Depression in adults: treatment and management (update)

Consultation on draft guideline - Stakeholder comments table
18 July to 12 September 2017

Comments forms with attachments such as research articles, letters or leaflets cannot be accepted.

Organisation name	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Association for Counselling and Psychotherapy				**References** Ahn, H.-n., & Wampold, B. E. (2001). Where oh where are the specific ingredients? A meta-analysis of component studies in counseling and psychotherapy. *Journal of Counseling Psychology, 48*(3), 251-257. Barth, J., Munder, T., Gerger, H., Nüesch, E., Trelle, S., Znoj, H., ... & Cuijpers, P. (2013). Comparative efficacy of seven psychotherapeutic interventions for patients with depression: a network meta-analysis. *PLoS medicine*, *10*(5), e1001454. Barkham, M., Lutz, W., Lambert, M. J., & Saxon, D. (2017). Therapist effects, effective therapists, and the law of variability. In L. G. Castonguay and Hill, C. E. (Eds.), *How and why are some therapists better than others?: Understanding therapist effects*. Washington, DC: American Psychological Association Barkham, M.; Moller, N. P. & Pybis, J (2017) How should we evaluate research on counselling and the treatment of depression?	Thank you for your comment and for bringing these references to our attention. Please see below for details of what has happened to each reference that you have provided. • Ahn 2001: this is a meta-analysis of dismantling studies and dismantling studies are outside the review protocol, except where the 'dismantled' intervention meets criteria for a specific intervention class, for example behavioural versus cognitive behavioural. • Barth 2013: we have cross-checked our included/excluded studies list against the reference list from this systematic review, and through this process have identified 14 additional studies that have now been added to the NMA for treatment of a new depressive episode. • Barkham 2017 ('Therapist effects, effective therapists, and the law of variability') and Saxon 2012: therapist factors were outside the scope of this review so these papers have not been included.

Organisation name	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				A case study on how NICE's draft 2018 guideline considered what counts as best evidence. *Counselling and Psychotherapy Research* Brown, E., Moller, N., & Ramsey-Wade, C. (2013). Recording therapy sessions: What do clients and therapists really think?. *Counselling and Psychotherapy Research*, *13*(4), 254-262. Carroll, K. M and Nuro, K. F (2002). One size cannot fit all: a stage model for psychotherapy manual development. Clinical Psychology: Science and Practice, 9(4): 393-406. Corney, R., & Simpson, S. (2005). Thirty-six month outcome data from a trial of counselling with chronically depressed patients in a general practice setting. *Psychology and Psychotherapy: Theory, Research and Practice*, *78*(1), 127-138. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M. (2008) Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ; 337:a1655.	• Barkham 2017 ('How should we evaluate research on counselling and the treatment of depression? A case study on how NICE's draft 2018 guideline considered what counts as best evidence'), Carroll 2002, Craig 2008, Gyani 2012, Gyani 2013, Ioannidis 2009, Kriston 2013, NHS Digital 2014, NHS Digital 2015, NHS Digital 2016, Pybis 2017, Rhodes 2015, Salanti 2011, Salanti 2012, Salanti 2014, Smith 2014, Spiegelhalter 2002, Stiles 2006 Stiles 2008, Turner 2012, Williams 2016: These papers do not meet the study design criteria for inclusion as they are not systematic reviews of RCTs or RCTs. • Brown 2013 and Timulak 2009: These papers are about experience of care, which was excluded from the scope of this update. • Corney 2005: this RCT was not included because the study's definition of chronic depression (≥6 months) does not meet our inclusion criteria for the chronic depression review (MDD for a duration of at least 2 years or dysthymia). • Cuijpers 2016 ('Are all psychotherapies equally effective in the treatment of adult depression? The lack of statistical power of comparative outcome studies') and Munder 2013: These papers do not meet the study design criteria for inclusion in

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				Cuijpers, P. (2016) Are all psychotherapies equally effective in the treatment of adult depression? The lack of statistical power of comparative outcome studies. *Evidence Based Mental Health, 19,* 39-42. Dias S, Welton NJ, Sutton AJ, Caldwell DM, Lu G, Ades AE. Evidence synthesis for decision making 4: inconsistency in networks of evidence based on randomized controlled trials. Med Decis Mak 2013; 33: 641-656. Gyani, A., Pumphrey, N., Parker, H., Shafran, R., & Rose, S. (2012). Investigating the use of NICE guidelines and IAPT services in the treatment of depression. *Mental Health in Family Medicine*, *9*, 149-160. Gyani, A.; Shafran, R.; Layard, R. & Clark, D. M. (2013) Enhancing recovery rates: Lessons from year one of IAPT. *Behaviour Research and Therapy, 51,* 597-606. Ioannidis JPA. Ranking antidepressants. Lancet. 2009; 373: 1759-1760; author reply 1761-1762. Kriston L. (2013) Dealing with clinical heterogeneity in meta-analysis. Assumptions, methods, interpretation. International Journal of Methods in Psychiatry Research, 22(1):1–	the review because they are systematic reviews of systematic reviews rather than an RCT or a systematic review of RCTs. • Dias 2013: The authors of this paper were involved in conducting the NMA analyses included in the guideline and consistency checks were carried out on the NMA as part of this analysis. • Linde 2015a: we have cross-checked our included/excluded studies list against the reference list from this paper. No new studies were identified for inclusion beyond additional studies that had already been identified through other means. • Linde 2015b: we have cross-checked our included/excluded studies list against the reference list from this systematic review. One additional study (Levesque 2011) has been included in the review of treatment of a new depressive episode. • Linde 2016: This study, and issues relating to transitivity, were considered by the technical team when designing and conducting the NMA, when interpreting the results, and when making recommendations. • Lindhiem 2014 could not be included as the comparison of active choice condition relative to no involvement in shared decision making does not match the review protocol. Patient preference,

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				15. Linde, K., Rücker, G., Schneider, A., & Kriston, L. (2016). Questionable assumptions hampered interpretation of a network meta-analysis of primary care depression treatments. *Journal of clinical epidemiology*, *71*, 86-96. Linde, K., Sigterman, K., Kriston, L., Rücker, G., Jamil, S., Meissner, K., & Schneider, A. (2015a). Effectiveness of Psychological Treatments for Depressive Disorders in Primary Care: Systematic Review and Meta-Analysis. *Annals of Family Medicine*, *13*(1), 56–68. http://doi.org/10.1370/afm.1719 Linde, K., Rücker, G., Sigterman, K., Jamil, S., Meissner, K., Schneider, A., & Kriston, L. (2015b). Comparative effectiveness of psychological treatments for depressive disorders in primary care: network meta-analysis. *BMC family practice*, *16*(1), 103. Lindhiem, O., Bennett, C. B., Trentacosta, C. J., & McLear, C. (2014). Client preferences affect treatment satisfaction, completion, and clinical outcome: A meta-analysis. *Clinical Psychology Review, 34, 506 - 517*	choice and the principles of shared decision making were considered by the committee during the interpretation of evidence and making the recommendations. • Rosso 2013: this was included in the analysis but mislabelled 2012 and missing from the references. This has now been amended. • Saxon 2012: Therapist effects are outside the scope of this guideline • Saxon 2017: this is a protocol rather than an RCT with extractable evidence. Therefore it was excluded from the guideline. • Scott 1992: This RCT was already included in the NMA for treatment of a new depressive episode although this reference was missing from the reference list in chapter 16. This omission has been corrected.

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				Munder, T., Brütsch, O., Leonhart, R., Gerger, H., & Barth, J. (2013). Researcher allegiance in psychotherapy outcome research: an overview of reviews. *Clinical Psychology Review*, *33*(4), 501-511. NHS Digital (2014). Psychological Therapies: Annual report on the use of IAPT services. England, 2013-2014. http://content.digital.nhs.uk/catalogue/PUB14899 NHS Digital (2015). Psychological Therapies: Annual report on the use of IAPT services. England, 2014-2015. http://content.digital.nhs.uk/catalogue/PUB19098 NHS Digital (2016). Psychological Therapies: Annual report on the use of IAPT services. England, 2015-2016 http://content.digital.nhs.uk/pubs/psycther1516 Pybis, J., Saxon, D., Hill, A., & Barkham, M. (2017). The comparative effectiveness and efficiency of cognitive behaviour therapy and counselling in the treatment of depression: Evidence from the 2nd UK national audit of psychological therapies. *BMC Psychiatry, 17,* 215.	

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				Rhodes KM, Turner RM, Higgins JPT. Predictive distributions were developed for the extent of heterogeneity in metaanalyses of continuous outcome data. J Clin Epidemiol 2015; 68: 52-60. 6. Rosso, G., Martini, B., & Maina, G. (2013). Brief dynamic therapy and depression severity: A single-blind, randomized study. *Journal of affective disorders*, *147*(1), 101-106. Salanti, G. (2012). Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. *Research synthesis methods*, *3*(2), 80-97. Salanti G, Giovane CD, Chaimani A, Caldwell DM, Higgins JPT. Evaluating the quality of evidence from a network metaanalysis. PLoS One 2014; 9: e99682. Salanti G, Ades AE, Ioannidis JPA. Graphical methods and numerical summaries for presenting results from multipletreatment meta-analysis: an overview and tutorial. J Clin Epidemiol 2011; 64: 163-171. 11.	

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				Saxon, D., & Barkham, M. (2012). Patterns of therapist variability: Therapist effects and the contribution of patient severity and risk. *Journal of Consulting and Clinical Psychology, 80,* 535–546. Saxon, D., Ashley, K., Bishop-Edwards, L….(2017). A pragmatic randomised controlled trial assessing the non-inferiority of counselling for depression versus cognitive-behaviour therapy for patients in primary care meeting a diagnosis of moderate or severe depression (PRaCTICED): Study protocol for a randomised controlled trial, Trials, 18:93 Scott, A. I., & Freeman, C. P. (1992). Edinburgh primary care depression study: treatment outcome, patient satisfaction, and cost after 16 weeks. *Bmj*, *304*(6831), 883-887. Smith, D.J., Court, H., McLean, G., et al. (2014). Depression and multimorbidity: a cross-sectional study of 1, 751,841 patients in primary care. Journal of Clinical Psychiatry. 75(11): 1202 – 8. Spiegelhalter DJ, Best NG, Carlin BP, Van Der Linde A. Bayesian measures of model complexity and fit. J R Stat Soc Ser B Stat Methodol 2002; 64: 583-639. 8.	

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				Stiles, W.B., Barkham, M., Twigg, E., Mellor-Clark, J., & Cooper, M. (2006). Effectiveness of cognitivebehavioural, person-centred, and psychodynamic therapies as practiced in UK National Health Service settings. *Psychological Medicine, 36,* 555-566. Stiles, W.B., Barkham, M., Mellor-Clark, J., & Connell, J. (2008). Effectiveness of cognitivebehavioural, person-centred, and psychodynamic therapies in UK primary care routine practice: Replication in a larger sample. *Psychological Medicine, 38,* 677-688. Timulak, L. (2009). Meta-analysis of qualitative studies: A tool for reviewing qualitative research findings in psychotherapy. *Psychotherapy Research*, *19*(4-5), 591-600. Turner RM, Davey J, Clarke MJ, Thompson SG, Higgins JP. (2012). Predicting the extent of heterogeneity in meta-analysis, using empirical data from the Cochrane Database of Systematic Reviews. Int J Epidemiol; 41: 818-827. 5. Williams, R., Farquharson, L., Palmer, L., Bassett, P., Clarke, J., Clark, D. M., & Crawford, M. J. (2016).	

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				Patient preference in psychological treatment and associations with self-reported outcome: national cross-sectional survey in England and Wales. *BMC Psychiatry, 16:*4.	
Association of Dance Movement Psychotherapy UK				We are concerned that this recommendation has omitted important evidence-based contributions from embodied psychological interventions such as dance movement psychotherapy. This form of embodied psychotherapy, currently registered with UKCP and largely recognised as one of the arts psychotherapies, has had documented evidence of its potential value in the treatment of depression. Note: the discipline can also be found as dance movement therapy, dance therapy or movement psychotherapy. Missing evidence includes: **Cochrane Review on Dance Movement Therapy for Depression:** Meekums B, Karkou V, Nelson EA. (2015) Dance movement therapy for depression. *Cochrane Database of Systematic Reviews*, Issue 2. Art. No.: CD009895. DOI: 10.1002/14651858.CD009895.pub2. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009895.pub2/epdf Although this study concludes that that	Thank you for your comment and for bringing these references to our attention. The Röhricht 2013 RCT has now been included in the chronic depression review. The Meekums 2015 systematic review has been checked and as your response highlights 1 of these studies (Padopoulos 2013) does not meet our inclusion criteria due to mean age <18 years, and the other study (Xiong 2009) also does not meet inclusion criteria as it is a non-English language paper.

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				further research in needed with stronger methodological rigour in order to draw firmer conclusions, it also claims that for adults with depression: "There is some evidence to suggest dance movement therapy is more effective than standard care for adults..." (Meekums et al 2015, p.1). Furthermore, the subgroup analysis that was performed for the two adult studies (107 participants) showed that: "…there was evidence of a reduction in depression for group dance movement therapy conducted over a period between 4 and 10 weeks with a total of 20 sessions and combined with standard care, as compared with standard care alone" (Meekums et al 2005, p. 25). **Key RCTs:** The two adult RCTs that included in the Cochrane review are summarised here: Röhricht F, Pa Padopoulos N, Priebe S. (2013) An exploratory randomized controlled trial of body psychotherapy for patients with chronic depression. *Journal of Affective Disorders* 151: 85–91. [DOI: 10.1016/j.jad. 2013.05.056] 31 adults, both male and female aged 18-65 took part in the study. They were referred through community mental health team with a DSM-IV diagnosis of moderate to severe	

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				recurrent depressive disorder. 15 people were randomised to waiting group (7 women and 8 men), while 16 people were randomised to intervention (6 women and 10 men). All participants in both study arms were offered an intervention titled 'body psychotherapy' delivered by a qualified dance movement psychotherapist, either immediately or after a 12-week waiting period, in addition to standard care which included ongoing antidepressant medication and outpatient clinical management. The group size was limited to 8 participants in each group and consisted of 20 sessions of 90 min each over 10 weeks. Primary outcome was the level of depressive symptoms as assessed on the 21-item Hamilton Rating Scale for Depression (HAM-D) (Hamilton 1960). Statistical analysis for HAM-D scores through ANCOVAs adjusted for baseline differences in scores indicated a statistically significant difference with the intervention group scoring lower on level of depression [intervention group mean: 20.9; SD: 8.9 (n = 11) vs control mean: 29.5; SD: 9.1 (n = 12)] Xiong L, Li M, Li Q. (2009) Influence of dance therapy on self-efficacy and rehabilitation of patients with depression, *Chinese Nursing Research,* 23(12A):3138–3139.	

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				This was a two-armed randomised controlled trial, DMT plus standard care versus control group being standard care (routine medication and psychological support nursing), using a standardised test of depression. The intervention took place in China in an urban-based hospital and involved 76 patients (33 males & 43 females), mean age 32.26 ± 8.71 years who met the CCMD-3 (Chinese Classification and Diagnostic Criteria of Disorders) diagnostic criteria for depression. They joined the study voluntarily with informed consent and were willing to make improvements. 38 people were randomised to the standard care group (21 women and 17 men). The intervention was group dance movement therapy informed by Chace methods, with 8 to 9 people in each group. The treatment lasted for 4 weeks, 5 sessions per week (Monday to Friday), 2 hours for each session, over a 4-week period. All received standard care, which consisted of medication and nursing psychological support. Primary outcome measure used was the 24-item Hamilton Rating Scale for Depression (HAM-D) with end scores suggesting statistically significant differences between the intervention and the control groups [intervention group mean: 10.13; SD:± 3.20 (n = 38) vs control mean:	

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				17.20; SD: ± 8.34 (n = 38)]	
Association of Dance Movement Psychotherapy UK				Further evidence in dance movement psychotherapy that is relevant to this NICE guideline can be found in the following meta-analyses: **Meta-analyses** Koch S, Kunz T, Lykou S and Cruz R (2014) Effects of dance movement therapy and dance on health-related psychological outcomes: A meta-analysis, *The Arts in Psychotherapy*, 41, 46-64. http://www.sciencedirect.com/science/article/pii/S0197455613001676 This meta-analysis looked at the effectiveness of dance movement therapy and dance from 23 primary trials (N = 1078) on variables such as quality of life, body image, well-being, and clinical outcomes, with sub-analysis of depression, anxiety, and interpersonal competence. Results suggest that these interventions are effective for increasing quality of life and decreasing clinical symptoms such as depression (including DMP's suitability for both geriatric and adolescent forms) and anxiety. Empirical evidence supports an increase in quality of life, well-being, mood, affect, body image, and clinical outcomes, and particularly for a	Thank you for your comment and for bringing these references to our attention. Please see below for details of what has happened to each reference that you have provided. • Koch 2014 and Ritter 1996: we have cross-checked our included/excluded studies list against the reference list from these papers. No new studies were identified for inclusion beyond additional studies that had already been identified through other means. Please note that only papers reviewed at full-text are documented in the included and excluded studies list; if a paper has been excluded on the basis of only the title and/or abstract then it may not appear in these lists. • Cruz 1998: This paper does not meet the study design criteria for inclusion as it is not a systematic review of RCTs or an RCT.

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				decrease of depression and anxiety. Furthermore the clinical outcomes sub-analysis suggests that these interventions showed moderate effects for depression and anxiety, with an overall moderate pooled effect on interpersonal competence (although this last result is inconclusive due to heterogeneity of results). Cruz, R., & Sabers, D. (1998). Dance/movement therapy is more effective than previously reported. *The Arts in Psychotherapy*, 25(2), 101–104. http://link.springer.com/article/10.1023/A%3A1013041723005 Cruz and Sabers (1998) report on their recalculation of Ritter and Low's (1996) meta-analysis and argue that dance/movement therapy is more effective than reported before due to an error on calculating effect sizes for repeated measures. They also argue that the effect of dance/movement therapy is comparable with other psychological interventions. Ritter, M. & Low, K. G. (1996). Effects of dance/movement therapy: A meta-analysis. *The Arts in Psychotherapy*, 23, 249–260. http://www.sciencedirect.com.edgehill.idm.oclc.org/science/article/pii/0197455696000275	

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				Ritter and Low (1996) report on a meta-analysis of 23 studies on dance/movement therapy for a number of different client groups. 781 clients were included in total. An array of benefits from dance/movement therapy were reported in these studies including improvements in motor skills, body awareness, muscle control and balance, special awareness, attention, participation and relaxation, as well as expressivity.	
Association of Dance Movement Psychotherapy UK				Other relevant studies in dance movement psychotherapy are listed here: Bräuninger I. (2012) Dance movement therapy group intervention in stress treatment: A randomized controlled trial (RCT). The Arts in Psychotherapy, 39:443-50. Hilf Z. (2009) Efficacy of Dance Therapy in the Treatment of Somatoform Disorders [Wirksamkeit von Tanztherapie bei Somatoformer Störung]. Unpublished Diploma thesis. Faculty for Sport and Health Sciences of the Technische Universität München, Germany. Horrocks A, Naidoo J, Daykin N. (2009) 'I didn't think I'd feel like this': Evaluation of the Rock-a-Bye groups, Dance Movement Therapy for postnatal women and their	Thank you for your comment and for bringing these references to our attention. Please see below for details of what has happened to each reference that you have provided. • Hilf 2009, Horrocks 2009, Konstantinidou 2005, Lauža 2011, Rasa 2011, Reinemann 1998 and Zemite 2011: These are dissertations so have not been included. • Bräuninger 2012: This intervention is targeted at stress in a non-clinical population, rather than symptoms of depression. • Karkou 2010: This is a book section so has not been included. • Martin 2013, Pylvänäinen 2010, Pylvänäinen 2015 and Stewart 1994: These papers do not meet the study design criteria for inclusion as they are not systematic reviews of RCTs or RCTs.

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				infants. University of the West of England, UK. Karkou V, Fullarton A, Scarth S. (2010) Finding a Way Out of the Labyrinth through Dance Movement Psychotherapy: Collaborative Work in a Mental Health Promotion Programme for Secondary Schools. In: Karkou V editor(s). Arts Therapies in Schools: Research and Practice. London: Jessica Kingsley, 59-84. Konstantinidou M.(2005) Effects of DMT program in the psychosocial health of elderly. Unpublished PhD Thesis, University of Komotini, Greece. Lauža S. (2011) Dance movement therapy for decreasing symptoms of depression in the patients with chronic musculoskeletal pains. Unpublished Masters Dissertation: Riga Stradins University, Latvia. Malkina Pykh IG. (2012) Effectiveness of rhythmic movement therapy for disordered eating behaviors and obesity. Spanish Journal of Psychology, 15(3):1371-87. Mannheim EG, Helmes A, Weis J [German]. (2013) Dance/movement therapy in oncological rehabilitation [Tanztherapie in der	• Price 2006 and Malkina Pykh 2012: The intervention was not targeted at depression symptoms (no depression outcome reported) so this has not been included. • Mannheim 2013: This is a non-English language paper and so has not been included. • Osteras 2012, Payne 2010 and Selman 2012: these are trials that specifically recruited participants with a particular physical health condition in addition to depression, and therefore this is a different population to that in our scope.

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				stationären onkologischen Rehabilitation]. Research in Complementary Medicine [Forschende Komplementarmedizin] 20(1):33-41. [DOI: 10.1159/000346617] Martin S, Martin G, Lequertier B, Swannell S, Follent A, Choe F. (2013) Voice movement therapy: Evaluation of a group-based expressive arts therapy for nonsuicidal self-injury in young adults. Music and Medicine, 5(1):31-8. Osteras H, Osteras B, Torstensen TA. (2012) Medical exercise therapy, and not arthroscopic surgery, resulted in decreased depression and anxiety in patients with degenerative meniscus injury. Journal of Bodywork and Movement Therapies, 16(4):456-63. Payne H, Stott D. (2010) Change in the moving bodymind: Quantitative results from a pilot study on the use of the BodyMind approach (BMA) to psychotherapeutic group work with patients with medically unexplained symptoms (MUSs). Counselling & Psychotherapy Research (CPR), 10(4):295-306. Price C. (2006) Body-oriented therapy in sexual abuse recovery: A pilot-test	

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				comparison. Journal of Bodywork and Movement Therapies, 10(1):58-64. Pylvänäinen, P. M., Muotka, J. S., & Lappalainen, R. (2015). A dance movement therapy group for depressed adult patients in a psychiatric outpatient clinic: effects of the treatment. *Frontiers in psychology*, *6*. Pylvänäinen, P. (2010). The dance/movement therapy group in a psychiatric outpatient clinic: explorations in body image and interaction. Body, Movement and Dance in Psychotherapy, 5(3), 219-230. Rasa I. (2011) Late maturity, depression, dance and movement therapy. Masters dissertation, Riga Stadins University, Latvia. Reinemann D. (1998) ROM dance: a treatment for symptoms of depression and anxiety in adults with mental retardation. EdD dissertation, Northern Illinois University. Selman LE, Williams J, Simms V. (2012) A mixed methods evaluation of complementary therapy services in palliative care: yoga and dance therapy. European Journal of Cancer Care, 21(1):87-97. Stewart NJ, McMullen LM, Rubin LD. (1994)	

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				Movement therapy with depressed inpatients: a randomized multiple single case design. Archives of Psychiatric Nursing, 8(1):22-9. Zemite SS. (2011) Dance movement therapy for reducing depression symptoms of women prisoners. Masters dissertation, Riga Stradins University, Latvia.	
Association of Dance Movement Psychotherapy UK				The NICE guidelines support Coping Strategies of a physical (e.g. gardening) or creative (e.g. poetry) nature (4.4.12), and Exercise/Physical Activity (7.1.4.2) as a treatment. Dance should be mentioned here, being both active and creative, even without the structured psychotherapeutic aspects of DMP. The benefits of engaging in dance sessions for adults with depression have been reported in studies such as those following: Akandere M, Demir B. (2011) The effect of dance over depression. Collegium Antropologicum, 35(3):651-6. Alpert PT, Miller S, Wallman H. (2007) Modified jazz dance effects on balance cognition and mood in older women. Communicating Nursing Research, 40:359.	Thank you for your comment and for bringing these references to our attention. Dance interventions were included in the guideline providing that the study met other eligibility criteria. For example, Haboush et al. (2006) 'Ballroom dance lessons for geriatric depression: An exploratory study' is included in the NMA under the exercise class. Please see below for details of what has happened to each reference that you have provided. • Haboush 2006: this was included in the NMA of treatment of a new depressive episode but was missing from the reference list in Chapter 16. This omission has now been amended. The following references have not been included because they do not meet the inclusion criteria for the following reasons: • Akandere 2011 and Eyigor 2009: The sample do not have clinically important symptoms of depression (or symptoms

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				Birks M. (2007) Benefits of salsa classes in treatment of depression. Nursing Times 2007;103(10):32-3. Eyigor S, Karapolat H, Durmaz B, Ibisoglu U, Cakir S. (2009) A randomized controlled trial of Turkish folklore dance on the physical performance, balance, depression and quality of life in older women. Archives of Gerontology & Geriatrics, 48(1):84-8. Haboush A, Floyd M, Caron J, LaSota M, Alvarez K. (2006) Ballroom dance lessons for geriatric depression: An exploratory study. The Arts in Psychotherapy, 33(2):89-97. Hackney ME, Earhart GM. (2010) Social partnered dance for people with serious and persistent mental illness: a pilot study. Journal of Nervous and Mental Disease, 198(1):76-8. Kaltsatou A, Mameletzi D, Douka S. (2011) Physical and psychological benefits of a 24-week traditional dance program in breast cancer survivors. Bodywork Movement Therapy, 15(2):162-167. King E. (2010) Jump for joy: Irish Ceili dancing with mental health patients. Unpublished MA dissertation, Autonomous	just below threshold) at baseline. • Pinniger 2013 ('Intensive tango dance program for people with self-referred affective symptoms'): the sample were not restricted to participants with symptoms of depression ('feelings of stress, anxiety, and/or depression'). • Alpert 2007: This is a conference abstract. • Birks 2007: Extractable data are not reported in this article. • Hackney 2010: does not meet the study design criteria as it not a systematic review of RCTs or an RCT. • Kaltsatou 2011 and Pinniger 2013 ('Tango programme for individuals with age-related macular degeneration'): the trials specifically recruited participants with a physical health condition, which is excluded from the scope of this guideline. • Koch 2007 and Pinniger 2012: The depression outcome measure was not in the list of included outcome measures in the review protocol. • Puyvelde 2014: This was excluded due to overlap with the antenatal and postnatal mental health guideline. • King 2010 and Reinemann 1998: These are dissertations. Having carefully considered the evidence of

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				University of Barcelona, Spain. Koch SC, Morlinghaus K, Fuchs T. (2007) The joy dance: Specific effects of a single dance intervention on psychiatric patients with depression. Arts in Psychotherapy, 34(4):340-9. Pinniger R, Brown RF, Thorsteinsson EB, McKinley P. (2012) Argentine tango dance compared to mindfulness meditation and a waiting-list control: A randomised trial for treating depression. Complementary therapies in medicine, 20(6):377-84. Pinniger R, Brown RF, Thorsteinsson EB, McKinley P. (2013) Tango programme for individuals with age-related macular degeneration. British Journal of Visual Impairment, 31(1):47-59. Pinniger R, Thorsteinsson EB, Brown RF, McKinley P. (2013) Intensive tango dance program for people with self-referred affective symptoms. Music and Medicine, 5(1):15-22. Puyvelde, M., Rodrigues, H., Loots, G., Coster, L., Du Ville, K., Matthijs, L., ... & Pattyn, N. (2014). Shall we dance? Music as a port of entrance to maternal–infant intersubjectivity in a context of postnatal	clinical and cost effectiveness of treatment for a new depressive episode, the committee did not think there was enough evidence to recommend dance as an intervention.

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				depression. *Infant mental health journal*, *35*(3), 220-232. Reinemann D. (1998) ROM dance: a treatment for symptoms of depression and anxiety in adults with mental retardation. EdD dissertation, Northern Illinois University.	
British Psychoanalytic Association				***2 The rigour of the Tavistock Adult Depression Study (TADS)*** We consider the importance of this study under three headings: A the careful design of the study B the significance of its results C the implications for treatment of chronic, severe and complex forms of depression. **A Design of study:** This is a carefully thought-through design, comprising an RCT of long-term intensive psychotherapy, with additional qualitative measures and case studies. • The research was designed to provide the rigour of an RCT while preserving the integrity of the psychoanalytic process. It aimed rigorously to test the	Thank you for your comment. Also for providing such detailed information about the design and results of the Tavistock Adult Depression Study; how this study differs from other studies of psychotherapy and reasons why LTPP is different from other forms of psychological therapy. Fonagy 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') is included in the review for further-line treatment.

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				validity of the claim of psychoanalysis to be more effective over time than Treatment As Usual (TAU) for this group of patients. • Patients recruited for the study by referral from local GP practices were entered into the TAD Study on an intention-to-treat basis with all eligible consenting participants (N=129). All had a diagnosis of major depressive disorder of at least 2 years, a minimum of two failed attempts of treatment, at least one with antidepressant medication, and complex personality and/or social difficulties. Most had been unwell for over 10 years; over half were unable to work. They were not selected for suitability for treatment (e.g. 'psychological mindedness') but were randomly allocated to two groups: a LTPP intervention group receiving a target of 60 sessions of once-weekly LTPP, and a Treatment As Usual/control group managed by the referrer following NHS guidelines. • Therapy followed the model of once-weekly psychoanalytic sessions for 18 months, as has been practised widely within the NHS. • The therapists were all	

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				psychoanalytically trained and shared a conceptual model of psychoanalysis. A manual (Taylor 2010) of psychoanalytic principles and treatment, designed by Dr Taylor, was permissive rather than prescriptive, so that therapists were free to work in their usual way, within this particular conceptual model (Taylor 2015). All sessions were video-recorded and the key elements of psychoanalytic practice identified in the manual, which was used by trained independent observers of the video records. Psychoanalytic process was differentiated from the process of other treatment, including CBT, supportive, or counselling therapies, so as to confirm (or refute) that the study was of specifically psychoanalytic practice. A high degree of adherence to treatment protocols was in fact found. • The length of post-therapy follow-up of both groups (3.5 years from start of treatment) contrasts with the often much shorter follow-up employed in research of medication or short-term therapies. This is particularly important in view of the often remitting and relapsing natural history of	

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				depression, with often temporary recovery at 3-6 months. • Axis 1 and 2 diagnostic measures were taken for all participants of both groups at baseline, end of treatment, and 6-,12- and 24-month follow-up. Standard depression ratings, both objective and self-reporting, along with a range of qualitative measures including social and personal functioning and quality of life, were taken at 3-monthly intervals during treatment, and at 6-, 12- and 24-month follow-up. No analysis of these was carried out before all subjects had reached the 6-month follow-up point. References: Taylor D (2010) Das tavistock-manual der psychoanalytischen psychotherapie. *Psyche: Zeitschrift fur Psychoanalyse und ihre Anwendungen.***64**(9-10): 833-861; Taylor D (2015). Treatment manuals and the advancement of psychoanalytic knowledge: the treatment manual of the Tavistock Adult Depression Study. *International Journal of Psychoanalysis* **96:** 845-875. **B Summary of the Results (Taylor et al 2015)**	

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				• There were observable differences between the two groups, with those who received Long Term Psychoanalytic Psychotherapy doing better than those receiving Treatment As Usual from early in the treatment and on completion of treatment. • Both groups showed partial remission at the end of treatment • On follow-up there were statistically significant differences between the two groups. the LTPP intervention group tended to maintain their improvement over time, and some improved further. The TAU group tended to lose the gains they had made in treatment. • The results showed these differences : at 6 month follow-up,(p= 0.03,), at 12 month follow-up (p= 0.008) and at 2 year follow-up (p=.0001). • Global Assessment of Functioning improved for both groups during treatment but at 2 year follow-up the LTPP group showed significant benefit over the TAU group (p=0.001) • There was a statistically highly significant finding at 2 years post-treatment follow-up, where 50% of the psychoanalytic group no longer met	

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				the criteria for Major Depressive Disorder, while this was the case for only 10% of the TAU group. (p=0.0002) Reference: Taylor D, Carlyle JA, Fonagy P, McPherson S, Rost F, Thomas R (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). *World Psychiatry* **14**(3): 312--321. ***C The implications of the Tavistock Adult Depression Study for treatment*** The TADS is an impressive study of the treatment of a group of patients with treatment-resistant /refractory depression. The use of an RCT, as NICE requires, for a psychoanalytic therapy has been very carefully thought–through and rigorously applied. The Study is very unusual in NHS psychotherapy research for three reasons: • The employment of an RCT to investigate the effectiveness of a psychoanalytic psychotherapy • The length of treatment - 18 months rather than the 6-month brief therapies often offered in the NHS,	

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				• the length of follow-up: three and a half years rather than end-of-treatment or only at 3 or 6 months. The nature of LTPP as a psychoanalytic psychotherapy is different from the other psychological interventions for severe forms of depression that are recommended in the revised (2017) guidelines by NICE. These focus on cognition, behaviour, and interpersonal dynamics. Psychoanalytic psychotherapy provides a different approach; it is also different from psychodynamic psychotherapy, which is recommended for less severe depression. *Psychoanalytic psychotherapy seeks to understand the* intra*personal factors that can militate against positive change. From the start, LTPP works at a deep level with these intrapsychic conflicts, as experienced in the relationship between patient and therapist. For example, anxieties attendant on developing trust, intimacy and potency may result in the patient losing any gains made in treatment.* *In Long Term Psychoanalytic Psychotherapy, over time, the patient gradually internalises the therapist's ability to contain these conflicts, building inner resilience so that improvement is sustained. Extending other forms of therapy, while giving support and*	

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				symptom relief, has not been shown to build maintained improvement in this way. Long-term prescription of medication itself carries risks of significant problems around withdrawal, and of ineffectiveness.	
Northumberland Tyne and Wear NHS Foundation Trust				The full guidance well outlines the social circumstances associated with depression and interventions should take account of this. Further reference is needed on the importance of supportive communities, workplaces and schools and the need for services that prevent the escalation of depression eg debt advice. There is recent public health evidence supporting a range of preventative approaches The importance of holistic formulation needs referring to in the Guidance. The argument for psychosocial formulations has been well made by the British Psychological Society, the Royal College of Psychiatry and is also mentioned in Skills for Health http://www.bps.org.uk/system/files/Public%20files/DCP/cat-842.pdf) (http://www.rcpsych.ac.uk/usefulresources/publications/collegereports/op/op103.aspx) (http://www.skillsforhealth.org.uk/services/item/146-core-skills-training-framework). .It is helpful to take an approach to helping people with depression through	Thank you for your comment. The guideline included review questions looking at the different models for co-ordination and delivery of services, different settings for delivery of care and ways to deliver services to promote access in vulnerable groups. The recommendations made in these areas were based on the evidence that was identified. Unfortunately no evidence was identified on supportive communities or workplaces and schools and as such the Committee did not make recommendations about these. A holistic approach to dealing with depression is covered in chapters 4 and 6 of the full guideline. These sections from the 2009 guideline did not form part of this update and consequently we are not able to amend the recommendations that they contain.

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				understanding the personal meaning of their distress, how they identify their needs and goals from treatment, with reference to their preferences for medication and/or psychological or social interventions. This is different to an illness based approach and puts more control back with the person seeking help.	
Northumbria healthcare NHS Trust- North Tyneside Talking Therapies		general	general	North Tyneside Talking Therapies (NTTT) has found increasing effectiveness in using IPT (Interpersonal Psychotherapy) to treat severe cases of depression over the last few years since investing in training of practitioners and supervisors in this mode of therapy, as illustrated by the following information taken from service IAPT data collection:- **North Tyneside Talking Therapies** **IPT Figures - August 2016 to July 2017** Figures include any patients that entered the IPT treatment pathway stage on IAPTus. Total patients 83 **Recovery** **Improvement** **GAD-7 Severity** **PHQ-9 Severity**	Thank you for your comment and providing these data from North Tyneside Talking Therapies on IPT.

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				2016 42% 63.16% 78.95% 74.63% 2017 58% 81.25% 68.66% 72.73% Grand Total 54% 77.11% 70.93% 79.07% The above stats represent recovery and improvement in all IPT cases.	

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				PHQ severity % means the percentage of patients who started therapy with severe depression. Recovery and improvement rates are for the corresponding % i.e. in 2016 74.6% of IPT cases had higher severity i.e. above 18 , at start of treatment and 42% of them recovered and 63% showed reliable improvement (iapt definition).	
Northumbria healthcare NHS Trust-North Tyneside Talking Therapies		general	general	North Tyneside Talking Therapies (NTTT) practitioners who are trained in both CBT (Cognitive Behavioural Therapy) and IPT (Interpersonal Psychotherapy) have found that discussing different therapy approaches with patients at assessment allows for collaborative selection of therapy type which best suits the client's needs and engagement style, thus providing patient choice increasing chances of engagement and recovery.	Thank you for your comment. Recommendations about recognition and assessment of depression are made in Chapter 6 of the full guideline. As this section of the 2009 guideline did not form part of this update, the evidence in this area has not been reviewed and we are unable to make any changes to the recommendations. However, we agree that a discussion of different therapy approaches is sensible and the evidence-based recommendations made in the rest of the guideline about different treatment options should inform this discussion.
Northumbria healthcare NHS Trust-North Tyneside Talking Therapies		general	general	North Tyneside Talking Therapies have invested significant staff resource over the last few years into training staff to be qualified IPT practitioners, to allow for clients to be offered an additional choice of therapy. This was very resource intensive for the service which reduced capacity at times, but we felt it	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the

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				was an important investment for client treatment choice within IAPT. We have found that having IPT as a treatment choice benefits clients and supported client outcomes and service performance. The IPT training was also funded by HENE. We would like to request that IPT remain an IAPT treatment choice for severe depression.	NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. IPT remains an option for the treatment of less severe depression. It has also been added to the treatment options for more severe depression.
United Kingdom Council for Psychotherapy				In response to question 3**: '*What would help users overcome any challenges?'*** we offer the following recommendations: **Patient choice of psychotherapy modalities** Patients should be offered a choice among psychological treatments, and this should be reflected within the guidelines such that CBT is not regarded as the default treatment. Given the evidence for improved completion rates, superior clinical outcomes and higher patient satisfaction linked to patient choice of treatment, as well as the evidence for differential responses to treatment based on patient characteristics, we recommend that the principle of patient choice and matching should be endorsed throughout the guidance in relation to all forms of depression. We recommend that patients must be offered	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline an offer of treatment. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When making the recommendations for specific

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				a choice of treatments for which there is evidence of clinical benefit, including psychodynamic psychotherapy and couples therapy for depression, and that clients should be matched to their treatment, instead of CBT being the primary treatment offered.	interventions, the committee took into account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective.
United Kingdom Council for Psychotherapy				**References** Bifulco A, Kwon J, Jacobs C, Moran PM, Bunn A, & Beer N. (2006). Adult attachment style as mediator between childhood neglect/abuse and adult depression and anxiety. *Social Psychiatry and Psychiatric Epidemiology, 41,* 796-805. Cooper M, Messow C, McConnachie A, et al. (2017). Patient preference as a predictor of outcomes in a pilot trial of person-centred counselling versus low-intensity cognitive behavioural therapy for persistent sub-	Thank you for your comment and for bringing these references to our attention. Röhricht 2013 has now been included in the chronic depression review. Unfortunately, none of the other studies meet the inclusion criteria for the review questions in this guideline. Reasons for exclusion are given below. • Bifulco 2006, Lin 2005 and Wallace 2013: These are post-hoc subgroup analyses of RCTs and are not relevant

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				threshold and mild depression. http://www.tandfonline.com/doi/abs/10.1080/09515070.2017.1329708 Department of Health (2013). *Achieving parity of esteem between mental and physical health.* https://www.gov.uk/government/speeches/achieving-parity-of-esteem-between-mental-and-physical-health DeRubeis RJ, Cohen ZD, Forand NR, Fournier JC, Gelfand LA, & Lorenzo-Luaces L. (2014). The Personalized Advantage Index: Translating Research on Prediction into Individualized Treatment Recommendations. A Demonstration. *PLoS ONE 9 (1):* e83875. Fournier JC, DeRubeis RJ, Shelton RC, Hollon SD, Amsterdam JD, & Gallop R. (2009). Prediction of Response to Medication and Cognitive Therapy in the Treatment of Moderate to Severe Depression. *Journal of Consulting and Clinical Psychology, 77*, 775–787. Hansson, M, Chotai, J, & Bodlund, O. (2010). Patients' beliefs about the cause of their depression, *Journal of Affective Disorders*, *124,* 54–59.	to the review protocol on relative clinical efficacy of interventions. • Cooper 2017: Secondary analysis of a study already included in the NMA for treatment of a new depressive episode (Freire 2015). • Department of Health 2013 and Hepgul 2016, Kessler 2003, Lamers 2011, Moffitt 2007, NHS Digital 2017, NHS England 2016, RCGP/NSPCC 2014, Röhricht 2015, Van Rijn 2013, Van Rijn 2016: do not meet the study design criteria as they are not systematic reviews of RCTs or RCTs. • DeRubeis 2014 and Fournier 2009: Secondary analyses of a study (DeRubeis 2005 – was considered for inclusion in the NMA of treatment for a new depressive episode. However it was excluded from this review as mean duration of MDD >2 years which means that this study is ineligible for this review. DeRubeis 2005 could also not be included in the chronic depression review as no minimum duration of MDD was specified as part of the entry criteria for that trial and it is unclear what proportion of participants in the study would meet criteria for chronic depression). • Van Rijn 2016: does not meet the study

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				Hepgul N et al. (2016). Clinical characteristics of patients assessed within an Improving Access to Psychological Therapies (IAPT) service: results from a naturalistic cohort study (Predicting Outcome Following Psychological Therapy; PROMPT). BMC Psychiatry. https://bmcpsychiatry.biomedcentral.com/articles/10.1186/s12888-016-0736-6 Huibers MJH, Cohen ZD, Lemmens LHJM, et al. (2015). Predicting Optimal Outcomes in Cognitive Therapy or Interpersonal Psychotherapy for Depressed Individuals Using the Personalized Advantage Index Approach. *PLoS ONE 10 (11):* e0140771. Kessler RC, Berglund P, Demler O, et al. (2003). The epidemiology of major depressive disorder: results from the national comorbidity survey replication, *JAMA, 289,* 3095-3105. Lamers F, van Oppen P, Comijs HC et al. (2011). Comorbidity patterns of anxiety and depressive disorders in a large cohort study: the Netherlands Study of Depression and Anxiety (NESDA). *Journal of Clinical Psychiatry, 72,* 341-8.	design criteria as it is not a systematic review of RCTs or an RCT. • Hansson 2010: The aetiology of depression is outside the scope of this guideline. Qualitative evidence is also outside the scope of this update as the experience of care section is not being updated. • Huibers 2015: Secondary analysis of a study that was already included in the NMA of treatment for a new depressive episode (Lemmens 2015/2016). • Lindhiem 2014 and Swift 2011: could not be included as the comparison of active choice condition relative to no involvement in shared decision making does not match the review protocol. Patient preference, choice and the principles of shared decision making were considered by the committee during the interpretation of evidence and making the recommendations. • Steinert 2017: This systematic review was checked for relevant references but no additional studies that met the inclusion criteria were identified.

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				Lin P, Campbell DG, Chaney EF, et al. (2005). The influence of patient preference on depression treatment in primary care. *Annals of Behavioral Medicine, 30,* 167–173. Lindhiem O, Bennett CB, Trentacosta CJ, & McLear C. (2014). Client preferences affect treatment satisfaction, completion, and clinical outcome: A meta-analysis. *Clinical Psychology Review*, *34*, 506–517. Moffitt TE, Harrington H, Caspi A, et al. (2007). Depression and generalised anxiety disorder: cumulative and sequential comorbidity in a birth cohort followed prospectively to age 32 years. *Archives of General Psychiatry, 64,* 651-660. NHS Digital (2017). *Psychological Therapies: Annual Report on the use of IAPT services, England, 2015-16.* http://www.content.digital.nhs.uk/catalogue/PUB22110/psyc-ther-ann-rep-2015-16_v2.pdf NHS England (2016). *Improving outcomes through personalised medicine*. https://www.england.nhs.uk/wp-content/uploads/2016/09/improving-outcomes-personalised-medicine.pdf RCGP/NSPCC (2014). *Adult survivors and*	

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				disclosures of historical abuse. Safeguarding children toolkit for General Practice. http://www.rcgp.org.uk/clinical-and-research/toolkits/the-rcgp-nspcc-safeguarding-children-toolkit-for-general-practice.aspx Röhricht F. (2015). Body psychotherapy for the treatment of severe mental disorders–an overview. *Body, Movement and Dance in Psychotherapy, 10,* 51-67. Röhricht F, Papadopoulos N, & Priebe S. (2013). An exploratory randomized controlled trial of body psychotherapy for patients with chronic depression. *Journal of Affective Disorders, 151,* 85-91. Steinert, C., Munder, T., Rabung, S., Hoyer, J ., and Leichsenring, F. (2017). Psychodynamic therapy: As efficacious as other empirically supported treatments? A meta-analysis testing equivalence of outcomes. https://doi.org/10.1176/appi.ajp.2017.17010057 Swift JK, Callahan JL, Vollmer BM. (2011). Preferences. *Journal of Clinical Psychology, 67,* 155-65.	

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				Van Rijn BV & Wild, C. (2013). Humanistic and integrative therapies for anxiety and depression: Practice-based evaluation of transactional analysis, gestalt, and integrative psychotherapies and person-centred counselling. *Transactional Analysis Journal, 43,* 150-163. Van Rijn BV, & Wild C. (2016). Comparison of transactional analysis group and individual psychotherapy in the treatment of depression and anxiety: Routine outcomes evaluation in community clinics. *Transactional Analysis Journal, 46*, 63-74. Van Rijn B, Wild C, & Moran P. (2011). Evaluating the outcomes of transactional analysis and integrative counselling psychology within UK primary care settings. *International Journal of Transactional Analysis Research & Practice, 2,* 34-43. Wallace ML, Frank E, & Kraemer HC. (2013). A Novel Approach for Developing and Interpreting Treatment Moderator Profiles in Randomized Clinical Trials. *JAMA Psychiatry*, 70, 1241–1247.	
Faculty of Occupational Medicine				Observations 1. inability to work mentioned as one of the serious consequences of relapse	Thank you for your comment and your observations. This guideline is about the treatment and management of depression in adults. Whilst there is an association

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				2. employment situation mentioned as a factor which might have influenced the course of the illness 3. people with depression may want help with employment problems 4. unemployment recognised as a complication of severe depression 5. employment now mentioned as one of the things that should be checked as standard (but no reason, no context and no guidance provided) Response 1. The small amount of guidance and information about work and employment is of course welcomed but it is disappointing that this guidance was not more detailed and more consistent. 2. Common mental disorders are now the most cited reason for periods of sickness absence but this strong association is absent from these guidelines. 3. One crucial piece of information is that there is little association between the "severity" of depression and its occupational consequences. Thus inability to work may a problem with all depressive episodes, not just ones	between depression and fitness for work, it is outside the scope of this guideline to make recommendations on how this should be dealt with in the workplace.

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				categorised as "severe". 4. It thus follows that everyone in employment who becomes depressed may want to discuss their job. Such discussions are not reserved for those with "employment problems". How to discuss with managers, impact of symptoms on shift length, safety critical roles etc should be standard. 5. Unemployment and falling out of the labour market can occur with any level of depression, not just severe. 6. The possibility of falling out of work should be seen as a "red flag" and specialist support from the Fit for Work service or Occupational Health should be sought. 7. Good that the categorisation has been altered. "mild-to-moderate" should be banned. This is a start. Depression divided into "less" severe and "more severe, but there could be more caveats here. Severe "to" whom or "for" whom…? 8. (The clear statements about residual symptoms should be drawn to the attention of the OH community. They potentially have a role in picking these up and drawing the attention of treating trans to their presence. The workplace is one area where the	

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				presence of such residual symptoms is more clearly seen).	
North East London Foundation Trust				I am writing on behalf of Waltham Forest IPAT – as a part of NELFT (North east London Foundation Trust). NELFT covers 4 boroughs and the response below is similar to that from my colleagues in other 3 boroughs and they have requested I include them in this response – being the London Boroughs of: Redbridge, Barking and Dagenham and Havering. Staff and managers at Waltham Forest wanted tom express their grave concerns at some aspects of the new draft guidelines. In particular the impact on the provision of Interpersonal Therapy (IPT) for depression is very worrying. IPT has been Relegated to a second line treatment for less severe depression)up to PHQ9 – 17). In our service this makes no sense – clinical assessment of each case is made and the nature of the difficulty, context such as relationships and life situation are included in our assessment of needs. We are also working to meet clients own choices and preferences as best we can. Some assessments clearly indicate CBT as a good first option but in other cases the context of the depression indicates (and clients often ask for and wish to undertake) a	Thank you for your comment and providing this interesting information about your service. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. IPT remains an option for people with less severe depression (who would like help for interpersonal difficulties that focus on role transitions or disputes or grief) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication individual CBT or BA) have not worked well in a previous episode of depression or in those who do not want the other recommended interventions. The committee made this a 'consider' recommendation because of the small

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				more reflective, exploratory, interpersonally based approach to managing their depression, particularly when the level of depression is at the higher end of the range (15 to 17 on PHQ9). It often makes no sense, either clinically or financially, to offer some form of CBT first and only later try IPT as a second line option. Assessed need and patient choice suggests a more flexible approach to treatment options would optimise our use of resources within NELFT. Of greater concern is the removal of IPT as a treatment for more severe depression. In Waltham Forest IPT has become one of the major front line treatments for severe depression in our patient group. The range and number of patients coming into WF IAPT has increased year by year and resources have changed dramatically – with more money coming into IAPT services and consequently a huge increase in patient referrals with severe and complex, long term difficulties that would previously have been seen in secondary care services. These patients are now expected to be treated in IAPT, many have a personality disorder diagnosis. Below are the guidelines for referral into NELFT secondary care. For Clusters 4 to 8. Psychology: severe and/or enduring depression, anxiety disorders and personality	benefit on the SMD outcome, the larger benefits on the other two clinical outcomes, and the lower cost effectiveness of IPT compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of IPT was likely to be higher in the subpopulation specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). IPT has also been added to the treatment options for more severe depression. The guideline does not recommend that any high intensity interventions should be provided by staff at a particular grade. However, in developing the economic model that underpins the cost-effectiveness data used to inform committee decision making, sensitivity analysis are often undertaken to explore the robustness of the analyses. The committee are clear that all interventions should be delivered by staff who are appropriately trained, for interventions such

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				difficulties. Psychotherapy: Suitable for those asking for an opportunity to explore emotions, relationships and what has shaped them as a person People are likely to present with some or all of the following: a history of childhood trauma (e.g. abuse, loss or traumatic separation), become overwhelmed by and struggle to manage emotions, experience persistent anxiety or depression, repeated destructive or unhelpful patterns in relationships, find it difficult to develop trusting and meaningful relationships In actuality large numbers of our referrals with cluster 4 and many with a cluster 7 are being seen in IAPT. They present with almost all the issues listed above and frequently have had several previous episodes of treatment. Most will have tried CBT at some point and not found it helpful or wish to try another approach. IPT along with Dynamic |Interpersonal Therapy (DIT) are the main alternatives available in WF IAPT to CBT for this client group. The long term nature of the difficulties and complexity of cases often rules out CBT: IPT and DIT are now the only alternatives. Many of our patients present with underlying difficulties in regulating their emotional reactions, which in turn leads to destructive, unhelpful and	as IPT this will mean that staff need to have completed an approved training course (such as that delivered by the IAPT programme). Current PWP courses do not include such training. The text that you cite about banding of therapists has been removed from the guideline.

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				repeated patterns of interactions with others. With IPT we frequently seeks to address these issues through the focus of 'Interpersonal sensitivities'. Some in house evidence from WF IAPT – the statistics below are somewhat crude but all the cases listed were scored initially at PHQ9 of 15 to 27. Representing a diagnosis of severe to very severe depression in most cases. 164 clients 92 in reliable recovery Recovery rate for reliable improvement 56% This recovery rate includes those who only attended an assessment session for IPT and did not engage in full treatment. Given the complexity of cases we are now seeing – the recovery rate is very positive and losing IPT as a first line treatment for severe to very severe depression would be a huge loss to our service. Data extracted from IAPT services nationally also has rated IPT as the most successful of all the face to face therapies in treating depression. We broadly welcome the inclusion of DIT and counselling as treatments for severe depression but disagree with the draft guidelines placing them as second line treatments after CBT – this does not accord with the research outcomes to date and does	

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				not accord with the needs and choices of our patient group. In particular we are disturbed at the exclusion of IPT as a treatment option for severe depression and urge you as strongly as we can to change this and include IPT as a first line treatment for more severe depression where the patient's needs and life context suggest this would be the best treatment option. We also think that IPT is a more gentle approach when clients have more severe depression as some clients struggle to complete CBT homework at that stage. Banding Below are 2 paragraphs from the draft guidelines which have alarmed us at NELFT. The GC also noted that the economic analysis assumed that all individual psychological interventions are delivered by a Band 7 clinical psychologist and that their relative cost effectiveness improved if these were effectively delivered by therapists paid at a lower Band. The relative cost effectiveness of high intensity psychological interventions, alone or combined with antidepressants, improves when these are delivered by less specialised therapists, such as Band 5 psychological well-being practitioners -PWPs- 1 or Band 6 therapists (instead of Band 7 clinical psychologists)	

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				Our band 5 PWP's are already experiencing heavy caseloads with many patients of far greater severity of symptoms and complexity than they were trained to work with and many are complaining of burnout and stress from the level of work they are facing – they are facing expectations of delivering 30 minute sessions of supported self help to patients with severe and enduring difficulties well beyond the level of their training or skills they have been taught. Many are feeling overwhelmed by this. We were therefore shocked to see these statements in print – which, whilst not stating directly that high Intensity treatments should be delivered by PWP's or band 6's do appear to give a 'green light' to trusts to down band these posts in order to save money. The clinical work our therapists undertake is difficult and very challenging. It is unsettling to read these statements which do not point out the danger of trusts attempting to go down this road of – in our view – highly unethical cost cutting. IAPT services across the country have been feeling the pressure for some years now and many staff are close to breaking point with the ever increasing demands placed upon them and reduced support available. We would like to see these paragraphs removed from the draft and replaced with a commitment to improved staff support and	

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				terms and conditions of working.	
RCPsych				Primary Care The following are some areas that need to be addressed: 1. **Explicit guidance**: Though there has been evolving consensus in the evidence base that Serum Lithium levels in the elderly (over 65 years) should be in the lower ranges, the future national clinical guidelines need to be more explicit about prescribing principles, frequency of monitoring of Lithium levels and renal functions including specific recommendations of maintaining a certain range of serum Lithium levels in elderly. 2. **Primary Care Prescribing**: In addition to the guidance to adhere to certain serum Lithium levels, the guidance should also specify to the GPs and other clinicians to monitor physical health (infections, diarrhoea, sickness, and being in temperate climate), neurological signs (e.g. coarse tremors) and cognitive status (delirium of the elderly patient and prescribing considerations (NSAIDs, ACE inhibitors, diuretics etc.). The renal functions, renal clearance and other	Thank you for your comment. In light of feedback from stakeholders and a coroner's report on lithium toxicity the recommendations for monitoring lithium have been significantly revised. Primary care 1. More detail has been added about frequency of monitoring, prescribing principles and appropriate plasma lithium levels. We have highlighted the particular importance of these recommendations for older people but we were not able to give a specific plasma lithium level for older people as we do not have evidence to base this on. 2. Additional information has been added to the recommendation about monitoring for signs of lithium toxicity, reviewing test results in light of the person's overall physical health and reviewing polypharmacy. We have increased the frequency of renal and thyroid monitoring to every 3-6 months. 3. We have not recommended that the POMH should be made available to all GPs as we cannot endorse the content of externally produced material. However we have recommended that people who are

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				related monitoring could be done more frequently to rule out risk of emerging toxicity than once every 3-6 monthly as recommended by the NICE. A practice primer for mental health in Older People aimed at primary care teams, particularly GPs is a timely initiative.[1] More details about this are given below. 3. **Information dissemination to primary care**: The up to date Lithium purple book (POMH) needs to be made available to all GPs. Repeat prescriptions for Lithium should only be issued after satisfactory serum lithium levels and renal functions in the previous 3 months. 4. **Shared care considerations**: The local CCGs, acute care and mental health should work towards developing shared care guidelines (e.g. Greater Manchester Medicines Management Group), which need to be widely shared within the local CCGs, primary care clinicians and mental health providers and subject to CQUIN and local audit. In cases where the GPs are in doubt about prescribing or monitoring, there needs to be prompt communication with the catchment area	taking lithium should be given information on how to do so safely and clarified that people should be provided with a lithium treatment pack which is available from the BNF. We have also clarified that repeat prescriptions should not be started until lithium levels and renal function are stable. 4. We have added a recommendation that lithium prescribing should be managed under shared care arrangements. The development of guidelines on this will be a matter for local implementation. 5. We have also recommended that for older people, their lithium prescribing should be managed in specialist secondary care services if there are any concerns. Older age adults Thank you for providing an extract from the Practice Primer September 2017. As noted above, we have made amendments to the recommendations to cover the issues raised in your comment. We have cited older people as a group who require particular consideration when prescribing lithium.

[1] https://www.england.nhs.uk/wp-content/uploads/2017/09/practice-primer.pdf

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				Old Age Psychiatrist. 5. **Lithium prescribing for more complex patients**: In elderly patients, where renal clearance and other comorbidities are likely to result in increased serum lithium levels as well as increased patient vulnerabilities to develop Lithium toxicity, consideration should be given to whether it is in the patient's best interest for them to remain in contact with secondary care mental health services. <u>Older Age Adults</u> The recommendations from the Old Age Faculty of the Royal College of Psychiatrists are: NHS England and NHS Improvement together with the Faculty of Old Age Psychiatry have recently published A practice primer for Mental health in older people. The summary is aimed primarily at colleagues in the primary care team, particularly GPs. Older people (or the elderly) in this primer is defined using the shorthand and traditional definition of 65 years of age as the start of old age, recognising that this chronological definition (introduced by Bismarck in 1880's	

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				as the age that pensions started) is much less relevant today and successive cohorts of people are living longer and healthier (one in five women born today can expect to live until they are 100). Lithium Monitoring guidance is included within the primer as follows below. The key points to note are: 1. Monitoring lithium levels involves more than just scheduling blood tests. The test results and any changes in patients' physical presentation or medication should be proactively reviewed and considered, including consideration of seeking a specialist opinion. Laboratory normal ranges are only part of the assessment when interpreting results. 2. In older people in particular, the exact therapeutic range can vary between individuals and is based on the individual's response to the lithium, the extent of any side effects and their ongoing physical health conditions. 3. The main factors influencing lithium levels are dehydration and polypharmacy.	

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				See guidance below from the Practice Primer September 2017:[2] Lithium has a narrow therapeutic window. Therefore, lithium levels need to be monitored to detect toxicity (diarrhoea, vomiting, coarse tremor, confusion, convulsion which can lead to death). Lithium toxicity warrants discontinuation and urgent investigation The main factors influencing lithium levels are dehydration and polypharmacy. Unpredictable Lithium dose increases (up to 4 fold) are reported with: • ACE inhibitors / A2 blockers (develops over weeks). • Thiazides (develops over days) – loop diuretics are safer. • NSAIDs (develops over days to months) - these have a very unpredictable and sometimes dramatic effect on lithium levels and are best avoided with lithium unless absolutely necessary. These medications can still be prescribed, but at stable doses (not prn) and under close	

[2] Ibid.

<table>
<tr><th>Organisation name</th><th>Document</th><th>Page No</th><th>Line No</th><th>Comments
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Please respond to each comment</th></tr>
<tr><td></td><td></td><td></td><td></td><td>lithium level monitoring. Seek specialist psychiatric or pharmacist advice if prescribing these drugs with lithium.

At normal levels, long-term lithium use can cause hypothyroidism and reduce renal function. If either of these occur, contact the Community Mental Health Team for advice.

To detect toxicity and adverse effects (on thyroid and kidney), regular monitoring is necessary (see Table 3).

Table 3: Lithium monitoring
<table>
<tr><td>Test</td><td>Frequency</td><td>Notes</td></tr>
<tr><td>Plasma Lithium level</td><td>Every 3 months</td><td>Bloods to be taken hours after last dos mmol/L might be effective in unipola depression; 0.6-0.8 mmol/L in bipolar i in elderly).
If stopping; reduce slowly over at least month; avoid incremental plasma reductions of >0.2 mmol/L.</td></tr>
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				U&Es (e-GFR), TFTs, Calcium, FBC | Every 3 months	
RCGP		6	5	Define mental health assessment- should this be the same across all professional groups	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
RCGP		6	16	Need to add with the patient's permission	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
RCGP		8	4	Need to define suicide risk assessment further and identify how a practitioner matches services/ help to need	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content

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					has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
RCGP		8	20	Need to add with patient's consent	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
RCGP		9	12	Active monitoring challenging in primary care without additional resources	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
RCGP		9	27	Need to add with patient's or their legal representative's consent	Thank you for your comment. These are recommendations on how services should be configured to provide care for people with

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					depression. As such a variety of different information could be shared so we do not think your suggested change is appropriate.
RCGP		10	9	Should include attempts to follow-up pts who do not comply with treatment	These are recommendations on how services should be configured to provide care for people with depression. As such we do not think your suggested change is appropriate. Follow-up is covered in other sections of the guideline.
RCGP		11	1-23	Which professional group does this refer to? It is not describing recognisable primary care	Thank you for your comment. The recommendations in the 'general principles of care' section would apply to both primary and secondary care.
RCGP		11	18-21	There should be attempts to match the expertise of therapists with the needs of patients	Thank you for your comment. This would be a matter for local implementation of the guideline.
RCGP		11	16-17	Should also be guided by co-morbidities, social situation. Are these standardised across providers across England?	Thank you for your comment. The treatment manuals referred to in the recommendation are published both nationally and internationally. Consideration of form and length of interventions in respsect of co-morbidities and social situation would be a matter of clinical judgement and therefore has not been specified in the recommendation.
RCGP		11	15	Scales are not used routinely by Primary care to monitor response to therapy	Thank you for your comment. IAPT successfully use scales to monitor response to therapy and this is often primary care based. Therefore we do not anticipate signifcant challenges to implementing this recommendation.

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RCGP		11	23	What are sessional outcome measures and are they equally appropriate across different types of interventions	Thank you for your comment. We have defined sessional outcome measures in the glossary more explicitly. We have amended the recommendation to clarify that routine use of sessional outcome measures should be considered.
RCGP		11	25	Whose responsibility is it to discuss this with the pt – therapist, GP, MH	Thank you for your comment. It would be the responsibility of the person delivering and supervising the intervention to monitor and evaluate treatment adherence.
RCGP		12	5	Whose responsibility is it to monitor this – CQC, MH Trusts or other providers of services	Thank you for your comment. Primary review would be done by healthcare professionals as part of supervision.
RCGP		12	13	Impractical to expect GPs to deliver this in a 10 minute consultation	Thank you for your comment. The recommendations give guidance on what information people need to have in relation to taking antidepressant medication. They do not specify when this information should be provided. This will depend on the individual and the current wording of the recommendation allows for this flexibility.
RCGP		13	23-24	This would require guidance from MH team for primary care and also advice about future monitoring for risk of relapse	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.10 to ensure that when stopping medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the

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					timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms.
RCGP		14	14	State medication to be prescribed by name	Thank you for your comment. It is not possible to name a specific antidepressant in this recommendation as what is used would vary between different individuals.
RCGP		14	20	Need guidance about how suicidality is to be assessed; whether this should always be the responsibility of MH services	Thank you for your comment. The prescriber will be responsible for reviewing the person, which may be a GP or a nurse prescriber. Mental health specialist referral would only be appropriate if the person was deemed to be at significantly increased risk of suicide.
RCGP		15	20-21	Will MH services be responsible for this?	Thank you for our comment. Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. We have clarified in the recommendations about monitoring antipsychotics that this should be done in specialist services for the first 12 months or until optimal treatment has been reached.
RCGP		15	11	Target lithium level / range should be defined	Thank you for your comment. We have

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				for each patient	clarified in the recommendations about lithium monitoring that the plasma lithium levels should not exceed 1.0 mmol/L.
RCGP		15	13	MH services generally don't have access to ECG, need to agree with Primary Care about monitoring and feeding back information. Need to clearly state roles and responsibilities of primary and secondary care in prescribing, monitoring and physical healthcare management when initially prescribed and thereafter- if dose changes and through stabilisation periods.	Thank you for your comment. Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. It will be a matter for local implementation to have effective arrangements in place between primary care and MH services.
RCGP		15	25	Role of shared care here?	Thank you for your comment. Based on the page reference given we think you are referring to recommendation 1.4.20. In line with NICE processes, this has been carried across from the 2009 guideline but the evidence has not been updated so we are not able to make any changes.
RCGP		16	13-14	Medicines management (also links with definition on P34 lines 22-26); should include review of all medicines potential for drug-drug interactions, evaluation for and management of side-effects, what symptoms are and are not responding and whether these may be related to residual symptoms of depression or other comorbid problem. Need to also address supporting the pt on LT treatment to become an expert pt. Medicine management	Thank you for your comment. In light of feedback from stakeholders the recommendation about medication management has been deleted as the committee agreed that it was no longer a widely used treatment option and so inclusion of the recommendation could lead to confusion.

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				is not a treatment or interention per se	
RCGP		16	21-22	There needs to be greater clarity around the definition of less severe depression i.e. qualify by presence of social or functional impairment, present or absence significant co-morbidity. What diagnostic criteria are used to standardise it?	Thank you for your comment. We have added an appendix to both the full and short versions of the guideline to clarify the defintions of less and more severe depression and how these should be applied in practice.
RCGP		16	28	Is / will this be included in the psychological therapy manuals?	Thank you for your comment. Yes these will be included in the psychological therapy manuals.
RCGP		17	24-29	Pharmacological Interventions: there are significant differences between SSRIs with respect to safety, tolerability, interactions and discontinuation syndrome. It is inappropriate and not consistent with other guidelines to lump them together as one group. Need to make initial and subsequent choice on a range of factors including previous response where efficacy and tolerability / safety are considered separately i.e one drug may be well tolerated but pt does not respond; another may be less well tolerated but efficacy response is better. Also if a person has tolerability problems these may be dose and time related (some side-effects only occur in the longer term) but need to ensure that pt has an adequate therapeutic dose.	Thank you for your comment. We consider that these issues are covered by recommendation 1.9.5.
RCGP		17	13-15	Physical Activity: Not currently usually provided; will need investment and resources	Thank you for your comment. Physical activity programmes are currently available on prescription so we do not think implementation of this recommendation will

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					require a significant increase in resources. This recommendation was based on evidence that physical activity programmes are a clinically and cost effective treatment, so any increase in costs would be a cost-effective use of NHS resources.
RCGP		17	12	Will need considerably more resource	Thank you for your comment. The format for providing self-help with support as recommended in the guideline, is already in widespread use in IAPT so we do not think implementation of this recommendation will require a significant increase in resources. This recommendation was based on evidence that self help with support is a clinically and cost effective treatment when delivered in this format, so any increase in costs would be a cost-effective use of NHS resources.
RCGP		17	22	Physical activity: It will be difficult to get numbers to commitment for this	Thank you for your comment. This recommendation was based on evidence that physical activity programmes are a clinically and cost effective treatment when delivered in this format.
RCGP		18	8-10	Evidence suggests these pts from pharmacological intervention. Need to include this as an option here as a priority especially if have history of relapse and certain LT co-morbidities	Thank you for your comment. Recommendations on the assessment of depression are made in section 1.2. It will be a matter for clinical judgement to determine who is at risk of developing more severe depression.
RCGP		18	19-21	Recommendation has important commissioning and resource implications	Thank you for your comment. The use of these interventions is already part of the

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					IAPT programme so we do not think implementation of this recommendation will require a significant increase in resources. This recommendation was based on evidence that individual CBT, BA or IPT are clinically and cost effective treatments when delivered in this format, so any increase in costs would be a cost-effective use of NHS resources.
RCGP		18	25-27	Recommendation has important commissioning and resource implications. What about follow-up for people who do not complete the course	Thank you for your comment. We have amended the recommendation to clarify that follow-up is also needed for those people who show a clinically signficant improvement. We do not think there will be significant resource impact from these recommendations as approximately 50% of people will recover and 10% more will show a significant improvement.
RCGP		19	7-8	Need greater clarification about when to recommend IPT (see previous comment) vs counselling	Thank you for your comment. The recommendations have been updated to indicate the sequence in which the different interventions should be used and the specific groups of people they are most effective in.
RCGP		19	19-20	Need greater clarification about when to recommend IPT, counselling or STPT	Thank you for your comment. The recommendations have been updated to indicate the sequence in which the different interventions should be used and the specific groups of people they are most effective in.
RCGP		20	1-2	Need to choose treatment dependent on previous response that considers previous efficacy and tolerability as well as co-	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the

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				morbidities and drug-drug interactions. Medication can be started immediately but CBT often takes 4 wks or more to initiate. Recommendation has important resource and commissioning implications	treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the two are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). Section 1.4 (short version) makes

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					recommendations on general principles that need to be applied when choosing treatments, which includes previous response.
RCGP		20	8-9	Need to choose treatment dependent on previous response that considers previous efficacy and tolerability as well as co-morbidities and drug-drug interactions.	Thank you for your comment. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable. Section 1.4 (short version) makes recommendations on general principles that need to be applied when choosing treatments, which includes previous response.
RCGP		20	17-18	What about role of counselling or IPT here?	Thank you for your comment. IPT has been included as an option for people with more severe depression. The committee noted that counselling showed a lower effect compared with pill placebo on SMD in more severe depression. Also it was not possible to include counselling in the economic analysis because it had been tested on less than 50 participants across RCTs included in the NMA, on each of the 3 main outcomes of the economic analysis (discontinuation for any

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					reason, response in completers, and remission in completers). Given this the committee were uncertain of the clinical and cost effectiveness of counselling in people with more severe depression and agreed not to make any recommendations about it for this group.
College of Mental Health Pharmacy (CMHP)		20	1	Again the SSRIs are put together as if one drug. This is not useful. Also need to consider if there has been any previous response to pharmacological treatment. However it is good to focus on using medication and psychological therapies together.	Thank you for your comment. The committee considered the evidence from the NMA on the effectiveness of different SSRIs. No particular drugs within this class were shown to be more effective, so the committee were unable to recommend specific drugs. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable.
RCGP		21	6	Need to include assessment of risk for relapse and then discuss. Primary Care may consider they do not have expertise to do this so refer to MH services	Thank you for your comment. We have added more detail to the recommendation about the content of the discussion about relapse. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and

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					effective collaboration and management of people with depression.
RCGP		21	24	Add – at the therapeutic dose to which they have responded here rather than 1.8.6	Thank you for your comment. We have amended recommendation 1.8.3 as you suggest.
The Mindfulness Initiative		21 22	25 25	We are concerned that the stipulation in 1.8.4 & 1.8.9 that MBCT is only offered to those who have recovered following treatment with antidepressant medication is not supported by evidence and will lead to an unhelpful restriction in patient choice. The Kuyken et al. (2016) meta-analysis found that MBCT significantly reduced risk of relapse in studies that included patients who had received no treatment for depression. We fear that these guidelines will be interpreted in a way that prevents access to MBCT amongst those seeking alternatives to anti-depressant medication for the treatment of depression and subsequent relapse presentation. Policymakers and patients have consistently called for greater patient choice, and particularly alternatives to antidepressants. 33% of respondents surveyed for the Mental Health Task Force's 2015 Five Year Forward report cited needing a choice of mental health treatments. The Task Force reported that people, especially young African Caribbean men, described what was currently provided as too heavily reliant on medication.	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. One of these factors was that in the majority of trials of MBCT (including those in Kuyken et al, 2016) participants either had a history of antidepressant treatment or were continuing to use antidepressants at enrolment. Consequently the committee agreed that MBCT should be recommended for people who have recovered following treatment with medication.

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				Unfortunately, this new guideline as currently drafted would make things worse. The Secretary of State for Health Jeremy Hunt specifies in the mandate to NHS England for 2016-17 that the government wants "…people to be empowered to shape and manage their own health and care and make meaningful choices". In October 2015 the Minister for Social Care and Communities Rt. Hon. Alistair Burt MP said, "I am keen to see more IAPT providers offer a greater range of NICE approved interventions, including mindfulness where it is appropriate."	
RCGP		22	19-20	Pts need to be educated about residual symptoms and early signs of recurrence and to seek medical advice about these as soon as possible	Thank you for your comment. We have amended recommendation 1.8.1 to clarify this.
College of Mental Health Pharmacy (CMHP)		22	19	Timescale for further review: 12 months is too long. A minimum of 6 months would be more relevant	Thank you for your comment. The committee discussed your suggestion but agreed that the current wording was appropriate since it defines the maximum amount of time between reviews (no more than 12 months) rather than specifying that further review should take place only at 12 months. The current wording would allow for further review to happen sooner than 12 months if that was needed.
RCGP		22	24	Also discuss residual symptoms and early	Thank you for your comment. We have

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				signs of recurrent	amended recommendation 1.8.1 to clarify this.
The Mindfulness Initiative		22 23	25 1	We are concerned that the draft wording of 1.8.9 & 1.8.10 would be mistakenly understood as saying that group CBT should be the default option, prioritised ahead of MBCT. The Kuyken et al. (2016) meta-analysis found that, contrary to early findings and previous NICE guidance, the number of previous episodes was not a moderator of relapse prevention outcome. We would recommend that this condition be removed. Further, the phrase "if initial psychological therapy had no explicit relapse prevention component" in 1.8.10 does not appear to be evidence-based. This caveat assumes that explicit relapse prevention components in initial psychological therapy are as effective as MBCT in preventing relapse and it is not clear that this has been demonstrated in randomised controlled trials. Finally, the evidence for the inclusion of group CBT here seems to be slim and wouldn't normally meet the NICE criteria for inclusion (of the two referenced studies, one is a definitive trial but in a non-UK sample, the other is a small trial described as a pilot	Thank you for your comment. The bracket in recommendation 1.8.5 (1.8.9 in the consultation version) was in the wrong place. It has now been moved to after MBCT. The decision on the effectiveness of an intervention is not taken on the basis of an analysis of individual trials which meet the criteria for inclusion in a review but from a pooling of the results of several trials. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. One of these factors was that of the trials of MBCT which specified a previous number of episodes as an entry criteria, 7 out of the 9 trials considered as part of the guideline evidence review had 3 or more episodes as their entry criteria. You raise the possibility that the lack of a finding of number of relapses as a mediator support the dropping of this qualifier from the recommendation. However, Kuyken et al note the low heterogeneity of the populations in the included trials may well impact on the analysis of any mediators. They also report in some analyses an association between

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				with equivocal findings). As such, we would suggest that the wording is changed to reflect that the evidence-base warrants priority for MBCT.	the number of episodes and relapse. When these factors were taken into account the committee considered that it was appropriate to include this qualifier in the recommendations. In developing recommendation 1.8.5 (1.8.10 in the consultation version) the committee were aware that a number of psychological interventions, such as CBT and BA, have built into them components that are explicitly focused on relapse prevention. They therefore agreed it was appropriate to include this in the recommendations for MBCT. NICE processes do not stipulate a minimum amount of evidence that must be idenfied before recommenations can be made. As described in Developing NICE guidelines: the manual, the wording of recommendations reflects the level of certainty that the committee have in the available evidence. The committee's rationale for making the recommendations based on the available evidence is documented in the 'evidence to recommendations' sections in the full guideline. When developing the recommendation for

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					CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. After considering the cost-effectiveness analyses the committee decided to recommend group CBT over individual CBT. To adopt this approach is entirely consistent with NICE methods.
RCGP		23	27-28	Recommendation should link to text that considers IPT, STPT, Counselling. For the pt population Treatment Resistant depression referred to here does this mean resistant to current therapy or the usual definition of resistant to two different classes of antidepressant. If the former then this will need additional resource in Primary Care and potentially MH services.	Thank you for your comment. This recommendation is about providing additional support. Which psychological therapies to consider is covered in subsequent recommendations. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited

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					response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is a consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression

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					and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'.
RCGP		23	10	Add – and timeframe for future review	Thank you for your comment. We have added to the recommendation that the need for further follow-up should be considered. However it is not possible to give a specific timeframe as this would depend on the individual.
RCGP		23	11	How is higher risk of relapse defined? Review has implications for primary and secondary care	Thank you for your comment. Recommendations 1.8.1 and 1.8.2 give details of what factors would mean someone was at higher risk of relapse.
RCGP		24	9-13	Recommendation has significant resource implications for MH and IAPT services	Thank you for your comment. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between

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					primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
RCGP		24	20-24	Add requires specialist input from MH services	Thank you for your comment. Getting advice from MH services is already covered in recommendation 1.9.7 and we do not think this needs to be repeated here.
RCGP		24	1	Who does recommendation refer to and how will this be implemented practically?	Thank you for your comment. These recommendations refer to anyone who is involved in the delivery of care to people with depression. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining two medications.
RCGP		25	20-23	Need to add – providing pt has good tolerability and compliance has been confirmed	Thank you for your comment. We have amended the recommendation to clarify that referral to/consultation with specialist services would need to be considered if symptoms impair personal and social functioning.
RCGP		25	18-19	Should read – change to an antidepressant with a difference side-effect profile; this could be the same or a different class. For example different propensities for sexual dysfunction, somnolence.	Thank you for your comment. We have not made your suggested change because the current wording of the recommendation conveys the same meaning. We have not included examples of side-effects in the

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					recommendation as there is no justification for highlighting particular side effects over others.
RCGP		26	4-7	Impact on MH resources	Thank you for your comment. We have revised this recommendation so that it now says to consider a different combination of medication and psychological therapy, rather than to recommend CBASP in light of your comment.
RCGP		26	22-23	Add about checking physical co-morbidities and optimising their management plus exercise	Thank you for your comment. We do not have any evidence to support making the amendments you suggest.
RCGP		27	2	Amisulpiride- no licence. Also would require monitoring of metabolic indices – need to add	Thank you for your comment. There was direct data on the efficacy of amisulpride in chronic depression. However there was no data on the use of quetiapine. Hence a recommendation was made about amisulpride. Additional recommendations have been made in section 1.4 about monitoring for people taking antpsychotics.
RCGP		27	19	What is the evidence for treating depression first before PD etc?	Thank you for your comment. As stated in the 'evidence to recommendations' section in the full guideline, this recommendation was made based on the committee's clinical knowledge and experience. We have recommended referral to a specialist personality disorder treatment programme first as this is consistent with existing NICE guidance and also the clinical experience

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					that where depression is co-morbid with personality disorder, treating the personality disorder first can improve the depression.
RCGP		28	12	Need to ensure that MH services can refer directly to IAPT without referring back to Primary Care	Thank you for your comment. We agree but this will be an issue for local implementation when designing protocols.
RCGP		28	15	Need to agree who would do physical health monitoring – implications for resources in Primary Care	Thank you for your comment. We envisage that physical health monitoring would be undertaken by both primary and secondary care. Given that psychotic depression does not affect large numbers of people we do not think there would be significant resource implications from implementing this recommendation.
RCGP		31	25	Should mention specifically involvement of specialists for physical conditions and MDTs; need ONE holistic Care Plan that includes Anticipatory or Crisis plan that is shred between all relevant health & social care professionals. Impact on IT and Information Governance	Thank you for your comment. The management of people with depression and physical health problems is outside the scope of this guideline. The need for continuity of treatment is covered by recommendation 1.14.7.
RCGP		32	22-23	Requires data sharing between stakeholders to ensure only ONE holistic Care plan. Impact on IT and Information Governance	Thank you for your comment. In light of feedback from stakeholders we have made additional recommendations in section 1.3 to ensure that structures are in place to support effective and integrated delivery of interventions across primary and secondary care.
Hyperparathyroid UK Action 4 Change		36	1/3	I was told for years that I was just depressed. They tried Cymbalta, Wellbutrin, & Zoloft, nothing made me feel better. It was	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in

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				only when I was so fed up I decided to start googling because I knew something else was going on and they were being lazy. I googled my symptoms and parathyroid.com was the first thing that came up. I looked back on my blood work and noticed my calcium was getting higher and higher over the years. When I went back to my doctor I pointed this out to her and asked for the test. She told me I was too young for this but to make me feel better she would order it. Sure enough, I was right. I think anyone diagnosed with depression should have their calcium and pth checked. I often wonder how many people are walking around feeling like complete s**t that could be cured.	adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis of hyperparathyroidism or the management of depression associated with hyperparathyroidism. NICE is currently developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
University of York		200	27	The GC states that, "For a number of interventions specifically behavioural couples therapy, nortriptyline in older people, acupuncture, omega fatty acids and peer support the GC were concerned that the populations in these interventions may differ from the general population in both networks and so separate pairwise comparisons were undertaken for those groups." There does not appear to be any *a priori* criteria for excluding interventions from the NMA on the basis of the extent that trial populations differ from those in the interventions included in the NMA networks.	Thank you for your comment. The text has been amended to clarify why acupuncture was not included in the NMA. This was because the participants in acupuncture trials may have been selected populations that would be different from those in the more and less severe networks. In addition, the committee noted that a significant number of the studies on acupuncture were performed in healthcare systems that were very different to the UK where the use of acupuncture is more common place and expectations of treatment response are consequently likely to be higher. This may increase the likelihood of more positive

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				The 1273 patients in the 7 trials included in the pairwise meta-analysis represent a spectrum of patients that is not atypical of trials that have provided the evidence on other physical interventions or psychological interventions that are recommended by the GC. One of the acupuncture trials, for example, compares acupuncture to TAU (1), and is described by the GC as having "moderate quality" (Page 321, Line 13). It was funded by NIHR and recruited 755 patients who were representative of those with depression in primary care in the UK. It is argued therefore, that acupuncture vs. TAU should be included in the NMA, given the relevance of the UK primary care population and evidence of effectiveness and cost-effectiveness (see below) from this large UK-based acupuncture trial. The trials from China are addressing a different question, namely comparing acupuncture to medication, and therefore are not relevant for the comparison with TAU. Neither are the two other non-Chinese trials relevant to the TAU comparator as they compare acupuncture to sham acupuncture. Reference: (1) MacPherson H, Richmond S, Bland M, Brealey S, Gabe R, Hopton A, et al. Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled	outcomes. They also acknowledged that the availability of appropriately trained and competent people to deliver acupuncture for the treatment of depression was limited and that there was uncertainty about the consistency of the methods for delivering acupuncture. The comparator in studies was not a reason that acupuncture was excluded from the NMA. Neither was existing cost effectiveness evidence a criterion for inclusion of interventions in the NMA.

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				Trial. PLoS Medicine. 2013 Sep 24;10(9):e1001518.	
Belfast Health and Social Care Trust		252 293		Recommendations 61 and 68 downgrade IPT to a ' second - line' therapy for less severe depressions and eliminates it for more severe cases. We are surprised and deeply disappointed by this. In the Belfast Trust we have a full time IPT practitioner for a number of years who works alongside her colleagues in CBT and the other therapies. She consustently achieves excellent outcomes with patients across the spectrum of severity. Last year she (and several trainees she supervised) treated 56 patients. The PHQ9 scores at entry ranged from 11-26, with a mean of 19.0 The scores post treatment ranged from 0- 26, with a mean of 6.18 36 of the 56 patients treated (64%) had a baseline score of 18 and above and if these the guidelines were implemented these patients would have been denied treatment. It is of note that the IPT therapist works in the Department of Psychotherapy in the Trust, and her referrals come primarily from other mental health staff rather than GP's. Many of	Thank you for your comment and providing data on the outcomes achieved by your IPT practitioner. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. IPT remains an option for the treatment of less severe depression. It has also been added to the treatment options for more severe depression.

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				her patients have been in psychiatric services for quite a long time (some for nearly a decade!) and not a few have had CBT or other significant interventions. Our Trust has clear experience of IPT being highly effective, as the above figures show, in patients with the more severe depressions. Increasingly patients are wanting psychological therapy, either instead of or along with medication; to remove IPT from the repertoire of recommended treatments appears to the Trust to be a retrograde step, and would - as evidenced by the figures above - reduce the quality of care we can offer our patients. Of the other 20 patients treated (36% of the total) many had previously been partially treated, but then benefitted further from IPT. However the Trust believes it to be inappropriate to limit the use of this evidence based therapy to patients who have had first to try other treatments.	
Nottinghamshire Healthcare NHS Foundation Trust	11.8	671	20	It is unclear why MBCT is not recommended for people with less severe depression with a high risk of relapse. Numerous RCTs of MBCT for depressive relapse demonstrate reduced rates for people regardless of level of depression during episode. This	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence.

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				recommendation therefore does not fit with the evidence base.	One of these factors was that recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. Another factor was that the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). Consequently the committee agreed to recommend MBCT for people with more severe depression. The considerations made by the committee are documented in section 11.7 of the full guideline.
Nottinghamshire Healthcare NHS Foundation Trust	11.8	671	27	• The recommended use of MBCT only for people with severe depression does not follow the evidence base. Findings from RCTs (e.g., Teasdale et al, 2000) and meta-analyses (e.g., Kuyken et al, 2016) shows	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence.

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				significant benefit for people experiencing a range of depression levels during episode, not just those with severe depression • The stipulation that MBCT should be offered to those who have recovered from a severe which was treated with medication or with psychological therapies again does not follow the evidence from RCTs. The relapse prevention trials for MBCT didn't just include people who received this in combination with medication or a psychological therapy – this restriction to the recommended us of MBCT is not in line with the evidence base • The suggestion of group CBT appears based only on one large RCT and one small pilot study for older adults. This does not appear therefore to meet NICE threshold of evidence of at least 2 reasonably powered RCTs	One of these factors was that recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. Another factor was that the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). Consequently the committee agreed to recommend MBCT for people with more severe depression. The considerations made by the committee are documented in section 11.7 of the full guideline. Another factor considered by the committee was that in the majority of trials of MBCT (including those in Kuyken et al, 2016)

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					participants either had a history of antidepressant treatment or were continuing to use antidepressants at enrolment. Consequently the committee agreed that MBCT should be recommended for people who have recovered following treatment with medication. NICE processes do not stipulate a minimum amount of evidence that must be idenfied before recommenations can be made. As described in Developing NICE guidelines: the manual, the wording of recommendations reflects the level of certainty that the committee have in the available evidence. The committes rationale for making the recommendations based on the available evidence is documented in the 'evidence to recommendations' sections in the full guideline. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. After considering the cost-effectiveness analyses the committee decided to recommend group CBT over individual CBT. To adopt this approach is entirely consistent with NICE methods.

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Nottinghamshire Healthcare NHS Foundation Trust	11.8	672	3	• Again, my understanding is that NICE recommendations are on the basis of two definitive RCTs – there is only one definitive RCT of group CBT for relapse prevention cited • The criteria for the relapse prevention trials for MBCT did not include the criteria that patients had recovered from medication and wanted to stop taking this – this restriction is therefore not in line with the evidence cited	Thank you for your comment. NICE processes do not stipulate a minimum amount of evidence that must be idenfied before recommendations can be made. As described in Developing NICE guidelines: the manual, the wording of recommendations reflects the level of certainty that the committee have in the available evidence. The committes rationale for making the recommendations based on the available evidence is documented in the 'evidence to recommendations' sections in the full guideline. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. After considering the cost-effectiveness analyses the committee decided to recommend group CBT over individual CBT. To adopt this approach is entirely consistent with NICE methods. As mentioned in our previous response, in the majority of trials of MBCT (including those in Kuyken et al, 2016) participants either had a history of antidepressant treatment or were continuing to use antidepressants at enrolment. Consequently

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					the committee agreed that MBCT should be recommended for people who have recovered following treatment with medication.
Association for Cognitive Analytic Therapy (ACAT)	Appendix G	G.1	General	CAT is a promising treatment for acute depression and ACAT requests that this is acknowledged in the research recommendations.	Thank you for your comment. No evidence on the effectiveness of CAT meeting the inclusion criteria for our review questions was identified. We have recommended further research into the mechanisms of action of psychological interventions. CAT may well be included in such future research.
Society for Psychotherapy Research (SPR) UK Chapter	Appendix J3			**Exclusion Criteria** We were concerned about the decision that some studies were excluded based on the reason that "*data cannot be extracted*". It is not clear whether the authors of these studies were contacted and we thus recommend an inclusion of a sentence to that effect, or alternatively a rewording of this exclusion criteria to be more transparent. If authors were not contacted, we are questioning the validity of this exclusion criteria, in particular as some of the excluded studies (e.g. Barkham et al., 1996) had been rated as bona-fide trials using the same criteria previously (Leichsenring et al., 2015) and ought thus to be included in the analysis. **Reference:**	Thank you for your comment. The methods and processes used to develop NICE guidelines are documented in Developing NICE guidelines: the manual. It is not usual process to contact authors. In the Barkham 1996 study, the data is in figures and it is not possible to extract mean and standard deviation data from these. We have not added a sentence to clarify that authors of published papers were not contacted to provide additional data as this is not part of usual process. The Leichsenring 2015 systematic review was checked for relevant references, however, no additional studies that met inclusion criteria were identified.

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				Leichsenring, F., Luyten, P., Hilsenroth, M.J., Abbass A. et al. (2015). Psychodynamic therapy meets evidence-based medicine: a systematic review using updated criteria. Lancet Psychiatry, 2, 648-660.	
University of Essex	Appendix L	104		We are concerned that the Draft Revision applies GRADE inappropriately in respect of specific trials and generally. We request: • Specifically, that the GRADE scoring of Fonagy et al (2015) is reviewed. We think it should be upgraded • That the Revision's GRADE scorings generally should give increased weight to studies that have collected and reported long-term follow-up data (that is progressively, ≥12 months rather than narrowly end-of-treatment ratings • That GRADE scorings should no longer down-rate studies involving treatments where concealment is not possible: for example, those evaluating psychological forms of therapy; these involve sentient participation by sentient human subjects. Justification: Fonagy et al (2015) is currently rated on	Thank you for your comment. GRADE assessment is conducted consistently across all studies included in the pairwise analyses. In GRADE, RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. Although it is more difficult to blind participants and intervention administrators in psychological studies, it is possible, for instance by isolating the active ingredient and using an attention-placebo (that is similar in other aspects with the exception of the active ingredient). Blinding of outcome assessors is also taken into account in the GRADE system. The reason for the rating of

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CHESS (Centre for Humanities Engaging Science and Society), Durham University	Appendix L	104		We are concerned that the Draft Revision applies GRADE inappropriately in respect of specific trials and generally. We request: • Specifically, that the GRADE scoring of Fonagy et al (2015) is reviewed. We think it should be upgraded • That the Revision's GRADE scorings generally should give increased weight to studies that have collected and reported long-term follow-up data (that is progressively, ≥12 months rather than narrowly end-of-treatment ratings as now • That GRADE scorings should no longer down-rate studies involving treatments where concealment is not possible: for example, those evaluating psychological forms of therapy; these involve sentient participation by sentient human subjects. **Justification:** • Fonagy et al (2015) is currently rated	Thank you for your comment. GRADE assessment is conducted consistently across all studies included in the pairwise analyses. In GRADE, RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. Although it is more difficult to blind participants and intervention administrators in psychological studies, it is possible, for instance by isolating the active ingredient and using an attention-placebo (that is similar in other aspects with the exception of the active ingredient). Blinding of outcome assessors is also taken into account in the GRADE system. The reason for the rating of

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Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				Dijkers M (2013) Introducing GRADE: a systematic approach to rating evidence in systematic reviews and to guideline development. KT Update (Vol. 1, No. 5 - August 2013) [http://www.ktdrr.org/products/update/v1n5/]	
Society for Psychotherapy Research (SPR) UK Chapter	Chapter 17	6 7	20 – 44 1- 9	**Class Models** We are concerned about the class models adopted in the draft guideline. The justification for classing treatments appears to follow a circular argument. It states: "*Classes were formed based on the assumption that they have similar effects*". There is no evidence that this is in fact the case, and this statement stands in contradiction with the emphasis made in the introduction of the full version of the draft guideline. Moreover, we were concerned about the lack of an explanation or definition as to how similarity between and within classes was assessed. It states: "*The assumptions were based on expert opinion from the guideline committee*" (p. 7, l. 9) and we recommend the inclusion of a more thorough and transparent explanation. The decision that an estimate for variance was borrowed from other interventions where	Thank you for your comment. The sentence "Classes were formed based on the assumption that they have similar effects" appears nowhere in the full draft guideline, and it was never used as a justification for classing treatments. The only sentence in relation to classes and similar effects appears in Appendix N1, MA detailed methods and results (Chapter 17 in consultation draft), which states "Classes of treatments are groups of interventions which are thought to have similar effects". Classes are not formed on the assumption that they have similar effects; classes are formed of interventions that have a similar mode of action, treatment component or approach, as well as similar adverse events, so that interventions within a class are anticipated to have similar (but not identical) effects. In this sense, anticipated similar effects are not the basis for forming classes, but rather the result of classes being formed by similar interventions. Classes of interventions for the treatment of depression, including their shared mode of action or treatment

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				it was not available needs to be made more transparent and justified adequately. For example, Exercise borrowed variance from Counselling; Sort-term Psychodynamic Psychotherapy, Psychoeducation, and Interpersonal Psychotherapy, Self-help, and Behavioural Therapies borrowed variance from Cognitive Behavioural Therapy. It is currently not clear as to why this approach was chosen and we recommend the inclusion of a plausible rationale.	component, are described in the introduction of Chapter 7 (section 7.1). The main reason for developing class models was that the systematic review included a very large number of interventions and it would be infeasible to compare them all in pairs and also for the committee to consider all individual intervention effects when making recommendations. The class model retains the individual intervention effects, whilst borrowing strength from the other elements in the class; relative effects between classes are easier to interpret and more helpful to decision-making when there are many treatment options. More justification for the use of class models including the benefits of this approach is now provided in the full guideline (section 7.3.3 in the final guideline). The fit of the class models to the data was checked, as reported in detail in Appendix N1 (Chapter 17 in the consultation draft), and the data supported satisfactorily the modelling assumptions. Borrowing/sharing of within-class variances was required due to sparse number of interventions forming some classes in some of the analyses. It is an assumption that is explicitly acknowledged in Appendix N1 (Chapter 17 in the consultation draft: NMA detailed methods and results) and also

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					clearly stated within Chapter 7 (section 7.3.3 in the final guideline), with cross-reference to the relevant section of Appendix N1 (Chapter 17 in the consultation draft). The assumptions on variance borrowing/sharing were made using the expert advice of the committee due to lack of published evidence. Borrowing/sharing variance from/with another class was necessary to retain the individual treatment effects within classes formed by one or two interventions, and can be considered as a conservative assumption, since the alternative would be to assume no variance within the class, which would mean that all elements in the class would have the same treatment effect, which is a much stronger assumption. Again, the fit of all models was tested and was found to be adequate so that there was no evidence that the data were in conflict with the assumptions underpinning the analysis.
Society for Psychotherapy Research (SPR) UK Chapter	Chapter 17	7	24 – 42	**Reporting of NMA results** In addition to transparency adequate reporting of network meta-analysis is pivotal (Cipriani et al., 2013). Although the draft guideline in Chapter 17 includes a section (p. 7, l. 24 – 42) on *Inconsistency Checks*, the reporting of these are not clear and seem difficult to follow upon first reading. An	Thank you for your comment. For the assessment of potential inconsistency in each network we used global checks for inconsistency, as recommended by the NICE Decision Support Unit (DSU) Technical Support Document (TSD) 4, available at: http://scharr.dept.shef.ac.uk/nicedsu/wp-content/uploads/sites/7/2016/03/TSD4-Inconsistency.final_.15April2014.pdf. The

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	Full Chapter 17 Chapter 17	212 6 6	9 – 10 13 – 18 6 - 18	inconsistency plot including the loops and 95% CI would be helpful, as these are easier to comprehend. It would graphically be immediately obvious were inconsistency was found (i.e. loops where the CI excludes zero) and we thus recommend an amendment to that effect. The number of comparisons where significant heterogeneity was detected is not clearly specified in the guideline and we would recommend doing so in order to be transparent. It is not feasible to ask the reader to go through the various tables and figures in order to access that information. Most importantly, however, the draft guideline do not appear to report what was done when inconsistency was found. Were these studies checked and excluded? If not, why was that not done? A protocol describing a clear strategy on how it was dealt with should be included (Cipriani et al, 2013). Inconsistent loops would need to be scrutinised and primary data should be checked for errors, and other sources should be explored through meta-regression and sub-group analysis (ibid). It is not apparent that a thorough methodology was followed by which all effect modifiers were considered and we recommend including a clear statement to that effect.	results of these checks did not show any cause of concern in most analyses. Deviance plots have been added in the final guideline (Appendix N1). Undertaking a local assessment of inconsistency was not practical to do for all comparisons due to the size and complexity of the network. It would produce a very large amount of comparisons to analyse and interpret, leading to a very high risk of finding spurious results. Heterogeneity was estimated across all studies in every NMA, and therefore all comparisons have the same estimated heterogeneity for each outcome. Thus, specifying comparisons where significant heterogeneity was detected is non-applicable. When evidence of inconsistency was found, studies contributing to between-trial heterogeneity were checked for data accuracy and analyses were repeated if corrections in the data extraction were needed. However, following any data corrections and if inconsistency persisted, no studies were excluded from the analysis, as their results could not be considered as less valid than those of other studies solely because of the inconsistency findings. Nevertheless, the presence of inconsistency in the network was highlighted and results

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				Subgroup analyses as described on p. 212 were carried out for inpatient versus outpatient populations and older versus younger adults. But these were carried out to allow for comparison of differential effects and not, as far as we can gather, to explore heterogeneity and mitigate violations of assumptions. It states "*Only interventions and classes of interest were included in the calculations of the rankings. The interventions that were deemed not of interest by the guideline committee and therefore excluded from the rankings were (…)"* adding a list of excluded interventions. An explanation is needed as to how the above decision was made. It is furthermore not clear from the description in this section whether these treatments were excluded from all analyses and thus may need to be specified. A further concern of ours is that the draft guideline does not appear to report rankings and effect sizes together (Cipriani et al, 2013). As Cipriani et a; (2013) have stressed, a network meta-analysis enables estimation of the probability that each intervention is the best for each outcome, and	were interpreted accordingly. This information has now been added in Chapter 7, section 7.3.5. Effect modifiers were considered qualitatively for all NMAs, whether inconsistency was identified or not, as failure to identify inconsistency does not mean it does not exist. We did sub-analyses of inpatient versus outpatient populations and older versus younger adults to explore whether setting and age were potential effect modifiers with a substantial impact on the effects. The results of these sub-analyses, although limited, suggested that, overall, they were not, and thus studies in different settings or on specific age groups were not treated separately in the NMA. Some interventions and classes were not of interest per se as they were not part of the decision problem (i.e. they were not candidates for recommendation); nevertheless, they were included in the network either because they had been used as controls in several trials and thus allowed additional (indirect) comparisons between interventions and classes of interest (e.g. imipramine) thus reducing uncertainty and enhancing precision, or because they were the sole connectors of some interventions

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				thus, it is important to look at the probabilities rather than the naïve rankings before drawing conclusions. "Clinicians should always be interested in the effect size and the rakings because a good rank does not necessarily imply a large or clinically important effect size" (ibid, p. 135). Thus, we recommend a revision and amendment of the draft guideline accordingly. We are concerned about the choice of *relative intervention effect sizes* used. We recommend using Number Needed to Treat (NNT) as it is an effect size measure more relevant and easier to interpret for clinicians and in line with what other recent network meta-analyses have used (e.g. May-Wilson et al, 2014). Generally, odds ratios are not recommended as a measure of effect size (Kramer and Kupfer, 2006). **References:** Cipriani, A., Higgins, J., Geddes, J.R., and Salanti, G. (2013). Conceptual and technical challenges in network meta-analysis. Annuals of Internal Medicine, 159, 130-137. Kramer, H.C. and Kupfer, D. (2006). Size of treatment effects and their importance to clinical research and practice. Biological Psychiatry, 59, 990-996. Mayo-Wilson, E., Dias, S., Mavranezouli I, et	and classes within the networks, thus enabling connectedness of the networks or in order to increase evidence for combined interventions. The full list of interventions and classes that were of no interest per se, as well as the justification for their inclusion in the network is provided in Chapter 7, section 7.3.2 (Populations, interventions and classes considered in the NMAs). Ranking and effect sizes have been reported together (within the same table) in Chapter 7 (see results of NMAs in 7.4.1.2 and 7.5.1.2 where ALL tables with results report effects sizes alongside rankings for each class). Probabilities of each intervention being best were not presented as this is an unstable measure and does not give the full indication of the performance of each intervention (it only suggests the performance of each intervention being best). The mean/median ranks with their 95 Credible Intervals were reported instead, which suggested how 'good' each class/intervention was on average (taking into account not only how many times a treatment was best, but also second best, third best and so on) and the uncertainty around each treatment's performance. The committee looked thoroughly at both effect sizes and rankings of classes/interventions before making

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				al. (2014). Psychological and pharmacological interventions for social anxiety disorder in adults: a systematic review and network meta-analysis. Lancet Psychiatry; 1, 368–76.	recommendations. Number Needed to Treat (NNT) was not used as an effect size measure as it does not perform well, in particular when most of the effects are not statistically significant as was often the case in the NMAs. We note that the SMD was the main clinical measure, which was selected by the committee because it is a measure commonly used in research and the committee was familiar with interpretation of findings expressed in the form of SMD.
Parkinson's UK	Full	General	General	Parkinson's UK understands that there is an existing guideline which is parallel to this one 'Depression with a chronic physical health problem', however; it is not clear how this updated guideline will link to it. The NICE guideline on 'Depression with a chronic physical health problem' does not include specific advice about managing depression in Parkinson's, while the updated Parkinson's clinical guideline (July 2017) simply links to the depression and chronic physical health problem guideline. Currently no guidelines take into account the specific mental health needs of people with Parkinson's, despite the high prevalence as up to 40% of people with Parkinson's will have depression at any given time.(Aarsland, D. et al. Depression in Parkinson's disease – epidemiology, mechanisms and management. Nat. Rev.	Thank you for your comment. This guideline is about the treatment and management of depression in adults. People with depression and a chronic physical health problem, such as Parkinson's, are not within the scope of this guideline. Therefore it is not possible to make recommendations for people with Parkinson's in this guideline. CG91 on 'Depression in adults with a chronic physical health problem' covers identifying, treating and managing depression in people aged 18 and over who also have a chronic physical health problem such as cancer, heart disease or diabetes. We will pass your feedback to the NICE surveillance team so that people with Parkinson's who are experiencing

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				Neurol. 8, 35–47, 2012). We would welcome clarification on when 'Depression with a chronic physical health problem' will be updated and what steps NICE will take to improve outcomes for people with Parkinson's experiencing depression.	depression can be considered for inclusion in future updates of CG91.
Public Health England	Full	General	General	Public Health England (PHE) notes that there is little mention of drug or alcohol misuse or dependency in the guidance document. PHE would recommend a more substantial inclusion of drug and alcohol misuse or dependency given the significant level of comorbidity and the difficulties experienced by patients who suffer both conditions in accessing effective support. PHE would recommend that the NICE guidance make reference to the following three documents: 1. The newly published PHE guidance document 'Better care for people with co-occurring mental health and alcohol/drug use conditions. A guide for commissioners and service providers' which is available at : https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/625809/Co-occurring_mental_health_and_alcohol_drug_use_conditions.pdf	Thank you for your comment. Drug and alcohol misuse is outside the scope of this guideline and we are not able to make any recommendations on this issue. However, there is existing NICE guidance on these issues which may be useful: • Drug misuse in over 16s: psychosocial interventions (CG51) • Drug misuse in over 16s: opioid detoxification (CG52) • Drug misuse prevention: targeted interventions (NG64) • Alcohol-use disorders: diagnosis and management of physical complications (CG100) • Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence (CG115)

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				2. The newly published clinical guidance 'Drug misuse and dependence. UK guidelines on clinical management' which has a section devoted to coexisting problems with mental health and substance use (section 7.9), which is available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/628634/clinical_guidelines_2017.pdf 3. In addition, practical advice and guidance for working in Improving Access to Psychological Therapies (IAPT) services with people who use drugs and / or alcohol is available at: http://www.drugwise.org.uk/wp-content/uploads/iapt-drug-and-alcohol-positive-practice-guide.pdf	
Mental Health Foundation	Full	General	General	This NICE guideline, "Depression in adults: treatment and management" is at risk of missing out on a critical dimension of efforts to tackle depression, that is, how depression in adults can be prevented.	Thank you for your comment. Prevention of depression is outside the scope of this guideline and we are not able to make recommendations on this issue. We note your suggestion for a new guideline in the

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				Issues of preventing depression are almost wholly missing in the document. Whilst there is a section on Relapse Prevention (pages 626-675), there is no wider discussion of the interventions and approaches to protecting wellbeing and preventing depression in adults from taking hold. Overall, the guidance is weak in terms of the early stages of depression (step 1 and 2 interventions). A wide evidence base for preventing depression now exists, as detailed in Mental Health Foundation publications such as 'Surviving or Thriving' (2017), 'Poverty and Mental Health' (2016), 'Mental Health and Prevention: Taking Local Action for Better Mental Health' (2016) and 'Better Mental Health for All: A public health approach to mental health improvement (2016). There is now a compelling case for investing in upstream interventions to stem the increasingly intense demands on mental health services, which should be underpinned by robust review of their efficacy. We suggest that there is therefore an opportunity for NICE to develop a separate, additional set of guidelines which set out best practice for preventing depression amongst adults from a public health perspective. This would complement the current guidelines on	prevention of depression, however NICE's referrals for new guidelines come from NHSE.

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				treatment and management.	
Mental Health Foundation	Full	General	General	We urge NICE to take a more proportionate and pluralistic approach to evidence. Evidence on the efficacy of public health interventions for prevention may need to be drawn from more diverse range of sources than in the treatment and management arena. Whilst Randomised Control Trials (RCTs) provide important evidence, in the field of public health it is often possible to reach more robust conclusions by triangulating research from a range of disciplines and through mixed method studies. We recommend that NICE complement the evidence of RCT trials with qualitative, participatory, and other forms of quantitative research. A rigid approach of only accepting RCT evidence is particularly problematic when it doesn't consider the risks and costs associated with non-treatment, and issues of time-lag in the production of evidence. Mindfulness Based Cognitive Therapy (MBCT) has been undervalued by this approach. It is important to balance the evidence-threshold in proportion to the low levels of risk associated with using this treatment; and the higher levels of risk	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline.

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				associated with non-treatment (for example because of waiting times; individual resistance to Cognitive Behavioural Therapy (CBT); or resistance to taking medication). Additionally, the constraints of only accepting RCT evidence risks missing opportunities provided by new digital solutions. In the fast-moving field of digital innovation, it is crucial that guidelines on digital solutions are developed to respond to new advances in a valid but timely way. Guidance needs to be contemporaneous with digital technologies, rather than providing recommendations on apps or technology which have already become obsolete. The rigidity of the RCT evidence model compromises the extent to which NICE guidance can be timely and impactful in a context where the public is increasingly buying commercial products which claim to benefit mental health.	
Royal College of Occupational Therapists	Full	General	General	There is very little in the guidelines in relation to activities or activities of daily living which we would recommend.	Thank you for your comment. We did not find any evidence to support making a specific recommendation around activities of daily living. However we do recognise they are important particularly for people with more severe and complex depression who are cared for in secondary care mental health services. This is covered by recommendation 1.14.4

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Royal College of Occupational Therapists	Full			In relation to Recommendations for research - to effectively deliver a service that enables someone to participate in daily life (employment, independent living) despite symptoms or post depressive episode, research is required into the mechanisms to facilitate this and non – psychological interventions need to be designed and tested in clinical trails – there is no attention to this in the guidelines.	Thank you for your comment. The committee developed a number of research recommendations, including one on the mechanisms of action of psychological therapies. The number of research recommendations that the committee can develop is limited and they decided not to prioritise your suggestion for a research recommendation on participating in daily life as the other research areas identified were more likely to inform future revisions of the guideline.
University of Liverpool	Full	general		In general this is a high quality document with careful recommendations emerging from comprehensive and well- considered evidence.	Thank you for your comment.
Primary Care Neurology Society	Full	General	General	It's a positive that there is more choice around therapies - people can chose to have counselling for example rather than cbt, even if they've not tried it and it's "failed" before. Or can chose to only have medication even though it's probably better to also have psychological therapy too. This allows people to be offered an intervention they can engage with according to where they are in their recovery journey - and over time they may start with IPT or counselling and then use cbt for more focussed work.	Thank you for your comment and your support.
Primary Care Neurology Society	Full	General	General	Although there is separate guidance for those with physical health problems, there are brief references here and there. There is also	Thank you for your comment. This guideline is about the treatment and management of depression in adults. People with depression

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				advice that those with cognitive impairment should ideally be offered the same interventions which could be modified e.g. shorter, if needed. Many of our patients with Parkinson's do have mild cognitive impairment but would benefit from IAPT (Increasing Access to Psychological Therapy). However, they often don't access it. This may be due to lack of home visiting - and these services rarely have a transport budget. But many of our patients do have PIP (Personal Independent Payments) and use taxis. Despite promoting IAPT and cc their GP and Parkinson's nurse. (and in our area most IAPT practitioners have had specific mental health in physical health training) I find people don't seek referral or self refer. I suspect apathy plays a part in this. I haven't checked the relevant depression in physical health guidance but I think some reference to access and reasonable adjustment could be added here.	and a chronic physical health problem, such as Parkinson's, are not within the scope of this guideline. Therefore it is not possible to make recommendations on access and reasonable adjustments for people with Parkinson's in this guideline. This group of people are covered by CG91 'Depression in adults with a chronic physical health problem'.
Primary Care Neurology Society	Full	General	General	It's clearer to have 2 main categories of severity as the previous guidance made it a bit complicated - it's not always that easy to distinguish between sub threshold symptoms for 2 years and a relapsing depression for example.	Thank you for your comment and your support.
British Association for	Full	General	General	BACP have prepared this response to the 2017 NICE consultation on the revised	Thank you for providing this information about BACP and for your support for the

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Counselling and Psychotherapy				*Guideline for Depression in Adults: Treatment and Management*, in our role as a professional body for UK counsellors and psychotherapists. As the largest British professional body for those providing psychological therapies and as laid out in our mission statement (https://www.bacp.co.uk/about_bacp/) we aim to campaign for the highest standards of care for those experiencing depression. Moreover, our responsibility to both our members and the British public means that we campaign for a range of treatments to be available through the NHS for those with depression. This commitment reflects the considerable evidence of broad equivalence between therapies for depression (Gyani, Shafran, Layard & Clark, 2013; Pybis, Saxon, Hill, & Barkham, 2017; Stiles, Barkham, Twigg, Mellor- Clark, & Cooper, 2006; Stiles, Barkham, Mellor-Clark, & Connell, 2008) but also the evidence that it is important to give clients choice about treatment options because doing so improve treatment outcomes (Lindhiem, Bennett, Trentacosta, & McLear, 2014; Williams et al., 2016). It is important to note that this means that BACP has a commitment to support choice for all evidence-based therapies and as such welcomes the recommendations in the draft	recommendations on CBT, psychodynamic therapy and counselling.

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				Guideline for the three main modalities practiced in the UK, namely Cognitive Behavioural Therapy (CBT), Psychodynamic Psychotherapy, and what is termed in the Guideline 'Counselling'. This document however focusses predominantly on counselling.	
British Association for Counselling and Psychotherapy	Full	General	General	This document was prepared by members of the BACP Research Department and draws on feedback on the draft Guideline from senior counselling and psychotherapy academic researchers in the UK and beyond. The document also draws on two reviews by academic teams independent of both NICE and BACP that were specifically commissioned by BACP to review the network meta-analysis and the economic cost modelling that informed the revised Guideline.	Thank you for this information.
British Association for Counselling and Psychotherapy	Full	General	General	BACP welcomes the extension to the original consultation period. However, given the length and complexity of the consultation documents and the level of detail required to digest and interpret the analysis, plus the timing of the consultation period, falling at a time of year when many researchers take holiday, we consider that the extension was wholly insufficient to allow for a properly robust independent level of scrutiny of the proposed Guideline recommendations and the processes and evidence used to arrive at	Thank you for your comment. The standard consultation period for a draft guideline is 6 weeks. In recognition of the complexity of this guideline and the consultation period falling over the summer it was decided to increase the consultation period by 2 weeks to a total of 8 weeks, to allow stakeholders more time to respond to the consultation.

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				such.	
British Association for Counselling and Psychotherapy	Full	General	General	BACP maintains in the strongest possible terms that detailed scrutiny of not only the evidence but the methods utilised is critical because historically the NICE Guideline for depression in adults has been significantly influential in shaping service delivery, in particular in England. As described by Clark (2011), the NICE recommendations for depression from 2004 onwards contributed to the development and roll-out of the Improving Access to Psychological Therapies (IAPT) programme, which in England and Wales now provides the bulk of treatment for depression in primary care (Gyani, Pumphrey, Parker, Shafran, & Rose, 2012). One example of the impact of the revised 2009 Guidelines appears to have been the cutting of counselling jobs in the NHS, with IAPT workforce census data suggesting a 35% decline in the number of qualified counsellors working as high-intensity therapists between 2012 and 2015, in a period where the total IAPT workforce grew by almost 18% (IAPT Programme, 2013; NHS England & Health Education England, 2016). Workforce shifts that apparently follow revised NICE guidelines (e.g. counselling not being recommended as a first line treatment for depression) underline the importance of	Thank you for your comment. We agree that scrutiny of the evidence and methods used to develop NICE guidelines is very important. NICE guidelines are subject to rigorous and in-depth quality assurance throughout their development to ensure that the pre-specified methods have been adhered to and that there is appropriate justification for that have been made recommendations. Consultation with registered stakeholders on the draft guideline forms an integral part of this quality assurance process, as it enables their views to be taken into consideration. Counselling was recommended in the 2009 guideline and continues to be recommended in this guideline. As you point out there has has been significant expansion in IAPT workforces, and a significant number of counsellors will be employed in that service.

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				scrutinising guideline recommendations since a core assumption is that using 'best' evidence and guideline methodologies will lead to NICE recommendations that improve patient care. In view of this we would argue that NICE has failed to facilitate a rigorous response to the consultation and in doing so has not acted in the best interests of the public.	
British Association for Counselling and Psychotherapy	Full	General	General	**BACP would like to make the following critiquing comments on the methodology used to arrive at the revised guideline (please see individual comments below):**	Thank you for your comments. We have responded separately to each of the issues that you have raised.
British Association for Counselling and Psychotherapy	Full	General	General	***Privileging of RCT evidence:*** BACP cautiously welcomes the decision to retain counselling as a treatment. However, we are concerned about the recommendation to include counselling only as a second line intervention behind CBT and Behavioural Activation and we consider that this decision is based upon the privileging of RCTs above other relevant forms of evidence. We contend that the consideration of RCTs without the inclusion of very large routine practice-based datasets such as the IAPT dataset does not constitute 'the best available evidence', is unfit for purpose, and does not follow NICE's own procedural manual that	Thank you for your comment. When making recommendations for treatment of a new depressive episode, we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be

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				"other study designs (including observational, experimental or qualitative) may also be used to assess effectiveness or aspects of effectiveness" (NICE, 2014/2017; p.15). We strongly recommend that NICE review their methodology to allow for the inclusion of findings based on large routine practice-based data sets. We consider that there can be insufficient confidence in the results of RCTs for adult depression conducted to date that compare CBT with another therapy because they likely lack sufficient statistical power (Cuijpers, 2016). Similarly, meta-analyses of RCTs focused on treatment of depression are also vulnerable to low power (Cuijpers, 2016). It is our view that trials require much greater statistical power and less bias to determine differential effectiveness, and that from the existing RCT data it is unclear whether one therapy for adult depression is more effective than another to an extent which is clinically relevant (Barkham et al., 2017). In our view, this crucial point undermines the credibility that can be placed on the NICE-generated meta-analytic analysis that has been used to generate the recommendations contained in the draft consultation.	made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We do not consider routine datasets, such as the IAPT dataset, to be better or equivalent to RCT data as we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading. We do not agree that our comparisons lack statistical power because both our networks drew on large samples of several thousand participants. Cuijpers 2016a ('Interpersonal Psychotherapy for Mental Health Problems: A Comprehensive Meta-Analysis') was searched for studies relevant to the guideline. No additional studies matching our inclusion criteria were identified beyond those that have already been added through other means (for example through stakeholder comments).
British	Full	Gener	Gen	***Failure to include large standardised***	Thank you for your comment. When making

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Association for Counselling and Psychotherapy		al	eral	***routine datasets:*** The issues with power in RCTs and meta-analytic syntheses of such create in our view mean that there is little justification for relying solely on trials data and dismissing evidence from large standardised routine datasets such as the IAPT dataset since the size, methods of collection and analysis of routine datasets merit their inclusion (Barkham et al, 2017). The IAPT dataset also represents a considerable financial investment of taxpayers' money. It is our view that such large datasets collected at taxpayers' expense deserve greater respect and consideration and we contend that this data should be used in order to complement data from RCTs. It is important further to note that the evidence from the IAPT dataset is that counselling is as effective as CBT as an intervention for depression (Barkham et al, 2017). Existing evidence from IAPT annual reports (NHS Digital, 2014, 2015, 2016) demonstrates that patient recovery rates have been virtually equivalent between CBT and counselling (Barkham et al., 2017). Research on different portions of the IAPT dataset in relation to the treatment of depression have reported comparable outcomes between CBT and counselling	recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We did not consider routine datasets, such as the IAPT dataset, as part of the evidence base because we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading.

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				(Gyani et al, 2013; Pybis et al, 2017). Given this, it is our view that IAPT data now needs to be considered alongside evidence from trials to form a more complete and accurate assessment of the comparative effectiveness of psychological therapies.	
British Association for Counselling and Psychotherapy	Full	General	General	***Failure to consider therapist effects:*** We also consider that a major gap in the guideline is the absence of attention to therapist effects. There is a growing body of evidence to indicate that there exit major differences between therapist effects (Barkham, Lutz, Lambert, & Saxon, 2017) or site effects (Pybis et al, 2017) where there appear to be noticeable differences in patients' outcomes (Saxon & Barkham, 2012), with some studies finding that these effects are greater than the difference between alternative models of therapy it is our view that the current guideline risks being read by GPs and other front-line practitioners in such a way that they will expect that all CBT therapists, counsellors or other therapists are equivalent in effectiveness when this is not supported by the evidence. Inclusion of consideration of therapist or site effects would have the benefit of promoting greater attending to on-the-ground evidence of effectiveness of specific therapists and clinics.	Thank you for your comment. The guideline focussed on the effectiveness of different interventions to treat depression. Therapist effects were not an area that was prioritised for inclusion in the guideline, therefore the evidence on this has not been reviewed and we are not able to make any recommendations on this issue.

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British Association for Counselling and Psychotherapy	Full	General	General	The recommendations in the NICE draft Guideline for Depression in Adults were developed out of a network meta-analysis and subsequent economic analysis. However review by BACP has identified a number of significant issues in the conducted NMAs that in our view suggest that the analysis results should be treated with considerable caution. These issues are described in the following sections below: - Selection of studies for inclusion - Consideration of bias - Homogeneity of study population - Classification of interventions - Outcome variables selected - Statistical homogeneity - Inconsistency - Transitivity - Judgements related to Rankings	Thank you for your comments. We have responded separately to each of the issues that you have raised.
British Association for Counselling and Psychotherapy	Full	General	General	BACP is concerned that although the economic analysis undertaken has been conducted rigorously, that it is based on underlying assumptions which may mask the true comparability of the cost effectiveness of the interventions included (please see individual comments below)	Thank you very much for your comments. We have responded separately to each of the issues that you have raised.
British Association for	Full	General	General	In summary, the BACP review of the economic modelling of the cost effectiveness	Thank you for your detailed comments. Please see specific responses to your

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Counselling and Psychotherapy				of interventions for the treatment of depression in adults suggests that there are some inconsistencies in the analysis and that two key assumptions in the analysis are inappropriate for counselling. This is combined with the fact that the economic analysis builds out of the NMA which is itself – and as acknowledged in the draft Guideline – flawed in a number of ways. Overall, our conclusion is that the results are likely misleading and that the cost effectiveness of counselling as an intervention for depression in adults is not appropriately represented.	comments on the limitations of the NMA and the key assumptions underpinning the economic analysis with regards to counselling. The NMA was a complex analysis that included numerous studies and interventions across 2 populations of different depressive symptom severity. As any complex analysis, it is characterised by a number of limitations, which have been acknowledged and their impact has been explored through extensive statistical checks. The committee have taken into account the limitations characterising the guideline NMAs and, consequently, the guideline economic modelling, which was informed by the NMAs, when making recommendations.
IPTUK	Full	General	General	A significant area of concern lies in the lack of transparency about the evidence that has been used, and how it has been used, to produce the draft guidance. Transparency is a key principle underpinning NICE guidelines, and the inconsistencies in referencing across this document are highly concerning and cast considerable doubt over its credibility. Chapter 16 of the draft provides references for the studies that have been included in the NMA and which therefore inform the recommendations. On reviewing this chapter,	Thank you for your comment. We agree that transparency is crucial. The approach that had been taken in the consultation draft of the guideline was that where a study had been cited in the text in Chapter 7 it was referenced in Chapter 16. However if a study was included in the NMA of treatment for a new depressive episode but not cited in the text in Chapter 7, then it would not appear in Chapter 16. Instead there was a cross reference to Appendix T and the intention was that Appendix T would act as the full list of studies included in the NMA. However, we appreciate your point that this makes it

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				we identified several omissions: **Failure to reference studies that have been included in the analyses described in Appendix T:** o Blom et al (2007) Combination Treatment for Acute Depression Is Superior Only when Psychotherapy Is Added to Medication Psychotherapy and Psychosomatics, 76, 289-297 o Blom MB, Spinhoven P, Hoffman T, Jonker K, Hoencamp E, Haffmans PMJ, van Dyck R. (2007) Severity and duration of depression, not personality factors, predict short term outcome in the treatment of major depression. J Affect Disord. 104: 119-126. ○ ***cited in Appendix T, more severe (MS) discontinuation, line 114, but not included in the outcome analyses or referenced in Chapter 16 or Appendix J3.*** o Marshall C, Zuroff DC, McBride C, Bagby RM. (2008) Self-Criticism Predicts Differential Response to Treatment for Major Depression. J Clin Psychol; 64:231-244. ○ ***cited in Appendix T, LS SMD line 76, but not referenced in Chapter 16***	difficult to identify which studies were included and that Appendix T does not include the full bibliographic reference. Therefore, in response to your comment, we have added all the references of included studies for the NMA of treatment of a new depressive episode (and other reviews) to Chapter 16. To confirm, the following studies were already included in the NMA but references will be added to Chapter 16 to make this clearer: • Marshall 2008 • Luty 2007 • van Scheik 2006 • Schramm 2007 • Reynolds 1999 • Reynolds 2006 • Blom 2007 ('Combination Treatment for Acute Depression Is Superior Only when Psychotherapy Is Added to Medication'). This study is also in Appendix J3. The outcome data had been previously omitted from the model in error but has now been added to the analysis and to Appendix N3 (which replaces the former Appendix T). Please note that for SMD we only included ITT continuous data (i.e. in those randomised). Continuous completers data has been included in the

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				o Luty et al (2007) Randomised controlled trial of interpersonal psychotherapy and cognitive behavioural therapy for depression BJPsych 190, 496-502 ○ ***cited in Appendix T, LS analyses, but not referenced in Chapter 16*** o van Scheik et al (2006) Interpersonal psychotherapy for elderly patients in primary care. Am J Geriatr Psychiatry. 2006 Sep;14(9):777-86. ○ ***cited in Appendix T, LS analyses, but not referenced in Chapter 16*** o Schramm, E., Van Calker, D., Dykierek, P., Lieb, K., et al. (2007) An intensive treatment program of interpersonal psychotherapy plus pharmacotherapy for depressed inpatients: Acute and long-term results. American Journal of Psychiatry, 164 (5), 768-777. ○ ***cited in Appendix T, LS analyses, but not referenced in Chapter 16*** o Swartz, H.A., Frank, E., Zuckoff, A., et al. (2008) Brief interpersonal psychotherapy for depressed mothers whose children are receiving psychiatric treatment. American Journal of Psychiatry, 165 (90), 1155-1162. ○ ***cited in Appendix T, LS***	response in completers analysis • Swartz 2008. The outcome data was included in the model but please note that for SMD we only included ITT continuous data (i.e. in those randomised). Continuous completers data has been included in the response in completers analysis • Bodenmann 2008. Data has been checked and numbers have been entered correctly. Please note that in Appendix N3 (which replaces the former Appendix T), the column code t refers to the number/code of intervention, n is the denominator (depending on the outcome, it would be N randomised or N completers) and r is the number of events • Beeber 2010 • Menchetti 2014 • Carter 2011. The outcome data had been previously omitted from the model in error but has now been added to the analysis and to Appendix N3 (which replaces the former Appendix T). In response to your comments regarding missing references; Swartz 2016 has been included in the NMA, thank you for bringing our attention to this study. Thank you also for drawing our attention to Barth 2013. This

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				discontinuation, line 63, but not included in the outcome analyses or referenced in Chapter 16 o Bodenmann et al(2008) Effects of Coping-Oriented Couples Therapy on Depression: A Randomized Clinical Trial. Journal of Consulting and Clinical Psychology, Vol. 76, No. 6, 944–954 ○ ***cited in Appendix T, MS analyses, but not referenced in Chapter 16*** ○ ***numbers in each group are incorrectly entered*** o Beeber (2010) Short-term in-home intervention reduces depressive symptoms in Early Head Start Latina mothers of infants and toddlers. Research in Nursing & Health, 33, 60Y76. ○ ***cited in Appendix T, LS Discontinuation, line 45, but not referenced in outcome analyses or chapter 16*** o Menchetti (2014) Moderators of remission with interpersonal counselling or drug treatment in primary care patients with depression: randomised controlled trial. The British Journal of Psychiatry	systematic review was checked for relevant references and as a result 14 additional studies were included in the NMA. The other studies identified as missing did not meet our inclusion criteria for the NMA of treatment of a new depressive episode for the following reasons: • Blom 2007 ('Severity and duration of depression, not personality factors, predict short term outcome in the treatment of major depression'): Secondary analysis of an RCT that was already included in the guideline. • Elkin 1995: Secondary analysis of a study already included in NMA (Elkin 1989). • Frank 2007 is not included in the NMA because it is not first-line treatment. It also does not meet the inclusion criteria for the relapse prevention review as the comparison is not of relevance to the review question as defined in the protocol (weekly versus twice-monthly versus monthly IPT). As outlined in the review protocol the objective of this review was to compare interventions against other active interventions or control arm(s) but comparing different intensities of the same intervention was beyond the aims and objectives of this

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				(2014) 204, 144–150. doi: 10.1192/bjp.bp.112.122663 ○ ***cited in Appendix T, MS analyses, but not referenced in Chapter 16*** o Carter (2011) Patient predictors of response to cognitive behaviour therapy and interpersonal psychotherapy in a randomised clinical trial for depression. Journal of affective disorders. 2011 Feb 28;128(3):252-61. ○ ***cited in Appendix T, LS discontinuation, line 44, but not included in the outcome analyses or referenced in Chapter 16*** o Reynolds CF, Dew MA, Pollock BG, Mulsant BH, Frank E, Miller MD, Kupfer DJ. Maintenance treatment of major depression in old age. The New England Journal of Medicine. 2006; 354(11): 1130–1138. http://dx.doi.org/10.1056/NEJMoa052619. [PubMed: 16540613] o Reynolds CF, Frank E, Perel JM, Imber SD, Cornes C, Miller MD, et al. Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression. The	review. • Cuijpers 2016 was searched for relevant studies and no additional studies were identified for inclusion beyond those that have already been added through other means (for example through stakeholder comments). • Ekeblad 2016: is not included in the NMA because it is not first-line treatment. • Toth 2013: It was not possible to extract continuous data as only means with no measure of variance was reported. Given the size of the evidence base it was not possible to contact all authors for missing data. • Power 2012: Data cannot be extracted (available for <50% of those randomised and disaggregated data threatens randomisation). • Karyotaki 2016: was searched for relevant studies and no additional studies were identified for inclusion beyond those that have already been added through other means (for example through stakeholder comments). In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be

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				Journal of American Medical Association. 1999; 281(1):139–145. ○ ***cited in Table 212 page 629 but not referenced in Chapter 16*** **Failure to reference or to explain why IPT trials, referenced in the 2009 guideline, have not been included in the current NMA:** o Elkin I, Gibbons RD, Shea MT, Sotsky SM, Watkins JT, Pilkonis PA, et al. Initial severity and differential treatment outcome in the National Institute of Mental Health Treatment of Depression Collaborative Research Program. J Consult Clin Psychol. 1995; 63(5):841–7 o Frank, E., Kupfer, D.J., Buysse, D.J., et al. (2007) Randomized trial of weekly, twice-monthly, and monthly interpersonal psychotherapy as maintenance treatment for women with recurrent depression. American Journal of Psychiatry, 164, 761-767. **Failure to include and reference all relevant evidence**: o Cuijpers et al (2016) Interpersonal Psychotherapy for Mental Health Problems: A Comprehensive Meta-	understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. Matsuzaka 2017 has not been included in the guideline because it was published after the cut off date of June 2016.

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				Analysis. Am J Psychiatry 2016; 173:680–687. o Ekeblad et al (2016) Randomised trial of Interpersonal Psychotherapy and Cognitive Behavioural Therapy for Major Depressive Disorder in a Community Based Psychiatric Outpatient Clinic. Depression and Anxiety, 33 1090-1098 o Toth, S.L. et al (2013) The efficacy of interpersonal psychotherapy for depression among economically disadvantaged mothers. Development and Psychopathology, 25, 1065-1078 o Completer (defined as complier) data are available. Did the committee contact the author to enable full extraction of the data? o Power M.J. & Freeman, C (2012) A Randomized controlled trial of IPT Versus CBT in Primary Care: With some cautionary notes about handling missing values. Clinical Psychology & Psychotherapy, 19, 159-169 o Swartz, H. A et al (2016) Brief Psychotherapy for Maternal Depression: Impact on Mothers and Children. J Am Acad Child Adolesc Psychiatry 2016;55(6):495–503 n.b. the children in this study are teenager not infants. o Barth et al (2013) Comparative Efficacy of Seven Psychotherapeutic Interventions	

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				for Patients with Depression: A Network Meta-Analysis PLOS Medicine, May, Vol 10, Iss 5, e1001454 o Karyotaki E, Smit Y, de Beurs DP, Henningsen KH, Robays J, Huibers MJH, et al. The long-term efficacy of acute-phase psychotherapy for depression: a meta-analysis of randomized trials. Depression and Anxiety. 2016;33(5):370-83. o Matsuzaka CT, Wainberg M, Pala AN, Hoffmann EV, Coimbra BM, Braga RF, et al. Task shifting interpersonal counseling for depression: a pragmatic randomized controlled trial in primary care. Bmc Psychiatry. 2017;17. Consequently, in addition to a lack of clarity on how existing evidence has been used, it appears that several studies on IPT containing relevant evidence and core analyses were overlooked. If the gaps in the evidence and referencing errors identified for IPT and misrepresentation of data with core analyses are representative of the way in which data have been managed and reported across all treatments, the credibility of the document is significantly undermined. Failure to review and reference accurately in a guideline that purports to report and	

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				recommend on the evidence raises serious questions over the validity of this document and its recommendations o **The guideline committee should make clear exactly what evidence was used to arrive at these recommendations. Inconsistencies in referencing between Chapter 16 and Appendix J3 creates confusion.** o **The guideline committee should revise the reference list to provide a comprehensive and accurate record of the evidence used.** o **The guidance committee should provide a full explanation as to why relevant evidence was omitted and recalculate with all relevant evidence included.**	
IPTUK	Full	Appendix T	LS Remission ITT	Appendix T, LS Remission ITT has been incorrectly coded, raising serious doubts over any conclusions based on this dataset. **The committee should recode and recalculate all analyses on LS (less severe) remission ITT and revise recommendations accordingly**	Thank you for your comment. All analyses have now been updated following inclusion of more studies in the review and changes in the classification (e.g. CBT and BT group therapies have formed a new class in the updated analyses). The treatment codes have been checked across all outcomes in the final analyses. In the updated analysis of less severe remission ITT, combined psychological and

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					pharmacological interventions (some of which, such as combined counselling with antidepressants, were new in the analysis and were based on small numbers randomised) showed moderate to very large effects, as in the previous (consultation) analysis. Behavioural therapy remained the most effective psychological intervention on this outcome. The effects of CT/CBT, IPT, psychoeducational interventions, SSRIs and TCAs were overall similar in the original and the updated analysis. The effects for counselling, short-term psychodynamic therapy and self-help with support were reduced in the updated analysis, with short-term psychodynamic therapy showing an effect similar to pill placebo in the updated analysis. The effects for exercise alone or combined with antidepressant/CBT and self-help without support were improved in the updated analysis (all 3 interventions showed effects similar to pill placebo in the consultation analysis, but better effects than pill placebo in the updated analysis).
South Tyneside	Full	General	General	We are concerned that these recommendations will result in clients who	Thank you for your comment and providing data on IPT use in south Tyneside Lifecycle

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Lifecycle Primary Care Mental Health Service				would benefit from Interpersonal Psychotherapy (IPT) not being able to access this effective treatment as a first line treatment or as a treatment for higher severity depression. During the period of 01/08/16 to 31/07/17, South Tyneside Lifecycle Primary Care Mental Health Service provided Interpersonal Psychotherapy (IPT) for 255 adult service users. Of those receiving Interpersonal Psychotherapy (IPT) treatment, 30.23% had a baseline PHQ-9 score of 10-17 (lower severity depression) and 60.98% had a baseline PHQ-9 score of 18+ (higher severity depression). The average PHQ-9 baseline score was 18. At the end of treatment, 61.29% of service users had a PHQ-9 score of less than 10, 21.14% of service users had a PHQ-9 score of 10-17 and 17.61% had a HQ-9 score of 18+. The average PHQ-9 end of treatment score was 9. Of the 169 service users who accessed Interpersonal Psychotherapy (IPT) as the sole treatment (not stepped up or across), 59.17% were in the higher severity range at the start of treatment and 32.54% were in the lower severity range. 60.95% of this group	Primary Care Mental Health Service. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues.

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				had an end of treatment PHQ-9 score of less than 10. Given the efficacy of Interpersonal Psychotherapy (IPT) in our service, both as a sole treatment and as a treatment for higher severity depression, it is concerning that, going forward, 81.96% of these service users would not be able to access Interpersonal Psychotherapy (IPT) if these draft guidelines for depression are implemented. Of the total number of adult service users receiving treatment for higher severity depression in our service, 11.47% received IPT, so a significant proportion of service users would be detrimentally affected by the withdrawal of this treatment option.	IPT remains an option for people with less severe depression (who would like help for interpersonal difficulties that focus on role transitions or disputes or grief) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication individual CBT or BA) have not worked well in a previous episode of depression or in those who do not want the other recommended interventions. The committee made this a 'consider' recommendation because of the small benefit on the SMD outcome, the larger benefits on the other two clinical outcomes, and the lower cost effectiveness of IPT compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of IPT was likely to be higher in the sub-population specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). An individual high intensity psychological

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					intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
British Psychoanalytic Council	Full	General	General	Narrow consideration of what constitutes evidence: The recommendations are derived from a narrow consideration of what constitutes appropriate evidence: RCTs and meta-analyses. Although RCTs and meta-analyses lend themselves well to scientific study, RCTs also use populations that are not representative of clinical experience. This is	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret

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				a significant problem, where treatment recommendations are then made for clinical populations, including choice of treatments, based on evidence that is not particularly clinically representative. This can only lead to recommendations which are not necessarily in the best interests of patients, based on a privileging of treatments which lend themselves to RCTs (CBT for example) but which have limited clinical utility. To briefly expand, the recommendations are largely drawn from RCTs with patients with a diagnosis of depression only. Yet, there is much evidence, in addition to clinical experience, that depression is frequently comorbid with other illnesses, such as anxiety. Patients typically present to clinicians with a wide range of difficulties such as bereavement, co-morbid physical ill health, relationship problems, and so on. Although one cannot question the validity of RCTs and meta-analyses as forms of scientific study, one can reasonably question the rationale for relying so much on RCTs and meta-analyses given the clinical reality of most people experiencing depression. We now quote from page 24 of the Full version:	this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We did not consider routine datasets, such as the IAPT dataset, as part of the evidence base because we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading. The references that you cite did not meet the evidence reviews' inclusion criteria because: • Hepgul et al. is not an RCT and is not of relevance to the review question as defined in the protocol • Kessler et al. and Lamers et al. are epidemiological studies on comorbidity not different treatment response.

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				'*Uses and limitations of clinical guidelines* *Guidelines are not a substitute for professional knowledge and clinical judgement. They can be limited in their usefulness and applicability by a number of different factors: the availability of high quality research evidence, the methodology used in the development of the guideline, the generalisability of research findings and the uniqueness of individuals with depression.* *Although the quality of research in this field is variable, the methodology used here reflects current international understanding on the appropriate practice for guideline development (AGREE-Collaboration 2003) ensuring the collection and selection of the best research evidence available and the systematic generation of treatment recommendations applicable to the majority of people with depression. However, there will always be some people and situations where clinical guideline recommendations are not readily applicable. This guideline does not, therefore, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual, in consultation with the person with depression*	

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				or their carer.' We are pleased that NICE emphasises the importance of professional knowledge and clinical judgement; but the fact is, the NHS psychological therapies programme defers to the recommendations of NICE, clinicians need to justify their demands for resources to budget holders, and adherence to NICE guidelines can help defend healthcare professionals and providers against claims of clinical negligence. These recommendations will affect what treatments are widely available to the millions of people experiencing depression. Until NICE also takes into consideration the wider range of available evidence from real-world settings and does not overly rely on RCTS which use patients with a sole diagnosis of depression, its treatment recommendations for depression in adults will not only be of questionable clinical utility for patients but will also be overwhelmingly deferred to. An example of real-world evidence which NICE should take into consideration is the IAPT dataset evidence concerning the effectiveness of psychodynamic psychotherapy and CBT. The dataset shows	

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				that both types of treatment have a recovery rate of 45.9%, with psychodynamic psychotherapy achieving this with 5.7 sessions on average, as opposed to 5.8 sessions on average for CBT. Why is real world evidence such as this not taken into consideration? This example immediately brings into question CBT as always being the first-line treatment. There are many studies on depression and comorbidity, including: Hepgul, N., King, S., Amarasinghe, M., Green, G., Grant, N., Grey, N., Hotopf, M., Moran, P., Pariante, C., Tylee, A., Wingrove, J., Young, AH., & Cleare, AJ. (2016). Clinical characteristics of patients assessed within an Improving Access to Psychological Therapies (IAPT) service: results from a naturalistic cohort study (Predicting Outcome Following Psychological Therapy; PROMPT), *BMC Psychiatry* 16:52 Kessler, RC., Berglund, P., Demler, O., Jin, R., Koretz, D., Merikangas, KR., Rush, AJ., Walters, EE., & Wang, PS. (1993). The epidemiology of major depressive disorder: results from the national comorbidity survey replication, *Journal of the American Medical Association*, 289, 3095-3105.	

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				Lamers, F., Van Oppen, P., Comijs, HC., Smit, JH., Spinhoven, P., Van Balkom, AJ., Nolen, WA., Zitman, FG., Beekman, AT., & Penninx, BW. (2011). Comorbidity patterns of anxiety and depressive disorders in a large cohort study: the Netherlands Study of Depression and Anxiety (NESDA), *Journal of Clinical Psychiatry*, 72(3):341-8.	
British Psychoanalytic Council	Full	General	General	<u>Separation of Treatment Resistant Depression from Chronic Depression:</u> Past versions of the guidelines did not use a Treatment Resistant Depression category, separate from Chronic Depression. Instead, they emphasised the myriad types of depression that are chronic and resistant to treatment, and which are often linked with co-morbid mental health disorders. Given that the draft guidelines emphasise the difficulty in, and problems of, classifying depression, we do not understand why a decision has now been taken to separate Treatment Resistant Depression and Chronic Depression. The European Psychiatric Association guidance (2016) and the APA (DSM-V) also both recommend a common persistent depression category.	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a

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				Given the importance and impact of these revised guidelines, and the commonality of patients experiencing treatment-resistant depression and chronic depression, we are concerned what long-term impact this may have on choice of treatments for people experiencing treatment-resistant and chronic depression. We suggest that NICE reverts to previous guidance on this matter and does not separate the two types of depression.	limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'.

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British Psychoanalytic Council	Full	General	General	<u>Due consideration of outcomes of treatment at long-term follow-up/observation:</u> The guidance notes that patients with treatment-resistant depression are likely to relapse or deteriorate following treatment. Despite this, there is little attention paid to long-term follow-up of treatments. It is concerning, for example, that the draft guidelines do not consider data from the Tavistock Adult Depression Study's (2015) long-term follow-up data, which demonstrated for example that at 2-year follow-up, nearly a third of the participants receiving long-term psychoanalytic psychotherapy (LTPP) were still in partial remission, compared with only 4% of those in the control group. The study also found that at 2-year follow-up, 44% of the LTPP group no longer met diagnostic criteria for major depressive disorder, compared with 10% of those in the control group receiving treatment-as-usual. One can reasonably argue that a treatment which demonstrates considerable effect at long-term follow-up is stronger than one which does not. A treatment which has little effect after a treatment ends is surely a weaker treatment than one which has a longer-lasting effect on a patient. We	Thank you for your comment. Fonagy 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') is included in the review for further-line treatment. We did not consider follow-up for further-line treatment as this data was not widely available across different intervention types and thus did not enable meaningful comparison. We did, however, include longer-term follow-up data in the relapse prevention review so we do have evidence in the guideline pertaining to longer-term effects of maintenance treatment. However, Fonagy 2015 does not meet the inclusion criteria for that review. It is also worth noting that if you do consider the 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although as you point out the effects on depression symptomatology are statistically significant at this time point. In GRADE RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias.

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				therefore suggest that, for ethical reasons and for cost-effectiveness reasons, NICE takes into due consideration all follow-up data on the effect of treatments for patients/service users, and takes this data into consideration when makings its recommendations. We also suggest that studies with no long-term follow-up data are downgraded.	Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. However we agree that it is important that long-term follow up data are collected in future research to enable comparison of this outcome across different interventions. We have therefore amended our research recommendations to specify that these data need to be collected.
British Psychoanalytic Council	Full	General	General	<u>Patient/service user experience:</u> We are concerned that the draft guidelines are based on low quality patient/service user experience research. Further, the guidelines do not seem to take due consideration of a number of themes arising from the patient experience accounts included in the full copy of the guidelines. We have various concerns with regard to the quality of the patient/service user experience research. We do not know, for example, if the thirty eight men and women who gave interviews which were collected by	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.

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				Healthtalkonline represented any under-represented groups of people. Page 68 refers to a number of themes found in accounts of people with depression, including: trauma or conflict in childhood as a perceived cause of depression, and the need for long-term psychotherapy for people with severe and chronic depression. These patient/service user themes seem to have had no influence on the draft recommendations. On page 97, under a section on 'Psychological therapy' under 'Experiences of treatments', the following is stated: '*There was a strong feeling within the service user and carer topic group that the excerpt from Howe (1995) in the section above highlights the reasons why many people opt for private therapy; that is, that psychological treatment offered by the NHS in the form of CBT does not go far enough in addressing the trauma experienced in childhood. The study by Ridge and Ziebland (2006) confirms the opinions of the topic group and the testimony from the personal accounts that people with 'deep and complex problems felt the need for longer term therapy'. Those that have had long-term psychodynamic therapy*	

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				report that it has been helpful in their understanding of themselves and their depression and that until they have worked through and repaired the damage experienced in childhood, depression will be a major factor in the person's life. The service user and carer topic group do acknowledge, however, that as there has been little research into the efficacy of long-term psychodynamic therapy, it cannot be recommended as a course of treatment in this guideline.' And yet in fact, good quality studies have now been carried out on psychodynamic psychotherapy for long-term depression. These include the Tavistock Adult Depression Study (2015). One wonders how far the patient/service user representatives in the guideline development group were made fully aware of these studies. We are also concerned that the guidelines do not seem to have taken due account of the many studies on patient/service user experience which have come out in recent years, including many more on under-represented patients. A selection includes: Alderson, SL., Foy, R., Glidewell, L., & House, AO. (2014). Patients understanding of	

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				depression associated with chronic physical illness: a qualitative study, *BMC Family Practice,* 20,15:37. Brenne, E., Loge, JH., Kaasa, S., Heitzer, E., Knudsen, AK., & Wasteson, E. (2013). European Palliative Care Research Collaborative. Depressed patients with incurable cancer: which depressive symptoms do they experience? *Palliative Support Care*, 11(6):491-501. Clarke, DM., Cook, KE., Coleman, KJ., & Smith, GC. (2006). A qualitative examination of the experience of 'depression' in hospitalized medically ill patients, *Psychopathology*, 39(6):303-12 Corcoran, J., Brown, E., Davis, M., Pineda, M., Kadolph, J., & Bell, H. (2013). Depression in older adults: a meta-synthesis, *Journal of Gerontological Social Work*, 56(6):509-34. Dekker, RL., Peden, AR., Lennie, TA., Schooler, MP., & Moser, DK. (2009). Living with depressive symptoms: patients with heart failure, *American Journal of Critical Care*, 18(4):310-8. Feely, M., & Long A. (2009). Depression: a psychiatric nursing theory of connectivity,	

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				Journal of Psychiatric and Mental Health Nursing, 16(8):725-37. Kokanovic, R., Bendelow, G., & Philip, B. (2012). Depression: the ambivalence of diagnosis, *Sociology of Health and Illness*. 35(3):377-390. Oliffe, JL., Ogrodniczuk, JS., Bottorff, JL., Johnson, JL., & Hoyak, K. (2012). "You feel like you can't live anymore": suicide from the perspectives of Canadian men who experience depression, *Social Science and Medicine,* 74(4):506-14. Scroggs, N., Shattell, M. & Cowling, WR. (2010). "An existential place of pain": the essence of despair in women, *Issues in Mental Health Nursing*. 31(7):477-82. Smith, JA., & Rhodes, JE. (2014). Being depleted and being shaken: An interpretative phenomenological analysis of the experiential features of a first episode of depression, *Psychology and Psychotherapy*. 88(2):197-209. Van Grieken, RA., Beune, EJ., Kirkenier, AC., Koeter, MW., Van Zwieten, MC., & Schene, AH. (2014). Patients' perspectives on how treatment can impede their recovery from	

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				depression, Journal of Affective Disorders. 167:153-9.	
British Psychoanalytic Council	Full	General	General	For the above reasons, and because of the considerable impact these guidelines will have on persons experiencing depression, we believe that any further revision of the draft guidelines should be subject to further scrutiny and consultation.	Thank you for your comment. Section 10.3 of Developing NICE guidelines: the manual clarifies when a second consultation may be needed. This states that "In exceptional circumstances, NICE may consider the need for a further 4-week stakeholder consultation after the first consultation. This additional consultation may be needed if either: • information or data that would significantly alter the guideline were omitted from the first draft, or • evidence was misinterpreted in the first draft and the amended interpretation significantly alters the draft recommendations. NICE staff with responsibility for guideline quality assurance make the final decision on whether to hold a second consultation." NICE judged that these criteria were not met, therefore no second consultation was conducted.
Relate	Full	General		We believe that NICE is over-reliant on Randomised Control Trials (RCTs) in considering evidence for interventions, and as a result is missing a valuable source of information on treatment effectiveness by neglecting practice-based routine outcome	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions

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				data. Both RCTs and routine outcome monitoring have their limitations. RCTs usually involve much smaller samples of only around 100 patients, whereas practice-based data sets allow for much bigger samples. We believe NICE should consider data from Improving Access to Psychological Therapies (IAPT) services – an enormous outcomes data set. Given that this data is collected routinely within IAPT, we would urge NICE to consider the data in developing guidelines. The IAPT data on recovery rates shows that couple therapy for depression is the most effective high-intensity psychological therapy.	compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We did not consider routine datasets, such as the IAPT dataset, as part of the evidence base because we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading.
Mind	Full	General		Clients appreciate the counselling approach and it should be fully offered as part of the menu of therapies– and clients should be deemed to have sufficient insight to decide from a menu of choice (this is not our experience of what happens in IAPT). Currently it is seen that counsellors offer mainly counselling for depression, but counsellors have trained to work with clients	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused

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				presenting with many problems and this remains unrecognised within IAPT generally (so anger, relationship issues, abuse, self-injury etc.). NICE have included counselling as a continued option within their draft review but there were concerns from various sources about whether this would happen – the fear being that counselling would be dropped as an option. This is because NICE seems fixated on Randomised Control Trial evidence, and seems to ignore practise based evidence. This is ironic since the whole of IAPT is essentially a massive data gathering system which should be offering lots of data about what is effective in the real world. If that data is not being used to inform NICE guidelines, then it begs the question as to why such huge amounts of data are being collected on a session by session basis nationwide.	on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We did not consider routine datasets, such as the IAPT dataset, as part of the evidence base because we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading. Making recommendations about the recognition within IAPT of what problems counsellors have been trained to deal with is not within the remit of this guideline.
Mind	Full	General		The removal of Mindfulness Based Cognitive Therapy (MBCT) from the NICE guidance as a first line treatment for less severe depression (Section 1.5) and more severe depression (Section 1.6) will result in a challenging change in practice, as the Mindfulness in Mind partnership has	Thank you for your comment. Whilst two studies of MBCT were included in the NMA for treatment of a new depressive episode, the committee did not consider that the evidence was strong enough to support recommending this intervention, which was primarily developed for relapse prevention,

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				successfully delivered MBCT as a first line treatment to more than 890 patients. Clients' recovery rates are strong, showing improvements in anxiety, depression and perceived stress.	for first line treatment.
Mind	Full	General		Patient satisfaction and retention: our wide-scale delivery of MBCT has resulted in significantly improved patient satisfaction and retention in the mindfulness groups. Demand increases year on year. We are finding that mindfulness-based interventions are a more acceptance choice to a large number of people from hard-to-reach and black and minority ethnic (BME) communities who are often excluded from accessing a psychological therapy.	Thank you for your comment and providing this information about patient satisfaction with MBCT.
Mind	Full	General		Limiting patient choice: reducing the role of MBCT for the treatment of depression will result in further limiting patient choice. Patient choice has been a strong ethos of Mind, and we have found that over 890 people across two local Minds have actively chosen mindfulness-based interventions over other treatment options, in particular those patient groups who are often excluded from a psychological therapy. Our waiting list is up to 100 people per week, and we have found the need to significantly increase our provision over the past couple of years. This	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline

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				has also resulted in Mind setting up a national teacher training programme for mindfulness, 'Mindfulness in Mind'.	an offer of treatment. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When making the recommendations for specific interventions, the committee took into account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective. Whilst two studies of MBCT were included in the NMA for treatment of a new depressive episode, the committee did not consider that the evidence was strong enough to support

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					recommending this intervention, which was primarily developed for relapse prevention, for first line treatment.
Mind	Full	General		Evidence-base: We have reviewed a recent meta-analysis of randomised controlled trials (Strauss, Cavanagh, Oliver, & Pettman, 2014) which found MBCT (for people meeting diagnostic criteria for a current episode of depression) demonstrated significant post-intervention between-group effects in comparison to control conditions on depressive symptom severity. This validates Mind CHWF's experience of patient recovery rates using MBCT. We have a clinical research partnership with City, University of London, and have been keeping abreast of the latest evidence of the efficacy of mindfulness. As such, we have undertaken neuroscience research into the effects of mindfulness-based interventions on depression and anxiety, and conducted two randomised controlled trials in partnership with City, University of London, which are being prepared for publication. We would be willing to submit our experience to NICE.	Thank you for your comment. Whilst two studies of MBCT were included in the NMA for treatment of a new depressive episode, the committee did not consider that the evidence was strong enough to support recommending this intervention, which was primarily developed for relapse prevention, for first line treatment. The Strauss 2014 systematic review has been checked for relevant studies. Only 1 study meets our criteria for inclusion and that had already been included. As the two randomised controlled trials you have conducted are not yet published we are not able to include them in this guideline. They may be included in future updates of the guideline.
South West London and St. George's Mental Health NHS Trust	Full	General	General	Overall, there is an over-emphasis in the draft guideline on an intrapsychic conceptualisation of depression which is at odds with earlier descriptions in the introductory chapters of the guideline that	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been

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				describe the social and interpersonal correlates of depression (pp. 37-38). The presence of caveats for the application for relationship-focused therapies (e.g., pp. 252, lines 1-3, 17-18, 28-30), combined with the absence of caveats for the application of cognitive and behavioural therapies, risks implying that the application of CBT is universal compared to a more limited application of relationship focused therapies. In practice no psychological therapy has universal application, social and relationship correlates of depression are common rather than exceptional (pp. 37-38) and choice can improve engagement and outcomes (pp.43, lines 5-8). Current IAPT practices in our Trust have emphasised matching evidence-based therapies to the goals of clients presenting with depression. This has proved a practical way to implement current 2009 guidance, but there seems little room for this level of choice in the 2017 draft guidance.	re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. The caveats for the application of IPT, counselling and STPT are based on the committee's consideration that the effectiveness and cost effectiveness of these interventions was likely to be higher in the sub-population specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis.
Tavistock and Portman NHS Foundation Trust	Full	General	General	**Conceptual framework of depression** We believe that the conceptual framework for depression within the draft guideline has	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline

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				consequences relating to clinical management and for research. In relation to the distinction between chronic depression and TRD, earlier versions of the Guidance decided not to use the TRD category. This was based on evidence for the existence of a more loosely defined heterogeneous group of long-term, difficult to treated depressive conditions, frequently associated with dysthymia and co-morbid common mental disorders, various personality disorders/traits and serious psycho-social disability. In many cases, depression manifests as a long term condition rather than an acute one, which requires long term management using a variety of approaches to treatment and management. Furthermore, the introduction to the section on complex depression refers to many studies noting the frequent comorbidity in depression with physical illnesses and other mental health disorders, nonetheless the definition of complex depression in the draft guidelines is only focussed on co-morbidity with personality disorder. It does not include other co-morbidities nor does it include other aspects of complexity, such as childhood and/or adult trauma, poor functioning and severe relationship difficulties. We are concerned that the draft guidelines exclude RCTs that	TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this

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				include dual diagnoses or co-morbidity with other mental health disorders apart from personality disorder. Furthermore, many patients with depression and personality disorder also fulfil criteria for chronic and/or TRD, again highlighting the overlap between these categories. • **The clinical setting:** In the case of TRD, this is often defined as being akin to a medical condition, and a language is used which relates to pharmacology, dose and response. Within a clinical setting, a rather different conception is used and the entire psychosocial functioning of the patient is considered. The draft guideline therefore do not correspond to the reality of the clinical setting. • **The research setting:** This has an impact on definitions used within research. The guidance implicit to the NICE guidelines for depression will not be consistent with the APA (DSM-5) and the European Psychiatric Association (EPA) guidance (2016) if the current conceptualisation are adopted. Both recommend a common "persistent" depression category with sub-categories for severity and	is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. The committee considered a number of comments on the use of the term 'complex depression' in this guideline. In the guideline 'complex depression' was limited to depression that was co-morbid with a personality disorder. A number of stakeholders pointed out that other factors such as other mental health co-morbidities, drug and alcohol misuse, social and environmental factors and a history of poor response to treatment can also contribute to a diagnosis of complex depression. The committee considered these factors and

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				degree of associated psycho-social disability. Furthermore, the guidance will complicate outcome research, as many participants in trials included in the TRD meta-analysis meet the guideline's definition of chronic depression and/or complex depression. We are concerned that the guideline set up false categories and trials classified within only one category. In particular, Fonagy et al.'s (2015) study is classified within TRD when in fact it should be categorised with chronic depression. REFERENCES APA. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: American Psychiatric Association. Fonagy, P., Rost, F., Carlyle, J., McPherson, S., Thomas, R., Fearon, R. M. P., Goldberg, D. & Taylor, D. (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). World Psychiatry, 14(3), 312-321.	noted that co-morbidity with a range of other mental disorders also occurred in participants in studies for first line treatment, TRD and chronic depression. The committee therefore considered that co-morbidity alone would not be useful in describing complex depression. The focus on depression that was co-morbid with personality disorder was because of the committee's knowledge and experience that it can complicate the treatment of depression (see for example the meta-analysis by Newton-Howes et al (2006) Personality disorder and the outcome of depression: meta-analysis of published studies. British Journal of Psychiatry, 188, 13-20)). The committee therefore decided to stay with the current definition of complex depression used in the guideline as alternative suggested definitions did not clarify the issue. However they acknowledge there are limitations with this definition of complex depression. APA 2013 and Jobst 2016 have not been included in the guideline as they do not meet the study design criteria (not RCT or systematic review of RCTs). Fonagy 2015 is included in the review of further line treatment.

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				Jobst A et al. (2016) European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. European Psychiatry, 33, 18 – 36.	
Tavistock and Portman NHS Foundation Trust	Full	General 343	General 24 - 27	**<u>The importance of long-term follow-up data</u>** The 8.2*Review questions* section indicates the high likelihood of relapse/deterioration in patients with depression, in particular in those falling under TRD. Indeed, the necessity for RCTs of interventions for depression to include longer term follow-up data are persistently made (e.g. Westen et al., 2004; Hepgul et al., 2016).The long-term costs of depression are substantial, both from the point of view of the well-being of the person suffering from it and those associated with them, and also from an economic point of view. It is thus crucial that studies report outcome data over a longer-term after treatment termination than is currently practiced. Most studies included in the data analysis in the draft guideline have a very brief follow-up period of 6 – 12 weeks, and thus not provide any evidence that the effects obtained were lasting and that changes in depression severity could thus be maintained over time. An example of a study which had	Thank you for your comment. Fonagy 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') is included in the review for further-line treatment. We did not consider follow-up for further-line treatment as this data was not widely available across different intervention types and thus did not enable meaningful comparison. We did, however, include longer-term follow-up data in the relapse prevention review so we do have evidence in the guideline pertaining to longer-term effects of maintenance treatment. However, Fonagy 2015 does not meet the inclusion criteria for that review. It is also worth noting that if you do consider the 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although as you point out the effects on depression symptomatology are statistically significant at

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				substantial long-term follow up data was that of Fonagy et al (2015) which was undertaken at the Tavistock and Portman NHS Foundation Trust. They obtained data over a two-year period after treatment ended and showed substantial improvements and statistical significant effects with full remission Numbers Needed to Treat (NNT)= 9.6; partial remission NNT = 3.9 at the 182-week follow-up. We are concerned that attention is only focused on outcome at treatment endpoint in all analyses carried out in the draft guideline. Promisingly, the draft guideline highlights in the introduction that "the aim of interventions is to restore health through the relief of symptoms and restoration of functioning, and in the longer term, to prevent relapse" (p. 4, l. 31-32). It seems contradictory to subsequently not pay attention to studies which indeed provide data on longer-term outcome. Where available, these data should be taken into account when making recommendations, and any recommendations for future research should include emphasis for further studies to include a long-term follow-up. REFERENCES	this time point. In GRADE RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. However we agree that it is important that long-term follow up data are collected in future research to enable comparison of this outcome across different interventions. We have therefore amended our research recommendations to specify that these data need to be collected. Hepgul 2016 and Westen 2004 have not been included because they do not meet the study design criteria (not a systematic review of RCTs or an RCT).

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				Fonagy, P., Rost, F., Carlyle, J., McPherson, S., Thomas, R., Fearon, R. M. P., Goldberg, D. & Taylor, D. (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). World Psychiatry, 14(3), 312-321. Hepgul N, King S, Amarasinghe M, et al (2016). Clinical characteristics of patients assessed within an Improving Access to Psychological Therapies (IAPT) service: results from a naturalistic cohort study (Predicting Outcome Following Psychological Therapy; PROMPT). BMC psychiatry, 16(1), p52. Westen, D., Novotny, C. M., & Thompson-Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. Psychological Bulletin, 130, 631– 663.	
Tavistock and Portman NHS Foundation Trust	Full	General/ 202 onwar	General	**Problems with the method of dividing trial populations by categorising baseline severity simply as more severe or less severe**	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of

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		ds		The method used to derive this distinction has not been validated and we are concerned that this leads to misleading impressions and conclusions/recommendations in which potentially valuable treatment effects are ignored. We suggest: • The revision of the draft guideline should identify and use categories and methods of analysis which are more appropriate as ways of determining the value of treatments than currently. • Use partial remission rates as well as full remission rates particularly where baseline severity is 'very severe' and/or where the prognosis is poor, for example, because of the complexity or chronicity/treatment resistance of the depressive disorder. Specifically, in relation to Fonagy et al (2015) which the draft guideline currently reports as 'Less severe' in Appendix J5 for baseline severity, when this trial employed the 17-item HAMD on which, as a matter of fact, the mean baseline score of the trial sample is in the 'severe' category. Please correct or alternatively demonstrate the greater reliability and validity of the chosen algorithm over the 17-item HAMD's thresholds	depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by

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				References: Fonagy, P., Rost, F., Carlyle, J., McPherson, S., Thomas, R., Fearon, R. M. P., Goldberg, D. & Taylor, D. (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). World Psychiatry, 14(3), 312-321.	the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogenous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterized. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and

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					other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be

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					analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that

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					were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if two or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered

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					whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe depression was to develop more homogenous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the

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					committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA. Fonagy 2015 is included in the review for further-line treatment.
British Psychoanalytic Association	Full	General	General	We urge NICE to include long-term psychoanalytic psychotherapy (LTPP) in their revised guidelines (July 2017) for the treatment of chronic and severe/relapsing forms of depression. In support of this we draw the attention of NICE to the evidence from the Tavistock Adult Depression Study (TADS), showing the effectiveness of LTPP in these complex mental disorders (Taylor et al 2015).	Thank you for your comment. Fonagy 2015 is the publication of the clinical results from the TADS trial using the Taylor 2015 manual. Fonagy 2015 is included in the review for further-line treatment as the study cites their inclusion criteria as "at least two failed treatment attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a

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				We base our case on: 1 The nature of depression 2 The rigour of the Tavistock Adult Depression Study 3 The need for NICE to improve its long-term recommendations and to inform patients of the results of the Study, so that they can exercise patient choice Reference: Taylor D, Carlyle JA, Fonagy P, McPherson S, Rost F, Thomas R (2015). Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). *World Psychiatry* **14**(3): 312--321.	psychological intervention". Fonagy et al 2015 does not report the proportion of people with comorbid personality disorder. We were not able to determine if it met the inclusion criteria for the review on complex depression and consequently it was excluded from that review. The committee decided not to recommend LTPP for further-line treatment as there was only data from a single study and the effects on both remission and depression symptomatology were not statistically significant. Stakeholders have commented that the guideline only considered endpoint and not follow-up data. However, if you consider 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although effects on depression symptomatology are statistically significant at this time point. Even with more consistent effects, the committee would be unlikely to make a recommendation on the basis of a single study.
British Psychoanalytic Association	Full	General	General	**1 The nature of depression** NICE estimate that depression will become the second most common cause of loss of	Thank you for your comment and providing details on the current provision of long term psychoanalytic psychotherapy. Fonagy 2015

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				disability adjusted years in the world by 2020. In addition to the suffering and the direct economic cost of depression to patients, their families and communities, there is an indirect economic cost to society, as those suffering from mental disorders such as depression are known to make more use of health care services. The increasing prevalence of depression therefore leads to an increase in health care costs. The Tavistock Adult Depression Study research team note that, worldwide, 'depressive disorders have consistently been shown to be the largest contributor to the burden of human disease' and that this statistic 'is connected with the fact that depression tends to pursue chronic or relapsing courses' (Taylor et al. 2012 p2). The condition is often complex and mixed with other psychological and/or social problems, and patient response to treatment may be only partial. As BPA psychoanalysts, psychotherapists, and supervisors of NHS psychotherapists, we have witnessed the suffering caused by depression, in varying degrees of severity, often over many years. We are aware of the painful experiences that go with relapse,	is the publication of the clinical results from the TADS trial using the Taylor 2015 manual. Fonagy 2015 is included in the review for further-line treatment.

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				following periods of remission, and of the possibility that patients may become suicidal or be at risk of self-harm. We have also observed the changes resulting from psychoanalytic treatment, as a consequence of which patients become able to tolerate emotional pain in new ways, to lead less restricted lives, and to act less destructively towards themselves and those who care for them. Until quite recently, long-term psychoanalytic psychotherapy for depression has not been subjected to satisfactory Randomised Controlled Trial (RCT), evidence-based studies. As a consequence of this under-investigation, there have been critical reductions in funding for NHS departments offering psychoanalytic psychotherapy. It is very important that the Tavistock Adult Depression Study has addressed this issue, with statistically significant results demonstrating the effectiveness of Long Term Psychoanalytic Psychotherapy. In particular, the study draws attention to positive effects over the long term (the 'sleeper' effect) and to the ability of patients to make deep-seated changes to their lives in the course of and following LTPP, including their capacity for relationships and productive work.	

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				However, what little remains of the current provision of long-term psychoanalytic psychotherapy from out-patient psychotherapy departments within the NHS is in danger of being cut further. Thus, while it is positive that Dynamic Interpersonal Therapy (DIT) as a therapy for mood disorders has been rolled out nationally within IAPT services as the brief psychodynamic model for the treatment of milder forms of depression, the provision of longer-term, in-depth psychoanalytic psychotherapy has become scarce to the point of non-existence within the public sector, despite evidence of enduring positive outcomes in both symptom reduction and personality change. Reference: Taylor D, Carlyle JA, Fonagy P, McPherson S, Rost F, Thomas R (2012). Tavistock Adult Depression Study (TADS): a randomised controlled trial of psychoanalytic psychotherapy for treatment-resistant /treatment–refractory forms of depression. *BMC Psychiatry* **12:** 60.	
Northumberland Tyne and Wear NHS Foundation Trust	Full Full Full	General	General	These guidelines are a very substantial revision of CG90 published in 2009. In particular there has been a very substantial increase in reference to psycho-social interventions. This is to be welcomed. In all	Thank you for your comment and support for our recommendations on psychosocial interventions. The IAPT programme has been central to

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				13 different interventions are described (CBT (individual and group), BA, IPT, STPT, BCT, MBCT, CBASP, self-help with support, physical activity programmes and rehabilitation programmes). The concern with such a broad range of therapies included in the recommendations for routine care is a) the lack of awareness of the range of treatments and the difference between them (e.g. between BA and physical activity programmes, CBASP vs CBT and MBCT); b) the lack of availability of such a range across the country and c) the degree of fidelity to each of the specific model 'in the field'. The emphasis and detail around psychosocial interventions in the guideline is in stark contrast to the reduction in focus on pharmacotherapy in the draft guideline compared with CG90. The concern is that many of the generic statements and those specifically related to medication have been drafted by experts who do not have experience of prescribing. For example there is an interesting choice of words in the footnote on page 25 regarding combining an antipsychotic with an antidepressant: "The prescriber should follow relevant professional guidance…." We are unclear what "professional guidance" the committee are referring to. Similarly, there is a general recommendation in section 1.4.5 for all	the implementation of NICE recommendations on treatment of depression. This programme is currently undergoing further expansion which should also enhance availability of interventions. In recognition of the current variation in the use of specific psychological interventions we have made recommendations about how they should be structured. The footnote you cite is standard text used in NICE guidelines when a recommendation is made for an off license use of an intervention. The wording was not constructed by the committee. The committee included a number of people with significant expertise and experience of prescribing medication. We have clarified that the use of sessional outcome measures should be considered as they do not currently apply to all interventions. In light of feedback from stakeholders the recommendation about medication management has been deleted as the committee agreed that it was no longer a widely used treatment option and so inclusion of the recommendation could lead to confusion.

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				interventions to use "sessional outcome measures". We are unclear what this means in relation to the prescription of medication. Recommendation 1.4.22 also appears to have been written by somebody who does not prescribe medication. It states "Do not routinely provide medication management on its own as an intervention for people with depression." 'Medication management' is defined on page 34 as "giving a person advice on how to keep to a regime for the use of medication (for example, how to take it, when to take it and how often). The focus in such programmes is only on the management of medication and not on other aspects of depression." With such a definition, we are in agreement with recommendation 1.4.22. However, this definition of 'medication management' bears little resemblance to what actually happens in the clinic in practice. When considering the pharmacotherapy recommendations in isolation, for example in the situation where a patient refuses psychological interventions, or such interventions are not available within a time scale that is clinically appropriate, there is concern regarding a) the limited extend of the recommendations; b) the nature of the recommendations in particular how different these are in relation to the previous NICE	In light of your comment we have made a number of changes to our recommendations for medication. In particular we have included further detail on the monitoring of lithium and antipsychotics, the need to be aware of potential interactions between antidepressant medications and the relative position of medication compared to psychological interventions. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				guidelines (CG90), other respected UK guidance (e.g. British Association for Psychopharmacology – Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525) and current clinical practice with it being unclear what new evidence underpins such a radical departure from previous guidelines; c) the potential impact of the recommendations on service provision. This last point is a particular concern given how hard pressed specialist mental health services currently are. Following the draft guideline, if a patient chooses medication and are prescribed an SSRI at a standard starting dose and they don't respond over 3-4 weeks, and then they don't respond to a dose increase, switch or addition of a second medication over a further 3-4 weeks, then recommendation 1.9.8 states that the clinician should "consider consulting with, or referring the person to, a specialist service. In theory this means that within just 6 weeks of presenting to their GP and failing to respond to just one antidepressant (with dose optimisation) could end up in specialist care. While there is concern about patients being treated for far too long in primary care before referral to specialist services, given the evidence that duration of untreated depression is associated with poorer outcomes (De Diego-Adelino et al. 2010 J	

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				Affect Disorders 120:221 – 225), our concern is that the guidelines prompts referral too early and potentially un-necessarily in too many situations. Recommendation 1.14.4 recommends referring people to specialist services if the person has more severe depression and "….complicating problems, for example unemployment, poor housing or financial problems". This will account for a very significant proportion of such patients. Given how common depression is, lowering the threshold for referral to specialist care even just slightly runs the risk of services becoming swamped. As such, we believe that the guidelines as drafted potentially will lead to vast increases in costs to the NHS and potential destabilisation of services.	
Northumberland Tyne and Wear NHS Foundation Trust	Full	General	General	Seems to put a lot of emphasis on CBT, psychology – not sure where the capacity will come from More advice given around information to patients – good but shame pharmacy (hospital and community) input cannot be mentioned Now states SSRIs or Mirtazepine for treatment for less severe depression if patients refuse CBT - ?cost impact and will this translate to pts where the service cannot be offered. I worry that basically everyone will	Thank you for your comment. The guideline emphasises a range of interventions including psychological, pharmacological and service level interventions (for example collaborative care). A significant provision of psychosocial interventions take place in the IAPT programme and as you will be aware this programme is currently undergoing a significant expansion with another 4000 therapists to be trained between 2016 and 2021. We envisage that the recommendations made about providing information (section

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				be started on medication because this is the easy thing to do. SSRIs used to be the definite first line – now some choice – we will need some guidance More severe – CBT and drug combo – again – capacity issues Lithium and antipsychotics seem to come in earlier in treatment vs going to SNRI/combo – implications of more lithium monitoring and risk Could the term medicines optimisation be used instead of medicines management to reflect that we want the patient to get the best out of their medicines. The guideline gives no guidance as to how to combine medication – just states to use a different class. No mention of where trazadone, venlafaxine, agomelatine, vortioxetine fits into treatment. No advice as to which antipsychotic to use in psychotic depression. In terms of medication, it doesn't seem that helpful!	1.4) would apply to all people involved in the multidisciplinary care of people with depression, including primary and secondary care and pharmacists. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). We are not clear which part of guideline you

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					are referring to but SSRIs remain the first choice antidepressant for less severe depression. There are a broad range of alternative first line treatments recommended in the guideline including guided self-help and exercise. The IAPT programme is currently undergoing significant expansion. This programme includes treatment of more severe depression. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the two are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to

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					recommendations' section (7.7). Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. In light of feedback from stakeholders the recommendation about medication management has been deleted as the committee agreed that it was no longer a widely used treatment option and so inclusion of the recommendation could lead to confusion. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable. We have now included a specific recommendation about vortioxetine.
University of Essex	Full	General	General	We are concerned that the Draft Revision's decision to separate the analyses of Chronic	Thank you for your comment. A number of stakeholders commented on the utility of the

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				Depression [CD] & Treatment Resistant Depression[TRD] (while also not conducting appropriate sensitivity analyses) will damage both the clinical treatments provided and future research. We suggest: • Restoring the position correctly taken in previous versions of the Guidance namely that the overlap of chronic depression and treatment resistant depression patient populations is so large as to render questionable the separation of TRD from CD as a means of structuring meta-analyses. • Cluster TRD with CD. Operationalise this in an additional meta-analysis and an evidence review (and possibly include other related categories). • Failing the above, undertake appropriate sensitivity analyses to ascertain the robustness of proposed recommendations. These analyses will not require great extra resources. But they will greatly increase the credibility of the Draft Revision's recommendations and the probability that they will be beneficial rather than damaging.	term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same.
		506		Justification: Earlier versions of the	A number of stakeholders argued that TRD

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			5 onwards	Guidance decided not to use the TRD category, citing strong evidence for the existence of a more loosely defined heterogenous group of long-term, difficult to treated depressive conditions, frequently associated with dysthymia and co-morbid common mental disorders, various personality disorders/traits and serious psycho-social disability. This well-evidenced position has been reversed in the Draft Revision - without apparent justification. The unfortunate sense of confusion that is conveyed is compounded by the Draft Revision beginning by reminding the reader of the uncertainty in classifications of depression and emphasising that false categories give rise to confusion. We agree. Left as it stands, as the draft predicts, but regardless of itself proceeds to generate: • Confusion in Clinical Service Provisions: The diagnostic inclusion criteria used in TRD studies are most often narrowly pharmacological (exact dose, duration and response). They are not those used in usual clinical settings where case identification is usually descriptive and involves complex evaluations of psychosocial functioning across several domains. • Confusion in Research: the UK guidance will be out of line with the	and chronic depression were essentially similar. The committee took the view that this is a consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. Jobst 2016 and Ruhe 2012 have not been included in the guideline as they do not meet the study design criteria for the review (not RCTs or systematic review of RCTs).

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				APA (DSM-V) and the European Psychiatric Association (EPA) guidance (2016). Both recommend a common "persistent" depression category with sub-categories for severity and degree of associated psycho-social disability. • Confounds in Treatment Research: The Revision currently gives credence to a false dichotomy. It treats as different, users who in fact are alike in nearly all ascertainable respects. The definition of chronic depression given in the Draft reads: *"Adults with chronic depression, defined by a diagnosis of depression according to DSM, ICD or similar criteria, or depressive symptoms as indicated by baseline depression scores on scales. The definition of chronic depression includes: meeting criteria for full MDD for 2 years; persistent subthreshold symptoms (dysthymia); double depression (an acute episode of MDD superimposed on dysthymia). In the case of mixed populations, if the study reports data for a subgroup with chronic depression, data for this subgroup will be extracted. If the study does not report data separately we will only include studies where*	

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				over 75% of the population have a diagnosis of chronic depression. Studies with mixed populations where less than 75% of the population have chronic depression will be included in other reviews." Many subjects in the trials included in the TRD meta-analysis will meet this definition of CD. Note Ruhe *et al (*2012): "because of their chronic clinical course, approximately 40% of CD patients also fulfil criteria for 'treatment-resistant depression'' (TRD)…… usually defined by the number of non-successful biological treatments". Most CD patients have received multiple courses of AD's. Most TRD patients have multidimensional psychosocial disabilities; the only difference is that TRD trials tend not to report such data. • Chronic depression/TRD conditions are persisting. Any self-respecting RCT or meta-analysis should include the comparison of long term follow-up outcomes, not only the endpoints of short-term treatments. Jobst A et al. (2016) European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. European	

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				Psychiatry, 33, 18 – 36. Ruhe HG, van Rooijen G, Spijker J, Peeters FP, Schene AH. (2012) Staging methods for treatment resistant depression. A systematic review. J Affect Disord, 137, 35–45.	
University of Essex	Full Appendix J5	General P201	General line 4 onwards	There are serious problems with the Draft Revision's method of dividing trial populations by categorising baseline severity simply as more severe or less severe. We are very concerned that it leads to misleading impressions and conclusions/recommendations in which potentially valuable treatment effects are ignored: We suggest: • The Revision identify and use categories and methods of analysis which are more appropriate as ways of determining the value of treatments than currently. • Use partial remission rates as well as full remission rates particularly where baseline severity is 'very severe' and/or where the prognosis is poor, for example, because of the complexity or chronicity/treatment resistance of the depressive disorder. • Specifically, in relation to, Fonagy et	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility,

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				al (2015) (of which the present commentator is an author): the Draft currently classes this as 'Less severe' in J5 for baseline severity. This trial employed the 17 item HAMD on which, the mean baseline score of the trial sample is in the 'severe' category. Please correct or alternatively demonstrate the greater reliability and validity of Draft Revision's algorithm over the 17-item HAMD's thresholds. **Justifications:** The Draft Revision uses a single reductive proxy estimate of severity, which depends on the unevidenced assumption that a valid, reliable equivalence algorithm combining different depression rating scales is established. Most of the component measures have their own range of severity categories, validated in the literature. The Draft Revision simply seems to have ignored these. The method developed for the Draft Revision does not seem to reflect their validated categories and therefore its reliability framing for the analyses of treatments for new episode depression is questionable. Furthermore, the Draft is inconsistent even in its use of this categorisation. On this insecure basis: • Trials are then categorised in the Draft	especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs

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				Revision by using mean patient scores rather than ranges of individual ones. As a result, trials can be assigned to "less severe" by being, for example, ≤ 1 point below the chosen threshold mean, while another is assigned to "more severe" merely by being ≥ 1 point above it. Several trials have essentially identical patient populations, with large overlaps of the baseline scores of individual patients, yet are subjected to different unequal standards of comparison. Furthermore, individual patients' symptom scores fluctuate greatly over time, yet the Draft Revision neglects follow-up and follow-along data. The single baseline severity score employed does not have a good correlation with the other important areas of disability that exist in depression. Yet after duly acknowledging their importance in preambles, the Draft Revision proceeds effectively to disregard measures of social functioning and quality of life as part of a necessary basis for recommendations. • The Draft Revision does not always use its own measure of baseline severity consistently: in the "Further-	which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the

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				line treatment" section it adopts instead another also dubious distinction, for example, that it draws between TRD and chronic depression. • For patient populations in whom baseline severity is 'very severe', the Revision needs to take more serious account of the implications of the evidence of the extreme difficulty for some users of achieving a target of 'full remission' (e.g. The STAR-D study). In the interests of these patients, it is essential that the Revision takes *partial remission rates* into account not just full ones. • Specifically, Fonagy et al (2015) is currently recorded in J5 as 'Less severe' for baseline severity. This trial used the 17 item HAMD. According to the latter's categories, the mean baseline score actually comes in the 'severe' band. We ask the GDG first to acknowledge this discrepancy and second to demonstrate exactly how the Revision's methodology is more valid and reliable than that of the source measure, or failing this to correct this misleading classification of the severity of this Study's patient population.	overall severity of depression. It is not clear how partial remission rates could be used as an outcome for complexity or chronicity. We have used remission, response and symptom severity at end point. This latter outcome would take into account the impact of the intervention including those who had not remitted and was also a more commonly reported measure than partial remission, the definition of which may vary across studies. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the two population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom

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				• Of course, baseline severity must be considered when judging trial outcomes. However, this can be achieved without resorting to crude dichotomising cut-offs. In this context, please note that given the wide variation in outcomes and in baseline severity, the SMD alone, as listed in J5, is inadequate from several angles, including statistically. A method for determining Reliable and Clinically Significant Change (Jacobsen & Truaux, 1991) offers a better assessment of how changes on different measures considering baseline severity, might be interpreted. For example, IAPT data records an overall 'recovery' rate of 46.3% (HSCIC, 2016). Whereas, analysis of 'reliable improvement' (which considers baseline and end-point severity, rather than only whether the case met 'clinical caseness' at either point) indicates a figure of 62.2%. Using 'reliable improvement' in the trials included in the guideline meta-analyses would offer a fuller picture; particularly important when trials have studied the treatment of markedly severe populations for whom currently there	severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine

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				are few moderately well-evidenced treatments available. Failing to report both partial remission or the reliable improvement rates assessed in such trials ignores the potential of the benefits that have been found for more severe and complex populations than studied generally. Again, Fonagy et al (2015) is an important case in point. Health and Social Care Information Centre (2016) Psychological Therapies: Annual Report on the use of IAPT services, England, 2015-16. Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology,* 59, 12-19. Trivedi, M.H; Rush, AJ; Wisniewski, SR, et al (2006) Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. American Journal of Psychiatry 163, 28–40.	which scale would be used to determine severity if two or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. The committee took into account not only the cut-offs suggested by developers but also data on the validity of the suggested cut-offs. For example, Fournier et al, 2010 JAMA. 6;303(1):47-53; which in a patient level meta-analysis identified 23 on the Hamilton DRS as the point at which the drugs were clinically significantly better than placebo. The committee took the view that such data provided better validation of the cut-offs developed by scale developers which were often not based on empirical data but on the expert opinion of scale developers. Another example which the committee took into account in developing their own cut offs is the PHQ-9 which classifies mild depression as a score between 5 and 9 when the PHQ-9 cut off for caseness in is a score of 10 or more. Unfortunately, the committee were not able

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					to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe

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					depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA. A number of stakeholders commented on the

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					utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD

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					and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. Given the available data it was not possible to calculate Reliable and Clinically Significant Change. This would have required access to the original trial data. Also as we mention above the studies would need to use the same definition of partial remission. Health and Social Care Information Centre 2016 and Jacobson 1991 cannot be included in the review as they do not meet the study

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					design criteria (not an RCT or systematic review of RCTs). Trivedi 2006 could not be included as data were only reported for the group receiving citalopram.
University of Essex	Full	General	General	We are troubled by the Draft Revision's failure to give proper attention to long-term follow-ups/observation periods and their outcomes rather than exclusively treatment endpoint. This omission is particularly difficult to understand when dealing with treatments for chronic/TRD/long lasting/ persisting depressions. We suggest: • When it is available, longer term follow-up data should be considered when making treatment recommendations. • When the Study has not collected, or has only a very short follow-up, recommendations should be downgraded. • Particularly in sections dealing with treatments of chronic/TRD/long lasting/ persisting depressions, upgrade (in GRADE system) any RCT with long post end-of-treatment follow-ups or periods of observation and that have analysed and reported this data. **Justifications:**	Thank you for your comment. Fonagy 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') is included in the review for further-line treatment. We did not consider follow-up for further-line treatment as this data was not widely available across different intervention types and thus did not enable meaningful comparison. We did, however, include longer-term follow-up data in the relapse prevention review so we do have evidence in the guideline pertaining to longer-term effects of maintenance treatment. However, Fonagy 2015 does not meet the inclusion criteria for that review. It is also worth noting that if you do consider the 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although as you point out the effects on depression symptomatology are statistically significant at this time point.

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				• Despite the 8.223 *Review questions* section in the Draft Guidance stating the high likelihood of relapse/deterioration in patients with depressions described under the heading of TRD, this - and indeed all other parts of the guidance evidence reviews/analyses – effectively ignore the necessity for long-term follow-up measures in the trials of depression treatment included; in fact, most have follow-ups of ≤ 8 weeks. The reviews of interventions in the draft guideline have taken the endpoint as the end of treatment in all cases. However, in those few trials with follow-ups and observation periods sufficiently long to offer data about the longer-term durability of end of treatment effects, the Draft gives them scant attention. Again, a prime example is Fonagy et al (2015): The Draft Revision focuses on treatment end-point; it omits the important data yielded by that study's exceptional 182-week observation period, which showed a substantial effect of considerable potential importance to sufferers (full remission Numbers Needed to Treat (NNT)=9.6; partial remission NNT = 3.9).	In GRADE RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. However, we agree that it is important that long-term follow up data are collected in future research to enable comparison of this outcome across different interventions. We have therefore amended our research recommendations to specify that these data need to be collected. Thank you for your drawing our attention to these references. Keller 2000 and Schramm 2011 are included in the chronic depression review. Kocsis 2007 is incuded in the relapse prevention review. Fonagy 2015 is included in the further-line treatment review. The other studies do not meet the inclusion

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				• Note that persistent depression is a long-term condition and NICE does not treat any other long-term condition in this inadequate way with regards to endpoints. Diabetes (type 2 adults) for example, includes examination of outcomes ranging from 2 years up to 10 and over as would be expected. The epilepsy guideline and arthritis guideline examined evidence including 1 and 2 years follow up data and in some cases longer. To treat depression, particularly any persistent form of depression, as a long-term condition on a par with long term physical conditions, follow-up data must be taken into account. • Calls for RCTs of interventions for depression to include longer term follow-up have been made repeatedly. Their importance in chronic/ resistant/persisting forms of depression is great (see for example McPherson et al, 2005; Goodyer et al, 2008; Goodyer et al, 2011; Goodyer et al, 2017). According to criteria adopted by NICE as well as the APA and EPA chronic forms of depression must last at least for 2 years. Various samples report mean duration of	criteria for the reviews in this guideline for the following reasons: • Goodyer 2008: Adolescent rather than adult sample • Goodyer 2011: Protocol. (We will forward this information to the NICE surveillance team for consideration.) • Hepgul 2016, Westen 2004: Do not meet the study design inclusion criteria (not an RCT or systematic review of RCTs) • McPherson 2005: Systematic review searched for relevant references but no additional studies that met inclusion criteria were identified. In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to

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				illness as 7.8 years (Keller et al (2000)); Kocsis et al (2007) 17.7 years; Schramm et al (2011) 21.2 years; Fonagy et al (2015) 24.4 years. Hepgul et al (2016) noted that 38% of IAPT attenders had attended IAPT previously, pointing to a high relapse rate. Given the actual mean duration of illness as opposed to the minimum to meet the criterion, there is an even stronger case for looking at data from follow-up periods in chronic forms of depression (including TRD). Westen et al (2004) argue that since many patients who respond initially to treatments will relapse and/or present to other services subsequently. Long term follow up data is therefore critical in any truly evidence-based evaluation of the therapeutic effects of treatments for depression. • An RCT should be considered stronger for including a significant follow-up period and reporting data analysis of those follow-up points (which should be at least 12 months and ideally 24 months or more to reflect the chronicity of the condition). Any treatment which shows significant impact at the end of treatment but for	publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. Consequently Goodyer 2017 cannot be included in the guideline as it was published afer the search cut-off date.

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				which nothing is known about in terms of follow-up is arguably a weak study, particularly in relation to chronic forms of depression. All treatments deemed to be effective and recommended for depression ought to have demonstrated an impact beyond the end of treatment. If the effects of the treatment wear off as soon as (or soon after) the treatment finishes (or the long-term effects are unknown) then the treatment can at best be considered a reasonable sticking plaster. Treatments for physical illnesses that stopped working immediately after the end of treatment would not typically be recommended. • Any RCT that has included significant follow-up periods after the end of treatment and have analysed and reported this data, should be upgraded for quality and the data must be included in the reviews of effectiveness and considered when making research recommendations. The Draft's GRADE evaluations of trial quality currently disregard the importance of length of follow-up/ observation period in rating the value of the effect reported at treatment	

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				end-point. RCTs of persisting/chronic/TRD depressions should have follow-ups of at least 12 months and ideally 24 months, and should report data for these follow-up points. They should be rated higher than trials with follow-ups of a few weeks, other things being equal. Goodyer IM, Reynolds S, Barrett B, Byford S, Dubicka B, Hill J, Holland F, Kelvin R, Midgley N, Roberts C, Senior R, Target M, Widmer B, Wilkinson P, Fonagy P. Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial. *Lancet Psychiatry.* 2017;4(2):109-119. Goodyer IM, Tsancheva S, Byford S, Dubicka B, Hill J, Kelvin R, Reynolds S, Roberts C, Senior R, Suckling J, Wilkinson P, Target M, Fonagy P. Improving Mood with Psychoanalytic and Cognitive Therapies (IMPACT): A pragmatic effectiveness superiority trial to investigate whether specialised psychological treatment reduces the risk for relapse in adolescents with	

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				moderate to severe unipolar depression: study protocol for a randomised controlled trial. *Trials.* 2011;12(1):175. Goodyer IM, Dubicka B, Wilkinson P, Kelvin R, Roberts C, Byford S, Breen S, Ford C, Barrett B, Leech A, Rothwell J, White L, Harrington R. A randomised controlled trial of cognitive behaviour therapy in adolescents with major depression treated by selective serotonin reuptake inhibitors. The ADAPT trial. *Health Technol Assess.* 2008;12(14): iii-iv, ix-60. Hepgul N, King S, Amarasinghe M, et al (2016). Clinical characteristics of patients assessed within an Improving Access to Psychological Therapies (IAPT) service: results from a naturalistic cohort study (Predicting Outcome Following Psychological Therapy; PROMPT). BMC psychiatry, 16(1), p52. McPherson S, Cairns P, Carlyle J, Shapiro D, Richardson P & Taylor D (2005) The effectiveness of psychological treatments for refractory depression: A systematic review, Acta Psychiatrica Scandinavica, 111, 331-340. Westen, D., Novotny, C. M., & Thompson-	

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				Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. Psychological Bulletin, 130, 631– 663.;	
University of Essex	Full	General	General	We are concerned that the Draft Revision has considered outcomes based on symptom measures while neglecting measures of quality of life and psychosocial functioning. Service users regularly report these as being of greater importance to them. We request: • All the meta-analyses consider outcomes of measures of functioning where available as well as of symptoms • These findings should influence the recommendations made Justification: A re-analysis of the 2004 NICE review examining outcomes of measures of functioning showed a different order of comparative efficacy amongst interventions and would thus change the recommendations made (McPherson, Evans & Richardson, 2009). RCTs of treatments for depression need to include alternative outcome measures (McPherson et al, 2005). Trials including measures of psychosocial	Thank you for your comment. We agree that psychosocial functioning and quality of life measures are important. However these kinds of measures are rarely reported and they are often reported inconsistently across studies. For these reason these measures were not prioritised for inclusion in the review protocols for this guideline. GRADE assessment is conducted consistently across all studies included in the pairwise analyses. In GRADE, RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of outcomes other than clinical efficacy is not a valid reason for upgrading within GRADE and these outcome measures are outside the protocol for this review

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				functioning and quality of life should be upgraded. Please note again that Fonagy et al (2015) reporting on GAF, QLESQ and CORE wellbeing found clinically significant group differences at 2-year follow-up on these measures. McPherson S, Evans C & Richardson P (2009) The NICE Depression Guidelines and the recovery model: is there an evidence base for IAPT? Journal of Mental Health, 18(5). McPherson S, Cairns P, Carlyle J, Shapiro D, Richardson P & Taylor D (2005) The effectiveness of psychological treatments for refractory depression: a systematic review, Acta Psychiatrica Scandinavica, 111, 331-340.	When making recommendations, the committee interpret the evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. As you will be aware there is much more limited data on measures of social and occupational function. The limited nature of this data will inevitably mean any comparison using this data would have to be treated with considerable caution as it could be potentially misleading about the effectiveness of interventions, given that it does not exist in many of the trials we have examined. McPherson 2009 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs). McPherson 2005 has been searched for relevant references. However, no additional

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					studies that meet inclusion criteria were identified.
University of Essex	Full	General P68	General	We find it deeply regrettable that the service user experience evidence was not was not updated for the Draft Revision. We strongly suggest: • The Revision should update this section and improve its quality taking the comments below into account. It should then fully integrate the more recent findings of this type of research into its treatment recommendations. More recent literature extends client experience data to under-represented groups. It takes account of changes in socio-economic and cultural circumstances. This should be incorporated by means of a meta-ethnographic synthesis Justification: • A great deal of research on experiences of depression of patients and carers has been published since 2004 and this literature has been wrongly ignored by the GDG. Some of this literature is listed below • There were serious limitations in the	Thank you for your comment. The proposal not to include the experience of care section in this update was consulted on with registered stakeholders at the time of consultation on the draft scope. As this section was not included in the update we are not able to make the changes that you suggest or include the references that you have highlighted.

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				patient experience data collected for the previous guidelines. These should have been corrected. Thus, no demographic details are given for the 38 individuals whose accounts were taken from Healthtalkonline. It is unclear which elements of the population were represented. The extent to which the data represents under-represented populations such as BME, men, older adults, non-heterosexual clients is unclear. More recent literature extends client experience data to these under-represented groups. It should be incorporated in a meta-ethnographic synthesis (which the University of Essex Health and Care Research Service could be commissioned to produce). • P68 summarises the findings of previous qualitative analysis: "*Although the 6 questions were aimed at people with any form of depression, all of the personal accounts received were from people who have/have had severe and chronic depression, spanning many*	

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		P97 P100		*years. The themes that are most frequently expressed in the testimonies include trauma or conflict in childhood as a perceived cause of depression; the need for long-term psychotherapy for people with severe and chronic depression; the need to take personal responsibility for and understand the illness to improve outcomes; issues around diversity; paid and unpaid employment as an important part of the recovery process; the negative impact on daily functioning; concerns regarding stigma and discrimination in the workplace; and the relationship between people with depression and professionals."* These important points are reiterated in other qualitative studies in which service users are consulted. Yet these key themes are not taken account of in the design of the guideline or its recommendations. No recommendations are made relating to reducing stigma. • The experience of depression is intertwined with the social and	

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				economic context in which people live. It relates to levels of community cohesion, economic circumstances, social support, loneliness etc. The social and economic context in the UK has changed both since 2004 and 2009. There is growing evidence of the impact of austerity on depression and many clients with depression have been significantly affected by reductions in their benefits, loss of work or changes to employment conditions resulting from the economic downturn and political choices (see for example The Psychological Impact of Austerity: A Briefing Paper http://www.psychchange.org/uploads/9/7/9/7/97971280/paa-briefing-paper.pdf). Experiences of depression are therefore likely to have been affected by this and it should not be assumed that experience of depression is a static biological phenomenon. • There have also been changes which impact on the extent to which stigma features in client narratives.	

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				Campaigns such a Time to Change may or may not have had an impact on stigma. The Draft implicitly assumes that this has remained static. There have been significant policy changes which could have impacted on experiences of carers. The Carers Act 2014 has come into law and there have also been many changes made to benefits available to carers. These major changes to carers' rights as well as their benefits entitlements and social context mean that it should not be assumed carers' experience would be much the same as in 2004 or 2009. • P97 Notes experiences of psychological therapy: *"There was a strong feeling within the service user and carer topic group that the excerpt from Howe (1995) in the section above highlights the reasons why many people opt for private therapy; that is, that psychological treatment offered by the NHS in the form of CBT does not go far enough in addressing the trauma experienced in childhood. The study by Ridge and*	

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				Ziebland (2006) confirms the opinions of the topic group and the testimony from the personal accounts that people with 'deep and complex problems felt the need for longer term therapy'. Those that have had long-term psychodynamic therapy report that it has been helpful in their under-standing of themselves and their depression and that until they have worked through and repaired the damage experienced in childhood, depression will be a major factor in the person's life. The service user and carer topic group do acknowledge, however, that as there has been little research into the efficacy of long-term psychodynamic therapy, it cannot be recommended as a course of treatment in this guideline" • This last comment was true when it was made many years ago. Since then studies have been carried out on psychodynamic and psychoanalytic psychotherapies for long term depression (Fonagy et al, 2015; Town et al, 2017). It is important to connect	

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				the neglect of this data to how the Draft is constructed and its recommendations. If this perspective from service users had been really considered in the current Draft, its recommendations would have reflected this. They do not. • None of the recommendations (p100) deriving from service user and carer experiences relate to interventions. **Suggested Literature** McPherson S, Rost F, Sidhu S, Dennis M (under review) Non-strategic Ignorance: Making Sense of a Randomised Controlled Trial of Psychodynamic Psychotherapy. • Carers experiences: Priestly J & McPherson S (2016) Experiences of Adults Providing Care to a Partner or Relative with Depression: A Meta-Ethnographic Synthesis. Journal of Affective Disorders DOI: http://dx.doi.org/10.1016/j.jad.2015.12.011 which concludes the needs for: "couples and systemic therapy at initial stages of management addressing stigma to help those overcoming challenges of caring for their partner or relative and self-compassionate	

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				approaches for caregivers who may need support to look after themselves, avoid feelings of guilt and move forward towards acceptance" • Service users: Smith JA, Rhodes JE. (2014) Being depleted and being shaken: An interpretative phenomenological analysis of the experiential features of a first episode of depression. Psychol Psychother. doi: 10.1111/papt.12034 van Grieken RA, Beune EJ, Kirkenier AC, Koeter MW, van Zwieten MC, Schene AH. (2014) Patients' perspectives on how treatment can impede their recovery from depression. J Affect Disord. 2014 Oct; 167:153-9. doi: 10.1016/j.jad.2014.05.065 Alderson SL, Foy R, Glidewell L, House AO. (2014) Patients understanding of depression associated with chronic physical illness: a qualitative study BMC Fam Pract. 20; 15:37. doi: 10.1186/1471-2296-15-37. DeJean D, Giacomini M, Vanstone M, Brundisini F. (2013) Patient experiences of depression and anxiety with chronic disease: a systematic review and qualitative meta-synthesis. Ont Health Technol Assess Ser. 1;13(16):1-33. Oliffe JL, Rasmussen B, Bottorff JL, Kelly MT, Galdas PM, Phinney A, Ogrodniczuk JS	

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				Dekker RL, Peden AR, Lennie TA, Schooler MP, Moser DK. (2009) Living with depressive symptoms: patients with heart failure. Am J Crit Care.;18(4):310-8. doi: 10.4037/ajcc2009672. Lovasz N, Clarke J. (2007) Life beyond depression: the experience of gays and lesbians who self-identify as depressed. J LGBT Health Res.;3(4):53-73. Clarke DM, Cook KE, Coleman KJ, Smith GC. (2006) A qualitative examination of the experience of 'depression' in hospitalized medically ill patients. Psychopathology.;39(6):303-12 Brownhill S, Wilhelm K, Barclay L, Schmied V. (2005) 'Big build': hidden depression in men. Aust N Z J Psychiatry.;39(10):921-31. Danielsson U, Johansson EE. (2005) Beyond weeping and crying: a gender analysis of expressions of depression. Scand J Prim Health Care.;23(3):171-7.	
University of Essex	Full	General	General	This document is of such inconsistent/poor quality in methodology and content, any revisions of the draft guidelines should go out for further consultation	Thank you for your comment. Section 10.3 of Developing NICE guidelines: the manual clarifies when a second consultation may be needed. This states that "In exceptional

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					circumstances, NICE may consider the need for a further 4-week stakeholder consultation after the first consultation. This additional consultation may be needed if either: • information or data that would significantly alter the guideline were omitted from the first draft, or • evidence was misinterpreted in the first draft and the amended interpretation significantly alters the draft recommendations. NICE staff with responsibility for guideline quality assurance make the final decision on whether to hold a second consultation." NICE judged that these criteria were not met, therefore no second consultation was conducted.
Society for Psychotherapy Research (SPR) UK Chapter	Full	general	general	**The distinction between treatment-resistant depression (TRD), chronic depression and complex depression** The distinction between treatment-resistant depression and chronic depression adopted in the draft guideline is highly problematic and out of line with other clinical and research guidance, including the American Psychiatric Association (2013) and the European Psychiatric Association guidance (Jobst, 2016). The overlap between both are too large to ignore and there is no evidence	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had

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				that warrants such a distinction. Both, the American Psychiatric Association and the European Psychiatric Association recommend a common "persistent" depression category with sub-categories for severity and degree of associated psycho-social disability. We are concerned that no appropriate sensitivity analyses were carried out and that the guidance will cause confounds in treatment research, as many participants in the trials included in the treatment-resistant depression meta-analysis will meet the guideline's definition of chronic depression and/or complex depression. We recommend to restore the position taken in the previous (2009) version of the NICE guideline and to re-run the meta-analysis accordingly. **References:** American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: American Psychiatric Association Jobst, A., Brakemeier, E-L., Buchheim, A., Caspar, E., Cuijpers P. et al. (2016) European Psychiatric Association Guidance on psychotherapy in chronic depression	somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty

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				across Europe. European Psychiatry, 33, 18 – 36.	about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. APA 2013 and Jobst 2016 have not been included in the guideline as they do not meet thestudy design criteria for the review (not RCTs or systematic review of RCTs).
Society for Psychotherapy Research (SPR) UK Chapter	Full	General	General	**Application of the GRADE system** Although we recognise that the draft guideline adopts an approach that is being utilized more frequently, we are nonetheless concerned about the GRADE system upon which the grading of the quality of evidence as well as the statistical adjustments and penalisation of studies is based. Applying it without modifications reinforces the false belief that the medical paradigm can easily be applied to psychological treatments. A pertinent example is the downgrading of studies that did not follow a double-blind approach, marking these as *high risk.* We recommend adapting the GRADE system in order to reflect the complex endeavour of	Thank you for your comment. GRADE is used in line with the NICE guidelines manual. GRADE assessment is conducted consistently across all studies included in the pairwise analyses. In GRADE, RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. The availability of wider outcomes is also not a valid reason to upgrade within

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	Full	55	8 - 10	comparing medical and psychological treatments. More specifically, the revision of the draft guideline should include the following relevant quality criteria: - The inclusion of end of treatment long-term follow-up data. This would be in line with the draft guideline's emphasis stating the high likelihood of relapse/deterioration in patients with depression in several parts of the document. It is imperative for research to demonstrate that effects are long-lasting and any randomised controlled trails that aim to do so should be considered stronger and thus be up-graded. The call for the inclusion of long-term follow-ups extending the currently adopted time period of 3 – 6 months to several years after treatment termination has been stressed by many researchers and trial methodologists (e.g. Rawlins, 2008) given the episodic nature of depression. - Adequate sample sizes providing sufficient power to detect true effects. Most psychotherapy studies are not powered enough to detect a true difference (Leichsenring et al., 2013)	GRADE and these outcomes are not in the protocol of the reviews because they are inconsistently reported across studies and interventions and as such would not allow for a meaningful comparison. Although it is more difficult to blind participants and intervention administrators in psychological studies, it is possible, for instance by isolating the active ingredient and using an attention-placebo (that is similar in other aspects with the exception of the active ingredient). Blinding of outcome assessors is also taken into account in the GRADE system. The non-blinding of participants and intervention administrators presents a risk of bias, although we accept that this is more of a problem for psychological than pharmacological trials, it does not negate the fact that participant and intervention administrator knowledge of the treatment being received/delivered is likely to introduce some degree of performance bias due to an individual's inherent beliefs about that intervention. The imprecision judgement in GRADE does not only consider statistical significance but is based on the width of the confidence interval (i.e. whether the 95% confidence interval crosses the line of no effect and one

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				and relying on statistical significance of effects will create a paradox whereby small effects detected in well-powered studies is used to justify a recommendation, whereas a much larger effect undetected in under-powered studies will be disregarded (Wampold et al., 2016). - Utilization of a range of outcome measures, in particular the assessment of functioning in addition to targeted symptoms. As Dijkers (2014) has stressed the quality for each outcome may differ between outcomes within a single study and across a body of evidence. Thus, we recommend the guideline to adapt the methodology not to penalise but to include the revision of a range of outcome measures (Wampold et al., 2016). - Adequate statistical and methodological measures taken to control for error rates. The quality of assessment currently adopted does not examine whether studies have controlled for variability across therapist participants (i.e., therapist effects). A review of 71 therapist	or both thresholds for clinical importance). However, sample size for the pooled effect is also taken into account and the rules of thumb for optimal information size are events<300 or N<400. Thus if large effects are observed across a number of small studies then it is likely that the pooling of studies will reduce imprecision and increase the likelihood of statistical significance. It is also important to note that the GRADE system 'quality' rating is not a value judgement on the quality of an individual study but rather an estimate of the extent to which we are confident that an estimate of the effect is correct and is unlikely to change with further research. We are less confident of this if the effect has wide confidence intervals and is based on a small sample of studies/participants. Examination of therapist effects specifically is outside the scope of this guideline. However, within-study variability should be reflected by the precision of the effect estimate and between-study variability through consideration of inconsistency. Further detail about the information that is taken into account to make the GRADE judgements is presented in the review protocols in Appendix F, in the 'review

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				effect studies by Baldwin and Imel (2013) identified that therapist effects account for approximately 5-8% of patient outcomes: approximately 7% in naturalistic studies, and 3% in efficacy studies. Considering patient severity, Saxon and Barkham (2012) studied 10,786 patients seen by 119 therapists and identified that therapist effect sizes increased up to 10% as patient non-risk severity increased. Most patients in this sample presented with a level of depression (77.2%) and anxiety (84.6%). The evidence points to the presence of therapist effects: its robust nature (across research designs) and its increasing contribution to the outcome of more severe patient presentations. We are concerned that the evidence identifying effective treatment does not control for variability between participating therapists within respective studies. We suggest for the inclusion of a) a quality criterion to identify evidence where therapist effects have been controlled for, and b) if possible where therapist effects analyses have not been conducted, and data is accessible, to consider post hoc analysis to control for	strategy' subsection. Thank you for drawing our attention to these references. The following studies did not meet inclusion criteria for the review and hence have not been included in the guideline: • Baldwin 2013 and Saxon 2012: Therapist effects are outside the scope. • Dijkers 2013, Rawlins 2008, Wampold 2016: Do not meet the study design criteria (not an RCT or systematic review of RCTs). • Garfield's handbook of psychotherapy and behavior change: Book • Leichsenring 2015 systematic review was checked for relevant references, however, no additional studies that met the inclusion criteria were identified.

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				therapist effects. Although the GRADE system utilized is adequately referenced, in order to improve the guideline's clarity and for readers to be able to easily follow, we recommend that the five criteria focused on (limitations, inconsistency, indirectness, imprecision and publication bias) are not only listed but also defined in this section. The description provided in Table 5 (p. 58) is insufficient. **References:** Baldwin, S. A., & Imel, Z. E. (2013). Therapist effects: Findings and methods. In M. J. Lambert (Ed.), Bergin and Dijkers M (2013) Introducing GRADE: a systematic approach to rating evidence in systematic reviews and to guideline development. KT Update (Vol. 1, No. 5 - August 2013) [http://www.ktdrr.org/products/update/v1n5/] Garfield's handbook of psychotherapy and behavior change (6th ed.). Hoboken, NJ: Wiley. Leichsenring, F., Luyten, P., Hilsenroth, M.J., Abbass A. et al. (2015). Psychodynamic therapy meets evidence-based medicine: a systematic review using updated criteria. Lancet Psychiatry, 2, 648-660.	

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				Rawlins, M.D. (2008). De testimonio: On the evidence for decisions about the use of therapeutic interventions. The Lancet, 372(9656), 2152–2161. Saxon, D., & Barkham, M. (2012). Patterns of Therapist Variability: Therapist Effects and the Contribution of Patient Severity and Risk. Journal of Consulting and Clinical Psychology, 80, 535-546. Wampold, B. E., C. Fluckiger, A. C. Del Re, N. E. Yulish, N. D. Frost, B. T. Pace, S. B. Goldberg, S. D. Miller, T. P. Baardseth, K. M. Laska and M. J. Hilsenroth (2016). "In pursuit of truth: A critical examination of meta-analyses of cognitive behavior therapy." Psychotherapy Research, 27(1), 4-32.	
Society for Psychotherapy Research (SPR) UK Chapter	Full Full	General 40	General 32 - 37	**The sole focus on depression severity as outcome variable** The focus on depression severity as the only outcome stands in contrast to the draft guideline's emphasis in the introduction of the full draft that a range of outcomes ought to be focused on. We either recommend amending the emphasis in the introduction or advice on the inclusion of other outcome measures, in particular measures of quality of life and psychosocial functioning given that service users regularly stress the importance of such outcomes over symptom change, as indeed	Thank you for your comment. In our reviews of the effectiveness of interventions we considered a range of outcomes. These were remission, response, relapse (for relevant questions), depression symptomatology and discontinuation (for any reason and due to adverse events). Details of the review protocols are provided in Appendix F. For the question on treatment of a new depressive episode, depression symptomatology (SMD) outcomes were prioritised for interpreting the results of the NMA. This was based on the advice of the committee because there was the most data

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				reported in the service user experience chapter of the draft guideline. Not including additional outcome measures stands in contrast to the emphasis of the draft guideline in the introduction, which clearly states: "Where *possible, the key goal of an intervention should be complete relief of symptoms (remission), which is associated with better functioning (…) For this reason the GC examined a range of outcomes (where available), including response, remission, change in symptoms and relapse.*" (p. 40, l.32-37). The inclusion of several outcome measures would be in line with those who have stressed that the disease burden is primarily due to comorbidities and not merely to the additive effects of having more than one disorder (Wampold et al., 2017). Moreover, as the re-analysis of the 2004 NICE review carried out by McPherson, Evans and Richardson (2009) has shown, focusing on functioning as outcome provided a different order of comparative efficacy amongst intervention with the consequence of a different derived treatment recommendation. **References:**	for SMD and the most connected network. This decision is document in the 'evidence to recommendations' section in the full guideline. Therefore we think that the existing text is accurate and have not made further amendments. We agree that psychosocial functioning and quality of life measures are important. However these kinds of measures are rarely reported and they are often reported inconsistently across studies. For these reasons these measures were not prioritised for inclusion in the review protocols for this guideline. However, when making recommendations, the committee interpret the evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. McPherson 2009 and Wampold 2017 have not been included as they do not meet the study design inclusion criterion (not an RCT or systematic review of RCTs).

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				McPherson, S., Evans, C., and Richardson, P. (2009) The NICE Depression Guidelines and the recovery model: is there an evidence base for IAPT?, Journal of Mental Health, 18(5). Wampold, B. E., C. Flueckiger, A. C. Del Re, N. E. Yulish, N. D. Frost, B. T. Pace, S. B. Goldberg, S. D. Miller, T. P. Baardseth, K. M. Laska and M. J. Hilsenroth (2017). "In pursuit of truth: A critical examination of meta-analyses of cognitive behavior therapy." Psychotherapy Research, 27(1), 4-32.	
Society for Psychotherapy Research (SPR) UK Chapter	Full	General	General	**Long-term Follow-up** The introduction of the draft guideline clearly states that "*the aim of intervention is to restore health through the relief of symptoms and restoration of function, and in the longer term, to prevent relapse* "(p.40, l.31-32). The draft guideline, however, does not give adequate attention to long-term follow-up. The choice to omit long-term data points is particularly difficult to comprehend in the sections dealing with treatment-resistant depression and chronic depression. However, it is also important to provide evidence that treatment effects can be sustained for individuals experiencing their first episode of depression, precisely because the relapse rate, as pointed out in the	Thank you for your comment. We did not consider follow-up for further-line treatment as this data was not widely available across different intervention types and thus did not enable meaningful comparison. This has been mentioned in the 'evidence to recommendations' section. We did, however, include longer-term follow-up data in the relapse prevention review so we do have evidence in the guideline pertaining to longer-term effects of maintenance treatment. However we agree that it is important that long-term follow up data are collected in future research to enable comparison of this outcome across different interventions. We have therefore amended our research

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				introduction, is high. We recommend an amendment to the draft guidelines by including longer term follow-up data from studies where it is available when making treatment recommendations, and stressing the importance for future research to include a long-term follow-up extending to several years after treatment termination (e.g. McPherson et al, 2005; Goodyer et al, 2017). It is puzzling that the guideline appears to treat depression differentially to any other long-term condition. Type 2 diabetes in adults, for instance, includes several measurement points of the outcomes ranging from 2 – 10 years. The epilepsy guideline and arthritis guideline examined evidence including 1 and 2 years follow up data. Thus, we recommend treating depression, particularly any persistent form of depression, such as treatment-resistant depression and chronic depression as a long-term condition on a par with long term physical conditions. In case the GC decides against an amendment accommodating our recommendations to analyse and include the findings of long-term effect into the treatment recommendations, we would like ask to add a transparent note in the short and full version of the guideline stressing that treatment	recommendations to specify that these data need to be collected. The McPherson 2005 systematic review has been searched for relevant references but no additional studies that met the inclusion criteria were identified. In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with

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				recommendations are based on end-of-treatment data only, and that the treatments recommended currently do not hold a robust evidence base to support sustained, longer-term effects. **References:** Goodyer, I.M, Reynolds, S., Barrett, B., Byford, S., Dubicka, B., Hill, J., Holland, F., Kelvin, R., Midgley, N., Roberts, C., Senior, R., Target, M., Widmer, B., Wilkinson, P., and Fonagy, P. (2017). Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial. Lancet Psychiatry, 4(2),109-119. McPherson, S., Cairns, P., Carlyle, J., Shapiro, D., Richardson, P. and Taylor, D. (2005) The effectiveness of psychological treatments for refractory depression: A systematic review, Acta Psychiatrica Scandinavica, 111, 331-340.	NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. Goodyer 2017 was published after the search cut-off date of June 2016 and therefore has not been included in the guideline.
Society for Psychotherapy Research (SPR) UK Chapter	Full Chapter 17	General General	General General	**Network Meta-Analysis** The need for an adequate method to address the limitations of meta-analyses has been stressed and the utilisation of network meta-	Thank you for your comments. We do not agree that network meta-analysis (NMA) is characterised by unique risks. Heterogeneity in populations or interventions can be a problem in both pairwise and network meta-

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				analysis has gained popularity (Sutton et al., 2008). An advantage is that it can improve precision of the direct estimates (Bucher et al., 1997) and allows for the exploration of biases that are difficult to assess in standard meta-analyses (Cipriani et al., 2013). Thus, we welcome the decision of using an approach that aims at mitigating known limitations of standard meta-analysis, however, there are serious concerns and unique risks associated with network meta-analysis over and above that of standard meta-analyses that need addressing (Keefe, 2015; del Re et al., 2013; Kibet et al., 2014). We are concerned that these have not been adequately resolved in the approach adopted in the draft guideline, and would thus like to express our apprehension to accept the treatment recommendations resulting from the analyses. In line with the Canadian Agency for Drugs and Technologies in Health (Wells et al., 2009), we would like to stress that findings from indirect or mixed comparisons should only be used to supplement evidence derived from direct comparisons. We are concerned that neither the full guidelines nor Chapter 17 include a section that outlines the various conceptual challenges of network meta-analysis and	analysis and should be considered prior to conducting the meta-analysis, and when interpreting the results. Effects obtained from the NMA are exchangeable across populations if populations are similar enough and there are no underlying effect modifiers that are unequally distributed across populations - the same applies to pairwise meta-analysis. More detailed text reporting on these issues has now been added in section 7.3.1. The risks have been addressed by controlling for a large part of heterogeneity (splitting populations with less and more severe depression; using detailed treatment definitions [including treatment intensity and mode of delivery for psychological interventions] and categorising them using a class random effects model), examining for model fit and checking for inconsistency between direct and indirect evidence. Other potential effect modifiers, such as age and setting (inpatient versus outpatient) were assessed in sub-analyses, using pairwise meta-analysis. Other parameters, such as sex, socio-economic factors and therapist factors, may also contribute to heterogeneity, in particular in such a large and complex dataset, but this would also be a problem had pairwise meta-analysis of the 366 studies included in the systematic review been conducted.

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	Full	210	34 – 48	highlights the approach taken in the guideline to address these. Following a scientific approach would require a judicious summary of the full methodology used, which includes outlining the limitations, thus our recommendation is to include such a section. The main assumption underpinning the validity of network meta-analysis is that there are no important differences between the trials included. In other words, the indirect and mixed comparisons are only valid when the studies included in the synthesis are similar in their distribution of effect modifiers (Ciprinai et al., 2013). These include not only severity at baseline, number of previous episodes and quality of study, which the draft guideline tries to address, but also sample size, age, sex, socio-economic factors, therapist factors, as well as treatment dose and administration of treatment. The network meta-analysis included 351 studies comparing 81 interventions and combinations of interventions, which differed considerably in all these variables, thus violating the transitivity or consistency assumption (Baker & Kramer, 2002). The variable distribution and thus contribution of the different treatments included in the network meta-analysis is highly problematic.	Considering heterogeneity when assessing the hundreds of pairwise, independent comparisons of this dataset would make interpretation of the findings and conclusions as to which interventions are the best options highly problematic. Between-study heterogeneity in the NMA was formally assessed for each network; results of this assessment were taken into account when interpreting the results of the NMA and making recommendations. The full methods and results of the NMA, including examination of model fit, heterogeneity, and inconsistency checks, as well as limitations of the NMA, have been reported in detail in Appendix N1 (Chapter 17 in the consultation draft) with a summary provided in Chapter 7. Detailed results of inconsistency checks and comparison between mixed (NMA) and direct evidence have been provided in Appendix N3 of the final guideline (Appendix W of the consultation guideline). The committee considered all these issues when making recommendations. The Canadian Agency for Drugs and Technologies in Health may recommend that indirect or mixed comparisons only be used to supplement evidence derived from direct comparisons. However, this is a NICE guideline. According to the NICE Guidelines

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				It is evident that some treatments contributed very few studies (e.g. yoga and any AD contributed only two studies), whilst others (e.g. individual CBT contributed 35 and Amitriptyline contributed 43 studies). Thus, findings might not depict a representative range of treatment, thereby biasing an effect estimate compared with those with more studies (Keefe, 2015). As del Re et al. (2003) and Kibet et al. (2014) have stressed the risk of false positives is high in network meta-analysis when the number of comparisons is large, which it is indeed in the analyses carried out. It is not apparent that Type-I error corrections were used (Shadish et al, 2002). One appropriate means for addressing the error rate problem would be to conduct an omnibus test of the null hypothesis that there are no differences among treatment (Wampold et al., 2016). It is unclear whether the guidelines have done so and we recommend stating clearly in the document if that was done and if not, to justify why this issue was not addressed. Only the full guideline (p. 210, l. 34-38) deals with bias adjustment models. A section needs to be included in Chapter 17 as well. However, here it states that sensitivity	Manual [PMG20] "When multiple options are being appraised, a network meta-analysis should be considered." (p.104). The review question on treatment of new episodes included a very large number of interventions. Conducting pairwise meta-analyses would fragment the evidence and would not allow the committee to draw conclusions on the most effective (and cost-effective) interventions among them, as the majority of interventions assessed have not been compared to each other in head-to-head trials. The alternative option would be for the committee to implicitly make indirect comparisons by comparing direct effects of interventions versus a common comparator, which would again raise issues of heterogeneity and transitivity, without any formal, coherent statistical assessment. Therefore, a formal NMA was considered the best means to answer the review question that was in line with NICE recommended methodology. Moreover, conducting an NMA and obtaining the relative effects of all pairs of classes/interventions was the only way to conduct formal economic modelling that includes all relevant treatment options. It is true that there was very limited evidence for some treatments (e.g. yoga), and far more robust evidence for others (e.g.

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				analyses were carried out on selected outcomes, which adjusted for bias associated with small study size effects. It is unclear why it was carried out only on selected outcomes and we recommend the inclusion of a transparent rationale. **References:** Baker, S.G. and Kramer, B.S. (2002). The transitive fallacy for randomized trials: if A bests B and B bests C in separate trials, is A better than C? BMC Medical Research Methodology, 2, 13. Bucher, H.C., Guyatt, G.H., Griffith, L.E., and Walter, S.D. (1997) The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. Journal of Clinical Epidemiology, 50, 683-91. Cipriani, A., Higgins, J., Geddes, J.R., and Salanti, G. (2013). Conceptual and technical challenges in network meta-analysis. Annuals of Internal Medicine, 159, 130-137 Keefe, J. (2015). Heightened risk of false positives in a network meta-analysis of social anxiety. The Lancet, 2, 292-293. del Re, A.C., Spielmans, G.I., Flückiger, C., and Wampold, B.E. (2013). Efficacy of new generation antidepressants: Differences seem illusory. PLoS One, 8, e63509. Kibret, T., Richer, D., and Beyene, J. (2014). Bias in identification of the best treatment in a	individual CBT). This was a limitation of the evidence base and not of the NMA per se. This would also be a problem had a pairwise meta-analysis been conducted. Nevertheless, the NMA enabled use of all available evidence and improved precision by allowing combination of direct and indirect comparisons. Moreover, the NMA enabled the use of a class model, where the effects of individual interventions were pooled into a more robust and precise class effect, while interventions retained their own intervention effect. The uncertainty of the relative effects informed by few or small studies was reflected in the uncertainty (Credible Intervals) around the relative effects. Some interventions that were represented by very few and small studies demonstrated extreme, implausible effects in the primary studies, which were subsequently 'transferred' in the NMA, but these extreme results would also have been obtained if pairwise meta-analysis had been attempted. This is a flaw of the primary studies, not of the NMA per se. Nevertheless, the committee took into account the results of the NMA in the context of the available evidence. Results on classes and interventions tested on a small number of people were treated with great caution and the total number of people randomised to

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				Bayesian network meta-analysis for binary outcome: a simulation study. Clinical Epidemiology, 6, 451–60. Shadish, W.R., Cook, T.D., and Campbell, D.T. (2002). Experimental and quasi-experimental designs for generalized causal inference. Boston: MA: Houghton Mifflin. Sutton, A., Ades, A.E., Cooper, N., Abrams, K. (2008) Use of indirect and mixed treatment comparisons for technology assessment. Pharmacoeconomics, 26, 753-67. Wells, G.A., Sultan, S.A., Chen, L., Khan, M. and Coyle, D. (2009). Indirect Evidence: Indirect Treatment Comparisons in Meta-Analysis. Ottawa: Canadian Agency for Drugs and Technologies in Health.	each class/ intervention across the NMA studies was taken into account when making recommendations. The economic analysis was also updated following consultation and included only classes that had been tested on at least 50 people in every main outcome considered in the economic analysis (i.e. discontinuation, response in completers, remission in completers). All NMA results were assessed for their plausibility, using the committee's expert judgement. Regarding the potential for false positive results, this point is not applicable given that the interpretation of the NMA results and subsequent recommendations did not rely on p-values or statistical significance of effects. An NMA helps identify the optimum decision, in the presence of uncertainty. Multiple comparisons were made using a combined body of evidence. Results were not interpreted solely by looking at the level of statistical significance. Decisions were made taking into account the expected effect size and its uncertainty for each class. A number of other considerations were made in order to make recommendations including cost effectiveness, harms, and qualitative judgements on the robustness and quality of the evidence base, the plausibility of the results, the characteristics of the study

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					populations in the RCTs included in the NMAs, patient characteristics and preferences. The methods and results of the bias adjusted models were fully reported in Appendix N of the consultation guideline draft (Appendix N2 in the final guideline): Clinical evidence – network meta-analysis: bias adjustment methods and results. The full guideline only reported a summary of the bias adjustment models. Justification for outcomes selected for the bias adjustment models is provided in the full guideline, towards the end of section 7.3.6: "SMD of depressive symptom scores was selected for sensitivity analysis as it was the main efficacy outcome considered by the committee. The other 2 outcomes [discontinuation and response in completers] were selected for sensitivity analysis because they were the main NMA outcomes that informed the economic analysis, with the highest anticipated impact on the results."
Society for Psychotherapy Research (SPR) UK Chapter	Full	General	General	**Qualitative evidence for effectiveness since 2009** **Core argument** We are concerned that qualitative evidence for effectiveness of different psychological therapies has not been reviewed since 2009.	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is

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				We believe that failure to update the qualitative evidence will impoverish the relevance of the Guideline for clinical practice in the UK. We argue here for the essential role that case study and qualitative research play in managing complexity and heterogeneity in appraising the effectiveness of different psychological therapies. A literature review using three databases identifies and highlights some of the evidence published since 2009 for effectiveness that has been overlooked in the Guideline. We then briefly consider how effectiveness claims might be appraised in two sample studies identified from the literature. We conclude with a recommendation for how case study and qualitative evidence might be utilised to improve the clinical recommendations made in the Guideline. We envisage within the use of the GRADE system for appraising quality of evidence the danger of a systematic discounting of knowledge that is gained through observational studies. We draw particular attention to case studies (called 'case report' and 'case series' in the GRADE handbook) that are ascribed a maximum starting score of 2 in this system, meaning they can only realistically be graded as low to very low quality evidence. Given the methodological	the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We consider that the features of complexity and causality, contextualisation and heterogeneity that you describe as requiring qualitative evidence to address, are taken into account by this interpretation of the clinical context by the committee. We did not consider qualitative evidence/case series on the effectiveness of different psychological therapies because we do not consider this to be the best available evidence when differentiating the relative efficacy of different interventions. Thank you for providing details of the literature search you conducted for published

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				advancements in the field of case study research, this is an outdated assessment. Case study methodology has many variations, ranging from clinical observations (narrative designs), to systematic case studies (including qualitative, quantitative and/or narrative designs), and single-case experimental designs (including an experimental manipulation). The American Psychological Association (APA, 2006) recognizes the importance of these different types of case studies in order to develop an evidence-based practice in psychology. Creating sound public policy requires that we draw on a diverse range of evidence (Health Foundation, 2017; Thomas, 2017). Qualitative evidence maximizes the value of reviews to policy and practice decision-making (Cochrane Collaboration, 2011). We thus argue that case study and qualitative evidence should inform the existing Guideline as part of a 'multi-level synthesis' (ibid) in which qualitative evidence is not merely supplementary, but intrinsic to the generation of a clinically representative picture. The essential and complementary features that case study and qualitative evidence bring are summarized thus: 1. Complexity and causality – psychotherapy	case series and qualitative evidence. Also for providing details of how effectiveness claims can be appraised in case study research. However, as indicated above single case studies or case series do not provide the high quality evidence needed to support decisions on the relative effectiveness of different interventions. Consequently they have not been included in the guideline. An understanding of the mechanisms of causality is outside of the scope of this guideline. We accept that a greater understanding of mechanisms can play an important part in the development of interventions and so have made a research recommendation in this area. As described above, context is taken into account by the committee. Guidelines are explicitly a guide to judgment and not a substitute for it. We expect all users of the guideline to take into account personal factors when applying the recommendations in everyday practice and so take into account heterogeneity. Thank you for drawing our attention to these studies. APA 2006, Bohart 2011, Cartwright 2012, Cohen 2016, Cochrane 2011, Craig

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				is a complex intervention and any reduction of case data down to independent variables and linear models of causality is almost certain to miss influential factors and the interactions between these (Lieberson 2000; Bohart et al, 2011). The Medical Research Council's updated guidance on evaluating complex interventions recognizes that there is a 'length and complexity in causal chains linking intervention to outcome' (Craig et al, 2008). Randomised Controlled Trials are black box evaluations (Labin, 2008), while case studies can give insight in causal mechanisms, capturing a more realistic 'soft' or 'enabling' account of causality in effective therapy (Elliott, 2002). Case studies generate a unique type of knowledge that cannot be conveyed through randomized trials: 'whereas the experimental or quasi-experimental portion will assess effectiveness by determining the strength of a relationship between an initiative and its outcomes, the case study portion will offer an explanation of the relationship, indicating how the initiative actually worked (or not) to produce the relevant outcomes' (Yin, 2014, p. 221). 2. Contextualisation – appreciation of why different therapies worked with different cases. If quantitative evidence tells us that a therapy was effective in 70% of cases, qualitative evidence can help us to discern	2008, Donmoyer 2000, Edwards 2004, Elliott 2002, Health Foundation 2017, Labin 2008, Lieberson 2000, Roberts 2016, Thomas 2017 and Yin 2014 have not been included in the guideline because they do not meet the study design criteria (not an RCT or systematic review of RCTs).

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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				why therapy was not effective in the other 30% (Donmoyer, 2000); thus the circumstances under which we might expect an intervention to be effective (Cochrane Collaboration, 2011). Cartwright and Hardie (2012) pointed out that high quality evidence that an intervention worked somewhere, doesn't immediately prove that it will be effective here. Observational studies such as case studies can help to fill this gap: as they are more embedded in local practices and contexts that are relevant to the UK. 3. Heterogeneity – recognizing that every patient, every therapist and the context they work in is unique, case study and qualitative evidence accumulates across these unique settings and does not require heterogonous factors to be stripped away (Edwards et al, 2004). As Thomas (2017) recognizes, there are no true replications of evaluations of complex interventions but rather we should think about a 'continuum of similarity'. Methods of synthesis based on 'small N scenarios' are necessary in order to manage this heterogeneity (ibid). One of the main challenges for including case studies in review studies is the fact that published case studies are scattered across a large number of data-bases, making the search process for a specific set of cases highly time-consuming. This problem has	

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				been alleviated by the creation of two specialized journals (Clinical Case Studies and Pragmatic Case Studies in Psychotherapy) and a searchable online database of psychotherapy case studies (www.singlecasearchive.com). **Qualitative evidence since 2009 – literature search and results** Whilst the following literature search is not intended to provide a comprehensive picture, we decided to scope out existing case study and qualitative evidence since 2009 for the effectiveness of different psychological therapies in the treatment of depression. By presenting some of the results of our literature search, we want to demonstrate the wealth of knowledge produced since 2009, which is, in our opinion, a necessary complement for other forms of evidence that are being used to inform the Guideline. We performed a literature search using the Embase, Medline and PsycInfo databases, and searched for peer reviewed studies in the English language. Three banks of search terms were combined: depression AND	

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				case study OR case series OR cross-case OR multicase OR multi-case OR case report OR qualitative OR grounded theory OR phenomenolog* OR narrative OR ethnograph* AND therap* OR counsel* OR psychotherap* The raw search was performed on 24th August 2017 and generated 5134 results. We decided to look at a sample year and so scanned the titles and abstracts for 2016 results that made effectiveness claims about psychological therapies for depression. We included studies that offered detailed and contextualized accounts of change processes as, or corresponding to, therapeutic events. Out of 767 raw results for 2016, 15 studies met these inclusion criteria, and they are listed along with authors, abstracts, and publication details in the appendix below. If this prevalence were to be repeated throughout the entirety of the 2009-2017 search we would expect approximately 100 studies. The sample of studies represent therapies that would fall generically into each of the categories: counselling, psychodynamic psychotherapy and cognitive behavioural	

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				therapy. **Appraising effectiveness claims in two exemplar studies** In this paragraph, we provide a brief demonstration of how effectiveness claims can be appraised in case study research. The two studies sampled consider the application of Acceptance and Commitment Theory (ACT) interventions in local, complex contexts: Cohen, R. 2016. Getting into the Acceptance and Commitment Theory with psychoanalytic therapy: the case of "Daniel". Pragmatic Case Studies in Psychotherapy, 2016, Volume 12, Module 1, Article 1, pp. 1-30 Roberts, S.L. & Sedley, B. 2016. Acceptance and Commitment Therapy with Older Adults: Rationale and case-study of 89-year-old with Depression and Generalized Anxiety Disorder. Clinical Case Studies, 2016, Vol. 15(1) 53–67 1. Complexity and causality. According to the guidance provided by Bohart et al (2011) and Elliott (2002) for the evaluation of causal statements, we found that the Cohen study provided rich, contextualised detail through which to appraise any associations between therapeutic events and change processes.	

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				The study provided verbatim utterances by the patient session-by-session that exemplified shifts in perceptions and cognition over time. The study reported behavioural changes and relationship breakthroughs highlighting plausible associations to therapeutic events. The therapist is also honest about interventions that did not work/fell flat. However, we found limited evidence in the Roberts and Sedley study for causal associations between therapeutic events and outcomes. Six weeks after the final therapy session, the patient reported that depression and anxiety were reduced to non-clinical levels. Neither the patient nor the therapist linked these changes to the treatment. The positive change was observed very early in the treatment, as the patient noted a reduction of distress after the first session. According to the authors, experiential avoidance (what is done to try and rid, suppress, or avoid unwanted thoughts, feelings, or urges) is a major cause of psychopathology in this case. The authors noted that the patient was not willing to reduce experiential avoidance. There is sparse first-hand evidence of whether and how the patient believed the therapy had helped, however the study reports the patient's own endorsement of mindfulness	

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				techniques learned during therapy, which she continued to practice at home. 2. Contextualization. In the Cohen study the patient is a 44 year-old Caucasian male. The treatment took place in Michigan, USA in private practice and the integration of the Acceptance and Commitment Theory intervention was part of a longer-term psychoanalytic therapy. The patient came to therapy having had a number of ineffective short-term treatments. In the Roberts and Sedley study, by contrast, the patient is an 89-year old Caucasian female. The treatment took place in New Zealand in a specialist adult mental health service, and the patient had no prior experience of psychotherapy. The treatment was conducted by an experienced therapist who is a relative novice to Acceptance and Commitment Theory. The treatment consisted of six 1-hr Acceptance and Commitment Theory sessions over an 8-week period. Treatment was designed with explicit reference to gerontology theory and processes, and the study demonstrates that elderly patients can positively engage in Acceptance and Commitment Theory. 3. Heterogeneity. The Cohen study provided extensive detail on the patient's background and psychobiography. Given the patient's	

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				childhood relationship with his father, the therapist provides a model of a less-intimidating father figure through use of therapeutic transference as part of the treatment plan. The Roberts and Sedley study was able to contain and interpret relatively idiosyncratic relational factors in this very elderly person's treatment: namely her anxieties about the threat to her children's inheritance if she were to die before her husband, which were associated with the patient's murder fantasies. In this case the therapist did not validate the patient's preoccupation with contracting dementia at the same age that her mother did. Rather, using test results that cognitive function and cerebral atrophy showed no evidence for dementia, the therapist was able to demonstrate to the patient the role experience avoidance had in maintaining distress. **Concluding remarks and Recommendation** In this section, we have set out the reasons for our concerns that case study and qualitative evidence generated since 2009 have not been utilised in order to produce the Guideline. In our view this means the recommendations, in particular the relative weighting of some forms of	

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				psychotherapeutic intervention over others, may not make for a representative clinical picture. As we have demonstrated, claims made about the effectiveness of different psychological therapies are heavily contextualised. Case study and qualitative evidence could be utilised within the Guideline to produce vignettes that demonstrate the real-world and locally contextualised applications of different psychological therapies. Presentation of evidence in this way within the Guideline could improve and reinforce local decision making about the most appropriate therapy for the patient's needs. **References:** APA (2006) Evidence-Based practice in psychology. Am Psychol 61: 271-285 Bohart, A.C., Tallman, K.L, Byock, G. & Mackrill, T. (2011). The "Research Jury" Method: The Application of the Jury Trial Model to Evaluating the Validity of Descriptive and Causal Statements about Psychotherapy Process and Outcome. Pragmatic Case Studies in Psychotherapy, Volume 7, Module 1, Article 8, pp. 101-144 Cochrane Collaboration: Noyes, J., Popay, J., Pearson, A., Hannes, K. & Booth, A. 2011. Chapter 20: Qualitative research and	

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				Cochrane Reviews. Cochrane Handbook for Systematic Reviews of Interventions Cartwright, N., & Hardie, J. (2012). Evidence-based policy: A practical guide to doing it better. New York: Oxford University Press. Craig, P., Dieppe, P., Macintyre, S., Michie, S., Nazareth, I. & Patticrew, M. (2008). Developing and Evaluating Complex Interventions: The new Medical Research Council Guidance. BMJ 2008;337 Donmoyer, R. (2000). Generalisability and the Single-Case Study in Gomm, R., Hammersley, M. & Foster, P. 2000. Case Study Method: Key Issues, Key Texts. Sage Publications : London Edwards, D., Datilio, F.M. & Bromley, D.B. (2004). Developing Evidence-Based Practice: the role of case-based research. Professional Psychology Research and Practice 35(6):589 · December 2004 Elliott, R. (2002). Hermeneutic Single-Case Efficacy Design, Psychotherapy Research, 12:1, 1-21 Health Foundation (2017), Healthy Lives for People in the UK . Accessed via http://www.health.org.uk/publication/healthy-lives-people-uk on 24th August 2017 Labin, S. N. (2008). Research syntheses: Towards broad-based evidence. In N. L. Smith & P. R. Brandon (Eds.), Foundational issues in evaluation (pp. 89-110). New York:	

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				Guilford. Lieberson, S. (2000). 'Small N's and Big Conclusions' in Gomm, R., Hammersley, M. & Foster, P. 2000. Case Study Method: Key Issues, Key Texts. Sage Publications : London Thomas, J. (2017). Qualitative Synthesis and Systematic Reviews. https://www.youtube.com/watch?v=FXMM8ufcOos#action=share accessed 27th August 2017 Yin, R. K. (2014). Case study research: Design and methods. Thousand Oaks: Sage.	
United Kingdom Council for Psychotherapy	Full	General	General	The United Kingdom Council for Psychotherapy (UKCP) is the leading organisation for the education, training, accreditation and regulation of psychotherapists and psychotherapeutic counsellors in the UK. We exist to promote and maintain the highest standards of practice of psychotherapy and psychotherapeutic counselling for the benefit of the public. Our membership includes more than 9,000 individual therapists and more than 70 training and accrediting organisations. Our individual members work for the NHS, privately, and in third sector organisations	Thank you for your comment and providing this information on the United Kingdom Council for Psychotherapy.

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				offering a wide variety of psychotherapeutic approaches. Our support for the psychological therapies is research-based and recognises the diversity of modalities that can deliver better mental health outcomes for all. We hold the national register of psychotherapists and psychotherapeutic counsellors, which only includes practitioners who meet our exacting standards and training requirements and who agree to abide by our stringent ethical standards. We welcome the opportunity to respond to the consultation on NICE's draft guidelines for depression.	
United Kingdom Council for Psychotherapy	Full	General	General	Our views concerning the question of '***Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why***' are as follows: **Patient choice of psychotherapy modalities** We would like to see the draft NICE guidance endorse the principle of choice of psychotherapeutic approaches for patients, since there is a significant risk that lack of	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline

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				choice will have a large negative impact on clinical practice. While the draft guidance acknowledges the importance of offering patients a choice of treatments (full version, page 43/ line 5; page 248/line 1), the recommendations themselves do not reflect this principle. Instead, the guidance offered throughout regarding all forms of depression (less severe, more severe, chronic and complex depression) proposes Cognitive Behavioural Therapy (CBT) as the first-line treatment, either alone or in combination with medication. The guidance states that lay members of the Guideline Committee regarded patient choice within treatment type, such as psychological interventions, as being of less concern (full version/page 247/line 25). While we acknowledge the importance of lay opinion, it is not clear why the available clinical research evidence concerning the impact of choice of psychological therapy treatment on outcomes was ignored in this instance. Recent meta-analyses have shown that patients matched to their preferred therapy are less likely to drop out prematurely and also achieve greater improvement in treatment outcomes (Swift et al, 2011).	an offer of treatment. We have also added a recommendation to section 1.4 (short version of the guideline) to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When making the recommendations for specific interventions, the committee took into account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective. The text about patient choice (p 247, line 25 of the consultation version of the guideline) was incorrect and has been amended.

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				Meta-analyses also indicate that when clients with psychological disorders are involved in either shared decision-making, choice of treatment condition, or otherwise receive their preferred treatment, they report higher levels of satisfaction, better completion rates, and superior clinical outcomes (Lindhiem et al, 2014). These results are also applicable specifically to the treatment of depression, including persistent sub-threshold and mild depression, as well as more severe depression (Lin et al, 2005; Cooper et al, 2017). Patients' choice of treatment is also important in the light of evidence from several randomised controlled trials (RCTs) that demonstrate differential responses to treatment types based on patient characteristics (Fournier et al, 2009; Wallace et al, 2013; DeRubeis et al, 2014; Huibers et al, 2015). The need to optimise outcomes by matching individual patients to the most appropriate treatment for them personally is a principle that is endorsed as part of personalised medicine for treatment of physical ill-health, and is cost effective (NHS England, 2016). We therefore suggest that this principle is applied to mental health, consistent with the government's parity of esteem agenda (DH, 2013).	Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). Thank you for drawing our attention to these references. These have not been included in the guideline as they do not meet the inclusion criteria for the following reasons: • Lindhiem 2014 and Swift 2011: could not

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				We conclude from the evidence cited above that a 'one size fits all' approach involving CBT as the default treatment will seriously compromise patient mental health through its application of an exceeding limited range of psychological treatments when there is evidence for the efficacy of a wider range of treatments. In the light of such evidence, we also regard it as unethical that practitioners should be advised to disregard patient choice among psychological treatments. The guidance therefore challenges the ethical practice of clinicians, compromising the principles of good clinical practice, and reducing opportunities for the achievement of optimal mental health outcomes for patients.	be included as the comparison of active choice condition relative to no involvement in shared decision making does not match the review protocol. Patient preference, choice and the principles of shared decision making were considered by the committee during the interpretation of evidence and making the recommendations. • Lin 2005 and Wallace 2013: Mediator/moderator analyses do not match the review protocol. • Cooper 2017: this is a secondary analysis of a study already included in the NMA for treatment of a new depressive episode (Freire 2015). • DeRubeis 2014 and Fournier 2009: Secondary analyses of a study: DeRubeis 2005 – was considered for inclusion in the NMA of treatment for a new depressive episode. However it was excluded from this review as mean duration of MDD >2 years which means that this study is ineligible for this review. DeRubeis 2005 could also not be included in the chronic depression review as no minimum duration of MDD was specified as part of the entry criteria for that trial and it is unclear what proportion of participants in the study would meet criteria for chronic

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					depression. • Huibers 2015: this is a secondary analysis of study already included in the NMA for treatment of a new depressive episode (Lemmens 2015/2016). • NHS Engand 2016, DH 2013: These do not meet the study design criterion (not an RCT or systematic review of RCTs)
United Kingdom Council for Psychotherapy	Full	General	General	**Omission of psychotherapeutic modalities** The draft guidance omits reference to certain modalities of psychological therapy, which may negatively impact clinical practice. There is evidence for the effectiveness of various forms of Humanistic and Integrative Therapy, such as Transactional Analysis, Gestalt, Integrative Psychotherapy and Person-Centred Counselling (Van Rijn et al, 2011; Van Rijn and Wild, 2013, 2016). There is also growing evidence for body psychotherapy (Röhricht et al, 2013; Röhricht, 2015). Given NICE's endorsement of choice, and the evidence we have cited above on the positive impacts on clinical outcomes, we are extremely concerned that the omission of evidence concerning a broader range of modalities will have a negative impact on clinical practice.	Thank you for your comment. The guideline looked for RCT evidence on a wide range of psychological and psychosocial interventions. The interventions that were reported in the guideline were those where RCT evidence was identified. Röhricht 2013 has now been included in the chronic depression review. Röhricht 2015, Van Rijn 2011, Van Rijn 2013, Van Rijn 2016 were not included in the guideline as they do not meet the study design criterion (not an RCT or systematic review of RCTs).

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United Kingdom Council for Psychotherapy	Full	General	General	**Over reliance on RCT evidence** The guidance also challenges the ethical practice of clinicians and reduces opportunities for the achievement of optimal mental health outcomes for patients due to the highly selective nature of the evidence that the guidance is based on. The recommended psychological treatments for depression are derived from a narrow consideration of what constitutes appropriate evidence, namely RCTs and meta-analyses. We recognise the importance of RCTs as a source of evidence but would suggest that there is also a significant body of robust data from non-RCTs that also needs to be taken into account. The validity of findings from RCTs is compromised by the selection of populations that clinicians do not typically encounter. As such, the guidelines cannot be regarded as ethically sound, since conclusions drawn from a broader range of evidence involving patients more typically seen in primary and secondary care leads to alternative recommendations for practitioners to implement. The most significant of these conclusions concerns CBT as the first line treatment when there is recent evidence of the efficacy of other psychological	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We did not consider routine datasets, such as the IAPT dataset, as part of the evidence base because we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading. Based on feedback from stakeholders, the

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				approaches such as psychodynamic psychotherapy (Steinert et al, 2017). While RCTs have the advantage of controlling for extraneous factors that affect the conclusions that can be drawn concerning the causal effects of psychological intervention on outcomes, their often strict criteria for selection of participants compromises their application to real practice settings. RCTs within the NICE evidence base were predominantly based on selection of patients with the sole diagnosis of depression. However, evidence from epidemiological studies demonstrates that depression and anxiety are frequently comorbid (Kessler et al, 2003; Moffitt et al, 2007). Evidence from studies of clinical populations also shows high rates of comorbidity (Lamers et al, 2011; Hepgul et al, 2016). For example, Hepgul and colleagues' study of patients accessing 'Improving Access to Psychological Therapies' (IAPT) services found that as many as 72% met the criteria for two or more diagnostic conditions, with depression and anxiety being the most common co-occurring disorders. Patients seen for depression in primary and secondary care settings are clearly more complex than those that the NICE evidence base draws on. It is questionable therefore	data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). Evidence on people with coexisting anxiety or any other coexisting mental health condition has not been excluded from the guideline so long as participants have clinically important symptoms of depression and the intervention is targeted at depression symptoms.

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				as to how far the findings from the trials used as evidence by NICE can be applied to the clinical populations typically presenting with depression. Evidence from a broader spectrum of studies needs to be taken into account, since results from RCTs may have limited application in real word practice settings. Evidence from IAPT, generated in real world practice settings with large samples of patients with and without comorbidities, with the statistical power to control for extraneous variables, leads to different conclusions regarding the appropriateness of CBT as the first-line treatment. Psychodynamic psychotherapy has been shown to have equal efficacy to CBT in actual clinical practice according to metrics used by the NHS. The IAPT dataset shows that both modalities have a recovery rate of 45.9% for depression. However, psychodynamic psychotherapy achieves this result, on average, with slightly fewer sessions (NHS Digital, 2017).	The Hepgul study represents a very small population (n=147). It is unclear how representative a population of IAPT this is given there are many hundreds of thousands of referrals to IAPT annually. We do not think this supports your assertion that patients seen in primary and secondary care are more complex than those included in the NICE evidence base, which includes people with complex and psychotic depression. You draw attention to the NHS-D IAPT database and the recovery rate reported for a range of psychological interventions such as CBT and STPT. As you point out the recovery rates in this database are broadly similar. However we do not think this provides good evidence for the broad equivalence of these interventions. The diagnostic accuracy within current IAPT services is limited, with many services reporting a much higher proportion of mixed anxiety and depression diagnoses and under-reporting diagnoses such as PTSD or social anxiety disorder. The comparisons in this database are not randomised and it is very unlikely that they are based on similar populations. For example the percentage of people who receive STPT is very small compared to those that received CBT. The

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					pathways into care for different therapies are not the same. For example a large proportion of people receiving CBT for depression have been "stepped up" from a low intensity intervention. In contrast a large proportion of people receive counselling as their first line intervention. Therefore to make direct comparisons about efficacy for populations that there is good reason to believe have different characteristics is misleading. The Steinert 2017 systematic review was checked for relevant references but no additional studies that met the inclusion criteria were identified.
United Kingdom Council for Psychotherapy	Full	General	General	Our response to question 2: **'Would implementation of any of the draft recommendations have significant cost implications?'** is as follows: **Patient choice of psychotherapy modalities** The principle of optimising outcomes by matching individual patients to the most appropriate treatment for them personally as endorsed as part of personalised medicine for treatment of physical ill-health is a principle which should be adopted in relation to mental health. The cost effectiveness of	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline an offer of treatment. We have also added a recommendation to section 1.4 (in the short

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				this personalised approach to treatment of physical ill-health is recognised by NHS England (2016). Offering patient choice and tailoring psychological interventions to individual patients will also likely be cost effective for depression, given the evidence reviewed here which shows higher completion rates and superior clinical outcomes. We therefore suggest that this principle is applied to mental health, consistent with the government's parity of esteem agenda (DH, 2013). We specifically recommend that patients are given a choice of psychological therapy treatments rather than CBT being the default, and that STPT and couples therapy for depression should form an integral part of this choice, given the evidence for their efficacy (Steinert et al, 2017). We believe our suggestions are a better and more cost-effective way of improving access.	version of the guideline) to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When making the recommendations for specific interventions, the committee took into account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first-line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective. The Steinert 2017 systematic review was checked for relevant references but no additional studies that met the inclusion criteria were identified.
United	Full	Gener	Gen	**Over reliance on RCT evidence**	Thank you for your comment. When making

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Kingdom Council for Psychotherapy		al	eral	Evidence from a broader spectrum of studies needs to be taken into account, since results from RCTs may have limited application in real word practice settings. In particular, evidence from large scale, robust investigations of routine practice, as represented by the IAPT dataset, should be taken into account.	recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We did not consider routine datasets, such as the IAPT dataset, as part of the evidence base because we cannot be sure that the populations treated with various interventions are the same and to assume so would be potentially misleading.
University of Nottingham	Full	Gen eral	Ge ner al	When Lord Layard announced the government investment into psychological therapies for depression, counselling was originally omitted as a psychological	Thank you for your comment. Counselling was included as an intervention in the review questions. Unfortunately no specific RCT evidence on PCE-CfD (which was developed

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				approach. As a result of the feedback by BACP, person-centred experiential therapies (PCET) was included and named 'CfD': Counselling for Depression. For clarity we have advised CfD is renamed PCE-CfD so it describes what is being offered. The guidelines, as they stand, do not acknowledge the progress made by PCE-CfD over the last five years. We are very pleased that since 2013 at the University of Nottingham we have qualified over 100 therapists in the East of England - Nottinghamshire, Essex, Norfolk, Suffolk, Lincolnshire and have also accepted delegates from Coventry and Warwickshire and Manchester. We have 150 IAPT therapists still in training with new people qualifying every week. The feedback we receive from the service providers is very positive and their client outcomes are also reported as favourable. We train supervisors who are in place in services supporting the PCE-CfD workforce. There are 4 other institutes who are offering these courses so the numbers are increasing every year. Counselling has always been a popular resource in GP services and its place in IAPT has been important so there is still a counselling presence in NHS services. Clients frequently ask for counselling, a non-medical approach, as opposed to	for the IAPT programme) was identified and so no recommendation for the use of PCE-CfD was made. However, the committee have recommended counselling based on a model that is specifically developed for depression, which would be in line with the specific training programme for counselling developed as part of IAPT. The meta-analysis linked to in the comment only includes two references, Stiles 2006 and Stiles 2007. Neither of these studies meet the inclusion criteria for the review as they do not meet the study design criterion (not an RCT or systematic review of RCTs).

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				pharmacology or cognitive behavioural therapy. Investment in counselling, through IAPT, is relatively new and represents 1% of the entire IAPT budget. We are building up research and appreciate that published papers are the way committees access peer reviewed research and evidence. We are confident that over the next 5 years the research evidence for PCET will have increased. We urge you to recommend PCE-CfD (presently known as CfD) remains as an approach for people struggling with depression. This link takes you to a meta-analysis conducted in 2008 https://www.pce-world.org/about-pce/articles/102-person-centredexperiential-therapies-are-highly-effective-summary-of-the-2008-meta-analysis.html	
Royal College of Psychiatrists	Full	General	General	The omission of ketamine from the Guideline is of great concern. There are multiple RCTs (published well before this Guideline) demonstrating its acute antidepressant effects with relatively good tolerability. Given the lack of information regarding its longer term or repeated use a statement from NICE on its evidence based place in therapy would have been of value for clinicians and may have helped restrict its inappropriate widespread use.	Thank you for your comment. Ketamine was not prioritised for investigation by this guideline as it is not a currently available first-line intervention for depression, it is not licensed for use in depression and it is an abused drug. In these circumstance the committee did not think it was appropriate to review it.
Royal College	Full	Gener		**Problems with categorisation of treatment**	Thank you for your comment. A number of

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of Psychiatrists		al		**resistant depression, chronic depression and complex depression** We are concerned the categories defined in the draft guidelines TRD, chronic depression and complex depression overlap considerably, in that there is strong evidence for the existence of a more loosely defined heterogeneous group of long-term, difficult to treated depressive conditions, frequently associated with co-morbid common mental disorders, various personality disorders/traits and serious psycho-social disability. Moreover, despite in the introduction to the section on complex depression referring to the many studies that have noted the frequent comorbidity in depression with physical illnesses and mental health disorders, the definition of complex depression in the draft guidelines is only focussed on co-morbidity with personality disorder, does not include these other co-morbidities nor other aspects of complexity such as high levels of childhood and/or adult trauma, very poor functioning and severe relationship difficulties. We are therefore concerned that the guidelines are excluding RCTs that include dual diagnoses or co-morbidity with other mental health disorders apart from personality disorder. Moreover, many patients with depression and	stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same.

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				personality disorder will also fulfil criteria for chronic and/or TRD, again highlighting the overlap between these categories. These concerns will impact on: • **Research** - the UK guidance will be out of line with the APA (DSM-5) and the European Psychiatric Association (EPA) guidance (2016). Both of these recommend a common "persistent" depression category with sub-categories for severity and degree of associated psycho-social disability. Additionally, the guidance will cause confounds in treatment research as many subjects in the trials included in the TRD meta-analysis will meet the guideline's definition of chronic depression and/or complex depression. We are concerned that the guidelines set up false categories and trials classified within only one category. • **Clinical service provision -** Due to the overlap of these three categories, there will be confusion as to which category any one patient should be assigned to. Inclusion criteria in TRD studies are restrictive and do not reflect case identification in usual	A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. The committee considered a number of comments on the use of the term 'complex depression' in this guideline. In the guideline 'complex depression' was limited to depression that was co-morbid with a personality disorder. A number of stakeholders pointed out that other factors such as other mental health co-morbidities, drug and alcohol misuse, social and environmental factors and a history of poor

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				clinical settings which is usually descriptive and involves complex evaluations of psychosocial functioning. The EPA recommends that the type of psychotherapy should be individually chosen in consideration of early versus late onset, type of depression, number of episodes, early trauma, symptom severity, patient preference and comorbid personality disorder, and recommends a personalized approach based on the patient's preferences and needs, e.g. pharmacotherapy or psychotherapy, group or individual psychotherapy, in- or outpatient treatment. References Jobst A et al. (2016) European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. European Psychiatry, 33, 18 – 36. Ruhe HG, van Rooijen G, Spijker J, Peeters FP, Schene AH. (2012) Staging methods for treatment resistant depression. A systematic review. J Affect Disord, 137, 35–45.	response to treatment can also contribute to a diagnosis of complex depression. The committee considered these factors and noted that co-morbidity with a range of other mental disorders also occurred in participants in studies for first line treatment, TRD and chronic depression. The committee therefore considered that co-morbidity alone would not be useful in describing complex depression. The focus on depression that was co-morbid with personality disorder was because of the committee's knowledge and experience that it can complicate the treatment of depression (see for example the meta-analysis by Newton-Howes et al (2006) Personality disorder and the outcome of depression: meta-analysis of published studies. British Journal of Psychiatry, 188, 13-20)). The committee therefore decided to stay with the current definition of complex depression used in the guideline as alternative suggested definitions did not clarify the issue. However they acknowledge there are limitations with this definition of complex depression. Jobst 2016 and Ruhe 2012 have not been included in the guideline as they do not meet the study design criteria for the review (not RCTs or a systematic review of RCTs).
Royal College	Full	Gener		**Functional outcomes being neglected**	Thank you for your comment. We agree that

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of Psychiatrists		al		The draft guidance takes a narrow view of outcomes assessed in being only symptom based. It neglects the importance of functional outcomes such as quality of life, improved relationships with others, self-care, problem solving, improvements in social functioning, improvements in being able to attain and sustain employment, etc being. Such functional outcomes are considered important by service users, as reported in the service user experience chapter of the guideline. Trials including analysis of non-symptom data should be upgraded for quality and this data should be taken into account. References McPherson S, Evans C & Richardson P (2009) The NICE Depression Guidelines and the recovery model: is there an evidence base for IAPT?, Journal of Mental Health, 18(5). McPherson S, Cairns P, Carlyle J, Shapiro D, Richardson P & Taylor D (2005) The effectiveness of psychological treatments for refractory depression: A systematic review, Acta Psychiatrica Scandinavica, 111, 331-340.	psychosocial functioning and quality of life measures are important. However these kinds of measures are rarely reported and they are often reported inconsistently across studies. For these reasons these measures were not prioritised for inclusion in the review protocols for this guideline. When making recommendations, the committee interpret the evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. McPherson 2009 cannot be included in the review as it does not meet the study design criteria (not an RCT or a systematic review of RCTs). McPherson 2005 has been searched for relevant references. However, no additional studies that meet inclusion criteria were identified.
Royal College of Psychiatrists	Full	Gener al		**Concern regarding use of GRADE data**	Thank you for your comment. Although it is more difficult to blind participants and

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				Most studies reviewed in draft guidelines are rated as 'poor quality' or 'very poor quality' using GRADE criteria. The main reasons that studies are not rated highly by these criteria are that there are sources of bias, for example lack of blinding, and where the sample of a trial is too heterogeneous. However, it is very difficult in many psychological therapy trials to blind participants or researchers due to the complex psychological interventions that are being compared. Regarding heterogeneity, the larger the sample size of a single study, or the more studies considered which are reflective of the different populations seen in different settings, the more likely there will be significant heterogeneity, and the studies will be rated lower, in contrast to a single small study with well-defined population which will be given a higher rating, which gives the erroneous impression that treatments tested in the latter are more effective than those in the former. Trials which report long-term follow up should be reviewed and upgrading considered given that the guidelines highlight the importance of on-going symptom reduction and improvement in functioning in the long-term.	intervention administrators in psychological studies, it is possible, for instance by isolating the active ingredient and using an attention-placebo (that is similar in other aspects with the exception of the active ingredient). Blinding of outcome assessors is also taken into account in the GRADE system. The non-blinding of participants and intervention administrators presents a risk of bias, although we accept that this is more of a problem for psychological than pharmacological trials, it does not negate the fact that participant and intervention administrator knowledge of the treatment being received/delivered is likely to introduce some degree of performance bias due to an individual's inherent beliefs about that intervention. Studies have been considered across settings and judgements of heterogeneity are made at the outcome level rather than individual study level. Although it is true that heterogeneity is more likely with more studies (inconsistency is obviously not possible with a single study), conversely a larger pooled sample size is more likely to increase the precision of the effect estimate and reduce the likelihood of downgrading due to imprecision.

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					In GRADE RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE.
Royal College of Psychiatrists	Full	general		We have some concerns regarding the dates of the personal accounts: Case A uses date of 2008 Case B uses date 2008 and refers to the next couple of years = 2010 Case C refers to 1999 plus the next 15 years = 2007 Case D refers to 2003 Case E gives no dates Case F refers to 1999 and comments on 9 years later now getting back to work = 2008 Case G refers to 2000 then discusses the following 8 years of being unwell = 2008 Case H refers to 2009 Case I gives no dates We would like to express concerns that none of these are recent. As we all know ECT has changed quite significantly over the years.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.

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				ECTAS and NALNECT are now also more prominent. Changes have also occurred also in other therapeutic forms of treatment. We for one would like to see these personal accounts to be more recent, and to reflect the changes that have occurred over the past decade, rather than to rely on outdated accounts	
Royal College of Psychiatrists	Full	43 76 245	2-8 37-40 28-31	**Lack of patient choice** The guidance recognizes the importance patient choice but the recommendations do not support this. *"Psychological treatments generally have more widespread acceptance than medication from service users (Priest et al, 1996; van Schaik et al, 2004) with a recent meta-analysis suggesting a 3-fold preference for psychological treatment (McHugh et al., 2013). It is also increasingly recognised that individuals wish to have a choice of psychological treatment options, and that the provision of such choice may improve treatment engagement and outcome (Kocsis et al, 2009; Swift and Callahan, 2009)."* Personal account D: *I am encouraged to see that a lot of resources are being put into providing CBT for people with depression,*	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline an offer of treatment. We have also added a recommendation to section 1.4 (in the short version of the guideline) to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When

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		P. 247, lines 25-33, and repeated on p. 292 46-50, 293 1-4		*but CBT is not the right treatment for everyone with depression and this needs to be recognised.* We are concerned that the guidelines do not stress the fact that many psychological treatments, including psychodynamic, are as effective as each other, and that the most important decision the guidance uses for the ranking of interventions is cost effectiveness. It appears that the health economic analyses are used to justify treatment decisions with insufficient evidence. For example, it is stated "*The GC noted that, although long-term psychodynamic psychotherapy ranked in a higher place than CBT and behavioural therapies, this was not included in the economic analysis due to lack of suitable data, but, nevertheless, it was very unlikely to be cost-effective, given its high resource use intensity."* However, this assumption is not substantiated due to the lack of available evidence and longer term treatment may be more cost effective in the long run in reducing rate of relapse and better long term outcomes. Hence the need to recommend more studies in this area. The guideline thus recommends fewer treatments than if other factors were taken into account in the ranking system, limiting	making the recommendations for specific interventions, the committee took into account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The text in the guideline has been updated

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				treatment choice. *"The GC discussed the issue of patient choice, with the lay members offering the opinion that many people are happy solely with a choice of either evidence based psychological or pharmacological therapy, with choices between different therapies of the same modality being of less concern. They thought that there would be a subset of patients who would have researched therapies carefully and would have a strong preference, but that this would not apply to the majority of people. Other issues such as choice of the gender of the therapist, the setting in which interventions were provided and good information on the content of, potential harms or side effects and likely outcomes of an intervention were also considered important".* There is no information as to who the lay members were, how many, their characteristics and whether their views reflect the majority of individuals with depression. The statement that choices between different modalities were of less concern contradicts the accounts of individuals in the sections of service user experience who express a preference for a particular modality.	as a result. In this we clarify that the committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. Maljanen (2016) has now been excluded from the NMA for less severe depression because no endpoint data were available (previously follow-up data had been entered into the model in error). Therefore there is no longer any data on LTPP included in the analysis of less severe depression. LTPP remains as an intervention that is included in the NMA for more severe depression. As there are no longer any data on LTPP in the NMA for less severe depression the committee have not made a recommendation about this intervention for first-line treatment of a new depressive episode. For the economic analysis for more severe depression we needed discontinuation data,

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					response in completers data and remission in completers data. The single study on LTPP in more severe depression reported dichotomous data on discontinuation and remission (both in completers and those randomised). It also reported continuous data; however, these were reported for the ITT sample at baseline and completer sample at endpoint so it was not possible to include them in any analysis that utilised continuous data (i.e. either SMD, response in those randomised or response in completers). Due to lack of response in completers' data the study of LTPP could not be included in the economic analysis. Consequently no recommendation has been made about the use of LTPP for more severe depression. Full details of the committee's rationale for making the recommendations for treatment of a new depressive episode are documented in the 'evidence to recommendations' sections (7.4.5 and 7.7). The text about patient choice (p 247, line 25 of the consultation version of the guideline) was incorrect and has been amended. Details of the lay members of the committee are provided at the start of the full guideline document. Lay members of NICE guidelines

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					provide their own personal opinions and experiences. They do not 'represent' the experiences of all people with depression – given the large number of people who have depression this would not be practical. Consultation on the draft guideline is an effective way to elicit views from a wider range of people, including those of service users, about the recommendations that have been made. This feedback is then taken into account, in line with NICE processes, to form the final guideline. Thank you for bringing these references to our attention. These studies have not been included in the guideline because they do not meet the inclusion criteria: • Priest 1996 and van Schaik 2004: cannot be included in the review as they does not meet the study design criteria (not an RCT or systematic review of RCTs) • McHugh 2013 and Swift 2009: As defined in the protocols of this guideline the pre-specified comparisons of interest were active intervention relative to another active intervention or control arm(s). Therefore comparison of patient choice versus no choice is outside this protocol. This analysis also necessitates secondary analysis and

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					moderator/mediator analysis which are also outside the protocol of this review. Patient preference, choice and the principles of shared decision making were considered by the committee during the interpretation of evidence and making the recommendations. • Kocsis 2009: moderator/mediator analysis are outside the protocol of this review.
Royal College of Psychiatrists	Full	252 293	28-35 22-29	**Short-term psychodynamic psychotherapy (STPT)** We are concerned that the recommendations for the use of STPT do not reflect the available evidence. ***STPT should be recommended for first episode less severe and more severe depression*** States *"Consider short-term psychodynamic psychotherapy (STPT) if a person with less severe depression would like help for emotional and developmental difficulties in relationships and:* *· _has had group CBT, exercise or facilitated self-help, antidepressant medication or individual CBT for a previous episode of depression, but 32 this did not work well for them, or*	Thank you for your comment. **First episode less severe and more severe depression** Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently,

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				· _*does not want group CBT, exercise or facilitated self-help, antidepressant medication or individual CBT."* States *"Consider short-term psychodynamic psychotherapy, alone or in combination with 22 an SSRI or mirtazapine, for a person with more severe depression who would like help for emotional and developmental difficulties in relationships and:* · _*has had individual CBT in combination with an SSRI, group CBT, or individual CBT or BA for a previous episode of depression, but this did not work well for them, or* · _*does not want individual CBT in combination with an SSRI, group CBT, or individual CBT or BA."* However, based on a meta-analysis of STPT for 54 studies 3946 patients, individual SPTP should be a first line option for depression overall. Based on this body of research STPT should be treated the same as CBT and IPT as a first line option. Driessen E, Hegelmaier LM, Abbass A A, Barber JP, Dekker JJ, Van HL, Jansma EP, Cuijpers P (2015). The efficacy of short-term	the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. Short-term psychodynamic therapy remains an option for people with less severe depression (who would like help for emotional and developmental difficulties in relationships) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication, individual CBT or BA or IPT) have not worked well in a previous episode of depression or in those who did not want the other recommended interventions. The committee made this a 'consider' recommendation because of the moderate benefit on the SMD outcome and the lower cost effectiveness of short-term psychodynamic therapy compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the

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				psychodynamic psychotherapy for depression: A meta-analysis update. Clinical psychology review , 42,1-15. Certain varieties of STPT appear more effective than others in reducing depression. The emotionally focused varieties, called the Experiential Dynamic Therapy models are derived from the work of Habib Davanloo from Canada in the 1960's to 2000's in collaboration with David Malan from the UK since the 1980s. This type of STPT has a potent antidepressant effect in a short course yielding large within group effects (*d*=1.33) that increase significantly in follow-up (further *d*=0.30). EDT outperformed non active controls in all times frames and outperformed other bona fide treatment controls in follow-up (*d*=0.64). (Lilliengren et al, 2016). Lilliengren P, Johansson R, Linqvist K, Machler J, Andersson G (2016). Efficacy of Experiential Dynamic Therapy for Psychiatric Conditions: AMeta-Analysis of Randomized Controlled Trials, Psychotherapy, 53 (1), 90–104. In the Cochrane review of STPT for common Mental Disorders (Abbass et al, 2014) the EDT methods accounted for the lions share of all the effects of STPT on depression again	effectiveness and cost effectiveness of short-term psychodynamic therapy was likely to be higher in the sub-population in the recommendation compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). Short-term psychodynamic therapy, alone or in combination with an SSRI or mirtazapine, remains an option for people with more severe depression (who would like help for emotional and developmental difficulties in relationships) who do not want to have or who have had poor response to individual CBT, IPT or BA alone, antidepressant medication alone or combined CBT, IPT or BA with antidepressants for a previous episode of depression. The committee made this a 'consider' recommendation after considering the equal effects of short term psychodynamic therapy with pill placebo on the SMD and response in those randomised outcomes and the fact that pill placebo has an established, large effect in depression but it is not a realistic treatment option. The

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				with increasing effect sizes in follow-up. (Post Treatment *d*= 0.93, Short-term follow-up *d*= 1.4, Long-term follow-up *d*=1.59). Abbass AA, Kisely SR, Town JM, Leichsenring F, Driessen E, De Maat S, Gerber A, Dekker J, Rabung S, RusalovskaS, Crowe E (2014). Short-term psychodynamic psychotherapies for common mental disorders. The Cochrane database of systematic reviews, 7, CD004687. ***STPT should be recommended for treatment resistant depression*** For treatment resistant depression we recommend that STPT methods or more specifically ISTDP should be offered as a first line treatment to severely depressed patients who have not responded to medication treatment or other first line intensive therapies. The evidence is from studies of the method of EDT called Intensive Short-term Dynamic Psychotherapy (ISTDP). This method has been subjected to 11 studies of resistant and complex patient populations (Abbass, 2016). It meets empirically supported criteria for mixed personality disorders with comorbid symptom disorders. It has been studied in the	committee also considered that making this recommendation would improve patient choice. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). Driessen 2015, Lilliengren 2016 and Abbass 2014 systematic reviews were searched for relevant references but no additional studies that met the inclusion criteria were identified. It should be noted that the committee based their recommendations on the results of the network meta-analysis produced by this guideline, which had different inclusion criteria to Driessen et al (2015). The committee were also informed by cost effectiveness data when making their assessment of the relative effectiveness of the interventions. Similarly, with the Lilliengren et al (2016) review this included a greater number of studies arising from the use of different inclusion criteria. In our included studies we did not find any evidence to support differential recommendations for different models of psychodynamic therapy.

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				UK in a Pathfinder Study and found effective for treatment resistant patient populations many of who had chronic depression (Hajkowski and Buller, 2012). Following up on a pilot study suggesting strong effects for TRD (Abbass, 2006), ISTDP was recently subjected to a rigorous RCT in comparison to secondary mental health team care as usual (medications and psychotherapy as usual) (Town et al, 2017). 90% of patients were medically ill and had personality disorders making a robust challenge to the treatment arms. In this study ISTDP, averaging 16 sessions, outperformed the comparator even while medications were reduced in 2/3 of cases (meanwhile over half in controls had increases in medications). The full remission rate on the HAMD was 36% while the partial remission rate was 48% (compared to 3.7% and 18.7% for TAU). These results compare favourably to the very few existing RCT studies of any psychotherapy for TRD. Abbass A (2006). Intensive Short-term Dynamic Psychotherapy in Treatment Resistant Depression: A Pilot Study. Depression and Anxiety, 23, 449-552. Abbass A (2016).The Emergence of Psychodynamic Psychotherapy for Treatment Resistant Patients: Intensive Short-term	Again the position with Abbass (2014) is similar to the other reviews. It is also worth noting that Abbass et al conclude that, 'variability in treatment delivery and treatment quality may limit the reliability of estimates of effect for STPP.' **Treatment resistant depression** Abbass 2006, Abbass 2016 and Hajkowski 2012 could not be included in the further-line treatment review as they do not meet the study design criteria (not an RCT or systematic review of RCTs). In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the

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				Dynamic Psychotherapy. Psychodynamic Psychiatry 44(2):245-80. Hajkowski, S., & Buller, S. (2012). Implementing short-term psychodynamic psychotherapy in a tier 4 pathfinder service: Interim report. Derby, UK: Derbyshire Trust. Town JM, Abbass A , Stride C, Bernier D (2017). A randomised controlled trial of Intensive Short-Term Dynamic Psychotherapy for treatment resistant depression: the Halifax Depression Study. Journal of Affective Disorders , 214,15-25. ***STPT should be recommended for complex depression*** STPT should also be offered be offered as first line option in cases where there is personality disorder based on meta-analytic data from RCTs of STPT for patients with Depression and Personality Disorder. (Abbass et al, 2011). Abbass A, Town J, Driessen E (2011). The efficacy of short-term psychodynamic psychotherapy for depressive disorders with comorbid personality disorder. Psychiatry, 74(1), 58-71.	publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. During the consultation period it was identified that 12 studies had been included in the guideline that were published after the search cut-off date; June 2016. These were studies that had been identified by guideline committee members, rather than the searches. It was therefore necessary to remove the studies that had been erroneously included as we could not ensure systematic identification of all potentially relevant studies after this date. Town 2017 was one of the studies that was removed from the guideline. A review of the outputs of all affected analyses suggested that the removal of the studies did not substantially affect the results of those analyses. . The use of the term TRD in the context of

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					your comments applies to a much wider population than that covered by the term as used in this guideline and by most investigators in this area. The definition in this guideline is limited to participants who have had two antidepressant trials of adequate doses and duration and have not responded. This definition is not without its problems and we have made some changes to the structure of our recommendations in light of feedback from stakeholders on this issue. However, your definition is much broader encompassing chronic and complex depression which we deal with separately. We are not able to make any recommendations on Intensive Short-term Dynamic Psychotherapy (ISTDP) as we did not find sufficient evidence to support the conclusion in your comments. **Complex depression** The Abbass 2011 systematic review had been identified and searched for relevant references prior to consultation and was the source of 2 studies included in the complex depression review (Hellerstein 1998 and Liberman 1981). However, the committee did not think the evidence from these studies supported making a recommendation for STPT in complex depression.

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Royal College of Psychiatrists	Full	97 77 225 245	12-14 41-44 23-25 28-31	**Long term psychodynamic psychotherapy** Although the experiences of treatment section is not proposed to be updated, it is now inaccurate. For example, On it states: "The service use and carer topic group do acknowledge, however, that as there has been little research into the efficacy of long-term psychodynamic therapy, it cannot be recommended as a course of treatment in this guideline" – this statement should be amended given there is now as an evidence base (Leichsenring & Rabung 2008, 2009, 2011; Leichsenring et al, 2013; Fonagy et al. 2015; Knect et al, 2016) Some patients express a preference for psychodynamic psychotherapy: Personal account E: *Over the last 2 years I have paid privately to see a psychotherapist and had psychodynamic therapy. This has been the most helpful in terms of trying to repair and understand the damage I experienced as a child. Financially, though, this has been difficult, and I have had to get another job, in addition to my full time job to pay for this.* However, it is assumed not to be cost-	Thank you for your comment. As you note, the patient experience section was not included in this update and therefore the content from the 2009 guideline has been reproduced in line with NICE processes. As the evidence in this area has not been reviewed it is not possible for us to make any changes to the recommendations. However as the text you cite is now factually incorrect we have removed it from the guideline. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The text in the guideline has been updated as a result and no longer contains the text that you quote. Thank you for bringing these references to our attention. Fonagy 2015 is included in the further-line treatment review. Leichsenring 2008 and Leichsenring 2011

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				effective: "*Long-term psychodynamic psychotherapy showed a large benefit and was ranked fourth in both the SMD and response in those randomised analyses; no remission data were available for long-term psychodynamic psychotherapy.* *The GC noted that, although long-term psychodynamic psychotherapy ranked in a higher place than CBT and behavioural therapies, this was not included in the economic analysis due to lack of suitable data, but, nevertheless, it was very unlikely to be cost-effective, given its high resource use intensity.* This assumption is not substantiated due to the lack of available evidence and longer term treatment may be more cost effective in the long run in reducing rate of relapse and better long term outcomes. Hence the need to recommend more studies in this area. References Leichsenring F, Rabung S. Effectiveness of long-term psychodynamic psychotherapy: a meta-analysis. *JAMA* 2008; **300:** 1551–65.	systematic reviews were searched for relevant references but no additional studies that met the inclusion criteria were identified. Leichsenring 2009 and Leichsenring 2013 could not be included as they do not meet the study design criteria (not an RCT or systematic review of RCTs). Knekt 2016 could not be included as it is a secondary paper with follow-up outcomes only. The primary paper (Knekt 2004) could also not be incuded as it was a book.

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				Leichsenring F, Rabung S Analyzing effectiveness of long-term psychodynamic psychotherapy reply. *JAMA* 2009; **301:** 932-3. Leichsenring F, Rabung S. Long-term psychodynamic psychotherapy in complex mental disorders: update of a meta-analysis. Br J Psychiatry 2011; **199:** 15–22. Leichsenring F, Abbass A, Luyten P, Hilsenroth M, Rabung S. The emerging evidence for long-term psychodynamic therapy. Psychodyn Psychiatry 2013; **41:** 361–84. Knekt P, Virtala E, Härkänen T, et al. The outcome of short- and long-term psychotherapy 10 years after start of treatment. *Psychol Med* 2016; 1-14 Fonagy P, Rost F, Carlyle J-A, Mcpherson S, et al. Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study (TADS). *World Psychiatry* 2015; **14:** 312-21.	
Royal College of Psychiatrists	Full	General P202		**Problems with dividing trial populations by categorising baseline severity simply as more severe or less severe.**	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for

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		onwards		We have concerns regarding the draft consultation's method of dividing trial populations by categorising baseline severity simply as more severe or less severe, as this may lead to conclusions or recommendations in which potentially valuable treatment effects are ignored. The rationale for this is: • The draft guidelines make an assumption that different rating scales are equivalent in terms of their scores, an assumption for which there is little evidence. • Trials are categorised in the draft revision by using mean patient scores rather than ranges of individual ones. This means that trials can be assigned to "less severe" by being, for example, ≤ 1 point below the chosen threshold mean, while another is assigned to "more severe" merely by being ≥ 1 point above it, despite several trials have essentially identical patient populations, with large overlaps of the baseline scores of individual patients. Furthermore, individual patient's symptom scores fluctuate greatly over time but the	response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and

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				revision does not take account of follow-up and follow-along data. Measures of social functioning and quality of life are not included in guideline's baseline severity scores, despite these being important areas of disability that exist in depression. • Patients whose baseline is classified as very severe are more likely to have a poorer prognosis because of the complexity or chronicity/treatment resistance of the depressive disorder and are therefore less likely to achieve full remission (e.g. the STAR-D study) so it is necessary to take partial remission rates into account as well. References Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology,* 59, 12-19. Trivedi, M.H; Rush, AJ; Wisniewski, SR, et al: Evaluation of outcomes with citalopram for depression using	moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee was also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterized. In doing so they took into account a number of factors including what other factors had been considered important

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				measurement-based care in STAR*D: implications for clinical practice. American Journal of Psychiatry 163:28–40, 2006	in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline.

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					As the two population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method

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					which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if two or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending

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					on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more

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					severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA. Thank you for bringing these references to our attention. Jacobson and Truax 1991 are not included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs). Trivedi 2006 could not be included as data were only reported for the group receiving citalopram.
University of York	Full	general	general	The GC has found that there was "potentially promising results" for acupuncture (Full version, Page 323, Line 8). For the treatment	Thank you for your comment. The text has been amended to clarify why acupuncture was not included in the NMA. This was

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				of new depressive disorders, the GC states, "For acupuncture, there was evidence of a statistically significant effect of acupuncture on depressive symptoms compared with SSRIs and higher rates of remission and response in those with less severe depression."(Full version, Page 322, Line 43). The GC has also reported that, using a NHS perspective, acupuncture in primary care in the UK was found to be a cost-effective intervention with an ICER versus treatment as usual of £4,731/QALY (2015 prices).(Full version, Page 236, Line 40). These attributes support the case for acupuncture to be included within the NMA. However the GC was concerned about the uncertainty related to several aspects of the acupuncture data. These comprise: a concern that the populations in acupuncture trials may differ from the general population in both networks, a concern that the acupuncture intervention may not be generalisable, a concern that most of the trials are low quality, a concern about potential harms, and a concern that the evidence that acupuncture is highly cost-effective is compromised by potentially serious limitations. In the information provided below, each of these concerns is directly addressed.	because the participants in acupuncture trials may have been selected populations that would be different from those in the more and less severe networks. In addition, the committee noted that a significant number of the studies on acupuncture were performed in healthcare systems that were very different to the UK where the use of acupuncture is more common place and expectations of treatment response are consequently likely to be higher. This may increase the likelihood of more positive outcomes. They also acknowledged that availability of appropriately trained and competent people to deliver acupuncture for the treatment of depression was limited and that there was uncertainty about the consistency of the methods for delivering acupuncture. The 'potentially serious limitations' of the economic analysis did not contribute to acupuncture not being considered in the NMA. The committee noted that in the large RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is considered from 2 RCTs that compared acupuncture with sham

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				Overall, there needs to be a level playing field, and the evidence on acupuncture appears as good as, if not better than the psychological and other physical interventions recommended by NICE. Indeed on several counts, the evidence on acupuncture is substantially better. See for example the decision by the GC to recommend behavioural couples therapy which has "very low quality evidence" (page 323 Line 22) and moreover the GC accepts their recommendation is being made despite there being "no available economic evidence on behavioural couples therapy" (Page 322, Line 31). Aside from the disproportionate weight given to the uncertainties around acupuncture, the relative benefits of acupuncture need to be clarified. Acupuncture needs to be compared to psychological and other physical therapies by including acupuncture in a revised NMA. Further explanations and rationale making the case for this are set out below.	acupuncture, no statistically significant benefit was observed on depression symptomatology. The committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS, the committee decided not to make a recommendation for its use. This information has been added to the 'evidence to recommendations' section in the full guideline.
University of York	Full	general	general	The GC highlight that they considered collaborative care as an intervention for treating depression, and that 'considerable new evidence has emerged since the publication of the previous guideline' (p104).	Thank you for your comment. In developing the recommendations for service organisation the committee were mindful of the problems that people with depression and, in particular, people with more severe

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				The GC identified and included 53 RCTs showing the beneficial effects of collaborative care for adults. The GC also note that there was evidence from a number of UK and international trials that there were clinical benefits associated with the use of collaborative care for adults (p132). Furthermore, the GC state that 'simple collaborative care is likely to be a cost-effective model for delivering services to adults with depression' (p130). Given the level of evidence about the beneficial effects of collaborative care for adults (note this is not limited to older adults or those with more severe depression), it is surprising that the GC limit their recommendation for collaborative care to older people, particularly if they have significant physical health problems or social problems (page 134). It is also surprising that the GC also limit their recommendation for the use of collaborative care as a method for the delivery of care for people with more severe depression (page 134). Given the level of evidence cited for the clinical benefits and cost effectiveness of simple collaborative care, it is important that recommendations for its adoption is made for adults with depression more generally, rather	depression have in accessing and engaging with services in both primary and secondary care. The committee therefore considered the evidence on collaborative care and decided that the provision of a simple model of collaborative care could be effective in ensuring both greater engagement with and uptake of services for people with more severe depression. Also, given that engagement issues are even greater in older adults, in particular those with physical health problems, and that there was evidence of the cost-effectiveness of collaborative care in older people with chronic physical health problems the committee agreed to recommend collaborative care for this group of people. However the committee were mindful of the outcomes of a range of interventions, for example guided self-help, where the effect sizes identified in the analysis were equivalent to or better than those identified for collaborative care in less severe depression. Therefore they did not recommend collaborative care for this group of people.

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				than being limited to older adults and those with more severe depression.	
University of York	Full	general	general	The GC outline important economic data on cost-utility analysis of simple collaborative care compared with usual care, derived from NIHR-funded and peer reviewed trials in the UK population. These all show that simple collaborative care is cost effective at the NICE cost-effectiveness thresholds for adults. Indeed, on page 312 the GC also state 'There is evidence from 3 UK economic evaluations conducted alongside RCTs that simple collaborative care is potentially a cost-effective model for delivering services to adults with depression', and that 'the published economic evidence indicated that simple collaborative care is likely to be a cost-effective model for delivering services to adults with depression' (p130). It is surprising that this important evidence on the cost-effectiveness of collaborative care, which is directly applicable to the UK context is not taken more into account in making the recommendations. The cost effectiveness evidence make a clear case for recommending collaborate care more broadly, rather than limiting such recommendations to older people and those with more severe depression. The recommendations should therefore be	Thank you for your comment. In developing the recommendations for service organisation the committee were mindful of the problems that people with depression and, in particular, people with more severe depression have in accessing and engaging with services in both primary and secondary care. The committee therefore considered the evidence on collaborative care and decided that the provision of a simple model of collaborative care could be effective in ensuring both greater engagement with and uptake of services for people with more severe depression. Also, given that engagement issues are even greater in older adults, in particular those with physical health problems, and that there was evidence of the cost-effectiveness of collaborative care in older people with chronic physical health problems the committee agreed to recommend collaborative care for this group of people. However the committee were mindful of the outcomes of a range of interventions, for example guided self-help, where the effect sizes identified in the analysis were equivalent to or better than those identified for collaborative care in less severe depression. Therefore they did not

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				extended to include all adults in general.	recommend collaborative care for this group of people. In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of

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					June 2016. During the consultation period it was identified that 12 studies had been included in the guideline that were published after the search cut-off date; June 2016. These were studies that had been identified by guideline committee members, rather than the searches. It was therefore necessary to remove the studies that had been erroneously included as we could not ensure systematic identification of all potentially relevant studies after this date. 3 of the 4 UK economic studies previously included on collaborative care have been removed from the guideline. A review of the outputs of all affected analyses suggested that the removal of the studies did not substantially affect the results of those analyses.
British Acupuncture Council	full	general	general	In respect of acupuncture, the critical decision in the guideline was that it should be excluded from the main analysis. Network meta-analysis (NMA) requires that the populations receiving the different treatments can be considered to be similar. The acupuncture studies are said to be suspect in this respect but we can find no information in the guideline to explain or support this decision. There may be a good reason for this exclusion but if this is not made public	Thank you for your comment. The text has been amended to clarify why acupuncture was not included in the NMA. This was because the participants in acupuncture trials may have been selected populations that would be different from those in the more and less severe networks. In addition the committee noted that a significant number of the studies on acupuncture were performed in healthcare systems that were very different to the UK where the use of

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				there will be the suspicion that once again NICE has not ensured a level playing field. In the low back pain guideline (2016) different rules were applied to acupuncture than to other physical therapies as to what constitutes an effective treatment, with the result that acupuncture's cost effectiveness never came into the reckoning. Again, here, its cost effectiveness is not considered when making recommendations. This is strange because cost-effectiveness is said to be a primary determinant. Presumably this is a corollary of exclusion from the NMA: no NMA means no economic modelling, and hence no relative cost-effectiveness. And yet cost effectiveness is discussed for Behavioural Couples Therapy (BCT): despite having no such data it gets a recommendation. Acupuncture has solid evidence of cost effectiveness but is rejected. The step-wise procedure in NICE guidelines requires that you first have to establish clinical benefits before reaching the economic trade-off. Acupuncture is generally agreed to be a very safe intervention (there is considerable published evidence on this) and the trial data indicate it may be superior to sham, SSRIs and counselling to a small extent and moderately better than treatment as usual. Certainly there should be cautions	acupuncture is more common place and expectations of treatment response are consequently likely to be higher. This may increase the likelihood of more positive outcomes. They also acknowledged that availability of appropriately trained and competent people to deliver acupuncture for the treatment of depression was limited and that there was uncertainty about the consistency of the methods for delivering acupuncture. The 'potentially serious limitations' of the economic analysis did not contribute to acupuncture not being considered in the NMA. The committee noted that in the large RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is compared from 2 RCTs that compared acupuncture with sham acupuncture, no statistically significant benefit was observed on depression symptomatology. The committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS,

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				attached to these conclusions but this is so for all of the treatments reviewed. Acupuncture is represented by seven trials with 1262 participants, the most directly relevant being a large, high quality UK study with n=755, that demonstrated superiority over both counselling and treatment as usual (TAU). The BCT evidence amounts to 5 trials with a total of only 256 participants. Despite this, the GC concluded that only BCT (of those interventions excluded from the NMA) appeared to provide improved clinical evidence outcomes. It's hard to give this statement much credence. The GC mitigated the very low quality evidence for BCT by claiming it to be 'less uncertain' than for other (NMA-excluded) interventions and more likely to be generalisable. By contrast acupuncture (with somewhat higher quality data) is suspect because: - There is no provider blinding: but this surely applies to most/all of the non-pharmacological interventions. - Study context impacts on the results in the four Chinese settings: but no explanation is provided for this	the committee decided not to make a recommendation for its use. This has been clarified in the 'evidence to recommendations' section. Thank you for bringing these references to our attention. Hopton 2014 could not be included in the review as this trial specifically recruited participants with a particular physical health condition in addition to depression and that is an exclusion criterion for this review. NHS 2017 and Hopton 2012 could not be included as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				supposition. - There is a lack of generalisability: again, there is no explanation for this concern. In summary, we find that a number of crucial decisions affecting how acupuncture is dealt with appear to have been made in an arbitrary fashion with no pre-determined or even explicit protocol to explain their basis. The decision to exclude acupuncture from the NMA meant that it would not be evaluated by comparison against other treatments; instead, it was subject to evidence interpretations that appear to be coloured by suppositions and suspicions rather than knowledge. We are also disappointed to see that once again in a NICE guideline there is no place for considering co-morbidity except in a very restricted sense: depression plus personality disorder. A large number of people with pain and musculoskeletal issues have coexisting depression and acupuncture appears to be particularly beneficial for this population and superior to psychological treatment (Hopton et al, 2014). We would strongly suggest that acupuncture is a good fit for current national health care initiatives aimed at bolstering wellbeing (Next steps on the NHS five year	

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				forward view, 2017). It increases the treatment options available to doctors and to the public and particularly meets the needs of those who are averse to drugs and/or psychological therapy. People with psychological conditions are already the second most frequent presenters to professional acupuncturists (Hopton et al, 2012). It is likely that endorsement by NICE would tend to encourage referral by GPs to private acupuncture practice (as currently for headaches) rather than the provision of, and payment for, specific acupuncture services on the NHS. **References** Hopton A, Macpherson H, Keding A, Morley S. Acupuncture, counselling or usual care for depression and comorbid pain: secondary analysis of a randomised controlled trial. BMJ Open. 2014 May 2;4(5):e004964. Next steps on the NHS five year forward view. NHS. 31 March 2017 Hopton AK, Curnoe S, Kanaan M, Macpherson H. Acupuncture in practice: mapping the providers, the patients and the settings in a national cross-sectional survey. BMJ Open. 2012 Jan 11;2(1):e000456	

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University of Exeter	Full	General	General	We are grateful for the Guideline Development Group for their extensive identification, appraisal and synthesis of this huge and varied dataset. In particular, we support the recognition that the evidence for Behavioural Activation, including from our own very large NIHR HTA 'COBRA' non-inferiority trial of BA vs CBT, now places BA as a fully viable and effective front-line therapeutic choice for patients. More choice for patients in the treatment of depression is to be applauded. Equally, the inclusion of our CADET trial in the recommendations has we feel led to better recommendations regarding collaborative care. However, we would like to make the following comments: The two different methods of systematic review and network meta-analyses used by the guideline group has led to inconsistency in the recommendations. For example, our group's two major depression trials – CADET for collaborative care; COBRA for BA and CBT – are treated differently in the data reviews despite these trials being of the same population, with baseline clinical and demographic criteria being essentially identical. However, CADET is used to feed	Thank you for your comment. The guideline developed review questions around different issues. For CADET the trial was included in the review question on organisation of services where severity of depression was not a factor in determining the allocation of the study. The COBRA trial has been removed from the guideline as it was included in error. In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final

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				recommendations for an overall population of depressed people whilst COBRA is fed into the less severe treatment analysis. In our view, the latter is an incorrect use of our data. Whilst the baseline means of both trials are below 18 on the PHQ-9, in fact the distribution of participants' baseline scores places more participants above 18. Whilst this is of no consequence for CADET and collaborative care, given the guideline uses that data to make recommendations for all patients, it is a very severe misapplication of our COBRA data in the treatment analyses: • 247/440 (56%) of COBRA participants scores were above the 18+ cut off, with 193/440 (44%) below it We might also point out that all our participants (COBRA and CADET) were assessed by a diagnostic interview to exclude those with mild/sub-syndromal conditions. Therefore, our COBRA trial actually contains a greater proportion of participants *above* the guideline's 18+ severity cut off than below it. This means that for the purposes of the guideline network meta-analysis our results are at least, if not more, applicable to patients with severe depression than those with a less severe disorder. In fact, the guideline uses	analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. During the consultation period it was identified that 12 studies had been included in the guideline that were published after the search cut-off date; June 2016. These were studies that had been identified by guideline committee members, rather than the searches. It was therefore necessary to remove the studies that had been erroneously included as we could not ensure systematic identification of all potentially relevant studies after this date. COBRA was one of the studies that was removed from the acute treatment NMA. A review of the outputs of all affected analyses suggested that the removal of the studies did not substantially affect the results of those analyses. Unfortunately we cannot include mediator analyses in the review of relative efficacy as these do not match the review protocol inclusion criteria.

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				data from participants with more severe depression to make recommendations about the treatment of people with less severe depression. This is a very severe error in our view. Even more ironical is that the guidelines actually recommend collaborative care for people with more severe depression. Our CADET trial included Behavioural Activation as the psychological treatment in our collaborative care model. The consequence of these irregularities is that data from two trials of the same population (depressed people in primary care) receiving the same treatment (Behavioural Activation) is used inconsistently – CADET for severely depressed people as part of collaborative care; COBRA for less severely depressed people. Given our CADET process analysis published in the HTA report showed that the only mediator of outcome was the Behavioural Activation component of collaborative care, this inconsistent analysis is extremely significant. Finally, our full NIHR-HTA Journal report now published (Richards et al, 2017) contains data on moderators of treatment, including	Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the two are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between the two types of treatments. Full details of the committee's' rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).

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				within group treatment effect moderation, which indicates BA may be slightly *more* effective than CBT for participants with severe depression. This direction of effect is consistent with previous data from other historical trials. We would also like to point out that overall our CBT in the COBRA trial was equally effective as BA. The arguments above as to the merits of BA for more severe depression, therefore, also apply to CBT. We contend, therefore, that the COBRA trial in particular has been rather unfortunately skewered by the guideline's severity classification system and that, notwithstanding the population mean, because slightly more than 50% of our participant population lie in the 'more severe' range the COBRA trial results (for both BA and CBT) are actually more applicable to this 'more severe' group of patients. Ironically, the guidelines now offer conflicting advice to services – deliver BA to severe patients as part of collaborative care; deliver BA to less severe patients. With respect, we think this is a muddle. We think our data shows that BA should be offered as a routine treatment to severely depressed (PHQ-9 18+) patients, not merely if other options are refused.	

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				We do, however, note that the guidelines include BA with CBT and IPT as a recommended treatment for this group and we agree with this recommendation. Nonetheless, we are concerned that patients with depression classified as 'more severe' may not be offered, and indeed be denied, the possibility of benefit from a treatment (BA) that we have shown to be as effective as CBT and which is potentially more cost effective. The absence of our COBRA data from the guideline's analysis of outcomes in 'more severe' depression and a careful reading of the network meta-analysis results could lead to a general impression that BA is less helpful for this group of patients. The reverse is actually true. **Recommendation** Given the international significance of both the Guideline and the COBRA trial we would like to recommend that NICE conduct a sensitivity analysis in which the COBRA results are placed in the 'more severe' range in order to assess whether the apparently less favourable results (from very low n) for BA would be altered by its inclusion. NICE might also conduct the same sensitivity analysis with reference to the equally	

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				effective CBT arm of our COBRA trial. Secondly, we would suggest that some reference in the guideline's explanatory text, should be made to the possibility that BA may be a viable first line treatment for 'more severe' depression, and that you cite the COBRA trial as evidence for this proposition. We think it is extremely important that COBRA is given an explanatory context, including reference to the split across severity categories, given the very substantial public investment from the UK NIHR HTA board in the COBRA trial. **References** Richards DA, Rhodes S, Ekers D, McMillan D, Taylor RS, Byford S, *et al.* Cost and Outcome of BehaviouRal Activation (COBRA): a randomised controlled trial of behavioural activation versus cognitive behavioural therapy for depression. *Health Technol Assess* 2017;21(46) Richards DA, Bower P, Chew-Graham C, Gask L, Lovell K, Cape J, et al. Clinical effectiveness and cost-effectiveness of collaborative care for depression in UK primary care (CADET): a cluster randomised controlled trial. *Health Technol Assess* 2016;20(14).	

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				Please note that whilst I have sent these comments from the University of Exeter, they do not include members of the COBRA and CADET trial teams who are members of the Guideline Development Group and are conflicted.	
CHESS (Centre for Humanities Engaging Science and Society), Durham University	Full	General		We find it deeply regrettable that the service user experience evidence was not was not updated for the Draft Revision. **We strongly suggest:** • The Revision should update this section and improve its quality taking the comments below into account. It should then fully integrate the more recent findings of this type of research into its treatment recommendations. More recent literature extends client experience data to under-represented groups. It takes account of changes in socio-economic and cultural circumstances. This should be incorporated by means of a meta-ethnography synthesis **Justification:** • A great deal of research on experiences of depression of patients	Thank you for your comment. The proposal not to include the experience of care section in this update was consulted on with registered stakeholders at the time of consultation on the draft scope. As this section was not included in the update we are not able to make the changes that you suggest or include the references that you have highlighted.

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		P68		and carers has been published since 2004 and this literature has been wrongly ignored by the GDG. Some of this literature is listed below • There were serious limitations in the patient experience data collected for the previous guidelines. These should have been corrected. Thus, no demographic details are given for the 38 individuals whose accounts were taken from Healthtalkonline. It is unclear which elements of the population were represented. The extent to which the data represents under-represented populations such as BME, men, older adults, non-heterosexual clients is unclear. More recent literature extends client experience data to these under-represented groups. It should be incorporated in a meta-ethnography style synthesis (which the University of Essex Health and Care Research Service could be commissioned to produce). • P68 summarises the findings of previous qualitative analysis: "*Although the 6 questions were aimed*	

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		P97		*at people with any form of depression, all of the personal accounts received were from people who have/have had severe and chronic depression, spanning many years. The themes that are most frequently expressed in the testimonies include trauma or conflict in childhood as a perceived cause of depression; the need for long-term psychotherapy for people with severe and chronic depression; the need to take personal responsibility for and understand the illness to improve outcomes; issues around diversity; paid and unpaid employment as an important part of the recovery process; the negative impact on daily functioning; concerns regarding stigma and discrimination in the workplace; and the relationship between people with depression and professionals."* These important points are reiterated in other qualitative studies in which service users are consulted. Yet these key themes are not taken account of in the design of the guideline or its recommendations. No	

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		P100		recommendations are made relating to reducing stigma. • The experience of depression is intertwined with the social and economic context in which people live. It relates to levels of community cohesion, economic circumstances, social support, loneliness etc. The social and economic context in the UK has changed both since 2004 and 2009. There is evidence of the impact of austerity on depression. Many clients with depression have been significantly affected by reductions in benefits, changes to employment conditions, and political choices. • There have also been changes which impact on the extent to which stigma features in client narratives. Campaigns such a Time to Change may or may not have had an impact on stigma. The Draft implicitly assumes that this has remained static. There have been significant policy changes which could have impacted on experiences of carers. The Carers Act 2014 has come into	

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				law and there have also been many negative changes made to benefits available to carers (e.g.). These major changes to carers' rights as well as their benefits entitlements and social context mean that it should not be assumed carers' experience would be much the same as in 2004 or 2009. • P97 Notes experiences of psychological therapy: *"There was a strong feeling within the service user and carer topic group that the excerpt from Howe (1995) in the section above highlights the reasons why many people opt for private therapy; that is, that psychological treatment offered by the NHS in the form of CBT does not go far enough in addressing the trauma experienced in childhood. The study by Ridge and Ziebland (2006) confirms the opinions of the topic group and the testimony from the personal accounts that people with 'deep and complex problems felt the need for longer term therapy'. Those that have had long-term psychodynamic therapy report*	

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				that it has been helpful in their understanding of themselves and their depression and that until they have worked through and repaired the damage experienced in childhood, depression will be a major factor in the person's life. The service user and carer topic group do acknowledge, however, that as there has been little research into the efficacy of long-term psychodynamic therapy, it cannot be recommended as a course of treatment in this guideline" • This last comment was true when it was made many years ago. Since then studies have been carried out on psychodynamic and psychoanalytic psychotherapies for long term depression (Fonagy et al, 2015; Town et al, 2017). It is important to connect the neglect of this data to how the Draft is constructed and its recommendations. If this perspective from service users had been really considered in the current Draft, its recommendations would have reflected this. They do not.	

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				• None of the recommendations (p100) deriving from service user and carer experiences relate to interventions. **Suggested Literature** McPherson S, Rost F, Sidhu S, Dennis M (under review) Non-strategic Ignorance: Making Sense of a Randomised Controlled Trial of Psychodynamic Psychotherapy. • Carers experiences: Priestly J & McPherson S (2016) Experiences of Adults Providing Care to a Partner or Relative with Depression: A Meta-Ethnographic Synthesis. Journal of Affective Disorders DOI: http://dx.doi.org/10.1016/j.jad.2015.12.011 which concludes the needs for: "couples and systemic therapy at initial stages of management addressing stigma to help those overcoming challenges of caring for their partner or relative and self-compassionate approaches for caregivers who may need support to look after themselves, avoid feelings of guilt and move forward towards acceptance" • Service users: Smith JA, Rhodes JE. 2014 Being depleted and being shaken: An interpretative phenomenological analysis	

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				of the experiential features of a first episode of depression. Psychol Psychother. doi: 10.1111/papt.12034 van Grieken RA (1), Beune EJ (2), Kirkenier AC (3), Koeter MW (3), van Zwieten MC (4), Schene AH (5). 2014 Patients' perspectives on how treatment can impede their recovery from depression. J Affect Disord. 2014 Oct; 167:153-9. doi: 10.1016/j.jad.2014.05.065 Alderson SL (1), Foy R, Glidewell L, House AO. 2014 Patients understanding of depression associated with chronic physical illness: a qualitative study BMC Fam Pract. 20; 15:37. doi: 10.1186/1471-2296-15-37. DeJean D, Giacomini M, Vanstone M, Brundisini F. 2013 Patient experiences of depression and anxiety with chronic disease: a systematic review and qualitative meta-synthesis. Ont Health Technol Assess Ser. 1;13(16):1-33. Oliffe JL (1), Rasmussen B, Bottorff JL, Kelly MT, Galdas PM, Phinney A, Ogrodniczuk JS 2013 Masculinities, work, and retirement among older men who experience depression Qual Health Res. 23(12):1626-37. doi: 10.1177/1049732313509408	

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				Within the boundary fence: an investigation into the perceptions of men's experience of depression in rural and remote areas of Australia Aust J Prim Health.;20(2):162-6. doi: 10.1071/PY12106 Sandhu A (1), Ives J, Birchwood M, Upthegrove R 2013 The subjective experience and phenomenology of depression following first episode psychosis: a qualitative study using photo-elicitation. J Affect Disord.;149(1-3):166-74. doi: 10.1016/j.jad.2013.01.018 Brenne E (1), Loge JH (1), Kaasa S (1), Heitzer E (2), Knudsen AK (1), Wasteson E (1); European Palliative Care Research Collaborative (EPCRC).2013 Depressed patients with incurable cancer: which depressive symptoms do they experience? Palliat Support Care.11(6):491-501. doi: 10.1017/S1478951512000909.Epub 2013 Feb 7. Anderson C (1), Roy T. 2013 Patient experiences of taking antidepressants for depression: a secondary qualitative analysis Res Social Adm Pharm. Nov-Dec;9(6):884-902. doi: 10.1016/j.sapharm.2012.11.002	

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Hyperparathyroid UK Action	Full	general		How do I let go of the anger I feel at being misdiagnosed? We can't change the past, I	Thank you for your comment and for providing this information. This guideline is

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4 Change				don't intend to end up bitter and let this define who I am for the rest of my life BUT, we can try to ensure that others don't travel the journey that we all have and make a difference. 26 years of undiagnosed PHPT (and kidney stones).	about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis of hyperparathyroidism or the management of depression associated with hyperparathyroidism. NICE is currently developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	general		I'm really struggling with depression at the moment I've been thinking of seeing my GP for some antidepressants. It just feels like a dark mood that seems to come over me for no apparent reason which I can't seem to snap out of. I have hyperparathyroidism and am waiting to see a surgeon.	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis of hyperparathyroidism or the management of depression associated with hyperparathyroidism. NICE is currently developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of

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					interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	general		I descended into the depths of depression and anxiety following a knee replacement operation. At first I thought I had post-operative depression and although the knee recovered as expected, I didn't. I got more and more depressed and anxious which was something I had never experienced before. It was a 'raised' calcium reading of 2.6 from an incidental routine blood test that began to suggest hyperparathyroidism.	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis of hyperparathyroidism or the management of depression associated with hyperparathyroidism. NICE is currently developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.

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Hyperparathyroid UK Action 4 Change	Full	general		I was diagnosed with mild depression with anxiety in 2010 or 2011. I think my vit D was checked 1 or 2 years after because my joints and muscles were getting increasingly painful. It was low and their solution was "take vit D". When that didn't help I went to a pain specialist, who diagnosed me with fibromyalgia. Nothing he gave me ever helped long term so I've been wondering if it's been PHPT all along. No one ever made the link. My calcium wasn't checked until I saw the pain specialist.	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis of hyperparathyroidism or the management of depression associated with hyperparathyroidism. NICE is currently developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	general		I've suffered with depression for about 10 years on & off but been really bed the last 2 & half years. I have hyperparathyroidism. I am waiting for surgery,	Thank you for your comment and providing this information.
Hyperparathyroid UK Action 4 Change	Full	general		I really want a proper screening system in place, were when someone presenting with depressive systems is not just treated for depression but further investigation is done into physical causes.	Thank you for your comment. This guideline is about the treatment and management of depression in adults. It is outside the scope of this guideline to make recommendations on diagnosis and assessment for people who have depression as a symptom of

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					another condition. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	general		I believe depression can be a symptom of other conditions and should not always be a final diagnosis without further investigations for medical causes of depression.	Thank you for your comment. This guideline is about the treatment and management of depression in adults. It is outside of the scope of this guideline to make recommendations on depression that is a symptom of another condition. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	general		It is recognized in young people that some anti-depressants will give the side effect of 'suicidal thoughts' and should be monitored for. I have had so many side effects from all the meds I have been on. That is why I feel those thoughts were a side effect of those meds. Plus now having been diagnosed with fibromyalgia, that condition makes sufferers more sensitive to meds.	Thank you for your comment and providing this information. We are aware of the issues that you raise and the guideline includes recommendations about risk assessment and monitoring for people with depression.
Hyperparathyr	Full	gener		Please be aware of hyperparathyroidism with	Thank you for your comment and providing

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oid UK Action 4 Change		al		Depression in Adults. A well-publicised study by an American Psychologist states findings that one in four people with depression have hyperparathyroidism.	this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	general		Lithium induced hyperparathyroidism is well documented and is associated with hyperplasia (all glands affected). Patients treated with lithium commonly develop mild hypercalcemia. Lithium increases the set point for PTH suppression. Hypercalcemia usually but not always resolves if therapy with lithium is discontinued.	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest.

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					However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms. We have also added more details to our recommendations about lithium monitoring.
Janssen	Full	General	General	We recognise the difficulties of trying to undertake a NMA across different interventions in depression, however, we are concerned that trials have been combined despite there being significant variation between studies. We see the GDG have explored the statistical heterogeneity between studies. However, we have noticed from reading the full guideline the following differences between studies, which taken together adds to potential significant variation between studies which could impact the relative treatment effects between studies. These include: • Attempts by the GDG to identify cut offs to determine disease severity across studies (pg. 201-203), • Assumptions used to decide relevant outcomes measures between studies (pg.207-210), • Differences in trial design and population, notably psychological and	Thank you for your comments. Variation in studies is an issue that needs to be addressed whether studies included in a systematic review are synthesised in NMA or in pairwise meta-analysis. Variation in populations, interventions and study designs across studies included in meta-analysis increases heterogeneity. With a dataset of 366 studies included in the systematic review, heterogeneity was not unexpected. The NMA controlled for a large part of heterogeneity, as you have noted in your comment (by splitting populations with less and more severe depression; using detailed treatment definitions [including treatment intensity and mode of delivery for psychological interventions] and categorising them using a class random effects model). Model fit and between-study heterogeneity, as well as inconsistency between direct and indirect evidence was formally assessed for each network. Other potential effect modifiers, such as age and setting (inpatient

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				pharmacological studies (pg.232, ln.5-17) • Differences in trials being studied in primary and secondary settings (pg.163, ln. 9-21) • Variation in the interventions received for classes or groups of interventions (pg. 206, ln. 1-32) • Differences in when the studies were conducted, with significant variation with studies ranging from 1981-2016 (Appendix T) We are also concerned that there is no discussion regarding the length of follow up. Given the differences in follow up between interventions in the clinical studies. This is likely to have an important impact on study results, especially when comparing across pharmacological and psychological interventions. Whilst also noting that the evidence for several of the psychological treatments consist of a single trial with limited numbers of patients. Therefore, increasing the risk that the treatment effects in those studies may have occurred by chance rather than being powered to detect for meaningful differences within those trials. We note that there has been limited use of sensitivity and scenario analyses to control	vs outpatient) were assessed in sub-analyses, using pairwise meta-analysis. All these parameters and statistical assessments were taken into account by the committee when interpreting the results of the NMA and making recommendations. The alternative option to NMA would be conducting hundreds of pairwise, independent comparisons of interventions included in this dataset. However, the majority of interventions included in the review have not been compared with each other in head-to-head trials. Therefore, in order to make conclusions on the most effective interventions, the committee would need to implicitly make indirect comparisons by comparing direct effects of interventions versus a common comparator, which would again raise issues about heterogeneity, without any formal, coherent statistical assessment of its presence. Moreover, without conducting NMA it would have been impossible to make simultaneous inference on all treatments examined in head-to-head trial comparisons, which is essential in order to undertake formal economic modelling. In turn, formal economic modelling was necessary for the assessment of the relative cost effectiveness of all treatment options. Cost effectiveness is a central consideration

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				for differences between trials. We strongly suggest that the NMA is thoroughly tested to ensure that relative treatment effects are consistent across different analyses given the significant variations and heterogeneity in trials. Any recommendation regarding specific intervention should note the inherent uncertainty in the evidence networks seen with the NMAs. We do not believe the NMAs should currently be used as the basis for making strong recommendations regarding the relative effectiveness of interventions, but only to inform a range of interventions to be recommended. This will allow clinicians to make appropriate decisions from a range of effective interventions without relying entirely on less than perfect NMAs.	underpinning NICE recommendations. Prioritisation of clinical outcomes and of depressive symptom scales would occur whether a NMA or a pairwise meta-analysis was conducted. Determination of clinical outcomes is an essential element of any systematic review. Prioritisation of depressive symptom scales was necessary as it was not possible to extract all available scale data from the 366 studies included in the NMA. We are not sure what you mean by "Variation in the interventions received for classes or groups of interventions (pg. 206, ln. 1-32)" and why you identify this as a problem. This text refers to inclusion of additional studies that compared an intervention of no interest per se, but which belonged to a class of interest, with another intervention belonging to a class of interest. These studies were included in the NMA to allow connectedness of all interventions and classes of interest in the network. Differences between participants in pharmacological and psychological trials regarding preference for one type of treatment over another are possible, although, as highlighted in the same paragraph in the guideline, a number of trials included in the NMA recruited participants who were willing to be randomised to either

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					a pharmacological or psychological intervention. Potential differences in the population that might affect transitivity of effects were considered by the committee when interpreting the results of the NMA. Differences in the years in which studies were conducted (1981-2016) is true of any systematic review; there was no rationale to exclude older studies from the systematic review or the NMA, as there would be no rationale to exclude a priori older studies if we had done a pairwise meta-analysis. Regarding the length of follow-up, all data were obtained at treatment endpoints, regardless of duration of treatment. This has now been clarified in the full guideline. The committee was of the view that it is relevant and appropriate to compare interventions at treatment endpoints, following completion of a full course of treatment, in order to compare the effects of treatments as they would be provided in optimal clinical practice. The duration / intensity of treatments was captured in the economic analysis, in the estimation of intervention costs. We acknowledge the difference in treatment course duration between pharmacological and psychological interventions, but course duration is inherent in the type of intervention rather an effect

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					modifier. We agree that the evidence for several psychological interventions consisted of a single trial (or only few) with very small numbers of patients. This was a limitation of the evidence base and not of the NMA per se. The very limited evidence base for some of the interventions would also be a problem had a pairwise meta-analysis been conducted. Nevertheless, the NMA enabled use of all available evidence and improved precision by allowing combination of direct and indirect comparisons. Moreover, the NMA enabled the use of a class model, where the effects of individual interventions were pooled into a more robust and precise class effect, while interventions retained their own intervention effects. The uncertainty of the relative effects informed by few or small studies was reflected in the uncertainty (Credible Intervals) around the relative effects. Some interventions that were represented by very few and small studies demonstrated extreme, implausible effects in the primary studies, which were subsequently 'transferred' in the NMA, but these extreme results would also have been obtained if pairwise meta-analysis had been attempted. This is a flaw of the primary studies, not of the NMA per se.

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					Nevertheless, the committee took into account the results of the NMA in the context of the available evidence (both its quantity and its quality). Results on classes and interventions tested on a small number of people were treated with great caution and the total number of people randomised to each class/ intervention across the NMA studies was taken into account when making recommendations. The economic analysis was also updated following consultation and included only classes that had been tested on at least 50 people in every main outcome considered in the economic analysis (i.e. discontinuation, response in completers, remission in completers). All NMA results were assessed for their plausibility, using the committee's expert judgement. Although inconsistency models and analyses adjusting for small study size were conducted, it was not feasible to run additional sensitivity and scenario analyses to control for differences between trials. Heterogeneity across trials was accounted for by splitting populations in two different NMAs according to their level of symptom severity and by categorising interventions according to their specific characteristics, mode of action, intensity and mode of delivery. Low to moderate heterogeneity was

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					found in the majority of analyses. Where high heterogeneity was found (most notably in response and remission in completers in people with more severe depression), this was highlighted and taken into account be the committee when interpreting the results and making recommendations. Other potential differences in the trials were either assessed in pairwise meta-analysis (age and settings) or were qualitative considered by the committee when interpreting the results and making recommendations. The NMAs have not been used as the basis for making strong recommendations for any intervention. A range of interventions have been indeed recommended, after taking into account the NMA results including the uncertainty surrounding mean effects, the size and the quality of evidence, the plausibility of the results for each intervention, the characteristics and comparability of the participants in the RCTs, the relative cost effectiveness of interventions, their harms, patient characteristics and preferences.
Janssen	Full	General	General	We note that no NMA has been conducted for a population of adults whose depression has not responded or there has been limited response to previous treatment(s) for the	Thank you for your comment. We have considered conducting a NMA of interventions for people who have failed treatment. However, the study population is

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				current episode. We are seriously concerned that the GC have extrapolated the relative effectiveness results from a population receiving first line treatment to a population that has failed treatment. This in our view is not evidence based and worse maybe putting patient at risk. In section, 8.7.2 and 8.7.3 [Full Guideline], we note that: • 'GC drew on the evidence for first line treatments particularly in more severe depression where combination treatment was more clinically and cost-effective than medication alone. For people who had not responded to an initial psychological therapy the GC recommended a combination with medication, either adding an SSRI (for example, sertraline or citalopram) or mirtazapine. In developing this recommendation, the GC again drew on the evidence for first line treatments particularly in more severe depression where combination treatment was more clinically and cost–effective than medication alone. [pg. 500, ln 2-9].' • 'GC acknowledged that the economic evidence in this area is sparse and has limitations, and decided to draw	highly heterogenous, comprising people who have not responded to specific pharmacological, psychological or combined interventions and therefore a NMA was not appropriate to undertake. For example, it would not be appropriate to include in the same NMA people who have not responded to a SSRI (but may be treatment-naive to other drugs and psychological therapies) to people who have not responded to CBT (who may be treatment-naive to other psychological interventions and other drugs). When considering what psychological therapies to recommend for people who had no or limited response, the committee drew on the evidence base for first line treatment of more severe depression. This was because the committee agreed based on their expert knowledge and experience, that if a person hadn't responded to treatment they would need a treatment that had been identified as being effective for the majority of people with more severe depression. These were CBT, BA and IPT.

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				additional information from the economic analysis of treatments of a new depressive episode that was undertaken for the guideline. We believe that a NMA should be conducted in population that has failed treatment, as we do not believe the relative treatment effects between interventions will necessarily be consistent across different populations. This would ensure appropriate evidence is generated in this population who have failed previous treatments and that patients receive evidence based effective treatments.	
University of Essex	Full	342-584		The exclusively pharmacological criteria used to define TRD in the Draft, and its general application of the medical-model parameters of the short-term studies typically associated with drug treatments to psychological interventions, skew the Draft's analysis of the findings of studies of psychological treatment approaches to this group of depressive disorders. As a result, valuable benefits are blocked out. Again, the study of Fonagy et al (2015) is a case in point: based on a psychological model of "TRD" (and Chronic Depression) rather than applying an antibiotic model of drug resistance, it examined the benefit of LTPP (long-term psychoanalytic psychotherapy); at two-year follow-up, a clear difference had emerged in favour of the test	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited

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		342 Tables 119-121 Tables 119-121	Line 14 onwards	treatment, a difference the Draft fails to note. We suggest: • that the Revision should adopt a more nuanced approach to TRD. It should fully recognise the psychological and psychosocial theories of poor responses to drug treatments that exist. It should apply standards to grading RCT's of these treatments that are appropriate (for example, recognising that it is impossible to conceal allocation in respect of psychological treatments) and as well that long-term follow-up of any end of treatment effects reported is essential. • And/ Or to reassign studies like Fonagy et al (2015) to the Chronic Depression section (or combine TRD with chronic depression **Justifications:** • The definitions given of TRD (8.1.2) are exclusively pharmacological requiring operationalisation of dose and duration monitoring. They imply that the inadequate response to the agent was immediately recent or current. Trials in this category generally establish TRD solely by	response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression

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				means of a medical-model operationalisation. For example, the Kocsis (2009) criteria read: "Inadequate response to 12 weeks of antidepressant medication according to a pharmacotherapy algorithm. Inadequate response defined as failing to meet criteria for remission (≥60% reduction in HAMD score, a HAMD total score<8, and no longer meeting DSM-IV criteria for MDD for 2 consecutive visits during weeks 6 through 12)". Watkins (2011a) criteria similarly read "Inadequate response (score≥8 on the 17-item Hamilton Depression Rating Scale for Depression [HAMD] and score≥9 on the Beck Depression Inventory [BDI-II]) to antidepressant medication taken at a therapeutic dose as recommended by the British National Formulary and/or equivalent to 125 mg of amitriptyline for at least 8 weeks continuously during the current episode and within the past 2 months". All the studies in this category have these detailed medical criteria for defining TRD except for Fonagy et al (2015). The latter	and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. Fonagy et al 2015 cites their inclusion criteria as "at least two failed treatment attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a psychological intervention". This meets the inclusion criteria for our review questions on further line treatment and hence it was included in those reviews. Fonagy et al 2015 does not report the proportion of people with comorbid personality disorder. We were not able to determine if it met the inclusion criteria for the review on complex depression and consequently it was excluded from that review.

Organisation name	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				represents a fundamentally different approach to TRD/Chronic Depression. • Tables 119, 120 and 121 give more detailed information about trials included in the meta-analysis of augmenting the antidepressant with a psychological intervention versus continuing with the antidepressant-only (parts 1,2, and 3). This includes Fonagy et al (2015) as the Draft classes it as an 'augmentation strategy'. However, unlike the other trials in this class, Fonagy et al (2015) had a psychological model of the factors leading to poor responses to treatment interventions; as a pragmatic study, closely monitoring dose, duration, and responses to specific medications would introduce distortions, and so it was not done. There was no requirement in the inclusion criteria that the medication received need be recent or current: *ergo,* this study was not designed as an 'augmentation strategy'. The Draft Revision itself notes that the patient population studied by Fonagy et al (2015) meets its criteria for chronic	

Organisation name	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
				depression (J5 columns E and V. Following these criteria, it should be placed in that category). • In the row "Augmented/previous treatment", information on the antidepressant agented augmented is given for each trial. Fonagy et al (2015) provide a list of various previous treatments but since it is examining resistance to all forms of treatment it includes counselling and CBT and not only medication. There was no requirement that participants were currently or recently in receipt of medication. The intervention is not conceived as an 'augmentation' of medications and should not be misrepresented as though it did.	
CHESS (Centre for Humanities Engaging Science and Society), Durham University	Full	342-584		**T**he exclusively pharmacological criteria used to define TRD in the Draft, and its general application of the medical-model parameters of the short-term studies typically associated with drug treatments to psychological interventions, skew the Draft's analysis of the findings of studies of psychological treatment approaches to this group of depressive disorders. As a result, valuable benefits are blocked out. Again, the study of Fonagy et al (2015) is a case in point: based on a	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee

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				psychological model of "TRD" (and Chronic Depression) rather than applying an antibiotic model of drug resistance, it examined the benefit of LTPP (long-term psychoanalytic psychotherapy); at two-year follow-up, a clear difference had emerged in favour of the test treatment, a difference the Draft fails to note. We suggest: • that the Revision should adopt a more nuanced approach to TRD. It should fully recognise the psychological and psychosocial theories of poor responses to drug treatments that exist. It should apply standards to grading RCT's of these treatments that are appropriate (for example, recognising that it is impossible to conceal allocation in respect of these kinds of treatments) and as well that long-term follow-up of any end of treatment effects reported is essential. • And/ Or to reassign studies like Fonagy et al (2015) to the Chronic Depression section (or combine TRD with chronic depression. Justifications: • The definitions given of TRD (8.1.2) are exclusively pharmacological requiring operationalisation of dose	considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and
			28-30		
			Tables 119, 120, 121		
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		Tables 119-121		and duration monitoring. They imply that the inadequate response to the agent was immediately recent or current. Trials in this category generally establish TRD solely by means of a medical-model operationalisation. For example, the Kocsis (2009) criteria read: "Inadequate response to 12 weeks of antidepressant medication according to a pharmacotherapy algorithm. Inadequate response defined as failing to meet criteria for remission (≥60% reduction in HAMD score, a HAMD total score<8, and no longer meeting DSM-IV criteria for MDD for 2 consecutive visits during weeks 6 through 12)". Watkins (2011a) criteria similarly read "Inadequate response (score≥8 on the 17-item Hamilton Depression Rating Scale for Depression [HAMD] and score≥9 on the Beck Depression Inventory [BDI-II]) to antidepressant medication taken at a therapeutic dose as recommended by the British National Formulary and/or equivalent to 125 mg of amitriptyline for at least 8 weeks continuously during the current episode and within the past 2 months". All the studies in this	chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. Fonagy et al 2015 cites their inclusion criteria as "at least two failed treatment attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a psychological intervention". This meets the inclusion criteria for our review questions on further line treatment and hence it was included in those reviews. Fonagy et al 2015 does not report the proportion of people with comorbid personality disorder. We were not able to determine if it met the inclusion criteria for the review on complex depression and consequently it was excluded from that review.

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				category have these detailed medical criteria for defining TRD other than Fonagy et al (2015). The latter represents a fundamentally different approach to TRD/Chronic Depression. • Tables 119, 120 and 121 give more detailed information about trials included in the meta-analysis of augmenting the antidepressant with a psychological intervention versus continuing with the antidepressant-only (parts 1,2, and 3). This includes Fonagy et al (2015) as the Draft classes it as an 'augmentation strategy'. However, unlike the other trials in this class, Fonagy et al (2015) had a psychological model of the factors leading to poor responses to treatment interventions; as a pragmatic study, closely monitoring dose, duration, and responses to specific medications would introduce distortions, and so it was not done. There was no requirement in the inclusion criteria that the medication received need be recent or current: *ergo,* this study was not designed as an 'augmentation strategy'. The Draft	

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				Revision itself notes that the patient population studied by Fonagy et al (2015) meets its criteria for chronic depression (J5 columns E and V. Following these criteria, it should be placed in that category. • In the row "Augmented/previous treatment", information on the antidepressant agented augmented is given for each trial. Fonagy et al (2015) provide a list of various previous treatments but since it is examining resistance to all forms of treatment it includes counselling and CBT and not only medication. There was no requirement that participants were currently or recently in receipt of medication. The intervention is not conceived as an 'augmentation' of medications.	
University of Nottingham	Full	585-625		PCE-CfD is not represented. We welcome the recommendation for research into this area and would recommend PCE and where appropriate PCE- CfD is included as we are aware it is offered in all these context.	Thank you for your comment. The recommendation for research in psychotic depression is to investigate the most effective and cost effective interventions to manage this type of depression. It may well be that PCE-CfD is included as one of the investigations in future research in this area. However we do not think it would be

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					appropriate to highlight any particular interventions in the recommendation.
University of Nottingham	Full	67-101		We welcome the qualitative research undertaken although there seems to have been little by way of new qualitative research added to the review. We wish to draw attention to how counselling services, as a matter of course, receive written feedback from clients in regards to their experience of receiving counselling. This evidence could be a great resource for understanding the impact of PCE-CfD. Given there are numerous services with in-house PCE therapists, recovering this data would have been easily executed and would provide a more rounded qualitative perspective of the impact of PCE-CfD.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.
Lundbeck Ltd	Full	486-498		We would again make clear that all clinical evidence relating to the use of vortioxetine has been ignored as a result of the decision to exclude vortioxetine as an intervention of interest to this decision problem.	Thank you for your comment. As you mention in your other comments, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by

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					this guideline. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Society for Psychotherapy Research (SPR) UK Chapter	Full Chapter 17 Full	203 - 213 5 – 15 109	1-2	**Consistency and transparency of outcome measurement points** It is surprising that neither the *Methods* section (7.3), nor the *Review Questions* (7.4) in the full version, nor the *Methods* section (17.2) in Chapter 17 includes a detailed description of the measurement time points chosen, including the rationale as per the choice adopted in the draft guideline. We are very concerned about that and are asking for a revision of these sections to that effect. It currently is not transparent and immediately discernible which measurement time point other than baseline was chosen for which analysis. It seems that the only protocol mentioning measurement time points is that for the analyses of relapse prevention (i.e. at 12 months or 24 months follow-up), however, also here one becomes easily confused as it is not clear why the analysis for medication includes the end of treatment as well as	Thank you for your comment. We have made amendments to chapter 7 to take into account the issues you raise.

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				follow-up, whilst the analysis for psychological therapies includes only follow-up. How *follow-up* is defined for medication needs to be clearly stated in order to avoid confusion. A further example of an inconsistency appears in Table 11. It includes a column named *No of participants (studies) Follow-up.* In this column both *6 months* and *12 months* get mentioned. Again, this contributes to confusion as to the exact end measurement time-point that was actually included in the analysis and requires adequate description and a reasonable justification. We recommend a clear pre–post definition that is consistent for all studies included in the analysis. To us, the most obvious time point would be the end of treatment given that all studies will have data at that time point, whereas not all studies will have collected data at 6 or 12 months. Choosing the closest measurement point available, as indeed has been adopted in the draft guideline, has an inherent conceptual problem in that it is the end of treatment for some studies, whilst for others it is a measurement time point during treatment or indeed post treatment for others. The variability of occasion under which the data	

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				was collected is diverse and a comparison seems unfeasible to us. We recommend an amendment to that effect.	
Lundbeck Ltd	Full	40-48		Taken together, pages 40-48 suggest a potential bias on the part of the authors – these pages convey the impression of being 'anti-medication' and seem to be very critical of primary care services. We believe the draft guideline recommendations - with their increased focus on specialist services, reduction in the role of primary care, and limited pharmacological options - runs counter to the authors' conclusion "it is important that available healthcare resources are used efficiently to maximise the benefits for people with depression, their carers and family, and the wider society" (p48, line 23-24 in the draft full guideline).	Thank you for your comment. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
University of Nottingham	Full	180-188		As identified in this section the research omits diverse perspectives on depression. Understanding different paradigms is important and by limiting the evidence to a medical paradigm the scope of the research is not inclusive. Many clients do not consider their depression to be an illness and	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on

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				conceptualise it in a variety of ways. We recommend the report takes note of the outcome of the PRaCTICE trial which compares a medical approach (CBT) to a humanistic approach (PCE-CfD)	recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
IPTUK	Full	199-203	General	A distinction between lower and higher severity of depression is introduced in this draft guideline as a basis for treatment recommendations. This guideline does not present a clear epidemiological rationale for identifying the distinction at the chosen cut-off, rather than a few points lower (Sotsky et al., 1991) or a few points higher (Fournier et al., 2010), either of which would have a significant impact on subsequent analyses and recommendations and consequently access to treatments and service delivery. This distinction used throughout, is outdated and does not reflect accurately current heuristics for treatment decisions or access to services, due to the unreliability in the application of cut off metrics of self-report scales on an individual patient level, changing psychometrics, omission of key clinical factors that guide clinical decision making, such as context, complexity and behavioural indicators, to name but a few. The description of how the distinction point was calculated, including judgements on	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority

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				redundancy within scales and adjustments to widely used measures, such as the PHQ-9, is opaque and does not help readers to understand the process behind this decision. In addition, measures of depression, used to prioritise data for extraction and to determine baseline severity if more than one measure was used in a trial (Page 200, line 34-39), were organised into a hierarchy. The definitions and criteria for determining ranking in this hierarchy, which could move trials from one analysis to another if measures reported mean scores on different sides of the cut off (e.g. Toth et al., 2013, Blom, 2007) are not provided. Given the significance of this hierarchical ranking, this is an unacceptable lack of transparency and accountability. In the two studies cited above alone, the hierarchy could change the allocation of data for over 220 subjects from the analysis for more to less severe depression. This raises considerable doubts over the transparency of data management in this document, if this unexplained mechanism could influence the allocation of significant numbers from one analysis to another, due to commonly found measurement phenomena, such as self-report and blind rated measures reporting different mean scores and severity levels.	of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of

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				The guideline should explicitly report how many studies were excluded from the analysis based on an inability to classify according to this system (Page 201, line 3). Concerns over accurate classification is reported to have been of greater concern for studies claiming to report on moderate to severe depression, which is also identified as lacking data generally. It is therefore vital to the transparency of this document to explain what proportion of the available data were included in the analyses and how many studies and subjects were excluded due to an inability to categorise according to severity. Given the potential for the exclusion of studies to have greater impact on a smaller dataset, the committee should explain what efforts were made to engage the relevant authors to extract the relevant data for those studies which could not be classified. The guideline reports that the committee adopted this binary system because it was considered the most useful in guiding clinical decisions (page 201, lines 15-17). The rationale guiding this conclusion is far from self-evident. This conclusion has been widely criticised by the clinicians who will look to this document for guidance and who have employed assessment on the severity spectrum as one factor in formulating	different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression.

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				treatment options. As it is currently presented, the binary distinction risks simplistic misinterpretation, bypassing consideration of influential factors such as duration of symptoms, (Blom et al, 2007), past-history, (Frank et al., 2007, Carter et al, 2011) comorbidity (Frank et al., 2001) etc. in determining treatment recommendations. The rationale behind the severity distinction requires fuller explanation and empirical justification, given depression operates across a normally distributed continuum and this distinction results in a radical change in recommendations. If the severity distinction, solely based on cut offs of trial based measures, is upheld, it should be directly linked to the research recommendations in this guideline, promoting evaluation of existing treatments with more severe depression and examination of the techniques required to enhance the effectiveness of these interventions where there is limited evidence. Without this research, a lack of evidence with higher severity depression, especially for IPT, is equated to evidence of lack of efficacy. This logical error must be guarded against as it introduces significant bias and skew. especially in the light of the questions over data management raised previously and	The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors,

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<tr><td></td><td></td><td></td><td></td><td>service based outcomes for IPT with this population. The Psychological Therapies: Annual Report on use of IAPT services for 2014-15 and 2015-16 reported recovery rates of 53.9% and 54.3% respectively for packages of care in which IPT was the final intervention. While these outcome rates do not distinguish between packages of care for lower and higher rates of baseline depression, it should be noted that national training in IPT advises that case selection should use a recommended minimum of 15 on the PHQ-9 and many services delivering IPT report high levels of successful treatment with this more severe depression. Many IAPT services plan to contribute to the consultation directly to share these data. Anecdotally, data submitted to IPTUK to inform this response to the draft guidance are described below:

<table>
<tr><td>Gateshead Talking Therapies

(01.08.16-31.07.</td><td>IPT referrals n (%)</td><td>Recovery Rate ITT (%)

IPT alone</td><td>Recovery Rate ITT (%)

Multiples incl. IPT</td><td>Recovery Rate (Completers)

IPT alone</td></tr>
</table>
</td><td>such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity.

Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if 2 or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were</td></tr>
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				17)					not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe
				PHQ-9 (10-17)	58 (4.58 %)	74.14 %	75%	36.94 % of sample 88.64 % recovered	23.19 % of sample 85.71 % recovered
				PHQ-9 (18+)	98 (5.79 %)	44.9%	56%	62.42 % of sample 66.13 % recovered	72.46 % of sample 69.23 % recovered
				Steps to Wellbeing **Southampton**	IPT referrals n (%)	Recovery Rate	-	-	-

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				03.03.15-.03.03.17					depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA. Information about the number of studies that
				PHQ-9 (10-17)	10 (15%)	70%	-	-	
				PHQ-9 (18+)	57 (85%)	46%	-	-	
				North Tyneside Talking Therapies 2016-2017	IPT referrals n (%)	Recovery Rate	-	-	
				PHQ-9 (10-17)	-	-	-	-	
				PHQ-9 (18+)	2016: 74.63 % 2017:	42% 58%	-	-	

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					72.73 %				were excluded from the NMA because baseline severity could not be categorised is detailed in appendix J3.1. The number that were excluded from the NMA because baseline severity could not be categorised is 29. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the
				Talking Mental Health Derbyshire 08.09.16 – 08.09.17	IPT referrals n (%)	Recovery Rate	-	-	
				PHQ-9 (10-17)	72 (58.53 %)	75.5%	-	-	
				PHQ-9 (18+)	51 (41.46 %)	41.4%	-	-	
				Belfast Trust IPT Service **2016-2017**	IPT referrals n (%)				
				PHQ-9 (10-17)	20 (35.7 %)	-	80%	-	

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				PHQ-9 (18+)	36 (64.2 %(	-	66%	-	breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. IPT remains an option for people with less severe depression (who would like help for interpersonal difficulties that focus on role transitions or disputes or grief) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication individual CBT or BA) have not worked well in a previous episode of depression or in those who do not want the other recommended interventions. The committee made this a 'consider' recommendation because of the small benefit on the SMD outcome, the larger benefits on the other 2 clinical outcomes, and the lower cost effectiveness of IPT compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of IPT was likely to be higher in the sub-population specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new,
				Emotional Wellbeing Service Humber NHS Foundation Trust 2016-2017	IPT referrals n (%)				
				PHQ-9 (10-17)	2 (40%)	100%	-	-	
				PHQ-9 (18+)	3 (60%)	66%	-	-	
				Essex IAPT Service 01.9.16 – 31.08.	IPT referrals n (%)	Recovery Rate			

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				17 | | | | | PHQ-9 (10-17) | 50 (46.30 %) | 64% | - | - PHQ-9 (18+) | 49 (45.37) | 60% | - | - While these data are not the result of randomized and controlled testing, and must be interpreted with caution, they consistently report exceptional recovery rates for IPT with lower severity depression, well beyond the results of most RCTS. Additionally, they report lower, but very good recovery rates for IPT alone and in combination with other treatments for higher severity depression. These practice-based data from IAPT services across England are an illustration and highlight the need for additional research and warn against prematurely removing IPT from the range of first line treatments available to patients presenting with both lower (recommendation 61, page 252) and higher severity depression. The lack of peer reviewed evidence for a	less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). Thank you for bringing these references to our attention. Sotsky 1991 and Fournier 2010 could not be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs). Toth 2013 cannot be included as data

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				range of interventions for higher severity depression usefully identifies a significant gap in the existing literature and addressing this gap in understanding through targeted research should be a first step rather than premature conclusions based on scant evidence.	cannot be extracted (no measure of variance reported). Mediator/moderator analyses are outside the protocol for this review and it is therefore not possible to examine the impact on the analyses of the duration of symptoms, (Blom et al, 2007), past-history, (Frank et al., 2007, Carter et al, 2011) or comorbidity (Frank et al., 2001). However, when making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline.
University of Nottingham	Full	626-629		As referred to in comment 4 above, by limiting the paradigm, clients are frequently undermined if they believe there is a 'cure' as is implied by depression being characterised as an illness. It removes the capacity of the individual to recognise the processes they are going through as a natural response and reaction, admittedly often with an overwhelming and distressing impact. Despite the case that for some, perceiving it	Thank you for your comment. We do not agree that "an illness paradigm" is something that is commonly adopted by individuals providing treatment for depression. The approach adopted by many professionals, and the one use in this guideline, is one of collaborative assessment and determination of the most appropriate treatment, given the evidence for its effectiveness and an individuals' past experience and hopes for

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				as an illness may be helpful, for others we consider the illness paradigm prevents engagement through PCE-CfD with a focus on emotions and the resulting opportunity to process their distress.	future treatment.
British Association for Counselling and Psychotherapy	Full	201 - 203	General	Another such example of insufficient time for appropriate scrutiny can be found in the process described in section 7.2.1 in which cut-off scores to distinguish between 'more' and 'less' severe depression were arrived at; given the lack of a substantial literature base to inform the decision, a "practical approach" (p202) was developed specifically for this Guideline review. This process was utilised to distinguish two study populations and was thus foundational in the process through which Guideline recommendations for 'more' and 'less' severe depression was arrived at. As a brand new procedure, one central to the entire enterprise, it would be entirely appropriate to interrogate not only the process utilised but also to systematically examine the implications of different cut-offs on the final analyses. However, again the lack of time available through the consultation period has not allowed for this point to be properly explored.	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority

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					of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of

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					different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression.

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					The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors,

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					such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if 2 or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were

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					not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe

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					depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA. The standard consultation period for a draft

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					guideline is 6 weeks. In recognition of the complexity of this guideline and the consultation period falling over the summer it was decided to increase the consultation period by 2 weeks to a total of 8 weeks, to allow stakeholders more time to respond to the consultation.
Primary Care Neurology Society	Full	668 - 669	General	Advice on antidepressants - long term use for those who are at high risk of relapse is positive as it is common practice (albeit not a huge number of people relative to those on courses) and was certainly taught as best practice years ago. Some people have been on anti- depressants therefore for many years. And some of these are therefore on tricyclics or venlafaxine having not responded to or tolerated ssri or mirtazapine. It could be tempting to change them if we feel keen to follow the new guidance or not to be seen as a poor prescriber. (I have a patient that relapsed badly and never recovered to previous level after changing dosulepin a few years ago that they were well controlled on for 10 years.) There could be a comment - in the short text which most will read - that some people might be well controlled over time and so a decision to swap medication to be in line with new guidance should be based on careful discussion and monitoring.	Thank you for your comment. The decision to swap medication, for people who are well controlled, to be in line with the recommendations in this guideline would depend on the individual circumstances and therefore be a matter for clinical judgement taking into account patient preferences.
Primary Care	Full	668 -	Gen	There could usefully be a distinction between	Thank you for your comment. The

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Neurology Society		669	eral	new prescribing - whether longer term or a course, and those who have been stable on meds for many years.	recommendations for relapse prevention and medication are focussed on establishing people on appropriate pharmacological or combined pharmacological and psychological interventions, and their subsequent review and monitoring. We make no reference to people who are on medication long term other than to say this should be reviewed.
Relate	Full	37-38		We are pleased to see the inclusion of this important evidence on the bi-directional link between couple and family relationships and depression, and the recognition that couple relationship distress increases the risk of depression by a factor of three, and that up to 30% of severe depression could be prevented if couple relationship quality was improved. Given this link between couple relationships and depression, we believe it is essential that provision of couple therapy for depression is increased to enable people to access this – the most effective high-intensity therapy within IAPT, with recovery rates of 58.8%. We would therefore like to see the new NICE guidelines give greater prominence to this treatment in recognition of the strength of evidence linking depression and couple relationship distress.	Thank you for your comment. Based on the available evidence, the guideline includes recommendations for the use of behavioural couples therapy as an option for the treatment of a new depressive episode in less and more severe depression. The evidence does not support recommending this intervention elsewhere. Provision of behavioural couples therapy, in line with what is recommended in the guideline will be a matter for local implementation.
National School of Primary Care	Full	38-39		It would perhaps be valuable to mention here that the majority of depression is likely to be seen and treated in	Thank you for your comment. We have updated the references in light of your feedback and significantly revised the text,

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Mental Health Interest Group				a primary rather than secondary care context. The majority of the references in this section are very old - several from 20 to 30 years ago - 1988 to 1998 - and relatively few are later than 2000, none later than 2004. Given the number of initiatives put in place to try and improve GP detection of depression over the past 20 years and the concern about rising rates of antidepressant prescriptions, some more recent references might be appropriate included. One which may be relevant implies that, while the rates of GP diagnoses of depression may have remained static or fallen, more recently there has been a trend for an increased recording of the symptoms associated with depression. Rait G, Walters K, Griffin M, Buszewicz M, Petersen I, Nazareth I, 'Recent trends in the incidence of recorded depression and depressive symptoms in primary care', *British Journal of Psychiatry* 2009 vol. 195: 520-524. This may have been associated with various Quality and Outcomes Framework initiatives - something else which it might have been relevant to mention in this section of the guidelines.	including citing Rait 2009 as you suggest.
Royal College of Psychiatrists	Full	88-89	general	It is fallacious to quote frequencies of experience reported from the Healthtalk	Thank you for your comment. As specified in the scope, the experience of care section

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				modules. The method of analysis used in creating Healthtalk modules (thematic analysis) is explicitly designed to report the range BUT NOT the distribution of experiences. So, to say that 3 of 4 patients reported negative experiences with ECT is misleading. Clearly there is going to be a huge sampling bias, not to mention a tiny sample. Further, the specific ECT module on Healthtalk should be the source of information on ECT, not the Depression module. The ECT Healthtalk module (as opposed to the depression Healthtalk module) includes several accounts by patients and their families of their experience of having to work hard to persuade their psychiatrist to give them ECT, knowing that it is the only thing that helped them. Further information on the point of the general acceptability of ECT in the UK can be found in the paper by Maguire et al (Ulster Med J, 85, 1182-186, 2016) which showed a high compliance with ECTAS standards and that 80% of patients felt they had benefitted from ECT.	from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.
University of Nottingham	Full	482-483	22-51	This section excludes PCE-CfD resulting in falling short of the IAPT commitment to ensuring client choice. The evidence considered is mostly pharmacological, Cognitive Therapy and Cognitive Behavioural Therapy. As a training institute of PCE-CfD	Thank you for your comment and providing information on the positive impact of including PCE-CfD on services. Counselling was included as an intervention in the questions about further line treatment for depression. Unfortunately no specific RCT

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				for IAPT therapists we received evidence from NHS services suggesting they have noticed a positive impact on their services as a result of including PCE-CfD supported by trained PCE-CfD supervisors. This is excellent news considering the relatively low training costs for this approach.	evidence on PCE-CfD (which was developed for the IAPT programme) was identified and so no recommendation for the use of PCE-CfD was made.
Lundbeck Ltd	Full	502-503	40-44, 1-7	Question 1: We believe that recommendation 77 will be challenging to implement in practice. The recommendation states: If a person has had no response or a limited response to initial treatment after assessing the issues in recommendation 76, provide more support by increasing the number and length of appointments. Also consider: • changing to a combination of psychological therapy and medication if the person is on medication only, or • changing to psychological therapy alone, if the person is on medication only and does not want to continue with medication or • changing to a combination of 2 different classes of medication, in specialist settings, or after consulting a specialist, if the person is on medication only or a combination of medication and psychological therapy and does not want to continue with	Thank you for your comment. We have made amendments to recommendation 76 (removing the word 'initial') so that its meaning is clearer. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more

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				psychological therapy. [new 2017] The position of the recommendation to consider a combination of 2 different classes of medication means that a person who has not responded to initial (i.e. first line) treatment could feasibly be offered a combination of two medications as a second line option, requiring referral to secondary care or consultation with a specialist. Secondary care mental health services are facing significant pressures both in terms of funding and capacity. Recommending combinations of medication with specialist input so early in the treatment pathway is likely to result in primary care referring greater numbers of patients to secondary care which would put additional strains on the system and could increase waiting times for specialist services. We believe that in relation to Question 2, this recommendation is likely to result in a substantial increase in costs as more patients are referred to specialist services having had no or limited response to just one previous intervention.	efficient and effective collaboration and management of people with depression.
Janssen	Full	Pg 206-207	48-21	We note that the decision problem for both NMAs specified only select classes of pharmacological interventions. In sections, Table 43, pg. 212-214 and Table 49, pg. 253	Thank you for your comment. The justification of inclusion/exclusion of antidepressants in the NMA is provided in section 7.3.2.1 "Identifying antidepressants

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				these are specified as: • Class of SSRIs: citalopram, escitalopram, fluoxetine, sertraline • Class TCAs: amitriptyline, lofepramine • Mirtazapine (comprising its own class) Note that in order to maximise connectivity in the network specific drugs that are excluded and 'any antidepressant' or 'any SSRI' or 'any TCA' nodes will be added where they have been compared against a psychological intervention and/or combined with a psychological intervention but they will not be considered as part of the decision problem. We believe that other pharmacological classes such as SNRIs have been studied in these populations and are potential suitable first line treatment options for these populations, for example, if people were contraindicated or intolerant to SSRIs from a previous episode of care. We note that justification for excluding several interventions was made in section 7.3.2.1, pg. 206. We note the GDG identified secondary evidence to justify excluding several interventions. However, from our reading of the full guideline these studies do not seem to have been systematically	for inclusion in the NMAs". Please note that any pharmacological interventions that were not considered in the NMA as part of the decision problem (i.e. as candidates for recommendation), including the class of SNRIs and also individual SNRIs, were included in the network if they were compared with psychological or combined pharmacological interventions, in order to allow network connectedness. Imipramine was included in the network, although it was not of interest as an intervention (i.e. it was not part of the decision-problem) because it has been traditionally used as a control in many pharmacological trials and therefore it provided additional links across (mainly pharmacological) interventions, thus improving network connectedness. Interventions such as 'any TCA' or 'any SSRI' or 'any AD' were also not of interest per se (as we were interested in the effect of specific drugs at the intervention level) but were included in the network if they enabled network connectedness. Results for these intervention nodes, as well as for imipramine, were not reported (as they were of no interest). Criteria on additional studies and interventions included in the NMA to allow network connectedness have been fully reported at the end of section 7.3.2 "Populations, interventions and classes

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				identified or their evidence graded to inform the decision to exclude these interventions. The reason not to include most these interventions currently appears to be based on the GC agreeing 'to focus on those antidepressants which were most likely to be considered for use as first-line interventions in the English healthcare system.' We do not believe that this is an appropriate justification to excluded relevant interventions studied in the population of interest from the NMA. Other classes of antidepressants, such as SNRIs should be included in the NMA and we believe these should be considered further. We note that the CDG needed to maximise connectivity of the network by including other studies. We would argue that a more appropriate method would have been to include a wider network of all pharmacological treatments to solve the connectivity problems and provide greater precision with regards to the treatments estimates for the interventions that were decided to be relevant to the decision problem. The current approach where trials are selected and added into the network, such as imipramine, line 32-35, pg. 205, introduces a potential selection bias into the NMA. This	considered in the NMAs". Interventions of no interest that were included in the NMAs to allow network connectedness have been assessed in numerous RCTs (more than 200), although only a few of these trials (less than 10%) contributed to the network connectedness. We acknowledge that inclusion of all RCTs of interventions of no interest in order to achieve network connectedness (by, notably, only a small percentage of them) would be methodologically more robust but this was not feasible within the guideline timescales. Therefore, we chose to include only studies of those interventions that enabled the network to be connected. The purpose of the network was to look at the relative effectiveness of first line interventions. The committee did not consider SNRIs to be first line interventions and therefore they were not included in the network.

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				could have a significant impact where these treatments are used to connect other relevant treatments of interest within the network. Other interventions may have been able to provide a similar direct or indirect connection between treatment of interventions but were not included in the NMA. In our view, including a wider network of all possible interventions in the population of interest would address the current selection bias and provide a more reliable estimate, through direct and indirect connections, within the NMA. Furthermore, this will also reduce the risk that a single study selected to provide the connection in the NMA biases the whole network. We understand that it may not have been possible to use other studies to provide direct or indirect connections through the NMA, but this should be documented in the full guideline. If it was possible to use other interventions to strengthen the network of direct and indirect evidence, then we believe these should be included to provide a more robust NMA. Overall, we believe there are further intervention of interest that could be included in the network e.g. SNRIs. The inclusion of these interventions within the network would help address the potential selection bias of just including studies to connect the network	

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				of evidence. We therefore suggest that NMA is re-run on the basis of including other pharmacological classes to strengthen the overall network of evidence and to provide a more robust relative treatment effect for all interventions studied in the population of interest.	
Royal College of Psychiatrists	Full	Chapter 4 68	9-15	**Service user experiences and research sections need updating and findings integrated into treatment recommendations** Service user and carer experience research needs to be updated and then taken into account in the designing of treatment recommendations rather than standing alone and not integrated into treatment recommendations. Service user experience is central to the treatment of depression, as it is for any treatment. Since this section was written, there have been significant changes in society that are likely to impact on the experience of depression, for example increasing austerity, reduction in social support, reduction in benefits for both service users and carers due to government changes. The guidelines neglects consideration of the wealth of research published since 2004 on experiences of depression of patients and carers.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.

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				The guideline should also improve the quality of the service user experience research employed and properly incorporate this research into treatment recommendations and guideline development methodology. There are methodological limitations in the patient experience data collected for the previous guidelines, e.g. no demographic details of the 38 individuals so it is not known what populations of service users were represented in these extracts, for example, whether under-represented populations such as BME, men, older adults, non-heterosexual clients were included. Moreover, key themes reported in the findings of previous qualitative analysis have not been taken into the design of the guideline or its recommendations. The themes reported are: *"trauma or conflict in childhood as a perceived cause of depression; need for long-term psychotherapy for people with severe and chronic depression; the need to take personal responsibility for and understand the illness to improve outcomes; issues around diversity; paid and unpaid employment as an important part of the recovery process; the negative impact on daily functioning; concerns regarding stigma and discrimination*	

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				in the workplace; and the relationship between people with depression and professionals." The EPA guidelines recommend that level of trauma in childhood and impact on daily functioning should be taken into account when choosing treatment. Given that childhood trauma is frequently perceived by service users as one of the causes of their depression we would also argue that the patient's attribution of their depression should contribute to the choice of therapy for them. Moreover, there are no recommendations made relating to reducing stigma.	
Royal College of Occupational Therapists	Full	7	1.2.7	There is no mention of interventions to facilitate recovery, social outcomes or participation in daily life. Although it does say that HCP should consider the context in terms of social isolation, employment and living conditions there is no guideline of what action to take to resolve these issues e.g. referral to Occupational Therapy	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
Association for Cognitive Analytic	Full	Chapter 7	7.1.2 & Tabl	There is widespread evidence of CAT being used as a frontline treatment method for treating depression in the UK. CAT is also	Thank you for your comment. The studies that you cite on CAT (Bennett 1994; Hamill & Mahoney 2011; Dunn et al 1997; Marriott &

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Therapy (ACAT)			e 43	commonly used when CBT as the first intervention has been ineffective or has low patient acceptability. CAT is therefore widely used as a depression treatment in IAPT services (see for example in Somerset, Barnsley, Sunderland and Norwich). CAT has an established evidence base regarding the treatment of depression. This consists of two case studies (Bennett, 1994; Hamill & Mahoney, 2011), a follow-up study of routine practice showing durability of clinical effectiveness (Dunn, Golynkina, Ryle & Watson, 1997), a quasi-experimental study showing matched outcomes with CBT and counselling (Marriott & Kellett, 2009) and a clinical trial showing matched depression outcomes with psychodynamic therapy (Brockman et al. 1987). It would be therefore appropriate for CAT to be acknowledged as a putative treatment for acute depression at this stage and ACAT would request that CAT is included in the list of putative psychological therapies at various points in the guidance (EG: as a paragraph in 7.1.2 and in Table 43).	Kellett 2009) did not match the inclusion criteria for the review protocol for treatment of a new depressive episode because they were not RCTs. Brockman 1987: did not meet the inclusion criteria because it contained mixed diagnoses ('neurotic, personality, and interpersonal problems). Consequently these studies were not included in the network meta-analysis or economic analysis conducted for this question and we are not able to make any recommendations about the use of CAT.
Association for Cognitive Analytic	Full	Chapter 16 (Refer	Gen eral	There is a large (N = 95) randomized and controlled deconstruction trial of CAT for depression in IAPT that has not been	Thank you for your comment. The study you cite has not been included in the guideline because it is not yet published and therefore

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Therapy (ACAT)		ences)		referenced or considered. The paper was provided to NICE pre-publication in the call for evidence and acknowledged on the 30th September 2015 (Clinical trial number: 10/H0405/53). The paper is currently under review in the Journal of Affective Disorders. CAT was shown to produce significant reductions in depression ($p = 0.01$), with large associated effect sizes ($d_+>1.5$). The trial was a test of an innovative 8-session version of the model, bespoke for depression treatment in IAPT. The drop-out rate was low (16%) - with 64% of cases completing full (8 session) CAT treatment. This evidence of high patient acceptability dovetails with the overall CAT evidence base which indicates low overall dropout rates and high patient acceptability. When the recovery rate for 8-session CAT are compared against recovery rates for step 3 CBT for depression (typically of 16 sessions duration) – then the recovery rates were similar. This suggests that brief-CAT for depression offers good service efficiency at step 3 of IAPT services.	falls outside of the cut-off date for including evidence in the guideline. We will forward these study details to the NICE surveillance team for consideration.
British Association for Counselling and Psychotherapy	Full	Chapter 17	General	**Inconsistency** The researchers investigated the homogeneity of the NMA analyses which is important as another key assumption of network meta-analysis ***Global inconsistency:*** Network meta-	Thank you for your comments. We pre-specified a difference of ≥5 to be meaningful and this was taken into account together with an assessment of the overall model fit, inconsistency plots and estimates of heterogeneity. Results are displayed in Appendix N1. In addition the similarity of

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				analysis requires the assumption that treatment effect estimates from different sources (particularly form direct comparative trials and from indirect comparisons) are sufficiently homogeneous (it can be seen as the generalization of the homogeneity assumption from effect estimates within comparisons in pairwise meta-analysis to effect estimates across comparisons in network meta-analysis). This was done primarily by comparing a so called inconsistency model (not assuming consistency) with the main model (assuming consistency) regarding fit to the data (Section 7.3 and 17.2). This fit was assessed by comparing the deviance information criterion (DIC), a fit index, of the models. In these comparisons, a DIC difference of at least 5 points was considered as an indicator of difference between the models regarding their fit to the data, with no meaningful difference indicating that the consistency assumption is supported by the data. However, it has been suggested that a difference of two or three points can already be of practical relevance (Spiegelhalter et al., 2002), thus the threshold used by the Guideline authors may have been two conservative (missing important inconsistency). Furthermore, it is known that	studies and populations was carefully considered prior to synthesis. Heterogeneity and inconsistency are related concepts. Inconsistency may be hard to detect which is why we aimed to minimise heterogeneity by controlling for a large part of it; this was done by splitting populations with less and more severe depression; using detailed treatment definitions [including treatment intensity and mode of delivery for psychological interventions] and categorising them using a class random effects model), examining for model fit and checking for inconsistency between direct and indirect evidence. Other potential effect modifiers, such as age and setting (inpatient vs outpatient) were assessed in sub-analyses, using pairwise meta-analysis. Where heterogeneity and/or inconsistency were identified, results were interpreted accordingly and the presence of heterogeneity and/or inconsistency were taken into account when making recommendations. For the assessment of potential inconsistency in each network we used global checks for inconsistency, as recommended by the NICE Decision Support Unit (DSU) Technical Support Document

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				the presence of between-trial heterogeneity impedes the detection of inconsistency (Dias et al, 2013), and in some of the network meta-analyses reported in the Guideline considerable heterogeneity was identified (see above). ***Local inconsistency:*** A careful evaluation of inconsistency should include checking the agreement between direct and indirect evidence for each comparison of interest (Salanti et al., 2014). By definition, it is possible only for comparisons for which direct comparative trials have been performed. Although direct and indirect evidence was not contrasted explicitly in the Guideline, Appendix W reports direct effect estimates from inconsistency models. Although direct evidence is available only for a fraction of comparisons, some of them suggest that direct and indirect effect estimates disagree to a substantial extent (for example, in the analysis of SMD of symptom change for sertraline vs. waitlist in less severe depression, the median estimated effect was -0.60 from network meta-analysis with consistency assumption and -1.24 from direct evidence). A more thorough inspection and explanation of local inconsistency would have been desirable for the assessment of the reliability of the reported findings.	(TSD) 4. The results of these checks did not show any cause of concern in most analyses. Deviance plots have been added in the final guideline (Appendix N1). Undertaking a local assessment of inconsistency was not practical to do for all comparisons due to the size and complexity of the networks. It would produce a very large amount of comparisons to analyse and interpret, leading to a very high risk of finding spurious results. In the comparisons between the NMA (mixed) and direct (pairwise) evidence, the actual point estimates do not matter, i.e. they do not indicate inconsistency per se. What matters is whether or not the CrIs overlap – i.e. it is the uncertainty in the estimates that indicates inconsistency. The committee assessed the results of all NMAs in the context of the network structures, the respective evidence base, and their plausibility. The committee noted the presence of 2 sub-networks of primarily psychological and primarily pharmacological interventions in a number of outcomes in more severe depression (response in completers, remission in those randomised, remission in completers). They noted the sparseness of the overall networks and the connection of the 2 sub-networks by studies

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				Difficulties in testing inconsistency: Inconsistency cannot be assessed for comparisons without direct evidence (or only regarding different sources of indirect evidence, which is currently not common practice). However, a careful investigation of most networks that are depicted in the Guideline reveals that the decisive body of evidence consists of two weakly connected sub-networks: one testing pharmacological interventions and using placebo as control treatment, while another testing psychological or physical interventions with waitlist or TAU as control. Even if these sub-networks can be consistent for themselves, due to sparse comparisons between them an essential part of inconsistency (for example, for comparisons of pharmacological and psychological treatments) cannot be assessed empirically.	comparing psychological with pharmacological interventions which showed very large benefits, resulting in one part of the network (psychological interventions) showing very large effects versus the other part of the network, which consisted of drugs and pill placebo. These observations were taken into account by the guideline committee when making recommendations and have been captured in the 'Evidence to Recommendations' sections for more severe depression in Chapter 7. Notably, following interpretation of these results, the committee did not prioritise psychological over pharmacological treatments (or vice versa) for recommendations in adults with more severe depression. In addition to the results of the NMA (including heterogeneity and inconsistency checks), other factors such as cost effectiveness, anticipated harms, treatment acceptability and compliance, patient characteristics and preferences were taken into account by the committee when making recommendations in general, and specifically when considering psychological versus pharmacological treatments. Therefore, any potential inconsistency between pharmacological and psychological interventions that was not possible to identify

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					in sparse networks (i.e. those reported above for more severe depression) had little impact on recommendations.
British Association for Counselling and Psychotherapy	Full	Chapter 17	General	**Transitivity** The third key assumption of network meta-analysis is transitivity (sometimes termed similarity). Linde, Rücker, Schneider & Kriston (2016) define transitivity as the requirement that the included trials comparing partly different sets of treatments (i.e., having different designs) are sufficiently similar with regard to clinical and methodological characteristics (e.g., population and outcomes). This means mainly that populations and interventions should be similar across different comparisons and that each participant could be, at least theoretically, randomized to any of the investigated interventions. The study by Linde, Rücker, Schneider & Kriston (2016) is relevant because the authors conducted a network meta-analysis of both pharmacological and psychological trials for depression in primary care and discussed the outcomes of this NMA in comparison with NMAs conducted separately for medications and psychological interventions.	Thank you for your comment. Quantitative appraisal of transitivity of the results was done using inconsistency checks. We agree that assessment of 'transitivity' or 'exchangeability' of the results also needs qualitative appraisal. The Guideline Committee were aware that populations tested on different types of interventions (i.e. pharmacological versus psychological, self-help versus face-to-face) might be different regarding their preferences and acceptability of specific treatments and this was taken into account when making recommendations. These concerns were reported on page 232 of the consultation guideline draft: "it is noted that participants in pharmacological and psychological trials may differ to the extent that some participants find different interventions more or less acceptable in light of their personal circumstances and preferences (so that they might be willing to participate in a pharmacological trial but not a psychological one and vice versa). Similarly, self-help trials may recruit participants who would not seek or accept face-to-face interventions. […] The NMAs have assumed that service users are willing

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				The authors concluded that while their assessment of the transitivity of the separate NMAs was broadly acceptable, the assumption of transitivity for the joint analysis was questionable. Notably the authors did not identify substantial heterogeneity and only moderate inconsistency in the joint NMA. The authors cautioned that: "Reviewers might be tempted to conclude that their network estimates are valid, if neither heterogeneity nor inconsistency is seen, both of which can be at least in part investigated and quantified by existing statistical tools, thus suggesting comforting ''objectivity.'' Still, it is crucial to notice that transitivity can be violated even in a homogeneous and consistent network, and its assessment inevitably needs qualitative clinical and epidemiologic appraisal." Thus, the authors, state, it is important "to be extremely careful about the interpretation of the findings from a network meta-analysis if the transitivity assumption is implausible." It is the conclusion of BACP that similar caution should be exercised in the case of this NMA. Transitivity is difficult to assess empirically, and therefore in most cases careful epidemiological judgment is necessary, for example using the criteria of Salanti (2012). Based on the expertise of the	to accept any of the interventions included in the analyses; in practice, treatment decisions may be influenced by individual values and goals, and people's preferences for different types of interventions. These factors were taken into account when formulating recommendations". The committee noted the presence of 2 sub-networks of primarily psychological and primarily pharmacological interventions in a number of outcomes in more severe depression (response in completers, remission in those randomised, remission in completers). They noted the sparseness of the overall networks and the connection of the 2 sub-networks by studies comparing psychological with pharmacological interventions which showed very large benefits, resulting in one part of the network (psychological interventions) showing very large effects versus the other part of the network, which consisted of drugs and pill placebo (interestingly, the 'problematic' results in these networks were created by RCTs comparing pharmacological versus psychological interventions, in which 'heterogeneity' or 'transitivity' should not be an issue). These observations were taken into account by the committee when making recommendations and have been captured

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				Guideline Committee, we could assume that this judgment was made as well as possible however this is difficult to assess given the failure to discuss transitivity in the draft guideline. Further, recalling the discussion above on treatment preference as a possible direct or indirect effect moderator, on the clinical heterogeneity of active treatments and TAU, and on the presence of two sub-networks of primarily psychological and primarily pharmacological interventions, transitivity of the analyzed networks can certainly be questioned. As Linde, Rücker, Schneider & Kriston (2016) comment, the evaluation of transitivity in network meta-analysis requires clinical judgment that may be subjective, context dependent, and accompanied by uncertainty, and the practical interpretation of findings from a network meta-analysis with uncertainty regarding its assumptions is correspondingly difficult.	in the 'Evidence to Recommendations' sections for more severe depression in Chapter 7. Notably, following interpretation of these results, the committee did not prioritise psychological over pharmacological treatments (or vice versa) for recommendations in adults with more severe depression. In addition to the results of the NMA, other factors such as cost effectiveness, anticipated harms, treatment acceptability and compliance, patient characteristics and preferences were taken into account by the committee when making recommendations in general, and specifically when considering psychological versus pharmacological treatments. Therefore, the transitivity of the NMA effects between pharmacological versus psychological interventions (which appears to be your main concern) was only one factor among those considered when making recommendations.
British Association for Counselling and Psychotherapy	Full	Chapter 17; pg51	General	**Judgements related to rankings of treatments** In general, results regarding the ranking of treatment according to their efficacy (as compared to placebo) were strongly emphasized throughout the Guideline. As an	Thank you for your comment. Treatment rankings and their uncertainty (mean/median values and 95% CrI) have been considered in combination with efficacy and the uncertainty around it (mean relative effects and 95% CrI). Rankograms include the same information as the mean/median ranks and

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				example, on p51 of Chapter 17, counselling is described as "the lowest ranked active class" of interventions in the SMD outcome analysis. For this ranking of treatments, median and mean ranks were used, although more informative individual and summary approaches to ranking are available, such as the graphical display of rankograms and the calculation of the surface under the cumulative ranking curve (SUCRA) (Salanti, Ades & Ioannidis, 2011). However, treatment ranking altogether should always be interpreted with due caution (Salanti, Ades & Ioannidis, 2011; Ioannidis, 2009). For example, imprecision of treatment effect estimates is frequently associated with good (low) ranks. This is impressively demonstrated by the fact that in most analyses, interventions and intervention classes with the best (lowest) median ranks were tested in only a handful of patients, (usually less than 100, not rarely less than even 20) (Chapter 17).	95%CrI, as they are based on the same values, so presenting rankograms would not increase the information provided to the committee nor would it alter recommendations. Reference to treatment rankings in the guideline text helped in the presentation of results of multiple interventions on multiple outcomes. No recommendation was made based solely or predominantly on the results of the treatment rankings. Clinical efficacy (and the underlying uncertainty), cost effectiveness (also the underlying uncertainty), harms associated with treatment, the quality of the evidence and other factors such as patient choice, specific patient characteristics and circumstances and implementation issues have been considered when making recommendations. We have acknowledged the fact that some interventions and classes that have performed well in the NMA and/or economic analysis have only been tested in a small number of patients: please see considerations on the 'quality of the evidence' in 'Evidence to Recommendations' sections 7.4.5 and 7.7 in the consultation guideline draft. Following careful consideration, we have now removed from the economic analysis all classes that have been tested on fewer than 50 people across RCTs in any of the main outcomes that

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					informed the economic analysis, i.e. discontinuation (any reason), response in completers, remission in completers."
Royal College of Psychiatrists	Full	26	26 - 29	It would be helpful if it explicitly states that this guidance is intended for adults of all ages including older adults as the term "adults" has historically excluded older adults.	Thank you for your comment. We have made your suggested change.
University of Liverpool	Full	29		Please clarify whether or not the GDC rejects DSM-5's inclusion of grief reactions within the depressive diagnostic spectrum	Thank you for your comment. Diagnosis of depression is not within the scope of this update. Therefore we have not looked at the issue you mention and are not able to comment on it.
National School of Primary Care Mental Health Interest Group	Full	33-4		If older/ elderly adults are included in this guideline, there may be value in a section somewhere referring to the potential differences with this group - e.g. lower detection rates and the likelihood of poorer access to treatment.	Thank you for your comment. We have clarified that older adults are included in the guideline however we do not think the additional detail you suggest is needed.
National School of Primary Care Mental Health Interest Group	Full	30		The description is very detailed as regards the range of potential symptoms in a depressive illness, but relatively little is stated about the impact on function or quality of life, which is a crucial perameter to be looking at in terms of peoples' improvement/recovery and is part of the diagnostic criteria. This is not necessarily the same as disability. Stigma is an issue mentioned in Chapter 4. It might be mentioned already in the	Thank you for your comment. We have amended the text in section 2.1.3 to make the impact on quality of life more explicit. Stigma is also mentioned in section 2.1.3.

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				Introduction, as this can affect both people presenting to clinicians with their symptoms and the likelihood of them receiving a correct and timely diagnosis. It was also clearly an issue in several of the patient accounts and the qualitative analysis in Chapter 4	
National School of Primary Care Mental Health Interest Group	Full	31		Given its prevalence and significant associated morbidity, the concept of treatment resistant depression could perhaps be usefully introduced at an early stage in the guidance.	Thank you for your comment. We have not made this amendment. In light of feedback from stakeholders, we are unsure of the value of the term treatment resistant depression and have chosen to use the term 'no or limited response to treatment' instead.
Royal College of Psychiatrists	Full	31	15 - 19	The evidence used (Fava and Kendler 2000) and the statements accompanying it are misleading as the paper it's quoted from does not make this categorical assumption. The paper states that Major depression is not limited to adult and elderly populations, with a substantial proportion of patients having their first episodes in childhood and adolescence; the statement as its written in the guidance might appear to suggest that major depression is substantially an illness that has a continuum starting from adolescence and continuing on into old age, which is not always the case. It also contrasts with the studies used for economic modelling on page 699 which all state the mean/median age of	Thank you for your comment. We have removed the statement about a substantial proportion of people have their first depression in childhood or adolescence.

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				onset for depression is in the 30's in most countries.	
University of Liverpool	Full	33		Could also include evidence on trajectory of depression in primary care from *diamond* cohort – see Gunn J, Elliott P, Densley K, Middleton A, Ambresin G, Dowrick C, Herrman H,Hegarty K, Gilchrist G, Griffiths F. A trajectory-based approach to understand the factors associated with persistent depressive symptoms in primary care. J Affect Disord. 2013 Jun;148(2-3):338-46. doi: 10.1016/j.jad.2012.12.021	Thank you for your comment. We have not made this change as this level of detail would not be reflective of what the individual chapters have covered. Gunn 2013 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs).
Hyperparathyroid UK Action 4 Change	Full	34	41/50	Depression was one of my PHPT symptoms but because I had suffered from it long term prior, the mental health people thought it was just a recurrence and treated me accordingly. Fortunately the GP side were sufficiently switched on to go down the hyperparathyroidism diagnostic route which proved to be the case and the main cause of my depression and acute anxiety	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain

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					their symptoms.
Hyperparathyroid UK Action 4 Change	Full	34	34/35	My doctors repeatedly ignored symptoms of pain once they concluded I had several signs of depression. Depression is a symptom of hyperparathyroidism. I was given Seroxat in 2000. I came off it as I felt worse, I was offered other antidepressants in 2004, then 2010. I declined but accepted Prozac in 2011 once I had a diagnosis of primary hyperparathyroidism. I had a 15 year old adenoma removed 5 years ago and have not needed antidepressants since.	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	34	34/35	I've suffered depression on and off since the birth of my daughter in 1981 and there are times when this was very serious. I feel fine right now and happier still 2 weeks post op (parathyroidectomy)	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	34	41/42	I was told for years that I was just depressed and it was causing my aches and pains, insomnia, and so on. Now I know that depression was not the cause of my issues, but another symptom itself. I believe that	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on

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				everyone who is diagnosed with depression and Fibromyalgia needs to be tested for HyperPARAthyroidism. I am now cured of hyperparathyroidism.	the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Lundbeck Ltd	Full	35		Vortioxetine is erroneously described as a third-line agent. This is not correct. Vortioxetine is licensed by the European Medicines Agency for the treatment of MDE in adults, with no restriction as to line of therapy (Lundbeck Limited, 2017). Following a STA in 2015, vortioxetine is recommended by NICE as a "clinically and cost-effective treatment option for treating MDE in adults whose conditions has responded inadequately to 2 antidepressants within the current episode" (NICE, 2015). **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes.	Thank you for your comment. We have amended the text to reflect that used in the wording of TA367.

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				November 2015. Lundbeck Ltd. Vortioxetine Summary of Product Characteristics. January 2017.	
British Association for Counselling and Psychotherapy	Full	35	18 - 22	***Conceptualisation of depression:*** The Guideline is based on an assumption that, for practical purposes, depression can be treated as a discrete entity, with a strong emphasis on evidence from controlled studies of interventions for depression. While these studies serve an invaluable function in generating scientific knowledge and understanding of this condition, we argue that they are of less relevance in relation to policy and practice because few patients present with clear-cut depression, for example, it is highly co-morbid with anxiety (Kaufman & Charney, 2000). In most cases, depression is one element of a complex set of problems that may include anxiety, cultural minority status, relationship difficulties, a life of adversity and trauma, loss and bereavement, work stress, physical incapacity and illness, and other factors (Smith, Court, McLean et al., 2014). It is our view that effective help and support requires a capacity to acknowledge, and if possible address, all of these dimensions. While the Guideline makes some attempt to	Thank you for your comment. Mediator/moderator analyses are outside the protocol for this review and it is therefore not possible to examine the impact on the analyses of comorbidity with anxiety (Kaufman & Charney, 2000) or cultural minority status, relationship difficulties, a life of adversity and trauma, loss and bereavement, work stress, physical incapacity and illness, and other factors (Smith, Court, McLean et al., 2014). However, when making recommendations, the committee interpret the evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline.

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				consider these issues, for example in the section on social deprivation, we are concerned that this perspective does not sufficiently inform the main recommendations and, therefore, that patients who present with such comorbidities will not receive appropriate or effective treatment.	
Hyperparathyroid UK Action 4 Change	Full	35	16/17	I had primary hyperparathyroidism (surgery 5 years ago) I was hospitalised with 2 episodes of major depression in 3yrs before I was diagnosed with PHPT. The 2nd time I was put on heavier SNRI medication which I believe caused me to become 'suicidal' and I tried to harm myself and had constant thoughts of wanting to 'end it'. The thought that my husband or youngest daughter would be the ones to find me, stopped me harming myself a 2nd time. When I look back now I am mortified that I got that low, as I had before all this, been an optimistic positive person. No past history of depressive illness, anxiety at times, that had been all.	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	35	48/50	'It is clinically apparent that features of depression itself such as loss of independence and thoughts of helplessness further compound the disability": Helplessness due to prolonged misdiagnosis of hyperparathyroidism can also lead to depression as displayed by many members of our support group.	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on

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					Hyperparathyroidism: diagnosis, assessment and initial management which may be of interest. There is also existing NICE guidance on Depression in Adults with a chronic physical health problem. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
CHESS (Centre for Humanities Engaging Science and Society), Durham University	Full	35	5	We are concerned that the Draft Revision's decision to separate the analyses of Chronic Depression [CD] & Treatment Resistant Depression[TRD] (while also not conducting appropriate sensitivity analyses) will damage both the clinical treatments provided and future research. We suggest: • Restoring the position correctly taken in previous versions of the Guidance namely that the overlap of chronic depression and treatment resistant depression patient populations is so large as to render questionable the separation of TRD from CD as a means of structuring meta-analyses. • Cluster TRD with CD. Operationalise this in an additional meta-analysis and an evidence review (and possibly	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term

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				include other related categories). • Failing the above, undertake appropriate sensitivity analyses to ascertain the robustness of proposed recommendations. These analyses will not require great extra resources. But they will greatly increase the credibility of the Draft Revision's recommendations and the probability that they will be beneficial rather than damaging. **Justification:** Earlier versions of the Guidance decided not to use the TRD category, citing strong evidence for the existence of a more loosely defined heterogenous group of long-term, difficult to treated depressive conditions, frequently associated with dysthymia and co-morbid common mental disorders, various personality disorders/traits and serious psycho-social disability. This well-evidenced position has been reversed in the Draft Revision - without apparent justification. The unfortunate sense of confusion that is conveyed is compounded by the Draft Revision beginning by reminding the reader of the uncertainty in classifications of depression and emphasising that false categories give rise to confusion. We agree!	would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic

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				Left as it stands, as the draft predicts, but regardless of itself proceeds happily to generate: • **Confusion in Clinical Service Provisions**: The diagnostic inclusion criteria used in TRD studies are most often narrowly pharmacological (exact dose, duration and response). They are not those used in usual clinical settings where case identification is usually descriptive and involves complex evaluations of psychosocial functioning across several domains. • **Confusion in Research**: the UK guidance will be out of line with the APA (DSM-V) and the European Psychiatric Association (EPA) guidance (2016). Both recommend a common "persistent" depression category with sub-categories for severity and degree of associated psycho-social disability. • **Confounds in Treatment Research**: The Revision currently gives credence to a false dichotomy. It treats as different, users who in fact are alike in nearly all ascertainable respects. The definition of chronic depression given	depression' to 'chronic depressive symptoms'. Jobst 2016 and Ruhe 2012 have not been included in the guideline as they do not meet the study design criteria for the review (not RCTs or systematic review of RCTs).

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				in the Draft reads: *"Adults with chronic depression, defined by a diagnosis of depression according to DSM, ICD or similar criteria, or depressive symptoms as indicated by baseline depression scores on scales. The definition of chronic depression includes: meeting criteria for full MDD for 2 years; persistent subthreshold symptoms (dysthymia); double depression (an acute episode of MDD superimposed on dysthymia). In the case of mixed populations, if the study reports data for a subgroup with chronic depression, data for this subgroup will be extracted. If the study does not report data separately we will only include studies where over 75% of the population have a diagnosis of chronic depression. Studies with mixed populations where less than 75% of the population have chronic depression will be included in other reviews."* Many subjects in the trials included in the TRD meta-analysis will meet this definition of CD. Note Ruhe *et al (*2012): "because of their chronic clinical course, approximately 40% of CD patients also fulfil criteria for 'treatment-resistant depression'' (TRD)……	

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				usually defined by the number of non-successful biological treatments". Most CD patients have received multiple courses of AD's. Most TRD patients have multidimensional psychosocial disabilities; the only difference is that TRD trials tend not to report such data. • **Chronic depression/TRD conditions are persisting**. Any self-respecting RCT or meta-analysis should include the comparison of long term follow-up outcomes, not only the endpoints of short-term treatments. Jobst A et al. (2016) European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. European Psychiatry, 33, 18 – 36. Ruhe HG, van Rooijen G, Spijker J, Peeters FP, Schene AH. (2012) Staging methods for treatment resistant depression. A systematic review. J Affect Disord, 137, 35–45.	
University of Liverpool	Full	35	Paras 2 and 4	Good to see emphasis on severity, duration and course – but surely also need to include assessment of **function.** NB this does appear later eg. Page 186, bullet 20.	Thank you for your comment. We have made this change.
Hyperparathyr	Full	35	23	Depression was one of my primary	Thank you for providing this information.

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oid UK Action 4 Change				hyperparathyroidism symptoms but because I had suffered from it long term prior, the mental health people thought it was just a recurrence and treated me accordingly. Fortunately the GP side were sufficiently switched on to go down the hyperparathyroidism diagnostic route which proved to be the case and the main cause of my depression and acute anxiety. However, treatment with antidepressants did assist in getting me to surgery date without me throwing myself under a convenient bus. Believe me, in really bad times that was an option I considered.	
Hyperparathyroid UK Action 4 Change	Full	36	1/3	Hyperparathyroidism MUST be included with other endocrine conditions	Thank you for your comment. We have added hyperparathyroidism to the list of endocrine conditions.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	We surveyed 100 people with hyperparathyroidism. 70% experienced Depression/low mood/isolation. 72% experienced anxiety. https://www.hyperparathyroiduk.com/	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	Patients who have been diagnosed with depression or might have depression should be tested for Parathyroid Issues. I was told for years that I was just depressed, yet none of the anti-depressants ever helped me and some had bad side effects. Had my doctors looked into other causes for my fatigue, aches, trouble sleeping, etc I may have been diagnosed and cured a lot sooner. I have so	Thank you for your comment and providing this information. This guideline is about the treatment and management of depression in adults. Therefore it is outside the scope of this guideline to make recommendations on the diagnosis and treatment of hyperparathyroidism. However NICE is in the process of developing a guideline on Hyperparathyroidism: diagnosis, assessment

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				much damage to my body from having PHPT for so long including arthritis, bone spurs, weak teeth and my right kidney started to dent in and calcify.	and initial management which may be of interest. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain their symptoms.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	Depression and anxiety were my main symptoms of primary hyperparathyroidism. I am keen to contribute to any discussion on this subject. I was suicidal when first diagnosed.	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	Depression was one of my first symptoms. I told my doctor I had no reason to be depressed. Happened at the same time as brain fog and memory issues. I have hyperparathyroidism.	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	There are many conditions relating to hormones that cause depression and no amount of treatment for depression is going to solve them if there is an underlying physical cause.	Thank you for your comment. This guideline is about the treatment and management of depression in adults. Therefore it is outside of the scope of this guideline to make recommendations on depression that is a symptom of another condition. However, in light of your comments we have added to recommendation 1.9.1 that people with no or limited response should be assessed to establish if there is an underlying physical illness that could explain

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					their symptoms.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	Hyperparathyroidism and anxiety: I have never been so low at times as this year and it's when my calcium is heading for 2.7. My reading a fortnight ago was 2.68 and I could feel the dark mood. This then gives me social anxiety and apathy.	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	Frankly I didn't want to talk to the doctors about my completely uncharacteristic free floating anxiety and black moods. Mostly because I didn't want to be labelled as a hysterical woman and get referred down the mental health route. It has been a HUGE relief to see that Depression and Anxiety is on the list as symptoms for pHPT. The brain fog too. I thought I was getting early dementia.	Thank you for providing this information.
Hyperparathyroid UK Action 4 Change	Full	36	1/3	I was treated with a range of antidepressants all of which had a negative impact on my life and left me totally flat and a continuously vanishing promise of various other support and therapies in various NHS areas over 15 years. Following a parathyroidectomy I feel back to my old self	Thank you for providing this information.
Tavistock Relationships	Full	37	11	While we very much welcome the inclusion of this material on the links between couple relationships and depression on pages 37-38 of the full guideline, we do not understand why none of this material has made its way into the short guideline. We strongly urge the GC to include at least one sentence in this	Thank you for your comment. The purpose of this text is to explain why there needs to be NICE guidance on depression. Your suggested amendment would be too detailed for the context section and so we have not added it.

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				'Context' section highlighting the links between relationship difficulties and depression. For example, the following sentence could be added, perhaps after 'work life' in line 24: "Indeed, depression is related to family and couple stress and conflict in a bi-directional way: depression is both caused by and is itself the cause of difficult family relationships".	
Lundbeck Ltd	Full	40	3-19	We are surprised by how old some of the references are that are cited for the claim "With 50% of people with depression never consulting a doctor, 95% never entering secondary mental health services, and many more whose depression goes unrecognised and untreated, this is clearly a problem for primary care". (Kendrick et al. 2009 and Goldberg and Huxley 1980). Over the last 37 years there have been significant changes to the organisation of the NHS, the commissioning of specialist mental health services, the recognition and management of depression in primary care, including the provision of IAPT services, and the public's awareness and attitude to illnesses such as depression. In any event, the guideline authors imply that failure to enter secondary care is a bad thing,	Thank you for your comment. We have made a number of amendments to the text including updating the references and clarifying that sub-optimal care also occurs in secondary care. We consider it to be a balanced view. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short

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				when the whole direction of travel epitomised in the 2009 guideline was to equip primary care to play a leading role in the management of adults with depression. We are surprised by this apparent shift in the direction of travel – there appears to be no obvious evidence for such a shift and we would challenge whether secondary care will be able to cope with a large influx in the number of referrals from GPs who have exhausted the newly suggested and more limited options for primary care pharmacological treatment. This also runs counter to many STP plans, local commissioning intentions, and local NHS strategic objectives, many of which focus on the delivery of effective interventions in primary care and community settings to reduce admissions to hospital and specialist care, maintaining care closer to patients' homes and in settings viewed as less stigmatising by the patients themselves.	guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Lundbeck Ltd	Full	42	24-26	The draft guideline erroneously describes vortioxetine as "an SSRI with additional activity at the 5HT1A and 5HT7 receptors". This is not correct; vortioxetine is not a member of the SSRI class. Whilst vortioxetine does inhibit 5-HT reuptake, its mode of action is distinct compared to SSRIs and results in a profile	Thank you for your comment. We have amended the text to describe vortioxetine as a multimodal antidepressant. We have also used the text from chapter 7 about its mode of action, to ensure consistency.

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				similar to that of combining multiple single-modality ADs. It is therefore better described as a 'multimodal antidepressant'; it is categorised as an 'other' AD in the British National Formulary. In addition, vortioxetine's action on 5-HT receptors is more complex than simply 'additional activity at 5HT1A and 5HT7 receptors'. Studies have shown that vortioxetine has six pharmacological targets and two modes of action; in addition to inhibition of the serotonin reuptake transporter it is an agonist for 5-HT1A, a partial agonist for 5-HT1B receptors, and an antagonist of 5-HT1D, 5-HT3, and 5-HT-7 receptors (Lundbeck Ltd, 2017). This distinct profile results in modulation of neurotransmission in several systems, including predominantly the serotonin but also the noradrenaline, dopamine, histamine, acetylcholine, GABA and glutamate systems (Lundbeck Ltd, 2017). This multimodal activity is considered responsible for the AD and anxiolytic-like effects and the improvement of cognitive function (Lundbeck Ltd, 2017). We feel that vortioxetine's multimodal mode of action should be more accurately described to avoid any confusion with SSRIs.	

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				References: Lundbeck Ltd. Vortioxetine Summary of Product Characteristics. January 2017.	
National School of Primary Care Mental Health Interest Group	Full	43		The stepped care model in the Delivery of Care section needs clarification to explain where the different treatment steps are like to take place - i.e. primary, secondary or tertiary care. Again the references used to back up the statement that treatment often falls short of recommended guidelines are over 20 years old - 1995 and 1996. There is an implication that more patients should be being referred to secondary care, but in most areas of the country access to secondary care for non-psychotic disorders can be very limited with long waiting lists unless the patient is very unwell and patients may also be resistant to this - encouragement of an effective liaison model might be more appropriate and cost-effective.	Thank you for your comment. The purpose of this section is to introduce the concept of stepped care, not to make recommendations about how this is delivered. The references in this section have been updated. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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Society for Psychotherapy Research (SPR) UK Chapter	Full	43 247 292 293 79	2 -8 25-33, 46-50 1-4 38-41	**Patient choice and range of evidence-based treatments** We welcome the draft guideline's recognition and emphasis on patient choice in section 2.4., particularly, as the inclination to offer choice has been slow to grow (Dixon, 2009) despite the recognition of the need to integrate service user choice and shared decision making as an important part of the National Health Service reform (Department of Health, 2009; Coulter, 2010). Moreover, there has been an accumulating evidence base that patient preference has a significant impact on treatment outcome (e.g. Gelhorn et al, 2011; Williams et al., 2016). However, we are very concerned that recommendations made in the draft guideline do not support this as it seems to stress the ambition to recommend as few treatments as possible. We are very concerned that the guideline disregards the existing robust evidence base that many psychological treatments are as effective as each other (see Cuijpers, 2017, for an overview). There are serious problems with the ranking system applied in the draft guideline and particularly with the decision to place decisive emphasis on cost effectiveness over evidence of treatment effectiveness. By including a ranking system,	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline an offer of treatment. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When making the recommendations for specific interventions, the committee took into account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details

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				an arbitrary hierarchy of effectiveness of treatments has been created, which does not reflect what the current evidence says. We are furthermore concerned about the statement on p. 247, l. 25-33, repeated on p. 292, l. 46-50 and on p. 293, l. 1-4, which contradicts the previously made emphasis. It states: "*The GC discussed the issue of patient choice, with the lay members offering the opinion that many people are happy solely with a choice of either evidence based psychological or pharmacological therapy, with choices between different therapies of the same modality being of less concern. They thought that there would be a subset of patients who would have researched therapies carefully and would have a strong preference, but that this would not apply to the majority of people. Other issues such as choice of the gender of the therapist, the setting in which interventions were provided and good information on the content of, potential harms or side effects and likely outcomes of an intervention were also considered important*". We recommend an amendment to these sections in order to avoid contradictions within the document. We furthermore would like to highlight that no information is included as to who the lay members were and whether their views	of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective. The text about patient choice (p 247, line 25 of the consultation version of the guideline) was incorrect and has been amended. Details of the lay members of the committee are provided at the start of the full guideline document. Lay members of NICE guidelines provide their own personal opinions and experiences. They do not 'represent' the experiences of all people with depression – given the large number of people who have depression this would not be practical. Consultation on the draft guideline is an effective way to elicit views from a wider range of people, including those of service users, about the recommendations that have been made. This feedback is then taken into account, in line with NICE processes, to form the final guideline. The text you quote from personal account D comes from the patient experience section of the guideline. As specified in the scope, the

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				reflect the majority of individuals with lived experience of depression. This statement also contradicts the accounts of the individuals in section 4. For example, personal account D: "*I am encouraged to see that a lot of resources are being put into providing CBT for people with depression, but CBT is not the right treatment for everyone with depression and this needs to be recognised*." (p.76, l. 38-41). Patient informal and formal feedback shows that different modalities of psychotherapy has had different impacts at different periods in their life, and it is thus crucial that we ensure that our health service provides and offers a range of evidence-based treatments. **References:** Coulter, A. (2010). Do patients want a choice and does it work? BMJ, 341: c4989. Cuijpers, P., 2017. Four decades of outcome research on psychotherapies for adult depression: an overview of a series of meta-analyses. Canadian Psychology/Psychologie canadienne, 58(1), 7-19. Department of Health (2009). The NHS constitution. Dixon, S. Report on the national patient choice survey March 2009. Department of Health, 2009 Gelhorn, H.L., Sexton, C.C., and Classi, P.M.	patient experience section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on patient experience has not been reviewed or updated. Thank you for bringing these references to our attention. Coulter 2010, Cuijpers 2017, Department of Health 2009, Dixon 2009 and Williams 2016 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs) Gelhorn 2011 could not be included as the comparison of patient preference relative to no preference does not match the review protocol. Patient preference, choice and the principles of shared decision making were considered by the committee during the interpretation of evidence and making the recommendations.

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				(2011). Patient preference for treatment of major depressive disorder and the impact on health outcomes: a systematic review. Primary Care Companion CNS Disorder, 13(5), PCC.11r01161. Williams, R., Farquharson, L., Palmer, L., Bassett, P., Clarke, J., Clark, D.M., and Crawford, M.J. (2016). Patient preference in psychological treatment and associations with self-reported outcome: national cross-sectional surbey in England and Wales. BMC Psychiatry, 16:4	
University of Exeter	Full	43	10-11	please add behavioural activation as a high intensity therapy to the list	Thank you for your comment. We have removed mention of any specific psychologcial therapies here as on reflection we think it would not be appropriate to single out particular treatments.
Royal College of Psychiatrists	Full	44	12	"The efficacy of ECT probably exceeds that of pharmacotherapy". It is inappropriate to have the word "probably" here. There is clear RCT evidence that shows that ECT is superior to drugs in terms of both response and remission both as a first-line treatment and in the treatment of refractory illness. This was found by the UK Review group in 2003 (with a large effect size) and again by NCCMH in 2009 as part of CG90.	Thank you for your comment. We have reviewed the text in light of your comment and made some ammendments. This text is a brief introduction to ECT, discussion of the evidence on ECT is covered in Chapter 12.
Royal College of Psychiatrists	Full	44	16	"…which is a particular concern for older patients." Why is longer term autobiographical memory loss (which is	Thank you for your comment. Memory problems may well be a cause of concern for some older people so it was thought

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				relatively uncommon) more of a concern for older patients? We would have thought it was more of a concern for patients of working age required to remember things for their job etc. This unreferenced statement is inappropriate.	important to mention it here.
Royal College of Psychiatrists	Full	44	17	"Unilateral electrode placement is … less efficacious." This statement needs updating in the light of Semkovska et al 2016, an RCT which found that RUL ECT is as effective as BL ECT, with fewer cognitive adverse effects. http://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2015.15030372 This was also the conclusion of a systematic review and meta-analysis of RCTs comparing bi-temporal with high-dose unilateral ECT (Kolshus E, Jelovac A, McLoughlin DM (2016). Bitemporal v high-dose right unilateral electroconvulsive therapy for depression: a systematic review and meta-analysis of randomized controlled trials. Psychological Medicine, 47, 518-530.)	Thank you for your comment. We have removed this statement.
Royal College of Psychiatrists	Full	44	21	"… ECT is usually used for the treatment of severe, high risk depression or following unsuccessful treatment with pharmacotherapy." It is important to note that the positive evidence for ECT extends well beyond these groups and the restriction in its use is a phenomenon related to Guidelines including NICE Guidelines. Left to clinicians' evidence-based judgements, ECT would be far more widely used. (Please see more	Thank you for your comment. This text aims to describe the current use of ECT in the management of depression. As you note the NICE guidance restricted its use to the treatment of severe, high risk depression or following unsuccessful treatment with pharmacotherapy. Therefore the current text is accurate in terms of the current use of ECT.

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				detailed discussion on this point at comment number 15)	
The Society of Homeopaths	full	45	6	Given the inclusion of aromatherapy and acupuncture, we would like to point the committee towards three recent, high quality RCTs at low risk of bias, showing the efficacy of homeopathic medicines in the treatment of depression. (Adler et al. 2011 & 2013; and Macias-Cortez, 2013). Furthermore we would like to point the committee towards the recent publication of a pragmatic RCT conducted in the UK, demonstrating the effectiveness of treatment by homeopaths for depression with 566 patients (Viksveen et al.2017). An intention-to-treat analysis of the offer group at 6 months reported a 1.4-point lower mean depression score than the no offer group (95% CI 0.2, 2.5, p=0.019), with a small standardized treatment effect size (d=0.30). Using instrumental variables analysis, a moderate treatment effect size in favour of those treated was found (d=0.57) with a between group difference of 2.6 points (95% CI 0.5, 4.7, p=0.018). Results were maintained at 12 months. A meta-analysis of homeopathic treatment for depression is in press (Viksveen et al.) concludes that " Limited evidence from high	Thank you for your comment. The committee did not consider homeopathic medicines to be interventions that were in regular clinical use for the treatment of depression. Therefore these interventions were not specified in any of the review protocols and consequently the studies that you cite (Adler et al. 2011 & 2013; Macias-Cortez 2013; Viksveen et al 2017) would not have met the inclusion criteria for the reviews. As such the evidence on homeopathic medicines has not been appraised and we are not able to make any recommendations on their use.

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				quality placebo-controlled double-blinded trials suggests HMPs may be comparable to antidepressants and superior to placebo in depression, and patients treated by homeopaths in other studies report improvement in depression. Overall, the evidence gives a potentially promising risk benefit ratio". **References.** Adler UC, Paiva NMP, Cesar AT, et al. Homeopathic individualized Q-potencies versus fluoxetine for moderate to severe depression: Double-blind, randomized non-inferiority trial. *Evid Based Complement Alternat Med* Adler UC, Krüger S, Teut M, et al. Homeopathy for depression: A randomized, partially double-blind, placebo-controlled, four-armed study (DEP-HOM). *PLoS ONE* Macías-Cortés EC, Llanes-González L, Aguilar-Faisal L, et al. Individualized homeopathic treatment and fluoxetine for moderate to severe depression in peri- and postmenopausal women (HOMDEP-MENOP study): a randomized, double-dummy, double-blind, placebo-controlled trial. *PLoS One*	

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				Viksveen, P; Relton, C; Nicholl, J. (2017). Depressed patients treated by homeopaths: a randomised controlled trial using the "cohort multiple randomised controlled trial" (cmRCT) design. TRIALS: 18: 299 Viksveen, P; Fibert, P; Relton, C. (2017) Homeopathy in the treatment of depression: a systematic review. (*European Journal of Integrative Medicine*) In press.	
University of Liverpool	Full	46		Evidence on economic costs could also make reference to 'return on investment analyses' esp Chisholm D, Sweeny K, Sheehan P, Rasmussen B, Smit F, Cuijpers P, Saxena S.Scaling-up treatment of depression and anxiety: a global return on investment analysis. Lancet Psychiatry. 2016 May;3(5):415-24. doi:10.1016/S2215-0366(16)30024-4. Also, worth noting somewhere that overtreatment for depression can be costly. See e.g. Vasiliadis HM, Latimer E, Dionne PA, Préville M. The costs associated with antidepressant use in depression and anxiety in community-living older adults. *Can J Psychiatry* 2013;58:201-9.	Thank you for your comment. We have now included this evidence in the introductory section about the economic cost of depression.
Lundbeck Ltd	Full	46	9-15	The GC's apparent criticism of primary care is disappointing, given that this signifies a	Thank you for your comment. Feedback was received from stakeholders that there would

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				reversal of the policy adopted in the 2009 version of the guideline; namely, to manage a greater proportion of adults with depression in primary care. By relying on references that are more than 20 years old, this paragraph fails to take into account significant changes in terms of how NHS primary and secondary care are configured over the last two decades, as well as the improvements in care and outcomes which have been observed as a result of the 2009 guideline. We acknowledge that there is still some way to go to deliver the improvements in care and outcomes envisaged by the 2009 guideline fully and comprehensively across the whole of the NHS, but do not believe that this warrant the complete change of direction envisaged in this 2017 version: namely, that the prescribing of all pharmacological interventions, other than SSRI or mirtazapine monotherapy, must take place under the care of a specialist. We believe that this is a retrograde step; it will result in more people waiting for a referral from their GP and secondary care will struggle to cope with the influx of new referrals.	not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Lundbeck Ltd	Full	48		We are surprised that the references for the burden of illness and the costs of treating depression are so out-of-date. We are surprised that more up-to-date estimates are	The references included in this section were identified via a systematic search of the literature from year 2003 and up to year 2016. All relevant references were included

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				not available. We believe the figures stated here significantly under-estimate both the number of people with depression, as well as the costs to the NHS and society.	in this section. Reporting of relevant data depends on the availability of such data in the published literature. Nevertheless, we would not consider the review out-of-date: The section includes 2 studies published in 2003, 2 in 2006, 1 in 2007, 1 in 2008, 2 in 2011, 1 in 2012, 1 in 2014, 2 in 2015 and 1 in 2016. In addition, two studies published in 2013 and 2016, respectively, have been added in the review of the cost of illness.
British Association for Counselling and Psychotherapy	Full	50	General	***Consideration of service user voice in revised Guideline:*** We note the inclusion of service users in the development of the draft Guideline (section 3.3.2) however we argue that this has been insufficient to ensure that service user voices have been properly included in the draft Guideline. This is because NICE elected not to update the guidance derived from qualitative data in this review of the Guideline; rigorously reviewing and synthesizing (Timulak, 2009) qualitative studies on service user experiences of depression and depression treatment is, we would argue, the only empirically supported way to ensure that a broad range of service user experiences are incorporated into the Guideline. The failure to systematically include service user voices in this way is disappointing given that NHS England's business plan for 2016/17 sets out a commitment: "to make a genuine shift to	Thank you for your comment. As you note and as specified in the scope, the patient experience section from the 2009 guideline was not included in this update. However, consultation on the draft guideline is an effective way to elicit views from a wider range of people, including those of service users, about the recommendations that have been made. This feedback is then taken into account, in line with NICE processes, to form the final guideline. Therefore we do not think that we have failed to consider service user voices. We did not consider qualitative evidence on the effectiveness of different treatments for depression because we do not consider this to be the best available evidence when differentiating the relative efficacy of different interventions.

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				place patients at the centre, shaping services around their preferences and involving them at all stages" (NHS England, 2016, p.49). NICE has a similar commitment (NICE Patient and Public Involvement Policy, 2017). In our view, it is particularly egregious that NICE did not revisit the qualitative evidence around treatment of depression because while NICE processes do not (currently) allow such data to be included in the final summative analyses that shape key recommendations, a number of researchers (Hill, Chui, & Baumann, 2013; Midgley, Ansaldo, & Target, 2014) argue that qualitative outcome studies should be included. This is because they "offer a significant challenge to assumptions about outcome that derive from mainstream quantitative research on this topic, in relation to two questions: how the outcome is conceptualised, and the overall effectiveness of therapy" (McLeod, 2013, p.65). Reviewing existing literature, McLeod suggested patients themselves conceptualise outcome much more broadly than in terms of symptom or behavioural change (Binder, Holgersen, & Nielsen, 2010). Typically patients acknowledge ways in which therapy has been helpful but also where it has failed, suggesting that quantitative outcome	Thank you for bringing these references to our attention. Hill 2013, Midgley 2014, McLeod 2013 and Binder 2010 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				research may overstate therapeutic effectiveness. Qualitative studies can also help answer questions about patient experience and expectations of NHS services, including whether treatments are credible and acceptable to them, which have an impact on outcomes.	
South West London and St. George's Mental Health NHS Trust	Full	50	29	We are concerned that the expert advisor panel did not include an IPT specialist, despite IPT being a frontline recommendation in the 2009 requiring review, and despite the lack of an IPT specialist on the committee. Whilst we understand that the committee must remain objective, IPT is not adequately explained in the guidance, and we are concerned that this is due to the lack of an expert advisor. Page 195 includes a description of the utility of IPT which seems to be based on a description of the focal areas, and as such is inadequate in scope. The descriptions of the utility of both couples therapy and short-term psychotherapy could equally be applied to IPT and we believe this description should be revisited.	Thank you for your comment. Given the breadth of interventions available for the treatment of depression it would not be practical for the committee to include someone with expert knowledge of each potential intervention. However, consultation on the draft guideline is an effective way to elicit views from people with expert knowledge of specific interventions, about the recommendations that have been made. This feedback is then taken into account, in line with NICE processes, to form the final guideline. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for

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					treatment of less and more severe depression in line with the new results. IPT remains an option for the treatment of less severe depression. It has also been added to the treatment options for more severe depression. The caveats for the application of IPT, counselling and STPT are based on the committee's consideration that the effectiveness and cost effectiveness of these interventions was likely to be higher in the sub-population specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis.
Lundbeck Ltd	Full	52		The search strategy for the systematic review was developed to locate as much relevant evidence as possible, and the search strategy included the HTA database. We are therefore at a loss to understand why the GC did not consider NICE TA367 a relevant piece of evidence for this guideline, particularly in view that the final scope (appendix A) for this guideline stated that vortioxetine and TA367 was relevant to this guideline update.	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline.

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					However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Ltd	Full	52	11-21; 27-31	In our opinion, the search strategy put in place after the finalisation of the scope was not sufficiently comprehensive because it failed to include vortioxetine as a search term, even though the final scope for this guideline update specifically mentioned that the vortioxetine TA was "closely related" to the guideline update. It is inexplicable that a search that extended to the HTA database was unable to identify TA367 (NICE, 2015) as being a relevant source of clinical evidence for the purposes of this guideline update. We believe that the clinical search strategy was flawed. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes (November 2015).	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We therefore do not think that the search strategy in the guideline was flawed. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
British Association for Counselling and	Full	54	General	***Consideration of bias:*** BACP notes the various efforts to manage risk of bias. The Guideline authors did not use the	Thank you for your comment. In response to your comment regarding researcher allegiance, we agree that this is a potential source of bias. However, it is not captured by

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Psychotherapy				Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for rating the quality of evidence, "because GRADE was not developed with network meta-analysis in mind" (Section 7.4 and 7.5). Although it is true, at least two GRADE-based evaluation systems are available for network-meta-analysis (Salanti et al., 2014; Puhan et al., 2014). It is acknowledged that these systems are recent yet although the Guideline authors address important GRADE-related issues while rating the quality of evidence, the assessment of quality of evidence conducted falls short of what is required by the two referenced systems, particularly with regard to the assessment of direct and indirect evidence (along with their methodological quality) for each effect estimate as well as regarding ranking treatments. In addition, there does not seem to have been broader effort to systematically consider bias related to researcher allegiance (RA). This is problematic given evidence from a meta-meta-analysis that "across n=30 meta-analyses the RA–outcome association was r=.262, corresponding to a moderate effect size" (Munder, Brutsch, Leonhart, Gerger & Barth, 2013). This is important, the study authors argue, since the estimate of the	the Cochrane risk of bias tool that we used for this review. In head-to-head trials, one might assume, that this bias would balance out as the researchers for 1 study could be committed to 1 type of treatment whereas researchers of another study could show reverse allegiance, and thus across studies the positive and negative sources of bias should balance. In comparisons relative to a non-active control this would be partially captured but only where the source of funding or declared conflicts of interest can be used as a proxy for researcher allegiance to a specific intervention. We agree that in principle adjusting for risk of bias in individual trials would be a more rigorous analysis than the sample size (small study bias). However for these analyses to work, we would need to have a good spread of "good" and "bad" studies across the network, which is not the case. In the less severe network, only 14 (out of 205 RCTs included) would be rated as low risk of bias. In the more severe network, only 1 (out of 145 RCTs included) would be rated as low risk of bias. The number of studies that are rated as high risk of bias would mean that results would not be meaningful as we need to have a considerable body of low risk of bias studies in order to compare the high risk

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				impact of researcher allegiance is greater than the typical difference in effectiveness between different types of therapy. As the authors of a network meta-analysis focussed on depression state of their own results: "Because data on a comparison level like allegiance cannot be considered in network meta-analysis, it is likely that researcher preferences influence the treatment effects found in this study to some extent" (Barth et al., 2013; p11). BACP argues that similarly Researcher Allegiance also likely significantly biased the individual RCTs included in the network meta-analysis and thus the overall findings. The Guideline authors also performed a sensitivity analysis in which the treatment effect estimates were adjusted for bias assumed to be present in small studies (as a proxy for publication bias), as described in Section 7.3 and Appendix N. They estimated bias for comparisons of active treatments with controls (while assuming that no bias is present in the comparisons of active treatments), and adjusted the effect estimates to account for this bias. As reported in Section 7.4 and 7.5, these analyses generally did not change the main conclusions, but in some cases had a substantial impact (changing the results) and	of bias studies to them. In response to your comment we have justified this further in the guideline including the detail above and clarification that the small study adjustment is not only trying to compensate for publication bias but is also using the study size as a proxy for other quality factors – larger studies are usually better conducted.

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				sometimes were hard to interpret (bias in the opposite to the expected direction). Although these analyses may provide some rudimentary help for appraising the evidence, they are in general rather simplistic. Adjusting for risk bias in individual trials was not attempted, even though considerable variation in the methodological quality of the included trials was observed (Section 7.4 and 7.5). Overall it is clear that the NMA has in several areas not properly accounted for or managed risk of bias; this inevitably reduces confidence in the findings of the analysis.	
Lundbeck Ltd	Full	54	27-29	By excluding vortioxetine from all the review/research questions, evidence relating to this AD was excluded from both the network-meta-analysis (NMA). We understand this could be due to the initial treatment (or first line) focus of chapter 7. However, we do not understand why evidence relating to vortioxetine, including TA367, was excluded from the review questions for chapter 8. We therefore believe the methodology and results are flawed, meaning the pathway recommendations for chapter 8 should be interpreted with caution.	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We therefore do not think that the

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					methodology or results in the guideline are flawed. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Ltd	Full	60	33-44	In our opinion, the search strategy put in place after the finalisation of the scope was not sufficiently comprehensive because it failed to include vortioxetine as a search term, even though the final scope for this guideline update specifically mentioned that the vortioxetine TA was a TA that was "closely related" to the guideline update. It is inexplicable that a search that extended to the HTA database was unable to identify TA367[1] as being a relevant source of clinical evidence for the purposes of this guideline update. We believe that the clinical search strategy was flawed.	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We therefore do not think that the search strategy used by the guideline was flawed. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Ltd	Full	62	44-	We have concerns about the exclusion	Thank you for your comment. We have now

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			45	criterion, which states "Studies comparing healthcare costs of adults with depression receiving branded versus generic forms of drugs were not considered in the economic literature review". We would ask for clarity on this point. Does this relate to branded versus generic forms of the *same* drug/molecule, or to studies that compare branded drugs to different medications that are in generic formulation? If it relates to the latter, we are concerned that this appears to focus on the medicine's acquisition cost and not its cost-effectiveness, which is a different consideration. In TA367, vortioxetine was compared to a broad range of generically available ADs and found to be a cost-effective use of NHS resources as an "option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode" despite being a branded AD.	clarified in the text that branded versus generic forms of the same drug were not considered in the review. We have included studies comparing branded forms of 1 or more drugs with generic forms of other drugs in the guideline economic review.
Royal College of Psychiatrists	Full	68	lines 7-9	**Proper weight should be given to outcomes reported at long-term follow-ups/observation periods, where these are available, rather than exclusively treatment endpoint.** We are concerned that due weight has not been given to outcomes reported at long term	Thank you for your comment. We did not consider follow-up for further-line treatment or for chronic depression as this data was not widely available across different intervention types and thus did not enable meaningful comparison. We did, however, include longer-term follow-up data in the relapse prevention review so we do have

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				follow up, rather than exclusively treatment endpoint. This should be for all studies, but particularly those for chronic depression and TRD. This data, where available, should be taken into account when making recommendations, and any recommendations for future research should include the need for further studies. Chronic forms of depression are defined as being at least 2 years duration, and often longer (See Keller et al., 2000; Kocsis et al. 2007; Schramm et al., 2011; Fonagy et al. 2015. Referring to the individuals included in the previous qualitative analysis in the previous guidelines, it is stated that "all of the personal accounts received were from people who have/have had severe and chronic depression, spanning many years." Moreover there is a high relapse rate (e.g. Westen et al., 2004; Hepgul et al., 2016) Long term follow up data is therefore critical. We also recommend that any RCT reporting significant after end treatment follow up or periods of observation for at least 12 months, and ideally longer, should be reviewed and upgraded by the GRADE system. Trials that	evidence in the guideline pertaining to longer-term effects of maintenance treatment. In GRADE RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The availability of long-term follow-up data is not a valid reason for upgrading within GRADE. However we agree that it is important that long-term follow up data are collected in future research to enable comparison of this outcome across different interventions. We have therefore amended our research recommendations to specify that these data need to be collected. Thank you for bringing these references to our attention. Hepgul 2016 and Westen 2004 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				demonstrate treatment which shows significant impact at the end of treatment, but no data regarding follow-up, are arguably weaker studies, particularly in relation to chronic forms of depression. References Hepgul N, King S, Amarasinghe M, et al (2016). Clinical characteristics of patients assessed within an Improving Access to Psychological Therapies (IAPT) service: results from a naturalistic cohort study (Predicting Outcome Following Psychological Therapy; PROMPT). BMC psychiatry, 16(1), p52. Westen, D., Novotny, C. M., & Thompson-Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. Psychological Bulletin, 130, 631– 663. McPherson S, Cairns P, Carlyle J, Shapiro D, Richardson P & Taylor D (2005) The effectiveness of psychological treatments for refractory depression: A systematic review, Acta Psychiatrica Scandinavica, 111, 331-340.	McPherson 2005 has been searched for relevant references. However, no additional studies that meet inclusion criteria were identified.

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Royal College of Psychiatrists	Full	68 97 225	9-11 3-14 23-	**Need for more studies of long-term therapy and concerns over assumptions regarding their cost-effectiveness** In the service user section it is reported that two of the themes that are most frequently expressed in the testimonies include childhood trauma and the need for long-term psychotherapy for people with severe and chronic depression. *"The themes that are most frequently expressed in the testimonies include trauma or conflict in childhood as a perceived cause of depression; the need for long-term psychotherapy for people with severe and chronic depression"* Full, p. 78 lines 28-30 Personal account E "*I also feel that long-term psychodynamic therapy should be available, on the NHS, which can get to the root of the issues that cause depression. I now know that I will have depression until I can resolve my childhood issues.*" *"There was a strong feeling within the service user and carer topic group that the excerpt from Howe (1995) in the section above highlights the reasons why many people opt for private therapy; that is, that psychological treatment offered by the NHS in the form of*	Thank you for your comment. As specified in the scope, the patient experience section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline but the evidence on patient experience has not been reviewed. However, in light of your comment we have removed the text "The service user and carer topic group do acknowledge, however, that as there has been little research into the efficacy of long-term psychodynamic therapy, it cannot be recommended as a course of treatment in this guideline." as it is now factually incorrect. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The text in the guideline has been updated as a result and no longer contains the text that you quote about long-term psychodynamic psychotherapy. We have

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		245	25 28-31	*CBT does not go far enough in addressing the trauma experienced in childhood. The study by Ridge and Ziebland (2006) confirms the opinions of the topic group and the testimony from the personal accounts that people with 'deep and complex problems felt the need for longer term therapy'. Those that have had long-term psychodynamic therapy report that it has been helpful in their under-standing of themselves and their depression and that until they have worked through and repaired the damage experienced in childhood, depression will be a major factor in the person's life. The service user and carer topic group do acknowledge, however, that as there has been little research into the efficacy of long-term psychodynamic therapy, it cannot be recommended as a course of treatment in this guideline"* Since this statement was made several years ago, studies have been carried out on psychodynamic psychotherapy for long term depression (Fonagy et al, 2015; Town et al, 2017, so even if the service user experience section is not updated, it is nevertheless important to take these comments into account, as well as the role of trauma and importance of functioning reported by service users, in the current guideline. We have concerns over assumptions	now clarified that the committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. We agree that more long-term outcomes for depression studies for both initial treatments and for those with chronic depressive symptoms would be highly desirable. However, very few studies report long-term outcomes. There is increasing concern in the research field that longer-term outcomes need to be routinely reported and measured in studies of depression. We have drawn attention to this in our research recommendations.

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				regarding cost-effectiveness of long-term psychotherapy: The guidelines report that for first episode, non- severe depression: "*Long-term psychodynamic psychotherapy showed a large benefit and was ranked fourth in both the SMD and response in those randomised analyses; no remission data were available for long-term psychodynamic psychotherapy.*" "*The GC noted that, although long-term psychodynamic psychotherapy ranked in a higher place than CBT and behavioural therapies, this was not included in the economic analysis due to lack of suitable data, but, nevertheless, it was very unlikely to be cost-effective, given its high resource use intensity.*" These assumptions are not substantiated due to the lack of available evidence. Longer-term treatments may be more cost effective in the long run in reducing rate of relapse and better long term outcomes. It appears that the health economic analyses are used in the guidelines to justify treatment decisions with insufficient evidence and a failure to show sensitivity analyses. Hence the need to	

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				recommend more studies in this area.	
Norfolk & Suffolk Foundation Trust	Full	293/4		IPT does not appear to be recommended at all for severe depression unless several other interventions have been tried (for limited response and treatment-resistant depression) etc. My understanding of the key research on IPT is that it is an effective treatment for depression especially in combination with anti-depressants for severe depression and that the research for maintenance IPT is very strong. IPT has been getting very good results in IAPT services Nationally (2014-17) and I believe it has been the most effective face to face therapy for depression for the last two evaluations. Patients in the IAPT evaluation included patients with 'more severe' depression (PHQP 15 plus). Data from our Wellbeing Suffolk service has shown that most patients offered IPT were in the 'more severe' range and that comparably good outcomes were achieved for both 'more severe' and 'less severe' depression and that there were positive outcomes for patients who were put straight to IPT or 'stepped up' after a first intervention had not been sufficient. Wellbeing Suffolk is part of The Norfolk and Suffolk Foundation Trust providing Low and	Thank you for your comment and for providing us with data from the IAPTUS electronic patient record. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication.

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				High Intensity IAPT psychological interventions and Wellbeing services. IPT for adults in Suffolk is provided by 6 IPT-UK/IAPT accredited Therapists including one IPT-UK/IAPT accredited supervisor. A review of treated* cases using data from the IAPTUS electronic patient record showed that: • 87 Patients completed IPT in Wellbeing Suffolk between 26 May 2015 and 8th August 2017 • Overall 64 out of 87 patients recovered with IPT (i.e. Last PHQ9 = <10 and Last GAD7= <8) So **74% of depressed patients recovered with IPT** • 49 of 87 (56%) had a first PHQ9 score of 18+ so in the' More Severe Depression' range for the draft guideline Of these 35 reached recovery (i.e. Last PHQ9 = <10 and Last GAD7=<8) so **71% of 'More Severe Patients recovered with IPT** • 32 out of 87 (37%) patients were stepped - up to IPT after another intervention. Of these 22 patients recovered (i.e. Last PHQ9 = <10 and Last GAD7= <8). So **69% of patients stepped up to IPT after another**	Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).

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				intervention recovered with IPT *Patients were considered to be treated if they met an IPT therapist for more than 2 sessions. Patients who had 3 or more sessions and did not complete were included and recorded as dropped out - 7 patients dropped out and only 1 of those patients was in recovery (i.e. Last PHQ9 = <10 and Last GAD7= <8) when they discontinued.	
National School of Primary Care Mental Health Interest Group	Full	82		It is not obviously appropriate to draw conclusions from the Healthtalkonline transcripts, not necessarily a representative sample, prior to presenting data gleaned from published qualitative reviews.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.
National School of Primary Care Mental Health Interest Group	Full	97		The statement that long-term psychodynamic psychotherapy could not be recommended in this guideline does not seem entirely warrented given the apparently positive results for longer-term psychotherapy for more severe depression presented in Chapter 7 - page 265 - albeit for small numbers.	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. Maljanen (2016) has now been excluded from the NMA for less severe depression because no endpoint data were available (previously follow-up data had been entered into the model in error). Therefore there is no longer any data on

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					LTPP included in the analysis of less severe depression. LTPP remains as an intervention that is included in the NMA for more severe depression. As there are no longer any data on LTPP in the NMA for less severe depression the committee have not made a recommendation about this intervention for first line treatment of a new depressive episode. For the economic analysis for more severe depression we needed discontinuation data, response in completers data and remission in completers data. The single study on LTPP in more severe depression reported dichotomous data on discontinuation and remission (both in completers and those randomised). It also reported continuous data; however, these were reported for the ITT sample at baseline and completer sample at endpoint so it was not possible to include them in any analysis that utilised continuous data (i.e. either SMD, response in those randomised or response in completers). Due to lack of response in completers' data the study of LTPP could not be included in the economic analysis. The committee considered the results of the clinical analysis (using the SMD as the main

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					clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. Consequently no recommendation has been made about the use of LTPP for more severe depression. Full details of the committee's rationale for making the recommendations for treatment of a new depressive episode are documented in the 'evidence to recommendations' sections (7.4.5 and 7.7).
Royal College of Psychiatrists	Full	98	5	A quantitative analysis of the views of 4 patients has no place in guidance of this type. See details above in point 5 for more comprehensive data.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to this section.
Swansea University	full	104		The guideline issues advice to monitor patients for any adverse effects of their medicines in general terms, but no specific strategy is mentioned. Where scheduled follow ups are arranged, how should patients	Thank you for your comment. It is not possible to include detailed strategies for monitoring for adverse effects of all medicines. This would be a matter for clinical judgement. However additional detail has

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				be monitored for potential adverse effects? What steps are taken to check whether pregnancy is likely?	been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity.
British Association for Counselling and Psychotherapy	Full	15; 49; 50	General	***Guideline Committee membership:*** We note that the committee membership is broadly described in section 3.3 (p50) of the draft Guideline and that the group members are named on p15 of the same document. We point out however that no information is given about the specific professional allegiances of the members of the guideline group, such as which therapies and interventions they have been trained in, or which they research, train others in, and currently use/ recommend to patients. This information is necessary for transparency and, in our view, is vital in order that the work of the group can be properly scrutinised and assessed for possible bias (Munder, Brutsch, Leonhart, Gerger & Barth, 2013). What is termed 'researcher allegiance' is a known biasing factor in psychotherapy research and in our view it is something that NICE should be systematically considering and seeking to protect against. This is critical since, as stated in the draft Guideline, the	Thank you for your comment. NICE have a policy on declaring interests that all members of their committees abide by. The interests declared by the Depression committee are documented in Appendix B of the guideline. All the interests declared have been managed in line with NICE policy.

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				committee have a particular role in facilitating conclusions to be drawn in areas where there is a lack of data or findings are inconclusive (section 3.1, p49); in other words it is where the evidence is weakest that the role of the (potentially biased) committee is strongest.	
NHS England National IAPT Team	Full	134	7-17	Clarity about the components of collaborative care is helpful.	Thank you for your comment and your support.
Royal College of Psychiatrists	Full	134	3 - 4	Again a terminology issue – older people? Should it be explicitly clarified what is meant by the term older people or older adults?	Thank you for your comment. The committee debated whether or not it was possible to define older people by including a specific age range in the recommendations. However, they agreed that doing this could result in people being inappropriately excluded from the recommendations (for example if they were 1 year younger than the age specified). They therefore decided not to specific any age limit for 'older people'
British Psychoanalytic Association	Full	67 – 99	General	***3 The need for NICE to improve its long-term recommendations and to inform patients of the Tavistock Adult Depression Study results, so that they can exercise patient choice*** Chronic major depression is one of the most common major causes of disability, suffering and cost in the UK and world-wide, and yet the current NICE guidelines still do not include any satisfactory, evidence-based treatment showing effectiveness over the	Thank you for your comment. Fonagy 2015 is the publication of the clinical results from the TADS trial using the Taylor 2015 manual. Fonagy 2015 is included in the review for further-line treatment. The committee decided not to recommend LTPP for further-line as there was only data from a single study and the effects on both remission and depression symptomatology were not statistically significant.

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				long term. The requirement of NICE for RCT evidence of efficacy does not fit easily with the paradigm of the psychoanalytic approach. The 'sleeper' effect, whereby patients in psychoanalytic psychotherapy continue to show further improvement after the end of treatment, not only in symptoms, but in a range of relationships and social functioning, has been widely reported in psychoanalytic case reports and other publications for many years. The TADS research is impressive, in the way it has managed to accommodate an RCT with this psychoanalytic approach, without sacrificing the integrity of either. Psychotherapists have been able, as a result, to demonstrate the positive, long-term effect of psychoanalytic psychotherapy in the form required by NICE, and to produce results indicating that LTPP may offer profound and longer-term benefits to a significant number of patients for whom no treatment is currently available. This research offers NICE an opportunity to improve its recommendations. Among other reasons for including LTPP, we would note that patients have a right to this knowledge, in order to exercise their right to make informed choices, especially given that the	Stakeholders have commented that the guideline only considered endpoint and not follow-up data. However, if you consider 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although effects on depression symptomatology are statistically significant at this time point. Even with more consistent effects, the committee would be unlikely to make a recommendation on the basis of a single study.

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				section on patients' experiences in the draft revised NICE guidelines mentions a preference for psychodynamic or psychoanalytic psychotherapy[1]. The strength of the TAD Study and results allows NICE to recommend these forms of psychotherapy in response to stated preference. We therefore urge NICE to include Long Term Psychoanalytic Psychotherapy, on the basis of the Tavistock Adult Depression Study, and furthermore we suggest that this needs to happen as a matter of urgency, as the Study measures a form of NHS psychotherapy which has been regularly offered, but which is being put under pressure to conform to current guidelines for short-term treatments. Psychotherapy departments, which have the skilled resources to provide LTPP, therefore remain under threat. This risks depriving patients of the treatment they need and want and does not make good use of the skills and financial resources available.	
NHS England National IAPT Team	Full	166	39-40	Fully agree	Thank you for your comment.

[1] NICE Guideline: Depression in adults Draft for consultation 4.6.8

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British Autogenic Society	Full	168 191-194	14-32 36 to 36	PSYCHOLOGICAL INTERVENTIONS Recommended 1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. The number of lower cost healthcare professionals trained to deliver cost effective interventions at primary care level with groups whilst rising is low. Cost pressures and availability challenges continue in the NHS. Autogenic Training has been available through the NHS since the late 1950s and has been delivered successfully through GP offices in the Home Counties and Scotland since the mid 1980s. This form of therapy is easy to teach at the primary care level by trained case workers, psychological therapists, and GPs as it is a manualised programme of 8 weeks of 1.5 hour meetings with follow up over the course of 12 months. AT is readily taken up by patients, and is a cost-effective, high quality, acceptable approach which has been less accessible than the public would prefer (Patient Choice) and than the NHS can afford.	Thank you for your comment. We did not find any evidence to support making a recommendation for autogenic training. It was not possible to include the references cited as these were in non-depressed populations. Trials that specifically recruit participants with a particular physical health condition in addition to depression were also not included due to overlap with the NICE 'Depression in adults with a chronic physical health problem: recognition and management' (CG91) guideline.

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				Krampen (1999) notes: "While most of the treatment objectives of autogenic training are of relevance in the treatment of depressive disorders, this is especially true for the reduction of overwhelming negative affects. In addition, it is hypothesized that learning autogenic training contributes to the improvement of the activity level, structuring of everyday life, and self-control of patients with depressive disorders. Further, autogenic training aims to reduce psychosomatic symptoms which frequently accompany depressive orders as well as to reduce the individual's vulnerability to stressors and negative stress reactions. Therefore, it is hypothesized that the long-term effectiveness of combined treatment (i. e., psychotherapy and autogenic training) of depressive patients is better than that of psychotherapy without autogenic training. Treatment effectiveness criteria in the follow-up study presented here include relapse rates and treatment re-entry rates, as well as depressive symptoms and psychosomatic complaints" (p. 13). Hidderly and Holt's research carried out at with early stage breast cancer patients at the Derbyshire Royal Infirmary shows significant improvement in HADS scores for the AT group over the control group, yet no difference in T and B cell markers;	

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				importantly, whilst for those in the AT group who appeared to enter a meditative state as opposed to those who relaxed only, there was a difference in T and B cell markers and further study is required on this front (Hidderly, M & Holt, M. 2004, A pilot randomized trial assessing the effects of autogenic training in early stage cancer patients in relation to psychological status and immune system responses. *Eur J Oncol Nurs*. Mar;8(1):61-5. DOI: 10.1016/j.ejon.2003.09.003). There is continuing debate about the co-morbidity of anxiety and depression, which you have noted in the Guidance. We are happy to provide input to NICE database of qualitative and quantitative research on AT and anxiety, PTSD, and panic, and on "how AT works".	
The Pituitary Foundation	Full	168	38	Re: the accurate identification of depression is an essential first step in the management. This should incorporate patients being treated/investigated for other health conditions. Accurate identification is the key to ensure serious endocrine symptoms/conditions are not missed. Our organisation firmly believes that increased awareness by GP's of Pituitary	Thank you for your comment. This guideline is about the treatment and management of depression in adults. It is outside of the scope of this guideline to make recommendations on depression that is a symptom of another condition.

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				(and other serious endocrine conditions affecting hormone production) conditions is needed if patients are not to be dismissed and prescribed anti-depressants without any other relevant investigations being undertaken- i.e. failure to recognise serious conditions such as Cushing's Disease/Syndrome.	
University of Liverpool	Full	170		Discussion of practitioner perspectives focuses on therapeutic nihilism. But many thoughtful practitioners are also concerned about dangers of over-medicalisation of distress. See e.g. Dowrick C, Frances A. Medicalising unhappiness: new classification of depression risks more patients being put on drug treatment from which they will not benefit. BMJ. 2013 Dec 9;347:f7140. doi: 10.1136/bmj.f7140.	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section.
British Autogenic Society	Full References	172 60	1-15 34-35	DEFINITIONS – Case identification instruments We note that you have Referenced one article by Krampen, Günter (2015). We are concerned that this author's follow up study assessing long term effects of Autogenic Training with psychotherapy on depression was not included. This follow-up study and the short term study preceding it use the Beck Depression Inventory (German edition) and ICD-10	Thank you for your comment. Krampen 1997 is not included in the guideline as it does not meet inclusion criteria (non-English-language paper). Krampen 1999 could not be included as it was a follow-up to an excluded paper, and more generally, we did not consider follow-up for acute treatment as this data was not widely available across different intervention types and thus did not enable meaningful comparison. We did not find any evidence that met eligibility criteria in order to support making a

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				diagnostic criteria. We appreciate this opportunity to bring both studies to your attention. Krampen, Günter. (1999) Long-term evaluation of the effectiveness of additional autogenic training in the psychotherapy of depressive disorders. *European Psychologist*, 10169040, 19990301, Vol. 4, Issue 1 pp. 11-18. The prior study of short term effects of AT plus psychotherapy is: Krampen, G. (1997). Autogenes Training vor und begleitend zur methodenübergreifenden Einzelpsychotherapy bei depressiven Störungen[Autogenic training before and simultanous to integrative psychotherapy of depressive disorders]. Zeitschrift für Klinische Psychologie, Psychiatrie und Psychotherapie, 45, 214–232. Very briefly, the results of including Autogenic Training in the treatment are: "Depressive and Psychosomatic Symptoms at Follow-Up - BDI Scores for depression gathered at all five measurement times are presented for the three groups under study in Figure 2 (for details on means and standard deviations see Krampen, 1997)…. Thus, long-term lasting reduction of depressive symptoms is	recommendation for autogenic training.

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				significantly better for patients under psychotherapy with autogenic training than in those under psychotherapy without autogenic training" (1999, p. 17). There are further relevant results in relation to reduction in somatic symptoms in these two studies, and we ask NICE to review and include them in developing the final Guidance. Further studies using HADS are cited in following comments, and we would ask that NICE review these studies as well.	
Lundbeck Ltd	Full	189	24-26	In assessing the relative benefits and harms of interventions for the treatment of a new depressive episode, the GC has only reviewed evidence of interventions "that are suitable as initial interventions for depression". As such, any interventions deemed not suitable as initial interventions have been excluded from the decision problem and thus the resulting literature searches and NMA. We think this should be made clear in the short version of the guideline. It important that mental health professionals and commissioners understand that, for this particular review question, the GC reviewed evidence of interventions deemed suitable for use as initial interventions only, and did not	Thank you for your comment. The short version of the guideline only contains the recommendations for clinical practice and the research recommendations. It is not possible for us to put the detail that you request into this version. This detail is already included in the full version of the guideline.

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				consider evidence for all possible interventions.	
Lundbeck Ltd	Full	190	46-48	It is important to note that the NICE TA of agomelatine was terminated and, therefore, agomelatine is not recommended by NICE as a clinically- or cost-effective treatment for depression in any setting.	Thank you for your comment. This section describes the range of antidepressants that are available. It is an introductory section and as such does not need to specify which interventions have been appraised by the NICE Technology Appraisal programme.
Lundbeck Ltd	Full	190	25-26	Regarding the comment relating to mirtazapine; "...but is associated with weight gain in some people", according to the Summary of Product Characteristics, mirtazapine is associated with weight gain in as many as 1 in 10 people. **Reference:** MSD Ltd. 30 mg mirtazapine Summary of Product Characteristics. February 2017. http://www.medicines.org.uk/emc/medicine/21573. 2017.	Thank you for your comment. This is a general introduction to the pharmacological interventions used in the treatment of a new depressive episode. It is not intended to replicate the detail in the Summary of Product Characteristics for each drug.
Lundbeck Ltd	Full	190	24	"The main alternative to SSRIs is mirtazapine". We would be interested to know the reference(s) for this assertion.	Thank you for your comment. We have changed the text to clarify that mirtazapine is a commonly used alternative to SSRIs.
Lundbeck Ltd	Full	191	1-3	The draft guideline states that vortioxetine "is recommended by NICE as a third-line agent for treating major depressive episodes in adults" (NICE 2015). This is not an accurate reflection of NICE's recommendation; TA367 states that vortioxetine "is recommended as an option for treating major depressive episodes in adults whose condition has	Thank you for your comment. We have amended the text to reflect that used in the wording of TA367. We have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.

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				responded inadequately to 2 antidepressants within the current episode." (NICE, 2015) As such, vortioxetine is a relevant treatment option for consideration when a clinician is considering switching ADs in order to achieve a response or prevent relapse. We believe this inaccuracy could lead to confusion among prescribers and healthcare organisations about where vortioxetine should be used in the treatment pathway and the conclusions that NICE came to regarding the clinical and cost-effectiveness of vortioxetine in this setting. Classifying vortioxetine erroneously as a "3rd line" agent also risks it being used inappropriately when patients are referred from primary care to secondary care services. For example, if a person with depression had had an inadequate response to two SSRIs in primary care and is then referred to the local mental health trust, the secondary care prescriber could believe they were required to try two further medications before they could prescribe vortioxetine as a 'third line' agent. This is not the case. We would therefore urge the GC to accurately cite the full recommendation for vortioxetine: (1) as that this is a current, extant piece of TAG which is highly relevant to this depression guideline; (2) in order to eliminate	

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				any confusion amongst prescribers across care settings, and; (3) to ensure consistency between NICE's recommendations, primary and secondary care formularies, and local guidelines which may be updated to reflect the new clinical guideline. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015.	
Royal College of Psychiatrists	Full	195	21	Cognitive analytic therapy does not appear to be explicitly mentioned. Is this deliberate or classed under the psychodynamic therapies?	Thank you for your comment. The treatments listed here are intended only as examples, it is not intended to be an exhaustive list of all interventions.
British Acupuncture Council	Full	198	43-45	Traditionally, and as applied by professional acupuncturists, the therapy is not just about needle application. Holistic re-balancing approaches would also draw upon the therapeutic relationship and the lifestyle advice, for example.	Thank you for your comment. The purpose of this section is to clarify the specific elements of the interventions. We did not focus on the theraputic relationship in acupuncture.
British Acupuncture Council	Full	199	32-34	Exactly the same arguments would apply to combination therapy with acupuncture	Thank you for your comment. The purpose of this section is to clarify the specific elements of the interventions. We did not focus on the theraputic relationship in acupuncture.
University of York	Full	199	3	The GC confirms robust existing data on acupuncture safety, stating that, "The risk of serious adverse effects is reported to be low." These statement is supported by a very large prospective study of 2 million treatments.(1)	Thank you for your comment. A low risk of adverse events is not a reason to recommend an intervention, there also needs to be evidence of clinical and cost effectiveness.

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				Given this safety data, along with the clinical benefits, see below, and beneficial cost-effectiveness, there is a case for a wider choice being made available to patients, especially for those patients who do not want to receive pharmacological or psychological interventions. Reference: (1) Witt CM, Pach D, Brinkhaus B, Wruck K, Tag B, Mank S, et al. Safety of acupuncture: results of a prospective observational study with 229,230 patients and introduction of a medical information and consent form. Forschende Komplementarmedizin. 2009 Apr;16(2):91–7.	The committee noted that in the large RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is considered from 2 RCTs that compared acupuncture with sham acupuncture, no statistically significant benefit was observed on depression symptomatology. The committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS, the committee decided not to make a recommendation for its use. This information has been added to the 'evidence to recommendations' section in the full guideline. The cost effectiveness of acupuncture is based on 1 study with potentially serious limitations, as it was based on a RCT with high attrition rates and the results were very sensitive to the cost of acupuncture. Whilst the quality of the economic analysis is high, we believe that the quality of the evidence it contains is not. The committee's

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					interpretation of this evidence was that it does not show acupuncture is a cost-effective intervention. Thank you for bringing this reference to our attention. Witt 2009 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs)
British Acupuncture Council	Full	200	27-30	We understand the exclusion arguments for some of these interventions but not for acupuncture	Thank you for your comment. Additional text has been added to clarify why acupuncture and several other interventions were excluded from the NMA.
South West London and St. George's Mental Health NHS Trust	Full	201	12-15	The change to the severity distinctions seems to lack clinical utility from our perspective, and seems to have been made in an arbitrary fashion. Given the impact this new severity distinction has made to front line recommendations, with first line options for more severe depression being now entirely cognitive or behavioural rather than relationship oriented options being available, we would expect a more scientifically robust process to have informed this decision making. This change to the options now available to clients accessing our Trust IAPT services will now be reduced, which we consider a backwards step in the IAPT agenda for providing patient choice.	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment.

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					The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too

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					heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that

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					baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other

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					methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if 2 or more scales were reported in an individual study. The committee then reviewed relevant studies which provided

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					data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network.

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					As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way,

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					to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA.
British Acupuncture Council	Full	204	2-3	We can find no such details (about the reasons for considering acupuncture separately) in this chapter or anywhere else	Thank you for your comment. Additional text has been added to clarify why acupuncture and several other interventions were excluded from the NMA.
Lundbeck Ltd	Full	207	15	As noted in comment 25 above, it is incorrect to say that vortioxetine is "recommended by NICE as a third line agent". TA367 (NICE, 2015) recommends vortioxetine "as an option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode". **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015.	Thank you for your comment. We have amended the text to reflect that used in the wording of TA367.
British Association for Counselling and Psychotherapy	Full	208	General	An example of where there has been insufficient time to allow for proper scrutiny would be section 7.3.47 of the draft Guideline, which refers to the development of a "hierarchy of depression scales" "based on GC expert advice"; this hierarchy led to the inclusion in the network meta-analysis of data related to some scales but not others. No	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental

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				information is given in the documentation about either the rationale for the prioritising of some instruments over others or the impact of data 'lost' from the analyses; it is possible that the impact of these decisions on the findings of the analyses was considerable.	and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity

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					depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what

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					data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the

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					committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is

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					the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if 2 or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given

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					to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also

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					considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA.
British Association for Counselling and Psychotherapy	Full	208	General	**Outcome variables** ***Standardized mean difference*:** The main clinical outcome was standardized mean difference (SMD) of depressive symptom severity change from baseline to the end of treatment as measured by continuous scales. For calculating SMD for change scores, sample size, mean change, and the standard deviation (or standard error) of change for each investigated group are necessary. As described in Section 7.3, this information (particularly the standard deviation of change) was not always completely available in primary study reports; therefore information on change from baseline was estimated form	Thank you for your comment. SMD was selected by the committee as the main clinical outcome as it is a measure commonly used in research and the committee was familiar with interpretation of findings expressed in the form of SMD. Use of changes from baseline, when reported, or of baseline and endpoint data when these were available, was considered more appropriate than use of endpoint values, as the latter may be affected by the variation of baseline scores of the study sample in each arm within each trial. Such continuous scale data were also used to estimate response in trials that did not report dichotomous response data, to enhance the evidence

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				other figures (baseline end endpoint mean scores, standard deviations, and number of individuals in each group; or number of individuals responding in each group). Section 17.2 describes the detailed methods of this approximation, including the fact that it relies on information regarding the correlation of baseline and end-of-treatment scores as well as regarding the relationship between standard deviations at baseline and follow-up. While calculations of the Guideline authors in data from studies reporting necessary information support reasonable estimates for the latter, the correlation of baseline and-of-treatment scores ranged from 0 to 0.88 (Section 17.2). Based on these inconclusive empirical findings, the Guideline authors decided to assume a 6 correlation of 0.50, when it was not reported or directly calculable. Although sensitivity analyses assuming a correlation of 0.30 did not change the results, this assumption deserves further attention. In the analysis of SMD of symptom change for less severe depression, treatment effects in 86 of the 106 trials had to be estimated with the approximation method described above (Section 7.4), while this approximation was performed in 53 of the 68 trials for more severe depression (Section 7.5). Thus, the majority of the trial effect estimates was approximated. Even if the	base. Conversely, dichotomous response data were used to estimate changes from baseline, when other continuous data were not available. In order to estimate the SD of the change score in studies that did not report adequate data for its calculation, the correlation between baseline and endpoint score was needed. The methodology used to impute a correlation coefficient was consistent with the methods recommended in the Cochrane Handbook (version 5.1.0, section 16.1.3.2): a number of studies within and beyond the NMA dataset were first identified that reported data that could be used to estimate a correlation coefficient, however, available data were very sparse and the correlations estimated from these studies varied widely. This variation in correlations was not a systematic, robust finding that could be attributed to specific studies, interventions or scales. Therefore, assuming different correlations for different studies/interventions within the NMA based on this evidence was not possible. Instead, a correlation coefficient of 0.50 was assumed across all studies and interventions included in the NMAs, and the impact of this assumption was tested in sensitivity analysis, as recommended in the Cochrane Handbook.

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				correlation between baseline and end-of-treatment scores was varied in sensitivity analyses, it was still assumed to be the same in all trials that required approximation, even though it was shown by the authors themselves that this correlation varies strongly across trials. As far more data were reported on end-of treatment scores (including standard deviations), using SMD of symptom severity at the end of treatment would have clearly been a better choice (relying much less on approximation). ***Response:*** Due to missing information in trial reports, the analysis of response data also relied strongly on estimating response from other information, essentially with the same methods and limitations as described for the SMD of symptom change.	The methods used in the NMA together with their limitations have been clearly described in Appendix N1 (Chapter 17 in the consultation draft) - see section 1.4 for limitations of the NMA.
Society for Psychotherapy Research (SPR) UK Chapter	Full	208 209	38 – 47 1 - 7	**Outcomes** *Discontinuation due to side effects* was chosen as an outcome, however, it is not defined what this entails for psychotherapy trials and we recommend amending this section by including a detailed definition.	Thank you for your comment. As reported in the guideline, this outcome 'was selected to mainly inform the economic analysis'. Discontinuation due to side effects was extracted only from studies that assessed pharmacological interventions (alone or in combination with psychological interventions). This is stated in the respective review protocols under 'critical outcomes' (the protocols are provided in sections 7.4 for adults with less severe

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					depression and 7.5 for adults with more severe depression). For the economic analysis, only discontinuation due to side effects of medication was of interest, in order to attach a utility decrement associated with side effects of antidepressants where appropriate. This has now been clarified in the guideline text. No utility data on side effects of psychotherapy are available, and the number of psychotherapy trials reporting discontinuation due to adverse events is negligible, so it was not possible to incorporate this parameter in the economic analysis.
British Association for Counselling and Psychotherapy	Full	210	General	**Statistical homogeneity** The researchers investigated the homogeneity of the NMA analyses which is important as is a key assumption of network meta-analysis. ***Between-trial heterogeneity:*** It was assumed, that the statistical between trial-heterogeneity (the variation of the effect estimates) is the same for all comparisons of interventions. Although it simplifies statistical modelling, empirical findings suggest that this assumption is very unlikely to hold (Turner et al., 2016; Rhodes, Turner & Higgins, 2015). In addition, in some of the network meta-analyses moderate to high between-trial heterogeneity was present as compared to	Thank you for your comment. Considering common between-trial heterogeneity across the whole network is standard practice. Existing heterogeneity adds uncertainty to the relative effects of treatments, which is accounted for in the results and their interpretation. Comparing this heterogeneity to empirical studies is not helpful as each dataset has its own characteristics regarding populations, interventions and study designs. However, considering the magnitude of the between-study heterogeneity standard deviation as compared to the size of the relative treatment effect is helpful in order to understand the magnitude and the impact of heterogeneity in the dataset. Between-trial heterogeneity was considered by the

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				the average heterogeneity in a large number of meta-analyses (Salanti et al., 2014; Turner et al., 2016; Rhodes, Turner & Higgins, 2015), precluding firm conclusions regarding treatment effect estimates like in any meta-analysis. ***Within-class heterogeneity:*** Treatment effect estimates within intervention classes were assumed to be distributed around a mean class effect with a certain amount of within-class heterogeneity (unfortunately, within-class heterogeneity estimates are not reported in the Guideline). Due to sparse data, the prior distribution for this within-class heterogeneity parameter was informed by expert opinion (the network meta-analyses were performed in a Bayesian framework, in which 5 estimates are the result of updating prior distributions by data, with usually using uninformative priors that weigh data far more strongly than the prior). This prior, which strongly determined the estimated within-class heterogeneity due to the low amount of data, is described in Section 17.2 for binary outcomes (e.g., response, remission), defined for the logarithmic odds ratio. However, the sample code used for analysis of metric data with standardized mean differences reported in Section 17.6 uses this prior as well, although standardized mean	Guideline Committee in this context when interpreting the results of the NMA. The distribution of the within-class variability does not strongly influence the class effects. The prior distributions are quite wide, reflecting our uncertainty in the true value. These distributions, together with the variance sharing across some classes, result in posterior distributions for the within-class variability that imply moderate variability, which means that the class effects are close to the original intervention effects (i.e. those that would have been observed if no class effect was assumed). Random effects models were compared with fixed class effects models. The conclusions are included in the final guideline (Appendix N1, section 1.2.3: "We compared the fit of the random class effect models to that of fixed class effect models which assume that all treatments in a class have the same relative effect. In most cases the models had a very similar fit suggesting that the interventions had been grouped well into classes with small within-class variability." The priors on the SMD scale are wider in relation to the logOR scale; this means they are less informative and therefore more

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				differences are scaled on a somewhat smaller scale than logarithmic odds ratios. This means that the priority within-class heterogeneity for metric outcomes was higher than for binary outcomes. In addition, the within-class heterogeneity was per definition positive, leading to somewhat confusing findings. For example, in the analysis of standardized mean differences in comparison to pill placebo in patients with less severe depression, citalopram, escitalopram, fluoxetine, sertraline all have rather precise estimates (with -0.59 and 0.10 being the lowest of the lower and the highest of the upper bounds of the four 95% credible intervals, respectively, see Appendix W), but the credible interval for selective serotonin reuptake inhibitors as a class (consisting only of the four aforementioned interventions) is -0.74 to 0.28 (Table 44 in Section 7.4). Although one would expect that estimates become more precise with more information, they actually seem to become more imprecise. In the same analysis, exercise as an intervention shows a clear effect (with credible interval -0.57 to -0.11, but exercise as a class (consisting only of exercise as intervention) has a credible interval of -1.57 to 0.89. It is also difficult to interpret the fact that	"conservative" in the sense that they allow higher uncertainty. They define uninformative prior distributions which, however, are sufficiently tight to allow convergence. We do not understand the comment on the within-class heterogeneity being "per definition positive, leading to somewhat confusing findings". Is it meant to be non-zero? (as it cannot be negative). If a zero heterogeneity was assumed, it would mean that all interventions within a class have exactly the same effect, which would be a much stronger assumption. The estimation of the class effects allows for within-class variance, which, although it may be small, is not zero; this variance adds to the posterior variance of the class mean, which, consequently, is expected to be larger than the variance of each individual intervention within the class, in particular when the class is formed by a small number of interventions. We acknowledge that these assumptions are potentially allowing for extra variance in the class, which is a slightly more conservative analysis than if we just assumed a fixed class effect for each class (in the sense that it allows for extra uncertainty).

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				according to the analysis of standardized mean differences for more severe depression, none of the treatment classes shows a statistically significant effect against placebo (by "statistically significant" meaning that the 95% credible intervals do not include the value for zero effect; Table 50 in Section 7.5). Even if these phenomena are in part likely to be the consequences of the class models drawing individual intervention estimates towards a class mean (Section 7.3) and borrowing within-class heterogeneity estimates from other classes in some cases (Section 17.2), they remain deeply unintuitive.	In the SMD analysis in patients with both less and more severe depression, the 4 SSRIs had precise intervention estimates (with very small differences between them) as the respective evidence base was wide and, in addition, each of them borrowed strength within the class. However, for the estimation of the class effect the model allowed for extra within-class variance, which added to the posterior variance of the class mean, resulting in its being larger than that of each SSRI on its own, so that the SSRI class effect versus pill placebo was not statistically significant while the individual SSRI effects versus pill placebo were. In other classes with larger effects where individual intervention effects are statistically significant, such as TCAs, the class effect is also statistically significant, although the uncertainty of the class effect is wider than that of the individual intervention effects due to the within-class variance added to the posterior variance of the class mean. Regarding the observation that none of the treatment classes shows a statistically significant effect versus pill placebo: this is not necessarily the result of the within-class variance added onto the variance of the class effect. It may be attributable to the use

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					of pill placebo as the reference control so that classes that had been shown in previous studies to be statistically significantly effective against a different control, may not show a statistically significant effect versus pill placebo. This is explained in the consultation guideline draft (p292, lines 39-45): "as the pill placebo has a larger effect compared with waitlist and TAU, interventions that appear to be effective compared with waitlist or TAU may not appear to be effective compared with pill placebo, and this may be seen as a difference between previous meta-analyses that have used waitlist or TAU as the reference treatment (comparator) and the guideline NMA that has used pill placebo as the reference treatment. The committee noted that relative effects of interventions versus TAU on the SMD outcome were similar to those observed in published reviews". Please note that the committee did not make recommendations based on the statistical significance of the class and intervention effects; rather, they considered the magnitude of the effects, the uncertainty around them, the size and quality of the evidence base, the comparability of patient populations across studies and interventions

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					examined, and other factors including cost effectiveness, patient characteristics and choice.
Society for Psychotherapy Research (SPR) UK Chapter	Full	213		**Overly Broad Definition of "counselling" in NMA psychological intervention class definition** It is incongruous to see such a disparate range of therapeutic interventions grouped together under the label "counselling": "directive counselling, emotion-focused therapy, non-directive counselling and relational client-centred therapy". First of all, "directive counselling" does not even fall into the same family of humanistic-experiential psychotherapies as the rest. Second, Elliott et al., (2013) established that emotion-focused therapy, relational client-centred therapy, and nondirective counselling have very different effects, with nondirective counselling being clearly inferior to Cognitive Behavioural Therapy in direct comparisons, client-centred therapy being equivalent in effectiveness to Cognitive Behavioural Therapy and emotion-focused therapy being superior to Cognitive Behavioural Therapy. Lumping these interventions together is thus not justified by the evidence and moreover unfairly disadvantages client-centred therapy and emotion-focused therapy. We ask that	Thank you for your comment. Following consultation, the committee re-considered the mechanisms of action, mode of delivery and other similarities/differences of the interventions included in each class and made some changes in classification (for example, group CT/CBT and group Behavioural Therapies formed a separate class). Regarding the class of counselling, the committee concluded that there were no significant differences across interventions that would warrant re-classification of interventions into different classes. Please note that the majority of evidence on counselling came from studies assessing non-directive counselling and that, following recoding of interventions, 'directive counselling' is not included in the updated NMAs. In the NMAs of interventions for less severe depression, the numbers randomised to each intervention included in the counselling class (across outcomes) were as follows: non-directive counselling 493; relational client-centred therapy 17; emotion-focused

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				these interventions be separated out. **Reference:** Elliott, R., Watson, J., Greenberg, L.S., Timulak, L., & Freire, E. (2013). Research on humanistic-experiential psychotherapies. In M.J. Lambert (Ed.), Bergin & Garfield's Handbook of psychotherapy and behavior change (6th ed.) (pp. 495-538). New York: Wiley.	therapy 60; Wheel of wellness counselling 44; psychodynamic counselling 73; interpersonal counselling 286. In the more severe depression, respective numbers were: non-direct counselling 82; relational client-centred therapy 19; emotion-focused therapy 19; any type of counselling 52. Specifically on the SMD outcome (which was the main clinical outcome), the numbers randomised to each intervention were as follows: for less severe depression non-directive counselling 152; wheel of wellness counselling 44. For more severe depression non-directive counselling 82; emotion-focused therapy 19; relational client-centred therapy 19. Therefore, the overall effect of counselling as a class was primarily based on the effect of non-directive counselling, owing to availability of efficacy data. As reported above, the evidence for client-centred therapy and emotion-focused therapy was very limited, and therefore its impact on the effect of counselling as a class was very small. Moreover, this limited evidence would not have been possible to support recommendations specific to these interventions, had these interventions formed

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					separate classes. Section 7.3.3. of the full guideline documents the approach used to group interventions into classes. The committee reviewed the evidence on the effectiveness of counselling but did not think the evidence supported recommending one particular version of counselling over another. However, the committee have recommended counselling based on a model that is specifically developed for depression, which would be in line with the specific training programme for counselling developed as part of IAPT. Thank you for bringing this reference to our attention. Elliott 2013 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs). There is an ongoing RCT about counselling for depression (PRaCTICED). We will forward this information to the NICE surveillance team for consideration.
Royal College of Psychiatrists	Full	216		**Group CBT** We are concerned that group CBT has been	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the

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				recommended as a preferred treatment modality for less severe depression on the basis of flawed evidence. Table 44 shows the NMA of less severe depression which shows the highest ranking are IPT and antidepressants, followed by short term PDPT and antidepressants, followed by self-help with support, followed by long-term PDPT etc. However, the guidelines recommended group CBT as the treatment of choice the basis (a) of efficacy data coming from all CBT therapies (with mean rank of 8) and (b) health economic data which shows that group CBT being cheaper to deliver than other treatments. However, this assumes that group and individual CBT are equivalent therapies, despite there being no data available for the efficacy of group CBT. Individual and group treatments using the same modality e.g. CBT, are not equivalent treatments, and group delivery of any modality should be considered a separate category from individual treatments of any modality. Moreover, the health economic assumptions are based on group CBT being delivered by relatively junior healthcare professionals, whereas in trials, interventions are typically	treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes

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				delivered by more experienced therapists and "therapist effects" are a well-recognised problem in translating evidence to practice. It would be helpful, for example, to demonstrate from IAPT data whether the group CBT currently being provided is associated with a reasonable response rate and is superior to other modalities. It appears that the health economic analyses are used to justify treatment decisions with insufficient evidence and a failure to show sensitivity analyses. It is hard to accept group CBT as the preferred first-line treatment modality on the basis of the evidence presented.	are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5).
University of York	Full	236	40	In a large scale (n=755) RCT of acupuncture or counselling for depression conducted in the primary care in the UK, the GC correctly reports that, "Using a NHS perspective, acupuncture was found to be the most cost-effective intervention with an ICER versus treatment as usual of £4,731/QALY (2015 prices). Counselling was extendedly dominated." (Page 236, Line 49) the GC goes on to state that, "The study is directly applicable to the NICE decision making context but is characterised by potentially serious limitations, including the particularly high proportion of missing resource use data	Thank you for your comment. The fact that the trial randomised 755 people (MacPherson et al., 2013) but resource use data were available only for 150 (Spackman et al., 2014, Table 3) may be typical of longer term trials but is a wider limitation of the trial conduct, even if missing data were handled using multiple imputation. The use of multiple imputation has been reported (and thus acknowledged) in the description of the study within the guideline. We agree that the variation in intervention costs was handled using sensitivity analysis. However, this analysis showed that economic findings

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				and the sensitivity of the results to intervention costs." However the extent of the missing health economic data was typical of 12 month follow-ups in longer-term trials and was properly handled using multiple imputation, and the variation in intervention costs was handled using sensitivity analyses.(1) Taking these factors into account, the cost-effectiveness of acupuncture, which was analysed by the health economists at the Centre for Health Economics, University of York, provided high quality evidence that acupuncture could be considered within the NMA. Reference: (1) Spackman E, Richmond S, Sculpher M, Bland M, Brealey S, Gabe R, et al. Cost-Effectiveness Analysis of Acupuncture, Counselling and Usual Care in Treating Patients with Depression: The Results of the ACUDep Trial. PLoS ONE. 2014;9(11):e113726.	were particularly sensitive to the intervention costs ("A sensitivity analysis was undertaken assuming that each acupuncture session costs £65, the same as counselling. In this scenario counselling is preferred to acupuncture [...]. This demonstrates that the cost-effectiveness of acupuncture in this study is reliant on having a lower price than counselling." Spackman et al., 2014). Therefore, results of the economic analyses are not robust, as they are sensitive to intervention costs, which is what the guideline states (sensitivity analysis would strengthen the robustness of the results if it showed that these did not depend on intervention costs - in this case, it demonstrated the opposite). We agree that the quality of the economic analysis is high, but we believe that the quality of the evidence is not. The quantity or quality of the available economic evidence was not a criterion for the inclusion of acupuncture (or any other intervention) in the NMA. Please refer to guideline section 7.2 for a justification of populations and interventions to be included in /excluded from the NMA.
University of York	Full	242	9	The GC sates that, "Evidence from 1 single UK study conducted alongside an RCT (n = 755) indicates that acupuncture is likely to be cost-effective compared with counselling and treatment as usual in adults with a new	We agree that the methods of analysis are of high quality. However, the high rate of missing data (605/755) and the fact that the results of the analysis are highly sensitive to intervention costs constitute limitations of the

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				episode of less severe depression. The evidence is directly applicable to the UK context but is characterised by potentially serious limitations." As stated on Page 236, Line 49, these potentially serious limitations include, "the particularly high proportion of missing resource use data and the sensitivity of the results to intervention costs." As explained above, the missing data was handled using multiple imputation and the variation in intervention costs was handled using sensitivity analyses.(1) Taking these factors into account, acupuncture could be considered within the NMA. Reference: (1) Spackman E, Richmond S, Sculpher M, Bland M, Brealey S, Gabe R, et al. Cost-Effectiveness Analysis of Acupuncture, Counselling and Usual Care in Treating Patients with Depression: The Results of the ACUDep Trial. PLoS ONE. 2014;9(11):e113726.	evidence. Note that according to NICE criteria (See The Guidelines Manual, Appendix H, 2.12) a study with potentially serious limitations is defined as a "study [that] fails to meet 1 or more quality criteria, and this could change the conclusions about cost effectiveness". Conclusions on cost effectiveness in this particular study could change following a small change in intervention costs (it is noted that the intervention cost for acupuncture was not taken from NHS sources as it is "not currently financed by the NHS", and therefore this uncertainty is considered as a limitation. The quantity or quality of the available economic evidence was not a criterion for the inclusion of acupuncture (or any other intervention) in the NMA. Please refer to guideline section 7.2 for a justification of populations and interventions to be included in /excluded from the NMA.
Lundbeck Limited	Full	243	47-49	We note that response was the only outcome for which mirtazapine data were available. This makes the recommendation to use mirtazapine as a first-line option even more surprising bearing in mind remission might be seen as the ultimate goal for people with depression. This outcome is well-evidenced	Thank you for your comment. Based on feedback from stakeholders, the analyses of the clinically and cost effective treatments for a new depressive episode have been revised. The committee have carefully considered the updated data and as a result the recommendations for treatment of less

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				for other ADs.	severe depression have been amended. In light of feedback from stakeholders about the limited nature of the data on mirtazapine and the lack of SMD data, the committee have removed this intervention from the recommendations for less severe depression.
British Acupuncture Council	Full	245	1-51	[also this continues onto page 246, lines 1-16]. There are several instances here of treatments with rather poor cost effectiveness being recommended on the basis that they may be useful for particular groups of people, for example those who don't get on well with other interventions. This could apply equally well to acupuncture, which has higher cost effectiveness, and would be particularly useful for those with co-morbid physical pain (Hopton et al, 2014). The guideline committee had the necessary expertise to identify niche markets for the various psychological treatments and to offer a degree of flexibility in the options that will be offered to service users. It does not appear from its make-up that this would have been possible for acupuncture and we would once again press for an appropriately qualified person on the committee when acupuncture is being considered.	Thank you for your comment. The committee noted that in the large RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is considered from 2 RCTs that compared acupuncture with sham acupuncture, no statistically significant benefit was observed on depression symptomatology. The committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS, the committee decided not to make a recommendation for its use. This information has been added to the 'evidence to recommendations' section in the full guideline.

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					Thank you for bringing this reference to our attention. Hopton 2014 could not be included in the review as this trial specifically recruited participants with a particular physical health condition in addition to depression and that is an exclusion criterion for this review.
Lundbeck Ltd	Full	245	7-10	We note that there was limited data informing the economic analysis for mirtazapine and no data available on the standardised mean difference (SMD) outcome. This makes the recommendation to use mirtazapine as a first-line option even more surprising.	Thank you for your comment. Based on feedback from stakeholders, the analyses of the clinically and cost effective treatments for a new depressive episode have been revised. The committee have carefully considered the updated data and as a result the recommendations for treatment of less severe depression have been amended. In light of feedback from stakeholders about the limited nature of the data on mirtazapine and the lack of SMD data, the committee have removed this intervention from the recommendations for less severe depression.
British Association for Counselling and Psychotherapy	Full	246	General	Combining the impact of lower pay and fewer sessions for counselling would also improve relative cost effectiveness. While the GC "also noted that according to the guideline economic analysis the cost effectiveness of counselling improved when this was effectively delivered by therapists paid at Band 6 or when this was delivered in 8 sessions, and agreed that these scenarios tested in sensitivity analysis may comprise	Thank you for your comment. Please note that the intervention resource use estimates used in the economic analysis were based on resource use reported in the RCTs that informed the NMA and economic analysis. In the class of counselling, there were variations in reported resource use across studies, ranging from 4 weekly sessions (Kwon 2015, wheel of wellness counselling) to 20-30 sessions (Maina 2005, non-directive

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				variations of clinical practice in some settings" (p246), this was not systematically examined. An independent researcher commissioned to review the economic analysis for BACP modelled this and, holding all else constant, reducing the number of counselling sessions from 16 to 8 would mean counselling then being in the top 10 interventions for less severe depression and if also having a lower cost, e.g. using Band 5 costs, could even be in the top 5 interventions using the Net Monetary Benefit Approach for ranking.	counselling). The mean number of sessions in the studies that informed the NMA of response in those completing treatment, which was the main efficacy outcome in the economic analysis of interventions for less severe depression, was approximately 17. The studies informing this outcome and the respective number of sessions reported are as follows: Watson 2003 16 sessions of emotion-focused therapy; Serretti 2013 6 sessions of interpersonal counselling; Maina 2005 20-30 sessions of non-directive counselling; Beutler 1991 20 sessions of non-directive counselling. The committee took into account the improved cost effectiveness of counselling relative to other interventions when it was delivered by Band 6 or 5 therapists and when it was delivered in 8 sessions instead of 16 (provided that the effectiveness of counselling remains the same) when making recommendations. However, these scenarios were considered to reflect variations in clinical practice, rather standard, optimal practice for the delivery of counselling in the UK, hence the results based on these scenarios were not deemed to reflect the cost effectiveness of counselling across UK routine practice.

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					Moreover, the committee agreed that if counselling was delivered in a lower number of sessions compared with the number of sessions in the trials informing the NMA, its effectiveness might be lower than that reported, and this would have a negative impact on its cost effectiveness. Please note that variations in delivery were also reported for other individual psychological interventions, and that applying lower estimates of resource use to other interventions would have a positive impact on their cost effectiveness relative to counselling. Please refer to our detailed responses to other related comments of yours on this issue.
British Acupuncture Council	Full	247	25-28	Nevertheless large numbers seek unconventional health care options for depression even in the absence of any endorsement by the NHS.	Thank you for your comment. The text about patient choice (p 247, line 25 of the consultation version of the guideline) was incorrect and has been amended.
British Association for Counselling and Psychotherapy	Full	248	14 - 26	**The evidence to support Recommendation 7.4.5, that psychotherapy and counselling interventions should be based on depression-specific treatment manuals, needs to be made explicit**. Studies in this area have produced mixed results, with some studies supporting the use of manuals, and other studies showing no advantage compared to treatment as usual	Thank you for your comment. The committed wanted to ensure the interventions recommended in the guideline are provided in routine care. One way to do this was to advise practitioners to follow the treatment as set out in the treatment manuals. The committee agreed to do this as there is evidence that treatments inappropriately applied can be harmful. We have made separate recommendations on patient

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				(Carroll & Nuro, 2002). This is important because few manuals incorporate responsiveness to patient preferences (Ahn & Wampold, 2001). The use of manualised treatment therefore has the potential to undermine the principle of patient choice. There is also evidence that patient choice does not reflect existing brand-name established therapies. Instead, patient preferences tend to reflect a heterogeneous set of factors.	choice. Thank you for bringing these references to our attention. Carroll and Nuro (2002) and Ahn and Wampold (2001) cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).
British Association for Counselling and Psychotherapy	Full	248	14 - 26	**Recording sessions** BACP welcomes the recommendation that 'healthcare professionals delivering interventions for people with depression should receive regular high-quality supervision'. However we are unclear on what is meant by 'external audit' as a way to monitor and evaluate competence. Whilst we can also see the benefits of recording sessions in regards to training and supervision, we believe that there remains the potential for issues to arise in the near future following the introduction of the impending GDPR legislation in May 2018. In addition we urge caution as there is a significant lack of research around the impact of recording on the client experience.	Thank you for your comment. We have removed 'external audit' from the recommendation. Dealing with any issues resulting from the GDPR legislation will be a matter for local implementation.

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University of Liverpool	Full	249	13	The statement that patients cannot get addicted to antidepressants is too dogmatic, in my view, and should be modified. Careful distinction between physical addiction and psychological habituation is also needed.	Thank you for your comment. The committee noted that whilst people will not become addicted to antidepressants, they can experience discontinuation symptoms if they stop taking them. The committee agreed that concerns about 'addiction' may be a reason why people are reluctant to take antidepressants and thought it was important that the recommendations highlight that this is not the case. However, in light of comments received from stakeholders the committee have amended recommendation 1.4.8 to include discussion of patients concerns about stopping medication.
Kent and Medway NHS and Social Care Partnership Trust	Full	250	29 - 34	This does not match the monitoring requirements in NICE guideline for bipolar, section 1.10.8. There does not seem to be aby rationale for this inconsistency	Thank you for your comment. Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. These are now more consistent with what is in the NICE guidance on Bipolar disorder, however there are still some differences because this is guidance for the use of antipsychotics in depression.
Kent and Medway NHS and Social	Full	250	29 - 34	This does not match the monitoring requirements in NICE guideline for psychosis, section 1.3.6.4. There does not seem to be	Thank you for your comment. Additional detail has been included in the recommendations about monitoring patients

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Care Partnership Trust				aby rationale for this inconsistency	who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. These are now more consistent with what is in the NICE guidance on Psychosis, however there are still some differences because this is guidance for the use of antipsychotics in depression.
Primary Care Neurology Society	Full	250	6	In following up those under 30 who have been prescribed antidepressants, does the 1 week review need to be face to face? Services are increasingly using phone reviews and this could leave them open to criticism. Many CMHT (Community Mental Health Teams) and GP are using the phone more and it's important to be very clear here.	Thank you for your comment. The 1 week review should be face to face which is why we have used the word 'see' in the recommendation.
Kent and Medway NHS and Social Care Partnership Trust	Full	250	25	This does not match the monitoring requirements in NICE guideline for bipolar, section 1.10.20. There does not seem to be aby rationale for this inconsistency	Thank you for your comment. Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. These are now more consistent with what is in the NICE guidance on Bipolar disorder, however there are still some differences because this is guidance for the use of lithium in depression.

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Swansea University	full	250	Recommendation 48	The guideline does not specify how, when and by whom, older people should be monitored for potential adverse effects?	Thank you for your comment. This recommendation would apply to all prescribers whether operating in primary care, secondary care or other healthcare settings.
South West London and St. George's Mental Health NHS Trust	Full	251	6	Our Trust IAPT services have a strong record in delivering safe and effective group CBT interventions to people with less severe depression. These are currently facilitated by a single competent practitioner, who has access to immediate staff support if required (i.e. in the event of a risk emergency). The recommendation that groups are delivered by two competent practitioners seems unnecessary from our experience, and would be challenging to implement due to the resource and cost implications this would have for the services. The number of groups we would be able to run would effectively halve, with consequences for the length of time clients would need to wait to access a group.	Thank you for your comment. The treatment manuals specify group CBT needs to be delivered by 2 competent practitioners. This is what has been used in economic analysis and based on this analysis group CBT was found to be a cost-effective option for treating less severe depression.
Norfolk & Suffolk Foundation Trust	Full	251	61	There is a change in the new NICE guidelines regarding the recommendations around use of IPT. The rationale for this is unclear. This is a major treatment approach used within our Trust and therefore clarity around this issue would be important. Previously IPT was recommended across all age groups (children, adults and older people) for all severities of depression. It now	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for

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				appears to be an optional treatment only in less severe depression "if the person …would like help with interpersonal difficulties".	treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. IPT remains an option for people with less severe depression (who would like help for interpersonal difficulties that focus on role transitions or disputes or grief) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication individual CBT or BA) have not worked well in a previous episode of depression or in those who do not want the other recommended interventions.

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					The committee made this a 'consider' recommendation because of the small benefit on the SMD outcome, the larger benefits on the other 2 clinical outcomes, and the lower cost effectiveness of IPT compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of IPT was likely to be higher in the sub-population specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make

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					firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
CHESS (Centre for Humanities Engaging Science and Society), Durham University	Full	252	17-27	**Problems with definitions of 'counselling'** This section recommends 'counselling' as an option for persons with less severe depression. However, 'counselling' remains an ambiguous term. The only further guidance for what this might mean is that is should be "based on a model developed specifically for depression". There are potentially two distinct forms of counselling: a nonspecific counselling that utilises generic and basic competences common to all forms of therapy, and a model-specific form of counselling, such as person-centred experiential counselling, which includes CfD (Counselling for Depression, which was developed to be a bona fide psychological therapy using an established methodology that involved defining a range of basic, generic, specific, and meta-competencies (Roth, Hill, & Pilling, 2009)). This distinction	Thank you for your comment. **Definitions of counselling** Counselling was included as an intervention in the question about treatment for a new depressive episode. Unfortunately no specific RCT evidence on PCE-CfD (which was developed for the IAPT programme) was identified and so no recommendation for the use of PCE-CfD was made. However, the committee took the training and model of CfD into consideration when developing the recommendations. Roth 2009 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs). There is an ongoing RCT about counselling for depression (PRaCTICED). We will forward this information to the NICE

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				between generic counselling and an active intervention implies critical differences in the level of training and competencies of a practitioner (comparable to the differences between low and high-intensity treatment in IAPT) and in the specificity of the model of intervention use. The proposed section does not make such a distinction, and despite suggesting that the counselling model be one that has been developed specifically for depression, it does not explicitly mention CfD. This suggests that guideline developers need to use definitions that specify the theoretical approach and potentially the level of professional training or competencies. **Counselling as a second-tier treatment** This section states: "Consider counselling if a person with less severe depression would like help for significant psychosocial, relationship or employment problems and has had group CBT, exercise or facilitated self-help, antidepressant medication, individual CBT or BA for a previous episode of depression, but this did not work well for them, or does not want group CBT, exercise or facilitated self-help, antidepressant medication, individual CBT or BA".	surveillance team for consideration. **Counselling as a second tier treatment** Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Counselling remains an option for people with less severe depression (and who would like help for significant psychosocial, relationship or employment problems) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication, individual CBT or BA or IPT) had not worked well in a previous episode of depression or in those who did not want the other recommended interventions. The committee made this a 'consider' recommendation because of the small benefit on the SMD outcome, the larger benefits on the other 2 clinical outcomes, and the lower cost effectiveness of counselling compared with other high intensity individual psychological

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				Counselling is therefore offered only as a second-tier treatment on this recommendation. However, it is unclear that this would lead to improved outcomes for clients with depression. Cape, Whittington, Buszewicz, Wallace, and Underwood (2010) carried out a meta-analysis and meta-regression of 34 studies focusing on brief psychological interventions for anxiety and depression, involving 3962 patients. Most interventions were brief cognitive behaviour therapy (CBT; n = 13), counselling (n = 8) or problem solving therapy (PST; n = 12). Results showed effectiveness for all three types of therapy: studies of CBT for depression (d -0.33, 95% CI -0.60 to -0.06) and studies of CBT for mixed anxiety and depression (d -0.26, 95% CI -0.44 to -0.08); counselling for depression as well as mixed anxiety and depression (d -0.32, 95% CI -0.52 to -0.11); and problem solving therapy (PST) for depression and mixed anxiety and depression (d -0.21, 95% CI -0.37 to -0.05). Controlling for diagnosis, meta-regression found no difference between CBT, counselling and PST. The authors concluded that brief CBT, counselling and PST are all effective treatments in primary care, but that effect sizes are low compared	interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of counselling was likely to be higher in the sub-population in the recommendation compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). Cape 2010 and Cuijpers 2012 systematic reviews were searched for relevant references but no additional studies that met the inclusion criteria were identified above those that had been identified through other means, (for example through stakeholder comments). Thank you for highlighting the Barth 2013 systematic review. This review has been checked for relevant studies and an additional 14 RCTs have been added to the NMA for for treatment of a new depressive episode through this process. It should be noted that the recommendations made in the guideline about CBT were not

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				to longer length treatments. Cuijpers et al. (2012) found that studies in which Non Directive Supportive Therapy (NDST) was compared with CBT resulted in a small and non-significant difference between NDST and CBT. The authors commented that NDST has been treated as a proxy for counselling although it specifically excludes active elements that may be present in bona fide counselling interventions (this confusion could be avoided by being clearer with what is meant by 'counselling' as suggested above). However, they found that the studies with researcher allegiance in favour of the alternative psychotherapy resulted in a considerably larger effect size than studies without researcher allegiance. Moreover, in studies without an indication of researcher allegiance, the difference between NDST and other therapies was virtually zero. The authors argued that such results suggested that NDST is effective. Barth et al. (2013) adopted a network meta-analysis – the same method used by the NICE Guideline Development Group – using 198 trials comparing seven forms of psychotherapeutic interventions, one of which was 'supportive counselling'. The analysis	for brief CBT. The committee did not think that the evidence supported a recommendation for any brief form of counselling or CBT. For briefer interventions the committee recommended self-help with support or exercise, based on the evidence of their clinical and cost-effectiveness. Therapist allegiance was not in the scope of the guideline and we did not examine the evidence for this.

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				found significant effects for supportive counselling compared against waitlist and that the evidence base for supportive counselling was broad. In summary, when studies with a low researcher allegiance against counselling together with evidence from bona fide counselling interventions are considered, the meta-analytic studies comparing counselling with CBT for depression suggest either broad equivalence of patient outcomes or, where differences do exist, that they are small. While there is minimal recent RCT evidence comparing counselling as a bona fide intervention with CBT head-to-head, this should not matter for the purposes of the guidelines, which are based on a network meta-analysis and not head-to-head RCTs. **Citations** Roth, A.D., Hill, A., & Pilling, S. (2009). The competences required to deliver effective humanistic psychological therapies. London, United Kingdom: Department of Health. Barth, J., Munder, T., Gerger, H., Nüesch, E., Trelle, S., Znoj, H., ... & Cuijpers, P. (2013). Comparative efficacy of seven psychotherapeutic interventions for patients	

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				with depression: a network meta-analysis. PLoS Medicine, 10, e1001454. Cape, J., Whittington, C., Buszewicz, M., Wallace, P., & Underwood, L. (2010). Brief psychological therapies for anxiety and depression in primary care: meta-analysis and meta-regression. BMC Medicine, 8, 38. Cuijpers, P., Driessen, E., Hollon, S. D., van Oppen, P., Barth, J., & Andersson, G. (2012). The efficacy of non-directive supportive therapy for adult depression: A meta-analysis. Clinical Psychology Review, 32, 280-291.	
British Association for Counselling and Psychotherapy	Full	252	24 - 27	**The evidence for the recommendation that any counselling intervention should be one developed specifically for depression (7.4.6) should be made explicit.** This requirement is only specified for counselling and short-term psychodynamic psychotherapy but not for CBT and IPT. What is the rationale for this?	Thank you for your comment. IPT and CBT were both developed specifically for the treatment of depression. In contrast, there has been less development of models of STPT and counselling that are specifically for treating depression. The committee thought it important to highlight this.
South West London and St. George's Mental Health NHS Trust	Full	252	1	Although we welcome the inclusion of IPT as an option for the treatment of less severe depression, the distinction between less and more severe depression as defined by the GC does not make conceptual sense when	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been

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				applied to IPT. National IAPT training recommends that IPT is offered for clients presenting with PHQ-9 scores over 15, creating an impractically small range (PHQ-9 score of 15 -17) for the application of IPT as a treatment option, especially given the absence of IPT as a treatment option for more severe depression in the draft guideline.	re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). The judgement of whether a person has more or less severe depression, should not be made solely on the basis of a score on the PHQ-9 scale.

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South West London and St. George's Mental Health NHS Trust	Full	252	7, 17, 28	We welcome the recommendation to offer alternative treatments, for low severe depression, such as IPT where CBT has been previously unsuccessful, or where clients decline a CBT intervention. It is our experience that providing access to an alternative therapy option is important where CBT is not acceptable to clients accessing out Trust IAPT services. As an example, in the last year, we offered IPT to 9 clients with less severe depression who declined a CBT intervention, or did not recover following a CBT intervention. 66% of these clients reached the IAPT threshold for recovery. We would be willing to submit the experiences of our Trust IAPT services to the NICE shared learning database.	Thank you for your comment. We will pass this information to our local practice collection team. More information on local practice can be found here https://www.nice.org.uk/about/what-we-do/into-practice/local-practice-case-studies
British Association for Counselling and Psychotherapy	Full	274	General	***Homogeneity of study population:*** Using symptom severity for the definition of study populations is likely to have accounted for effect modifiers that are associated with symptom severity. However, patients participating in trials testing different interventions may differ regarding factors that are only weakly related to severity. Even if the authors of the Guideline state that "a number of trials included... have successfully recruited participants who are willing to be randomized to either pharmacological or psychological intervention and to either self-help to face-to-face treatment" (Section 7.4	Thank you for your comment. The NMA controlled for a large part of heterogeneity, by splitting populations with less and more severe depression; using detailed treatment definitions [including treatment intensity and mode of delivery for psychological interventions] and categorising them using a class random effects model. Model fit and between-study heterogeneity, as well as inconsistency between direct and indirect evidence was formally assessed for each network. Other potential effect modifiers, such as age and setting (inpatient vs outpatient) were assessed in sub-analyses,

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				and 7.5), it is important to notice that the relative number of these trials is rather low. Furthermore, empirical findings suggest that participating in psychological vs. pharmacological trials is associated with clinically relevant patient characteristics and design factors (e.g., treatment duration, a certain type of control treatment) that are likely to influence treatment effect estimates (Linde, Rucker, Schneider & Kriston, 2016). In conclusion, although stratification by symptom severity probably reduced heterogeneity in the investigated populations, it is unclear whether these populations can be considered sufficiently homogeneous. This is problematic since a central assumption of network meta-analysis is that the populations investigated in a network are clinically homogeneous.	using pairwise meta-analysis. All these parameters and statistical assessments were taken into account by the committee when interpreting the results of the NMA and making recommendations. Notably, the committee did not prioritise pharmacological over psychological interventions (and vice versa) based on the results of the NMA. In addition to the results of the NMA and the assessment of heterogeneity, inconsistency, potential bias, plausibility of the results, quantity and quality of the evidence base, other factors such as cost effectiveness, anticipated harms, treatment acceptability and compliance, patient characteristics and preferences were taken into account by the committee when making recommendations in general, and specifically when considering psychological versus pharmacological treatments.
British Association for Counselling and Psychotherapy	Full	274	General	**Classification of interventions** ***Clinical heterogeneity of interventions:*** The considered interventions were allocated to classes (e.g., selective serotonin reuptake inhibitors, cognitive and cognitive behavioural classes) and inferences were drawn both regarding single interventions and classes. While the decision to include also interventions that are considered clinically	Thank you for your comment. When deciding on class membership the committee took into account the clinical and theoretical differences between interventions. They also took into account the outputs of previous guideline analyses both in terms of the classes used and the similarity in outcomes in these previous analyses This approach gave the committee confirmation that for most classes there is relatively little

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				unsuitable (in order to enlarge the evidence basis) corresponds to up-to-date standards, the decision how to define interventions and interventions classes remains immanently subjective (Kriston, 2013). As Linde et al. (2015a) state: "Because psychological treatments are considered complex interventions, grouping them can be performed along several dimensions and remains controversial" [see also Craig et al, 2008]. For example, treatment as usual (defined as an intervention in the Guideline) is likely to encompass a wide range of interventions and it is improbable that it is clinically as homogeneous as Cognitive Behavioural Analysis System of Psychotherapy or short term psychodynamic group therapy (both of which are also defined as interventions in the Guideline). The grouping of interventions into classes is also not straightforward. For example, some might consider computerized cognitive behavioural therapy with support as part of the class of cognitive and cognitive behavioural therapies instead of the class of self-help with support as done in the Guideline. The nomenclature and the exclusive classification system of the Guideline (which	heterogeneity. In addition, based on stakeholder comments the committee have revised the class membership developing a new class of cognitive and behavioural interventions. It should be noted that the classification corresponds with a number of other recent meta-analyses which have typically grouped interventions (such as CBT, IPT, STPT and exercise) under the heading we have chosen. It should also be noted that introduction of new classes such as group interventions has not led to a significant difference with the previous network which suggests that the classification of the classes is relatively robust. TAU is indeed a varied intervention which is why the committee took pill placebo as the primary benchmark against which to compare other interventions. We have added a comment to the 'evidence to recommendations' section to acknowledge the potential problems with TAU which may vary both within and between countries. Combination with TAU was considered and where an intervention was provided against the background of TAU this was noted.

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				was necessary for being able to perform network meta-analyses) thus structures clinical reality in one of several possible ways, without an empirical basis, based on theoretical and clinical considerations. Even if the definition and classification of interventions was approved by the Guideline Committee, of which members are likely to have attempted to create practically relevant and broadly useful categories, they rely on assumptions that may not be shared by everyone. Specific examples of potential disagreements are provided in the section above on 'Selection of studies for inclusion;' another example of the potential impact of clinical judgement in creating classes is provided by Linde et al. (2015b) whose network meta-analytic study focussed on treatment of depression included a class they labelled 'other approaches' which was comprised predominantly of counselling studies but included one RCT of psychoeducation. In summary, the NMA utilises categorisation of the included studies into classes but the judgement about class membership is necessarily subjective; it is thus entirely possible that different groupings would have resulted in different findings from the NMA. ***Treatment as usual (TAU):*** Besides being a	

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				per se clinically heterogeneous category, the inclusion of TAU raises further questions. First, what is considered "usual" depends on the context of the studies that used it as a comparator. For example, a "usual" depression treatment is likely to be different in the UK, US, and Germany. Second, it is somewhat surprising that no combined intervention category with TAU has been defined, although traditionally several studies in depression compare TAU with TAU that is enhanced by the intervention of interest. It remains unclear, how this issue has been dealt with in the network meta-analyses. Third, if TAU is to be interpreted as usual care, then the results on more severe depression are rather discouraging, showing TAU to be statistically significantly less effective than pill placebo regarding symptom reduction and response (Section 7.5). It is not easily comprehensible that these results may mean that usual care (by definition the most frequent intervention) for treating severe depression is not supported by evidence. In conclusion, the practice of using TAU as a comparator in the network meta-analyses can be questioned.	
British Association for	Full	288	General	**Inconsistent use of economic findings**	Thank you for your comment. We have now amended the text to clarify that the

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Counselling and Psychotherapy				The draft Guideline states that the GC used the results of economic modelling (cost effectiveness) as the main criterion for making recommendations and the NMA results on the SMD of depressive symptom scores outcome (ranking of interventions and relative effects versus pill placebo) as a secondary criterion. However, for severe depression the recommendations do not include the use of counselling because of uncertainty over the effectiveness evidence, yet in this case the economic findings suggested that counselling is cost effective compared to usual management. It is difficult to understand how the decision to exclude counselling as a recommended treatment for depression was arrived at given the claims about how decisions were made.	committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones.
British Association for Counselling and Psychotherapy	Full	290	General	The economic analysis is based on the assumption that all psychological therapies are delivered by practitioners who are on the same pay scale as a band 7 clinical psychologist. This is not correct, many counsellors and psychotherapists delivering psychological therapies at step 3 within IAPT services and more broadly within the NHS are working at band 6, which makes them considerably more cost effective than this analysis would suggest. The guidance does acknowledge that the	Thank you for your comment. The resource use estimates in the guideline economic modelling aimed to reflect reported resource use in the RCTs included in the NMA, also considering optimal delivery of psychological interventions in the UK. The skills and level of seniority of therapists delivering psychological interventions was not consistently reported across RCTs included in the NMA. Where reported, therapists delivering counselling ranged from master's or doctoral candidates in counselling psychology to experienced psychologists or

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				relative cost effectiveness of individual psychological interventions *en masse* will increase if any of these interventions can be delivered by a band 5 psychological wellbeing practitioner (PWP). There is also an option in scenario modelling to have a practitioner who has a unit cost halfway between the PWP and the psychologist unit costs. However, the guidance does not acknowledge that the relative cost effectiveness of these interventions will also change if one or more of the interventions can be delivered by Band 5 (or 6) practitioners while other still need to be delivered by Band 7 psychologists. Using Band 5 costings alone for counselling and keeping the higher costs for the other interventions would clearly increase the case for counselling. BACP would argue that the hourly costs of counselling are systematically lower than those for other psychological interventions and that as a result the relative cost effectiveness of counselling is underestimated.	psychiatrists. In short term psychodynamic psychotherapy trials, where reported, therapists in the RCTs were described as fully trained psychotherapists or experienced psychiatrists or psychologists. For other psychological therapies, including individual CBT, behavioural activation and IPT, therapists in the trials ranged from graduates of master's or doctoral degrees in social work, psychology, or psychiatry or mental health workers to experienced psychologists or psychiatrists. The committee acknowledged that psychological interventions can be delivered by appropriately trained Band 6 or Band 5 therapists in some settings, however this is not standard practice across interventions and settings. Therefore, delivery of interventions by therapists of a lower salary band was only tested in sensitivity analysis. Using Band 5 costings alone for counselling and keeping the higher costs for other interventions would clearly increase the case for counselling, but in the same way, using Band 5 costings alone for any other individual psychological intervention (e.g. behavioural activation, which has been delivered by mental health workers in RCTs conducted in the UK) and keeping higher therapist costs for other interventions would clearly increase the case for this specific

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					intervention relative to the other individual psychological interventions, too. We have added text in the economic chapter to clarify this point.
South West London and St. George's Mental Health NHS Trust	Full	292	22	Whilst we welcome the inclusion of an alternative treatment option to CBT in the guideline for more severe depression, and are delighted to see STPP remain an option for those clients who do not respond to CBT or are not willing or able to engage with it, we are unclear why STPPs are included, but IPT is not. IPT was ranked more highly than STPP in your review of the clinical effectiveness of a range of interventions. It was also ranked more highly than BA. In our experience, we would expect STPP and IPT delivery to be cost-equivalent, as both interventions are 16 session interventions provided by Band 7 therapists in IAPT services. The decision to include STPPs but exclude IPT as a consider option is not adequately explained in the guidance and does not seem to be justifiable on either clinical or cost effectiveness grounds. Removing IPT entirely as a treatment option for this group is a significant change in NICE guidance and will have an impact on our offer in Trust IAPT services. In the last twelve months, we offered IPT to 9 clients with more severe depression who declined a CBT	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication.

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				intervention, or did not recover following a CBT intervention. 44% of those clients reached the IAPT threshold for recovery by the end of the intervention. We would be willing to submit the experiences of our Trust IAPT services to the NICE shared learning database.	Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
South West London and St. George's Mental Health NHS Trust	Full	293	14	The recommendation to offer 1:1 CBT as a first line intervention for more severe depression only in circumstances where a client agrees to take an antidepressant medication in combination with the therapy, seems to us an impractical one. Clients may not be prescribed an anti-depressant for reasons other than a refusal to take one, for example due to a lack of tolerance for the side effects. To make the first-line offer of 1:1 CBT in our IAPT services contingent on an anti-depressant would be impractical and difficult to implement. Instead, we would prefer to recommend to clients that they consider anti-depressant medication with their GP, and inform them that the evidence base indicates that an anti-depressant medication alongside psychological therapy improves effectiveness. This would be in line with current practices within our IAPT services and enables a collaborative approach to treatment planning. Similarly we are not clear why clients might	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost

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				not be offered a CBT group as a first line intervention if they are willing to be prescribed an anti-depressant. We are concerned that this recommendation implies that access to group CBT might only be considered where clients are not taking antidepressants. In addition, there is no caveat for clients who are taking an anti-depressant and prefer to attend a CBT group over 1:1. In practice we would be unlikely to deny access to a CBT group to clients taking an anti-depressant where a group was preferred by the client. Whilst we understand that the absence of a recommendation for group CBT and antidepressant combined is likely to be a consequence of an absence of studies examining this combination in the evidence base, the resulting recommendation that group therapy may only be offered to clients who decline an anti-depressant is a clinically impractical one. Our experience of providing group CBT to clients with both less and more severe depression is that group CBT is a popular and acceptable intervention.	effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
British Association for Counselling and Psychotherapy	Full	92; 216	General	***Selection of studies for inclusion:*** The network meta-analysis and consequent economic modelling are based on a selected group or studies; the inclusion/exclusion of studies thus significantly shapes the findings. BACP notes that while the process for selection of studies is detailed in the draft	Thank you for your comment. We agree that transparency is crucial. The approach that had been taken in the consultation draft of the guideline was that where a study had been cited in the text in Chapter 7 it was referenced in Chapter 16. However if a study was included in the NMA of treatment for a

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				Guideline (section 4.5.2; p92) that the process is unclear and could have been improved. Specifically, we are concerned about the fact that it is difficult to understand which studies have been included in the various analyses conducted. For example, from Table 44 (Section 7.4.1.2; p216) it is not possible to determine which studies have been included to generate the N of 406 for counselling studies for the analysis pertaining to outcome related to SMD. We also note that it appears that different groups of studies have been included in each separate analysis for both the network meta-analysis and the economic modelling however again it is not clear which studies have been included in which analyses. The implication of the lack of clarity about the included studies is that a core process in the NICE analysis is not transparent and not thus amenable to review. More broadly we note what appears to be an arbitrary approach to selecting 'counselling' studies for inclusion. As an example, there is a notable lack of overlap with the studies included in Barth et al. (2013) who also conducted a network meta-analysis of	new depressive episode but not cited in the text in Chapter 7, then it would not appear in Chapter 16. Instead there was a cross reference to Appendix T and the intention was that Appendix T would act as the full list of studies included in the NMA. However, yours and other stakeholder comments have highlighted that it is difficult to identify studies that were included and Appendix T, which whilst listing the studies included in each outcome, does not include the full bibliographic reference. Therefore, in light of this feedback, we have added all the references of included studies for the NMA of treatment of a new depressive episode to Chapter 16. Appendix N3 (formerly Appendix T) will still list the studies included for each outcome in the less severe and more severe networks as not all studies report all outcomes so there is some variability in the 'included studies' list depending on the availability of data for each outcome. Thank you for highlighting the Barth 2013 systematic review. This review has been checked for relevant studies and an additional 14 RCTs have been added to the NMA treatment of a new depressive episode through this process.

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				treatments for depression and who also included counselling as a treatment. For example while the NICE analysis seems to have included eleven studies which included 'counselling' as an intervention, the Barth et al. (2013) study includes 37 studies. One study considered by NICE for inclusion was Cooper (2003); included in the Barth et al. (2013) analysis it was excluded from the NICE analysis on the grounds that the analysis focussed on post-partum depression although we are not sure why this was considered grounds for exclusion. As another example, the meta-analysis of psychological treatments for depression in primary care by Linde et al. (2015a) included a RCT on counselling by Corney and Simpson (2005) which does not appear to have been considered (e.g. it is not on the 'included' or 'excluded' list); the same meta-analysis included an RCT by Scott and Freeman (1992) comparing medication, CBT, counselling and routine care, which was included in the NICE analysis but, as far as we can see, not included in the analyses for counselling. The same point can be made about the RCT by Rosso, Martini and Maina (2013) which is included in the NICE analysis but although it includes a comparison between brief psychodynamic therapy with	The Linde 2015 systematic review has also been checked for relevant references and one additional RCT has been added to the NMA of treatment of a new depressive episode. The Cuijpers 2012 systematic review was searched for relevant studies but no new studies were included in the NMA, above any additional studies that had been previously identified through other means (for example through stakeholder comments). A difference in included studies lists will still exist between Barth 2013, Linde 2015 (or any other systematic review/network meta-analysis) and this review due to differences in inclusion criteria. Consequently the findings may also differ. Please see review protocols in Appendix F (and summarised versions at the start of each section in the full guideline document) for further details of the inclusion criteria for this guideline. The review protocols in Appendix F also outline in more detail the approach to double-coding. 10% of the initial references were double-screened (percentage agreement ≥90%) and at least 10% of data extraction (including risk of bias assessments) has been double-coded.

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				medication versus 'brief supportive therapy' with medication it does not seem to have been included in the 'counselling' analyses. The Guideline draft description of the method (section 3.5) also does not state whether data extraction and assessment of methodological quality were performed by independent raters, which is an established method to obtain reliable data. The inclusion of trials into any meta-analytic study is clearly critical in influencing the findings and we argue here that the decisions around inclusion/exclusion of studies in this network meta-analytic study can be criticised. We contend that this suggests the importance of not placing undue importance on the analysis results, especially considering the different conclusions drawn about 'counselling' by three other major and recent meta-analytic studies (Barth et al., 2013; Cuijpers et al., 2012; Linde et al., 2015b). For information, we also note that there are two trials currently underway which will contribute important data to the question of therapeutic effectiveness of Humanistic interventions: (1) a RCT on Emotion Focussed Therapy for depression being conducted in Portugal; (2) and the UK	Cooper 2003 and other studies that focus on postpartum depression are excluded from this guideline as guidance already exists for this population in the NICE Antenatal and Postnatal Mental Health guideline. Corney 2005 does not meet the inclusion criteria for the NMA of treatment of a new depressive episode as the population were described as chronically depressed. However, it also does not meet inclusion criteria for the chronic depression review as the study definition of chronic (≥6 months) is not the same as ours (MDD>2 years or dysthymia). Scott 1992 and Rosso 2013 are included in the NMA of treatment of a new depressive episode. Thank you for providing details of the 2 ongoing trials in this area. These data may be included in future updates of the guideline.

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				PRaCTICTED trial (Saxon et al., 2017).	
University of York	Full	321	16	The GC states, "However, very low quality evidence from the same RCT (N=604) suggests a clinically important but not statistically significant harm of acupuncture relative to counselling in terms of tolerability (as measured by discontinuation due to side effects), although the absolute numbers are small and no difference was found between acupuncture and counselling in terms of discontinuation for any reason." In terms of safety, the authors of the same RCT reported that, "The number of patients experiencing a serious adverse event (SAE) over the 12 months, as judged by a clinician (IW), was 16 (5.3%) of 302, 26 (8.6%) of 302, and nine (6.0%) of 151 from the acupuncture, counselling, and usual care groups, respectively, of whom nine had more than one SAE (range 2–4). No SAEs, including three deaths, were known to be related to treatment. The number of patients experiencing a non-serious adverse event (NSAE) was 56 (18.5%), 47 (15.6%), and 40 (26.5%), respectively, of whom 17 had more than one NSAE (range 2–4)."(1) The patients had been randomised to the three groups in the proportions 2:2:1 respectively. These data gives a clearer impression that adverse event rates were similar across treatment arms.	Thank you for your comment. The text quoted from MacPherson 2013 details the number of adverse events rather than discontinuation due to adverse events and only the latter is an outcome of interest in this review. However, as a result of your comment we checked the data that had been extracted for discontinuation due to side effects for MacPherson 2013 and discovered an error as this data is not reported in the paper and had been erroneously entered. This error has now been corrected and the data from MacPherson 2013 have been removed for discontinuation due to side effects. Thank you for bringing this to our attention.

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				Reference: (1) MacPherson H, Richmond S, Bland M, Brealey S, Gabe R, Hopton A, et al. Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled Trial. PLoS Medicine. 2013 Sep 24;10(9):e1001518.	
British Acupuncture Council	Full	322	31-40	Despite having no economic support BCT is recommended for a niche group of people. The contrast with how acupuncture is dealt with has already been highlighted. Acupuncture is not mentioned in this section but it is the only one of the NMA-excluded treatments that actually has economic data.	Thank you for your comment. As we have mentioned previously, the cost effectiveness of acupuncture is based on one study with potentially serious limitations, as it was based on a RCT with high attrition rates and the results were very sensitive to the cost of acupuncture. Whilst the quality of the economic analysis is high, we believe that the quality of the evidence it contains is not. The committee's interpretation of this evidence was that it does not show acupuncture is a cost-effective intervention. Also, the committee noted that in the large RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is considered from 2 RCTs that compared acupuncture with sham acupuncture, no statistically significant benefit was observed on depression symptomatology. The

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					committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS, the committee decided not to make a recommendation for its use. This information has been added to the 'evidence to recommendations' section in the full guideline.
British Acupuncture Council	Full	322	26-27	The earlier evidence statements do not support the contention that only BCT, and not acupuncture, provides improved clinical outcomes, so please could you explain the basis for this 'agreement'	Thank you for your comment. The committee noted that in the RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is considered from 2 RCTs that compared acupuncture with sham acupuncture, no statistically significant benefit was observed on depression symptomatology. The committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS,

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					the committee decided not to make a recommendation for its use. This information has been added to the 'evidence to recommendations' section in the full guideline. However it was the view of the committee that BCT could work for a particular subgroup of people. Hence they made a recommendation this should be considered.
Tavistock Relationships	Full	322	28	We note that this section on 'Trade-off between clinical benefits and harms' suggests that there is a risk of an "increase in relationship difficulties" from providing couple therapy as a treatment for depression. This is not what the research evidence relied upon says and should be removed or replaced by a statement that providing couple therapy for depression when there is a distressed relationship is associated with less clinical harm than providing individual therapy, and is therefore the treatment of choice. Beach & O'Leary (1992) suggest that giving cognitive therapy to highly martially distressed patients leads to less reduction in depression symptoms than giving marital therapy (ie cognitive therapy is not as effective with this group) p 523-524. Similarly, Emanuels-Zurveen (1996) did report higher	Thank you for your comment. The meta-analysis in this guideline that compared behavioural couples therapy with CBT included all 4 studies referenced in your comment for the discontinuation outcome (Beach 1992, Emmauels-Zurveen 1996, Bodenmann 2008 and Jacobson 1991) and showed a clinically important effect that just missed statistical significance (p=0.06) on discontinuation with higher drop-out in the behavioural couples therapy arm. This suggests potential clinical harms (higher discontinuation rates or a lack of acceptability of the intervention) that the committee agreed were important considerations when trading this off against the clinical benefit that was observed in the comparison of behavioural couples therapy against waitlist.

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				drop-out rates in the marital therapy arm. Importantly, however, some of these were because some couples were disappointed that the therapy was not a treatment for depression and they did not want to work on the relationship and others were because the couples decided to split up – which they considered a positive outcome. The study reported them as drop-outs, however, suggesting a failure of treatment. (p.186). A couple therapy intervention that works on depression would have prevented some of these drop-outs. Bodenmann et al (2008) doesn't mention any detrimental effects of couple therapy and Jacobson et al (1991) suggests that there was not differential drop out between couple and individual treatments.	In response to your comment, the evidence was checked for the risk of an increase in relationship difficulties and as you point out this was not identified so this statement ('increase in relationship difficulties') was removed from the guideline.
University of York	Full	322	42	"The GC noted that very low to low quality evidence had been found for acupuncture…" is a statement that is inconsistent with the GC's designation of one of the included trials providing "moderate quality" evidence (see Page 321, Line 13). This is the largest of the acupuncture trials, one which compares acupuncture to TAU and provides evidence that is relevant to the UK primary care context and found that acupuncture for depression is highly cost-effective.	Thank you for your comment. Only one outcome, out of the twenty considered for acupuncture, was rated as moderate quality and all others were low to very low quality. The moderate quality outcome was depression symptomatology for the acupuncture + TAU versus counselling + TAU comparison and neither a clinically important nor statistically significant effect was found. Therefore we think that the current description of the evidence is accurate in relation to the comparisons of

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					interest (namely acupuncture verus sham acupuncture, and acupuncture relative to treatment as usual).
British Acupuncture Council	Full	322	42	The acupuncture evidence is very low to moderate, not very low to low	Thank you for your comment. Only one outcome, out of the twenty considered for acupuncture, was rated as moderate quality and all others were low to very low quality. The moderate quality outcome was depression symptomatology for the acupuncture + TAU versus counselling + TAU comparison and neither a clinically important nor statistically significant effect was found. Therefore we think that the current description of the evidence is accurate in relation to the comparisons of interest (namely acupuncture verus sham acupuncture, and acupuncture relative to treatment as usual).
British Acupuncture Council	Full	323	4-5	Why is (no) blinding brought up in relation to acupuncture but not to BCT or any other psychological or physical treatment? You appear to be placing extra obstacles in the way of any acupuncture recommendation	Thank you for your comment. We agree that lack of blinding would apply to several interventions not just acupuncture. We have therefore removed this sentence.
British Acupuncture Council	Full	323	6-7	Please explain the basis for this idea about the context of the Chinese trials affecting the results. Are you aware of the current situation in China or is this concern based more on historical information?	Thank you for your comment. We have amended the text to clarify that because the studies had been conducted in China it may not be appropriate to extrapolate the results to the UK healthcare setting.
British Acupuncture Council	Full	323	9-10	Please explain the generalisability concerns. It does not seem like good practice to include studies that subsequently bar an intervention	Thank you for your comment. The text has been amended to clarify why acupuncture was not included in the NMA. This was

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				from the main review analysis. Acupuncture has been included without such a problem in NMAs for osteoarthritis and sciatica so why not here? One can only conclude that it's due to the preponderance of Chinese studies, in which case why not make this an exclusion criterion at the outset? 60% of acupuncture participants in the review trials populated the NIHR funded UK study (MacPherson 2013), which was purposely aligned with normal practice in the UK for each aspect of PICO.	because the participants in acupuncture trials may have been selected populations that would be different from those in the more and less severe networks. In addition, the committee noted that a significant number of the studies on acupuncture were performed in healthcare systems that were very different to the UK where the use of acupuncture is more common place and expectations of treatment response are consequently likely to be higher. This may increase the likelihood of more positive outcomes. They also acknowledged that availability of appropriately trained and competent people to deliver acupuncture for the treatment of depression was limited and that there was uncertainty about the consistency of the methods for delivering acupuncture. The sentence that you refer to has been deleted from the text as it was incorrect.
University of York	Full	323	4	The GC states that, "As blinding of provider is typically not possible in these studies, the GC were unsure of the possible impact of this on the findings." However this concern regarding lack of certainty should not be applied inequitably to acupuncture, as blinding of practitioners is not used in the trials informing evidence for other physical interventions or psychological interventions.	Thank you for your comment. We agree that lack of blinding would apply to several interventions not just acupuncture. We have therefore removed this sentence.

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University of York	Full	323	6	The GC states that, "They also queried whether the context of the study (4 of the studies were conducted in 7 China) may have impacted upon the apparent efficacy of the intervention." These four trials would only have an impact on the effectiveness of acupuncture vs. medication. They would have had no impact on the comparison of acupuncture vs. TAU, a comparison that has evidence provided by a large NIHR-funded trial (n=755) set in primary care in the UK, a context that is highly relevant to NICE, which provided not just statistically significant clinical benefits(1) but also showed acupuncture to be highly cost effective(2). References: (1) MacPherson H, Richmond S, Bland M, Brealey S, Gabe R, Hopton A, et al. Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled Trial. PLoS Medicine. 2013 Sep 24;10(9):e1001518. (2) Spackman E, Richmond S, Sculpher M, Bland M, Brealey S, Gabe R, et al. Cost-Effectiveness Analysis of Acupuncture, Counselling and Usual Care in Treating Patients with Depression: The Results of the ACUDep Trial. PLoS ONE. 2014;9(11):e113726.	Thank you for your comment. We have amended the text to clarify that because the studies had been conducted in China it may not be appropriate to extrapolate the results to the UK healthcare setting. Thank you for bringing these references to our attention. MacPherson 2013 and Spackman 2014 have already been included in the guideline.

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University of York	Full	323	8	The GC has found that there was "potentially promising results" for acupuncture, but "did not feel able to make recommendations on the basis of the available evidence as they had concerns about the generalisability of the intervention." In the large NIHR-funded trial of acupuncture for acupuncture or counselling for depression in primary care(1), a subsidiary paper presented useful evidence describing the intervention in detail along with evidence of its acceptability to practitioners, and its generalisability to a population of NHS patients with depression in primary care in the UK, along with data that would enable consistency in the delivery of this intervention.(2) References: (1) MacPherson H, Richmond S, Bland M, Brealey S, Gabe R, Hopton A, et al. Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled Trial. PLoS Medicine. 2013 Sep 24;10(9):e1001518. (2) MacPherson H, Elliot B, Hopton A, Lansdown H, Richmond S. Acupuncture for Depression: Patterns of Diagnosis and Treatment within a Randomised Controlled Trial. Evid Based Complement Alternat Med. 2013;2013:286048.	Thank you for your comment. The sentence that you refer to has been deleted from the text as it was incorrect. Thank you for bringing these references to our attention. Macpherson 2013 ('Acupuncture for Depression: Patterns of Diagnosis and Treatment within a Randomised Controlled Trial') could not be included as it was a secondary analysis of the MacPherson 2013 RCT ('Acupuncture and Counselling for Depression in Primary Care: A Randomised Controlled Trial') that had already been included in the guideline.

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University of York	Full	323	18	"The GC noted the low quality of the evidence for acupuncture, nortriptyline and omega-3 fatty acids and the fact that there was a lot of uncertainty over the effectiveness of these interventions." However similar levels of uncertainty exist across many of the psychological and physical interventions that are set to be recommended by NICE. The uncertainty about acupuncture involves a concern that the populations in acupuncture trials may differ from the general population in both networks, that the intervention may not be generalisable, that most of the trials are low quality, that there are harms associated with acupuncture, and that the evidence that acupuncture is highly cost-effective is compromised by potentially serious limitations. In the information provided above, each of these concerns has been addressed. Overall, there needs to be a level playing field, and the evidence on acupuncture appears as good, if not better than many of the psychological and other physical interventions. Indeed on several counts, the evidence on acupuncture is substantially better. See for example the decision to recommend behavioural couples therapy which has "very low quality evidence" (Page 323 Line 22) and for which the GC acknowledges that there is "no available	Thank you for your comment. The committee noted that in the large RCT comparing acupuncture to TAU there was a moderate statistically significant benefit for acupuncture on depressive symptomatology. In contrast when data is considered from 2 RCTs that compared acupuncture with sham acupuncture, no statistically significant benefit was observed on depression symptomatology. The committee were particularly interested in the data from the comparison between acupuncture and sham acupuncture because they were aware of a potentially very significant placebo effect with acupuncture. Given this data and the potential challenges with the training and implementation of acupuncture in the NHS, the committee decided not to make a recommendation for its use. This information has been added to the 'evidence to recommendations' section in the full guideline.

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				economic evidence" (Page 322, Line 31). To ensure a level playing field, acupuncture needs to be included in the NMA so that its relative benefit in relation to the other interventions can be properly assessed.	
British Acupuncture Council	Full	323	19	We disagree that there is a lot of uncertainty over the effectiveness of acupuncture. The large amounts of evidence in respect of migraine, back pain and osteoarthritis are very consistent with that on depression. In all these cases acupuncture has a moderately sized superiority over TAU and is at least as good as other active interventions. It has a small but statistically significant advantage over sham (MacPherson et al 2017). **Reference** MacPherson H, Vickers A, Bland M, Torgerson D, Corbett M, et al (Eds). Acupuncture for chronic pain and depression in primary care: a programme of research. Southampton (UK): NIHR Journals Library; 2017 Jan.	Thank you for your comment. In the comparison of acupuncture versus sham acupuncture in this guideline the only clinical efficacy outcome that had more than a single study suggests a non-statistically significant effect. MacPherson 2017 could not be included as trials that specifically recruit participants with a coexisting physical health condition are an excluded from the guideline.
CHESS (Centre for Humanities Engaging Science and Society),	Full	343		We are troubled by the Draft Revision's failure to give proper attention to long-term follow-ups/observation periods and their outcomes rather than exclusively treatment endpoint. This omission is particularly difficult to understand when dealing with treatments	Thank you for your comment. Fonagy 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') is included in the review for further-line treatment.

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Durham University			Line 17-p	for chronic/TRD/long lasting/ persisting depressions. **We suggest:** • When it is available, longer term follow-up data should be more considered when making treatment recommendations. • When the Study has not collected it, or has only a very short follow-up, recommendations should be downgraded. • Particularly in sections dealing with treatments of chronic/TRD/long lasting/ persisting depressions, upgrade (in GRADE system) any RCT with long post end-of-treatment follow-ups or periods of observation and that have analysed and reported this data **Justifications:** • Despite the 8.223 *Review questions* section in the Draft Guidance stating the high likelihood of relapse/deterioration in patients with depressions described under the heading of TRD, this - and indeed all other parts of the guidance evidence	We did not consider follow-up for further-line treatment as this data was not widely available across different intervention types and thus did not enable meaningful comparison. We did, however, include longer-term follow-up data in the relapse prevention review so we do have evidence in the guideline pertaining to longer-term effects of maintenance treatment. However, Fonagy 2015 does not meet the inclusion criteria for that review. It is also worth noting that if you do consider the 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although as you point out the effects on depression symptomatology are statistically significant at this time point. In GRADE RCT evidence is not upgraded, it starts at high quality and is downgraded for risk of bias, inconsistency, indirectness, imprecision and publication bias. Observational studies can be upgraded if a large effect is found, if the influence of all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect, or if a dose-response gradient is present. The

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				reviews/analyses – effectively ignore the necessity for long-term follow-up measures in the trials of depression treatment included; in fact, most have follow-ups of ≤ 8 weeks. The reviews of interventions in the draft guideline have taken the endpoint as the end of treatment in all cases. However, in those few trials with follow-ups and observation periods sufficiently long to offer data about the longer-term durability of end of treatment effects, the Draft gives them scant attention. Again, a prime example is Fonagy et al (2015): The Draft Revision focuses on treatment end-point; it omits the important data yielded by that study's exceptional 182-week observation period, which showed a substantial effect of considerable potential importance to sufferers (full remission Numbers Needed to Treat (NNT)=9.6; partial remission NNT = 3.9). • Note that persistent depression is a long-term condition and NICE does not treat any other long-term condition in this inadequate way with regards to endpoints. Diabetes (type 2 adults) for example, includes examination of outcomes ranging from 2 years up to	availability of long-term follow-up data is not a valid reason for upgrading within GRADE. However, we agree that it is important that long-term follow up data are collected in future research to enable comparison of this outcome across different interventions. We have therefore amended our research recommendations to specify that these data need to be collected. Thank you for your drawing our attention to these references. They do not meet the inclusion criteria for the reviews in this guideline for the following reasons: • Goodyer 2008: Adolescent rather than adult sample • Goodyer 2011: Protocol • Hepgul 2016, Westen 2004: Do not meet the study designinclusion criteria (not an RCT or systematic review of RCTs) • McPherson 2005: Systematic review searched for relevant references but no additional studies that met inclusion criteria were identified. In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be

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				10 and over as would be expected. The epilepsy guideline and arthritis guideline examined evidence including 1 and 2 years follow up data and in some cases longer. To treat depression, particularly any persistent form of depression, as a long-term condition on a par with long term physical conditions, follow-up data must be considered. • Calls for RCTs of interventions for depression to include longer term follow-up have been made repeatedly. Their importance in chronic/ resistant/persisting forms of depression is great (see for example McPherson et al, 2005; Goodyer et al, 2008; Goodyer et al, 2011; Goodyer et al, 2017). According to criteria adopted by NICE as well as the APA and EPA chronic forms of depression must last at least for 2 years. Various samples report mean duration of illness as 7.8 years (Keller et al (2000)); Kocsis et al (2007) 17.7 years; Schramm et al (2011) 21.2 years; Fonagy et al (2015) 24.4 years. Hepgul et al (2016) noted that 38% of IAPT attenders had attended IAPT	understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. Goodyer 2017 was published after the search cut-off date of June 2016 and therefore cannot be included in the guideline.

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				previously, pointing to a high relapse rate. Given the actual mean duration of illness as opposed to the minimum to meet the criterion, there is an even stronger case for looking at data from follow-up periods in chronic forms of depression (including TRD). Westen et al (2004) argue that since many patients who respond initially to treatments will relapse and/or present to other services subsequently. Long term follow up data is therefore critical in any truly evidence-based evaluation of the therapeutic effects of treatments for depression. • An RCT should be considered stronger for including a significant follow-up period and reporting data analysis of those follow-up points (which should be at least 12 months and ideally 24 months or more to reflect the chronicity of the condition). Any treatment which shows significant impact at the end of treatment but for which nothing is known about in terms of follow-up is arguably a weak study, particularly in relation to chronic forms of depression. All treatments deemed to be effective and recommended for depression ought to have	

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				demonstrated an impact beyond the end of treatment. If the effects of the treatment wear off as soon as (or soon after) the treatment finishes (or the long-term effects are unknown) then the treatment can at best be considered a reasonable sticking plaster. Treatments for physical illnesses that stopped working immediately after the end of treatment would not typically be recommended. • Any RCT has included significant follow-up periods after the end of treatment and have analysed and reported this data, those trials should be upgraded for quality and the data must be included in the reviews of effectiveness and considered when making research recommendations. The Draft's GRADE evaluations of trial quality currently disregard the importance of length of follow-up/ observation period in rating the value of the effect reported at treatment end-point. RCT's of persisting/chronic/TRD depressions should have follow-ups of at least 12 months and ideally 24 months, and should report data for these follow-up points. They should be rated higher	

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				than trials with follow-ups of a few weeks, other things being equal. Goodyer IM, Reynolds S, Barrett B, Byford S, Dubicka B, Hill J, Holland F, Kelvin R, Midgley N, Roberts C, Senior R, Target M, Widmer B, Wilkinson P, Fonagy P. Cognitive behavioural therapy and short-term psychoanalytical psychotherapy versus a brief psychosocial intervention in adolescents with unipolar major depressive disorder (IMPACT): a multicentre, pragmatic, observer-blind, randomised controlled superiority trial. *Lancet Psychiatry.* 2017;4(2):109-119.; Goodyer IM, Tsancheva S, Byford S, Dubicka B, Hill J, Kelvin R, Reynolds S, Roberts C, Senior R, Suckling J, Wilkinson P, Target M, Fonagy P. Improving Mood with Psychoanalytic and Cognitive Therapies (IMPACT): A pragmatic effectiveness superiority trial to investigate whether specialised psychological treatment reduces the risk for relapse in adolescents with moderate to severe unipolar depression: study protocol for a randomised controlled trial. *Trials.* 2011;12(1):175.; Goodyer IM, Dubicka B, Wilkinson P, Kelvin R, Roberts C, Byford S, Breen S, Ford C, Barrett B, Leech A, Rothwell J, White L, Harrington R. A randomised controlled trial of cognitive behaviour therapy in adolescents with major	

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				depression treated by selective serotonin reuptake inhibitors. The ADAPT trial. *Health Technol Assess.* 2008;12(14): iii-iv, ix-60.; Hepgul N, King S, Amarasinghe M, et al (2016). Clinical characteristics of patients assessed within an Improving Access to Psychological Therapies (IAPT) service: results from a naturalistic cohort study (Predicting Outcome Following Psychological Therapy; PROMPT). BMC psychiatry, 16(1), p52.Westen, D., Novotny, C. M., & Thompson-Brenner, H. (2004). The empirical status of empirically supported psychotherapies: Assumptions, findings, and reporting in controlled clinical trials. Psychological Bulletin, 130, 631– 663.; McPherson S, Cairns P, Carlyle J, Shapiro D, Richardson P & Taylor D (2005) The effectiveness of psychological treatments for refractory depression: A systematic review, Acta Psychiatrica Scandinavica, 111, 331-340.	
Lundbeck Limited	Full	343	23-30	With respect to the review questions for further line treatment: • "For adults with depression following no or limited response to previous treatment (of the current episode), or those not tolerating previous treatment (of the current episode), what are the relative benefits and harms of psychological, psychosocial, pharmacological, and	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the

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				physical interventions alone or in combination? • For adults with treatment-resistant depression, what are the relative benefits and harms of psychological, psychosocial, pharmacological, and physical interventions alone or in combination?" TA367 (NICE, 2015) has direct applicability to these review questions and we are surprised to note that it has been omitted from the draft guideline entirely. NICE concluded that vortioxetine was a clinically- and cost-effective option for patients who have had an "inadequate response to two previous antidepressants in their current episode" and yet this guidance has not been taken into account. Secondly, the REVIVE study (Montgomery et al., 2014) is directly applicable to the first review question having explored the effectiveness of vortioxetine or agomelatine in patients with an inadequate response to AD treatment. However, when reviewing the list of pharmacological interventions included as part of this review vortioxetine and all clinical/economic data available from the STA process and the broader publication database has been omitted. As noted	Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We therefore do not think that the methodology or results in the guideline are flawed. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.

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				previously, there is no mention or reference to vortioxetine or TA367 in the guideline recommendations in either full or shortened versions. Whilst we understand that it may have been felt unnecessary to duplicate work previously undertaken by NICE for the TA, we believe that if this was the case then it should be clearly stated that vortioxetine has already been found to be clinically- and cost-effective under an STA and so was excluded from this analysis, and a clear recommendation made in both the full and short versions of the guideline that vortioxetine should be considered as an option for adults whose condition has responded inadequately to 2 ADs within the current episode, in line with the conclusions made by TA367. **References:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015. Montgomery S A *et al.* Hum. Psychopharmacol Clin Exp 2014; 29: 470–482.	
Lundbeck Limited	Full	343	8-12	We are perplexed as to why vortioxetine is omitted from the list of potential next-step treatment options. It should be noted that vortioxetine is	Thank you for your comment. There is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes

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				approved by NICE in precisely this treatment setting, i.e. when a clinician is considering a switch to a different class of AD, or in the case where a person continues to have an inadequate response after two previous ADs.	on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Limited	Full	344	Table 92	We are perplexed as to why vortioxetine has not been included as a relevant pharmacological intervention in the decision problem for this review question. No explanation is given as to why vortioxetine alone has been excluded. Perversely, vortioxetine is recommended by NICE following TA367 in people who have not responded to initial treatment but was not included in these review questions, whereas none of the other pharmacological interventions listed in Table 92 have been subject to TA clinical and cost effectiveness review in this population but were included in these review questions.	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. However, in light of your comment we have

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					added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Limited	Full	346	2-20	Because vortioxetine is not included in the decision problem for this review question, no vortioxetine RCTs or other evidence of vortioxetine effectiveness was identified in the literature. No explanation is given as to why vortioxetine was not considered a relevant intervention in this setting. We consider the search strategy and results to be flawed.	Thank you for your comment. There is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We therefore do not think that the search strategy or results in the guideline are flawed. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Limited	Full	346	23-30	The results of the switching analysis are flawed because vortioxetine was not included as a relevant intervention.	Thank you for your comment. There is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in

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					Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We therefore do not think that the results of the swiching analysis in the guideline are flawed. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Royal College of Occupational Therapists	Full	81, 91, 125, 154		Occupational Therapy is only briefly mentioned on these pages and there is evidence that occupational therapy is beneficial for major depression. Please refer to following articles for information: https://bmcpsychology.biomedcentral.com/articles/10.1186/s40359-015-0097-9 https://www.cambridge.org/core/journals/psychological-medicine/article/adjuvant-occupational-therapy-for-work-related-major-depression-works-randomized-trial-including-economic-evaluation/9FF7CFE4B275869C51D99E957B5564C7	Thank you for your comment and providing these links to articles. We did not find any evidence to support recommending occupational therapy as an intervention for the management of depression. The studies that are linked to do not meet inclusion criteria for the following reasons: • Schene 2007 is a mixed population study with <80% meeting the criteria for first-line treatment, but <80% also meeting the criteria for further-line treatment or chronic depression • Gunnarsson 2015: Protocol
Lundbeck	Full	484	2-16	Relevant UK economic evidence in this	Thank you for your comment. As you

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Limited				treatment setting exists in the form of the vortioxetine TA367 (NICE, 2015). This has been omitted from the guideline. Also, the Scottish Medicines Consortium (SMC) has reviewed the cost-effectiveness of vortioxetine and recommended it for use in Scotland after the economic case for its use was demonstrated (SMC, 2016). This has also been omitted from review in the draft guideline. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015. Scottish Medicines Consortium Detailed Advice Document 1158/16. Vortioxetine for the treatment of major depressive episodes in adults. 2016.	mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the economic evidence on vortioxetine was intentionally not searched for or appraised by this guideline. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Limited	Full	499	22-39	We would again make clear that all clinical evidence relating to the use of vortioxetine has been ignored as a result of the decision to exclude vortioxetine as an intervention of interest to this decision problem.	Thank you for your comment. There is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by

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					this guideline. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Limited	Full	500	15-21	We believe the fact that the majority of anti-psychotics are not licensed to treat depression, either as monotherapy or in combination, should be explicitly stated in the full and short versions of the guideline and should not be relegated to a footnote. People with depression may also be at increased risk of physical health comorbidities so prescribing antipsychotics and anti-depressants that may worsen physical health comorbidities, such as increasing weight gain and worsening metabolic parameters (MSD Ltd., 2017; Gitlin, 2016; Rummel-Kluge, 2010; Laimer, 2006) does not appear to be in the best interests of people suffering with depression. **References:** MSD Ltd. 30 mg mirtazapine Summary of Product Characteristics. February 2017. http://www.medicines.org.uk/emc/medicine/21573. 2017. Gitlin M. International Journal of Bipolar Disorders 2016, 4:27.	Thank you for your comment. It is standard NICE process to highlight any off licensed use of interventions in the format of a footnote.

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				Rummel-Kluge C, et al. Schizophr Res 2010; 123: 225–33 Laimer M et al, Journal of Clinical Psychiatry 2006; 67(421-424).	
Lundbeck Lt	Full	502	21-29	These recommendations ignore the principles of rational prescribing and are contrary to the public health metrics contained within the NHS Outcomes Framework.	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications.
NHS England National IAPT Team	Full	502	31-39	Useful new guidance	Thank you for your comment.
Lundbeck Limited	Full	502	17-20	All of the recommendations in Chapter 8 are based on clinical and/or economic evidence of low or very low quality, and often on evidence derived from a single study. This is an important limitation, which should be made clear in the short version of the guideline. We do not believe it is sufficient to include this statement 500 pages into the full guideline.	Thank you for your comment. The short version of the guideline only contains the recommendations. Whilst it is not possible to replicate the 'evidence to recommendations' section in the short version, the limitations of the evidence that this section describes are reflected by the use of the word 'consider' in the recommendations about further line treatment. Higher quality evidence would have enabled recommendations to 'offer' specific interventions.
National School of Primary Care Mental Health Interest Group	Full	503		It was surprising to see that if someone had not responded to the initial medication prescribed for their depression, adding in another medication of a different group (recommendation 80) was put before	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a

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				switching to a single medication of another group (recommendation 82) - page 503, particularly as adding in another medication was (rightly) recommended to be under the supervision of a specialist. It is not clear how feasible such a strategy is, given the number of people seen in primary care who may not have a good therapeutic response to the initial medication prescribed. Would switching to another class of drug not be a logical first step?	combination of psychological therapy plus medication are options to consider before combining 2 medications.
Lundbeck Limited	Full	503	18-22	Recommendation 80 states "If a person wants to try a combination of medications and is willing to accept an increased side-effect burden, consider adding an antidepressant of a different class to their initial medication, for example, an SSRI with mirtazapine, in specialist settings, or after consulting a specialist." The position of this recommendation means that people could be offered a combination of an SSRI and mirtazapine after just one previous medication (i.e. second line). This could increase the likelihood of serotonin syndrome whilst increasing the side effect burden for individuals when there are alternative effective monotherapy options that could be tried in this position in the pathway. This recommendation could increase	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health

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				referrals to specialist services at a time when they are seeking to shift their focus to higher care clusters and improve primary care management of more common illnesses, such as depression. Currently, the primary care workforce is under increasing pressure and this guideline may result in GPs referring patients who they have used one anti-depressant with to specialist services, when a switch in class prior to this may be a more realistic proposition. This may also fit with current guidelines (including both local guidelines and the current NICE treatment pathway), clinical practice and service capacity. Recommendation 80 also runs counter to the evidence cited on pg. 47, lines 47-51 that "Non-adherence to antidepressant treatment leads, as expected, to increased symptom severity, decreased response and remission rates, increased risk of relapse, and higher rates of healthcare utilisation, leading to increased healthcare costs (Ho et al. 2016). Failure of treatment (due to either non-adherence or to inefficacy of treatment) considerably increases the cost of depression." Adherence to AD treatment is influenced by side effect burden, with greater side effects	services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				increasing the likelihood of non-adherence. Recommending a combination of ADs with a higher burden of side effects is likely to increase non-adherence to treatment, worsen outcomes, and therefore increase healthcare costs.	
Lundbeck Limited	Full	503	18-22	The strength of evidence for a combination of ADs also appears very weak. The recommendation is based on Carpenter et al.(2002), a study which included just 26 participants, only 11 of which received an SSRI + mirtazapine, and 15 of which received an SSRI + placebo. We are concerned that the relevant evidence base for vortioxetine has been excluded from the review questions, meaning a clinically- and cost-effective alternative further line treatment option has been completely overlooked, despite TA367 giving clear conclusions on vortioxetine's recommended position in the care pathway. Montgomery et al., 2014 explored the effectiveness of vortioxetine or agomelatine in patients who had had an inadequate response to SSRI/SNRI monotherapy. We believe it is a superior, and more relevant, source of evidence than the study reported by Carpenter. The Montgomery-reported REVIVE study included 502 participants, 255	Thank you for your comment, we agree the evidence for the combination of ADs is limited and so have been cautious in the development and wording of our recommendations. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally

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				of which were randomised to vortioxetine, and 246 of which were randomised to agomelatine. This compares to just 26 study participants in Carpenter 2002, only 11 of which were in the 'active' treatment arm Inclusion criteria for Carpenter 2002 were: "Adult outpatients were invited to participate if they met DSM-IV (American Psychiatric Association 1994) criteria for a current major depressive episode and had significant persistent depressive symptoms (total score 12 on the 17-item Hamilton Rating Scale for depression [HRSD-17] (Hamilton 1960)) despite at least 4 weeks of standard antidepressant monotherapy at maximum recommended or tolerated doses." Inclusion criteria for Montgomery 2014 were: "Eligible patients were aged ≥18 and ≤75 years, with a primary diagnosis of a single episode or recurrent MDD according to the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition Text Revision criteria (APA, 2000) and a current MDE of <12 months' duration [confirmed using the Mini International Neuropsychiatric Interview (MINI) (Lecrubier et al., 1997)]. Patients were required to have a Montgomery–Åsberg Depression Rating Scale (MADRS) (Montgomery and Åsberg, 1979) total score	not searched for or appraised by this guideline.

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				≥22 and item 1 (apparent sadness) score ≥3 at screening and baseline visits. Only patients with depressive symptoms considered nonresponsive or partially responsive to a single treatment course of an adequate dose (approved) and duration (≥6 weeks) were eligible for the study (stage I (Thase and Rush, 1997) and stage A (Souery et al., 1999) criteria). In addition, patients had to want to change their current treatment because of an inadequate response and to be considered by the investigators to be candidates for a switch." Baseline characteristics of study participants were similar between Carpenter 2002 and Montgomery 2014, as was severity of illness; CGI-S scores at baseline were 4.4 ± 0.6 for both vortioxetine and agomelatine arms in Montgomery 2014, and 4.5 ± 0.5 and 4.5 ± 0.6 in the mirtazapine and placebo arms, respectively, in Carpenter 2002. Whilst Carpenter 2002 was only a 4 week study, Montgomery 2014 was a 12 week study. The results of Montgomery 2014 demonstrated response rates in the vortioxetine arm of 61.5% at week 8, and 69.8% at Week 12, both of which were statistically significant versus the active comparator agomelatine. Carpenter 2002	

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				demonstrated a 63.6% responder rate for the SSRI + mirtazapine arm at week 4, and a 20% response rate in the placebo arm. Whilst Montgomery 2014 didn't report response rates at week 4, the Montgomery-Asberg Depression Rating Scale (MADRS) change from baseline was superior and statistically significant for vortioxetine over agomelatine at Week 4 ($p<0.01$). Discontinuations due to adverse events for SSRI + mirtazapine at 4 weeks were 9.1% in Carpenter 2002. Discontinuation rates due to adverse events for vortioxetine at 12 weeks were 5.9% in Montgomery 2014. We therefore believe the evidence for vortioxetine in this population is stronger than that for combining an SSRI with mirtazapine, and vortioxetine demonstrated similar efficacy with fewer discontinuations due to side effects, making it a more rational treatment choice. **References:** Carpenter L *et al.* Biol Psychiatry 2002; 51:183–188. Montgomery S A *et al.* Hum. Psychopharmacol Clin Exp 2014; 29: 470–482.	
Lundbeck	Full	503	18-	We are concerned that the draft guideline	Thank you for your comment. We have

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Limited			22	recommends the combination of two ADs very early in the treatment pathway, seemingly on the basis of very limited evidence and the increased risk of side effects and serotonin syndrome. However, stronger evidence in a similar patient population exists for vortioxetine, as well as a full TA recommendation (NICE, 2015). We feel that given the limited evidence, the increased risk of side effects and serotonin syndrome, the potential increased burden on secondary care specialist services, and the existence of a TA for vortioxetine, any recommendation to offer combinations of ADs such as an SSRI + mirtazapine should be made after the recommendation to offer vortioxetine as a treatment option. This approach is further supported because vortioxetine is a multimodal antidepressant (Lundbeck Ltd, 2017) Culpepper 2015 highlights; "Combining mechanisms of action provides a synergistic effect particularly for those patients who have failed on 1 or 2 drugs…Another way to target several mechanisms yet prescribe only 1 drug is to use multifunctional or multimodal antidepressant drugs…Multimodal antidepressants may provide less adverse effects than use of multiple single modality	revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. As we have mentioned previously, the committee reviewed the recommendations about input from secondary care and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				antidepressants" (Culpepper, 2015). A further benefit to this approach is that vortioxetine is suitable for use in primary care and does not require specialist input or monitoring, and would therefore be unlikely to lead to a rise in referrals to specialist services that is currently suggested when combining ADs in the current draft. **References:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes (November 2015). Lundbeck Ltd. Vortioxetine Summary of Product Characteristics. January 2017. Culpepper L *et al.* The American Journal of Medicine, 128 (9 Suppl):S1-S15, September 2015.	
Lundbeck Limited	Full	503 504	37-38 11-13	There appears to be a contradiction between recommendation 82 and recommendation 85. Recommendation 82 states: "If a person has had no response or a limited response to initial medication and does not want a psychological therapy or a combination of medications, consider: • continuing with the current medication, with extra support, close monitoring and an increased dose if	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so recommendation 85 has been removed so there is no longer potential for any contradiction.

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				the medication is well tolerated, or • switching to a medicine of a different class, or • switching to medication of the same class if there are problems with tolerability. [new 2017]" Recommendation 85 states: "If a person finds that their medication is helping them but they are having side effects, consider switching to another AD with a different side effect profile." [new 2017] These recommendations appear confusing. Medications of the same class have broadly similar side effect profiles and similar modes of action, whereas different classes of medication have different side effect profiles and different modes of action. If a person has had no (or an inadequate) response to their medication, and/or problems with tolerability, recommendation 82 suggests switching to another medication in the same class. Mode of action and side effect profile are likely to be very similar within class, and the person has already demonstrated that they have not responded to, or tolerated, that class of AD. A "within class" switch in these circumstances does not	

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				appear to be rational prescribing; it would seem more logical to switch to an AD that was better tolerated and also had a different mode of action. Conversely, recommendation 85 suggests that if the AD is helping but the person is experiencing side effects, consider switching to another AD with a different side effect profile. This implies changing class of medication because the side effect profiles between classes of medication are likely to be different, but very similar within class. Taken together these recommendations appear confusing: • If a person isn't responding to, or tolerating their AD, then switch to another medication in the same class that has the same mode of action and side effect profile, but • If a person is responding to, but not tolerating their AD, then change to a different class of AD that has a different mode of action and side effect profile.	
Lundbeck Limited	Full	503 504	37-38 11-13	Lundbeck would propose the following changes to recommendations 76-85 to address the issues outlined above: 76. If a person has had no response or	Thank you for your comment and suggested changes to the recommendations. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose,

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				limited response (within 3-4 weeks for antidepressant medication, or 4-6 weeks for psychological therapy) assess: • whether there are any personal or social factors that might explain why treatment isn't working • whether the person has not been adhering to the treatment plan, including any adverse effects of medication 77. When changing treatment for a person with depression who has had no response or a limited response to initial psychological therapy, consider: • combining the psychological therapy with an SSRI e.g. sertraline, citalopram, or mirtazapine, or • switching to an SSRI, e.g. sertraline, citalopram, or mirtazapine if the person wants to stop psychological therapy 78. If a person has had no response or a limited response to initial medication and doesn't want psychological therapy consider: • continuing with current medication, with extra support, close monitoring and an increased dose if the medication is well tolerated, or • switching to a medicine of a different class, or • switching to a medicine of the same	switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				class if there are problems with tolerability 79. If a person has had no response or limited response after assessing the factors above, provide more support by increasing the number and length of appointments. Also consider: • Changing to a combination of psychological therapy and medication if the person is on medication only • Changing to psychological therapy alone, if the person is on medication only and does not want to continue with medication, 80. If a person has responded inadequately to 2 antidepressants within the current episode, consider switching to vortioxetine (see NICE TA367) 81. If a person finds that their antidepressant is helping them but they are having side effects, consider switching to another antidepressant with a different side effect profile 82. If a person has had no response or limited response to alternative medication or treatment options above after 2–4 weeks, provide more support by increasing the number and length of appointments. Also consider: • Changing to a combination of psychological therapy and medication	

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				if the person is on medication only • Changing to psychological therapy alone, if the person is on medication only and does not want to continue with medication, or • Changing to a combination of 2 different classes of medication, in specialist settings or after consulting a specialist, if the person is on medication only, or a combination of medication and psychological therapy and does not want to continue with psychological therapy: o Inform the person of the likely increase in side effect burden (including the risk of serotonin syndrome) • Adding an antidepressant of a different class to their initial medication, for example an SSRI with mirtazapine, in specialist settings or after consulting a specialist • Combining an antidepressant with an antipsychotic or lithium in specialist settings or after consulting a specialist 83. If a person's symptoms do not respond to a dose increase, switching to another antidepressant or combination of medications after a further 2–4 weeks, review the need for care and treatment and consider consulting with, or referring the person to, a specialist	

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				service. 84. For people with depression whose symptoms have not adequately responded to a combination of medication and a psychological therapy after 12 weeks, consider: • Switching to an alternative medication with a different mode of action or side effect profile • Switching to a different psychological therapy, such as cognitive behavioural analysis system of psychotherapy (CBASP), CBT or MBCT 9 (see recommendation 86). Lundbeck would argue that whilst the draft full guideline states "there is limited evidence to support routine increases in dose of antidepressants or switching to a drug of a different class", the evidence presented for combination treatments ahead of these options also appears to lack robust evidence base (see Carpenter 2002). It makes practical sense to adopt the recommendations of TA367, before recommending a 'combination of medications' or augmentation strategy. After reviewing all clinical evidence, the appraisal committee for TA367 "accepted that the available evidence suggested vortioxetine leads to a lower probability of stopping	

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				treatment and fewer adverse effects than most other antidepressants in the short term" (NICE, 2015) Patients with depression may also be at increased risk of physical health comorbidities so prescribing a combination of medications that may increase side effects or AEs that could worsen physical health comorbidities, such as increasing weight gain (mirtazapine/second generations antipsychotics) and worsening metabolic parameters (second generations antipsychotics/lithium) (MSD Ltd., 2017; Gitlin, 2016; Rummel-Kluge, 2010; Laimer, 2006), does not appear to be in the best interests of the depressed patient. Conversely, vortioxetine has demonstrated placebo-level sleep disturbance and sexual dysfunction, weight neutrality, no QTc prolongation, and placebo-level effects on blood pressure, heart rate and renal or hepatic assessments (Lundbeck Ltd., 2017). It should also be noted that vortioxetine can be stopped immediately without discontinuation symptoms (Lundbeck Ltd, 2017). Also, NICE have provided robust and clear recommendations for monotherapy with vortioxetine for a person who has responded	

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				inadequately to two ADs within the current episode, affirming its clinical- and cost-effectiveness through the STA process. There is no cost-effectiveness base for all currently suggested combination medications in the draft guideline, but NICE conclude after "assuming equal efficacy between treatments, the incremental cost-effectiveness ratios (ICERs) for vortioxetine compared with all other antidepressants were £9000 per quality-adjusted life year (QALY) gained or below and the Committee agreed that treatment with vortioxetine was a cost-effective use of NHS resources" (NICE, 2015). Agomelatine, sertraline, venlafaxine (XR), duloxetine, citalopram and escitalopram, commonly used ADs, were included as comparators in this cost effectiveness analysis. In a similar HTA conducted by the Scottish Medicines Consortium for vortioxetine, a threshold-based sensitivity analysis to show the levels of reduction in adverse events for the comparators that would be required for the cost per QALY to reach £20k or £30k suggested that for adverse events where direct or indirect data were not available, the unadjusted comparator rates would have to reduce by approximately 70% and upwards for the vortioxetine ICERs to be above these	

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				acceptance thresholds (SMC, 2016). This reinforces that whilst ADs may share similar efficacy profiles, important differences exist between anti-depressants on AEs. This supports that a switch in class might be a sensible earlier option where a patient's lack of response may be due to not tolerating an effective dose of the prescribed AD. The SMC also concluded that vortioxetine was accepted for restricted use within NHS Scotland for the treatment of major depressive episodes in adults "who have experienced an inadequate response (either due to lack of adequate efficacy and/or safety concerns/intolerability) to two or more previous antidepressants" (SMC, 2016). This position is very similar to that recommended by NICE TA367 (NICE, 2015). We are also concerned that recommending combinations of medications that will require specialist consultation or initiation in a specialist setting may significantly increase the number of referrals to specialist services. This may place additional pressure on specialist MHT providers who may already have high demands on their services. GPs may not feel comfortable with prescribing combinations of psychopharmacological agents in primary care and may also not be able to manage the increasing side effect	

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				burden this could create. The alternative proposal above would allow GPs more options in primary care and reduce a potential increase in referral rates that the original draft recommendations might result in. Lundbeck hopes the proposed alternative pathway above would better represent current NICE TA367 recommendations, support current clinical practice more logically and allow the GP in collaboration with patient to select the class and mode of action of antidepressant that best balances efficacy and acceptability before considering specialist referral and specialist drug combinations. **References:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes (November 2015). MSD Ltd. 30 mg mirtazapine Summary of Product Characteristics. February 2017. http://www.medicines.org.uk/emc/medicine/21573. 2017. Lundbeck Ltd. Vortioxetine Summary of Product Characteristics. January 2017. Carpenter L *et al.* Biol Psychiatry 2002; 51:183–188 Gitlin M. International Journal of Bipolar	

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				Disorders 2016, 4:27. Rummel-Kluge C, et al. Schizophr Res 2010; 123: 225–33 Laimer M et al, Journal of Clinical Psychiatry 2006; 67(421-424) Scottish Medicines Consortium Detailed Advice Document 1158/16. Vortioxetine for the treatment of major depressive episodes in adults (2016).	
South West London and St. George's Mental Health NHS Trust	Full	503	10	Whilst we are pleased to see the inclusion of CBT, BA and IPT as options for treatment-resistant depression, we are disappointed to see that IPT only reappears for more severe depression after previous unsuccessful interventions. In practice we often have clients present with more severe depression whose problems have been triggered by a current interpersonal difficulty and whose goals are related to the resolution of this problem (e.g. marital conflict, stuck grief, difficulties adjusting to new roles). This is also described in the introductory chapters to the draft guideline (pp.37-38). Under the 2009 guideline we are able to offer an interpersonally focused intervention to match their goals (either BCT or IPT). In the introductory chapters to the draft guideline, it is noted that the provision of choice can improve patient engagement and outcomes (pp.43, lines 5-8). Under the draft guideline, clients with more severe depression would	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the two are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the

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				only be able to access IPT if they have first failed at two other interventions. This seems a clinically unhelpful and impractical recommendation, given the relatively high ranking of IPT (compared to BA and STPP) in your clinical effectiveness analyses for more severe depression.	committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). We have also revised the ordering of the recommendations on further line treatment. In doing so we have clarified that if a person has had no response or a limited response to treatment, is on medication only and does not want to continue with it, switching to a psychological therapy alone (CBT, BA, or IPT) is an option to consider.
Lundbeck Limited	Full	504	5-10	Recommendation 84 states: "For people with depression whose symptoms have not adequately responded to a combination of medication and psychological therapy after 12 weeks, consider: - Alternatives to combined treatment (see recommendation 87) - Switching to a different psychological therapy, such as CBASP, CBT or MBCT." Recommendation 87 states: If a person with chronic depression chooses	Thank you for your comment. We have amended the recommendations on further line treatment to remove this inconsistency.

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				not to have combined treatment, offer: • an SSRI alone, or • cognitive behavioural treatments (CBASP and CBT) alone. [new 2017] So, if a person has failed to respond adequately to AD medication combined with psychological therapy after 12 weeks, the recommendation is to withdraw one of these options and continue an SSRI alone, or psychological therapy alone. This makes little clinical sense. If a person has failed to respond to a combination of medication and psychological therapy after 12 weeks it is difficult to understand how further improvement could be expected by removing one of these two interventions and continuing a single treatment that has already been shown to deliver an inadequate response. This risks breaking the therapeutic alliance between patient and clinician and risks instilling hopelessness when further options could still be explored, such as switching to a medication with a different mode of action combined with a different form of psychological intervention.	
Royal College of Psychiatrists	Full	504	5-10	**CBASP** We are concerned with the implementation of the recommended treatment CBASP, as this	Thank you for your comment. In light of this we have removed CBASP from this recommendation.

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				is not an established treatment model in the UK, and raises questions of availability, training provision, and extra costs to do so.	
University of Nottingham	Full	508	16-36	PCE-CfD is again omitted. We receive numerous accounts of how PCE-CfD is frequently the approach offered in services where CBT and CT and pharmacology fail.	Thank you for your comment. Counselling was included as an intervention in the questions about chronic depression. Unfortunately no specific RCT evidence on PCE-CfD (which was developed for the IAPT programme) was identified and so no recommendation for the use of PCE-CfD was made.
British Acupuncture Council	full	508	10-11	One Chinese study (Zhang 2013) has a mean illness duration of 7.5 years in the base population: should it have been dealt with in the chronic depression group?	Thank you for your comment and bringing this to our attention. Zhang 2013 has been removed from the acute pairwise review of acupuncture because the mean duration of major depressive episode it reports means that this study does not meet the inclusion criteria for this review. It was not possible to add this study to the chronic depression review as the study had no minimum duration of major depressive episode as an eligibility criterion and it is not clear what proportion of participants in this trial would meet criteria for chronic depression.
British Autogenic Society	Full	General, 247, 292, 670 Medit	General, 25,46, 34 Medi	PATIENT CHOICE ISSUE: As the Draft guidance recommends a number of psychological interventions (page 101, l 36ff), some of which include meditative/relaxation therapeutic approaches,	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with

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		ation Relaxation Therapy 101	tation Relaxation Therapy 36ff	the Patient Choice issue leads to the ethical question of "which relaxation therapy for which client?". We are concerned that choices in this Guidance should include all the meditative/relaxation therapies now on offer within the NHS which have been shown to have the outcome of reducing depression as measured by HADS. This is particularly concerning because, as you have noted, patients consulting GPs often arrive with anxiety, somatic complaints and sleep disturbance whilst underlying depression may not be diagnosed as it may be co-morbid or sub-threshold depression. A recent report by Bowden, Lorenc and Robinson (2011, *Prim Health Care Res Dev*. Apr;13(2):175-85. Epub 2011 Jul 26. doi: 10.1017/S1463423611000181) found not only significant reductions in insomnia and sleep disturbance (p. 5), but also found reductions in depression and anxiety, as measured by HADS, for patients with a primary diagnosis of insomnia and who learned Autogenic Training (p.5) at the RLHIM. It may be that because HADS, depression and anxiety are not Keywords for this article, this report has been inadvertently overlooked.	depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline an offer of treatment. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person. We did not find any evidence to support recommending autogenic training as an intervention. Bowden 2011 does not meet the inclusion criteria for this review as the trial specifically recruits people with a coexisting physical health condition.

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				As Autogenic Training is already on offer in the NHS, at the Psychology Department, RLHIM and at other NHS and non-NHS locations, we urge that it be included in the NICE Guidance for Depression side by side with other psychological interventions or as a standalone first prescription for people with "subthreshold depressive symptoms" such as anxiety, panic and/or sleep disorders so that the dis-ease does not cross the threshold and raise costs to the NHS system as well as to patients.	
NHS Lothian	Full	581	37-45	We also welcome the consideration expressed by the Guideline Committee on the trade-off between net health benefits and resource use that acknowledges the need for CBASP training in the UK in order to increase effective treatments made available to people who suffer from chronic depression and the consequent reduction in longer term healthcare costs.	Thank you for your comment and your support.
NHS Lothian	Full	582	45-47	We welcome the additional clarity and guidance in the treatment of chronic depression, in particular the inclusion and recommendation of CBASP, as a treatment specifically developed to address the difficulties experienced by patients with chronic depression. This recommendation is consistent with the clinical evidence reviewed in these guidelines and summarised on	Thank you for your comment and your support.

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				Pages 574-577 and the conclusion reported on Page 581 (lines 4-5) that suggests "an advantage of CBASP over alternative psychological therapies".	
Royal College of Psychiatrists	Full	585	general	Section on Depression with co-morbidities – no specific reference to substance misuse; may be helpful to cross reference to the updated 2017 drug misuse clinical guidelines (Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group (2017) Drug misuse and dependence: UK guidelines on clinical management. London: Department of Health); in these guidelines chapter 3 examines psychosocial components of treatment – dual focus treatments (e.g. CBT) for both depression and substance misuse (3.7.3.2); chapter 7, section 7.9 looks at co-existing problems of mental health and substance misuse.	Thank you for your comment. The guideline is looking at complex depression, which is defined as depression that is co-morbid with a personality disorder. Although drug misuse can be part of the problem, it is not central to the characterisation or diagnosis of complex depression in this guideline and therefore we have not cross-referenced the document that you cite.
British Psychoanalytic Council	Full	585	4-42	<u>Narrow definition of complex depression:</u> We are concerned as to why, despite noting psychiatric comorbidities such as post-traumatic stress disorder, obsessive-compulsive disorder, eating disorders and generalised anxiety disorder, the guidelines only use depression with personality disorder as their criterion for complex depression. This means that a number of trials covering	Thank you for your comment. The committee considered a number of comments on the use of the term 'complex depression' in this guideline. In the guideline 'complex depression' was limited to depression that was co-morbid with a personality disorder. A number of stakeholders pointed out that other factors such as other mental health co-morbidities, drug and alcohol misuse, social and environmental factors and a history of poor response to treatment can also

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				complex depression have been excluded because they contain populations experiencing a wide range of psychiatric comorbidities (for example, the population used for the Tavistock Adult Depression Study).	contribute to a diagnosis of complex depression. The committee considered these factors and noted that co-morbidity with a range of other mental disorders also occurred in participants in studies for first line treatment, TRD and chronic depression. The committee therefore considered that co-morbidity alone would not be useful in describing complex depression. The focus on depression that was co-morbid with personality disorder was because of the committee's knowledge and experience that it can complicate the treatment of depression (see for example the meta-analysis by Newton-Howes et al (2006) Personality disorder and the outcome of depression: meta-analysis of published studies. British Journal of Psychiatry, 188, 13-20)). The committee therefore decided to stay with the current definition of complex depression used in the guideline as alternative suggested definitions did not clarify the issue. However they acknowledge there are limitations with this definition of complex depression. Fonagy et al 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') cites their inclusion criteria as

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					"at least 2 failed treatment attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a psychological intervention". This meets the inclusion criteria for our review questions on further line treatment and hence it was included in those reviews. Fonagy et al 2015 does not report the proportion of people with comorbid personality disorder. We were not able to determine if it met the inclusion criteria for the review on complex depression and consequently it was excluded from that review.
British Acupuncture Council	Full	585	4-42	The problems associated with co-morbidity are highlighted but only followed up for personality disorder. As discussed, acupuncture is particularly beneficial for depression with physical pain (Hopton et al, 2014), which was the case for half of the population in MacPherson 2013. Given the increasing NHS burden from chronic multi-morbidity acupuncture could be a useful option.	Thank you for your comment. We did not find any evidence to support making a recommendation for acupuncture for the treatment of depression that is co-morbid with personality disorder.
University of Essex	Full	585	4-28	We are concerned that the Draft takes comorbidity with PD as its only criterion of 'complex depression'; the cut-off threshold of 51% of participants having PD is also entirely	Thank you for your comment. The committee considered a number of comments on the use of the term 'complex depression' in this guideline. In the guideline 'complex

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				arbitrary. This approach is at odds with the EPA who adopt a nuanced approach to complexity in depression that is closer to the complexity that is more generally encountered in clinical services for depression. We request: • The Revision adopts an approach in line with EPA recommendations that type of treatment should be individually chosen in consideration of early versus late onset, type of depression, number of episodes, early trauma, symptom severity, patient preference and comorbid personality disorder (evidence level: 4; recommendation grade: Good Practice Point [GPP]). Justification: • The EPA Guidance Group (Jobst et al, 2016) sees complexity in terms of early versus late onset, type of depression, number of episodes, early trauma, symptom severity, patient preference and comorbid personality disorder, and that the type of treatment offered should be individually tailored accordingly.	depression' was limited to depression that was co-morbid with a personality disorder. A number of stakeholders pointed out that other factors such as other mental health co-morbidities, drug and alcohol misuse, social and environmental factors and a history of poor response to treatment can also contribute to a diagnosis of complex depression. The committee considered these factors and noted that co-morbidity with a range of other mental disorders also occurred in participants in studies for first line treatment, TRD and chronic depression. The committee therefore considered that co-morbidity alone would not be useful in describing complex depression. The focus on depression that was co-morbid with personality disorder was because of the committee's knowledge and experience that it can complicate the treatment of depression (see for example the meta-analysis by Newton-Howes et al (2006) Personality disorder and the outcome of depression: meta-analysis of published studies. British Journal of Psychiatry, 188, 13-20)). The committee therefore decided to stay with the current definition of complex depression used in the guideline as alternative suggested definitions did not clarify the issue. However they acknowledge there are limitations with this definition of complex

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				• The Draft's current terminology implies that the patients studied in other sections are not complex. Again as an example, Fonagy et al (2015) participants had high levels of childhood adversity (89% - unpublished data available on request); 47% musculoskeletal problems, 25% gastrointestinal problems plus high comorbidity of other physical problems; 91% had at least one other comorbid Axis 1 disorder; 84% had one or more Axis II disorder (therefore meeting the 51% threshold for the complex depression category anyway); 54% were unemployed; the mean baseline GAF score was 49.1; 45% had made at least one previous suicide attempt etc. Clinically this is a very complex population and yet this trial is classed as TRD only – rather than chronic and/or complex. Jobst A et al. (2016) European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe. European Psychiatry, 33, 18 – 36.	depression. The decision to include studies of mixed populations where at least 51% of the participants had a diagnosis of personality disorder was made after discussion with the committee. The reason for deciding on 51% as the cut off was because this would mean the majority of people in the study had depression comorbid with personality disorder. It would not be appropriate to adopt the recommendations on 'complex depression' from Jobst 2016 as these are for a broader population than that covered by this guideline and so could have considered evidence from studies which do not match our inclusion criteria. We have specified in the recommendations that complex depression is defined by this guideline as depression comorbid with a personality disorder. By doing this we intended to make it clear which specific population the recommendations applied to and do not think that this implies that other patients are not complex. Fonagy et al 2015 cites their inclusion criteria as "at least two failed treatment

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					attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a psychological intervention". This meets the inclusion criteria for our review questions on further line treatment and hence it was included in those reviews. Fonagy et al 2015 does not report the proportion of people with comorbid personality disorder. We were not able to determine if it met the inclusion criteria for the review on complex depression and consequently it was excluded from that review.
CHESS (Centre for Humanities Engaging Science and Society), Durham University	Full	585	4-28	We are concerned that the Draft takes comorbidity with PD as its only criterion of 'complex depression'; the cut-off threshold of 51% of participants having PD is also entirely arbitrary. This approach is at odds with the EPA who adopt nuanced approach to complexity in depression that is closer to the complexity that is more generally encountered in clinical services for depression. **We request:** • The Revision adopts an approach in line EPA recommendations that type of treatment should be individually	Thank you for your comment. The committee considered a number of comments on the use of the term 'complex depression' in this guideline. In the guideline 'complex depression' was limited to depression that was co-morbid with a personality disorder. A number of stakeholders pointed out that other factors such as other mental health co-morbidities, drug and alcohol misuse, social and environmental factors and a history of poor response to treatment can also contribute to a diagnosis of complex depression. The committee considered these factors and noted that co-morbidity with a

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				chosen in consideration of early versus late onset, type of depression, number of episodes, early trauma, symptom severity, patient preference and comorbid personality disorder (evidence level: 4; recommendation grade: Good Practice Point [GPP]). **Justification:** • The EPA Guidance Group sees complexity in terms of early versus late onset, type of depression, number of episodes, early trauma, symptom severity, patient preference and comorbid personality disorder, and that the type of treatment offered should be individually tailored accordingly. The Draft's current terminology implies that the patients studied in other sections are not complex. Again as an example, Fonagy et al (2015) participants had high levels of childhood adversity (89% - unpublished data available on request); 47% musculoskeletal problems, 25% gastrointestinal problems plus high comorbidity of other physical problems; 91% had at least one other comorbid Axis 1 disorder; 84% had one or more Axis II disorder (therefore meeting the 51% threshold for the complex depression category anyway); 54% were unemployed;	range of other mental disorders also occurred in participants in studies for first line treatment, TRD and chronic depression. The committee therefore considered that co-morbidity alone would not be useful in describing complex depression. The focus on depression that was co-morbid with personality disorder was because of the committee's knowledge and experience that it can complicate the treatment of depression (see for example the meta-analysis by Newton-Howes et al (2006) Personality disorder and the outcome of depression: meta-analysis of published studies. British Journal of Psychiatry, 188, 13-20)). The committee therefore decided to stay with the current definition of complex depression used in the guideline as alternative suggested definitions did not clarify the issue. However they acknowledge there are limitations with this definition of complex depression. The decision to include studies of mixed populations where at least 51% of the participants had a diagnosis of personality disorder was made after discussion with the committee. The reason for deciding on 51% as the cut off was because this would mean the majority of people in the study had depression comorbid with personality

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				the mean baseline GAF score was 49.1; 45% had made at least one previous suicide attempt etc. Clinically this is a very complex population and yet this trial is classed as TRD only – rather than chronic and complex.	disorder. It would not be appropriate to adopt the recommendations on 'complex depression' from Jobst 2016 as these are for a broader population than that covered by this guideline and so could have considered evidence from studies which do not match our inclusion criteria. We have specified in the recommendations that complex depression is defined by this guideline as depression comorbid with a personality disorder. By doing this we intended to make it clear which specific population the recommendations applied to and do not think that this implies that other patients are not complex. Fonagy et al 2015 cites their inclusion criteria as "at least two failed treatment attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a psychological intervention". This meets the inclusion criteria for our review questions on further line treatment and hence it was included in those reviews.

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					Fonagy et al 2015 does not report the proportion of people with comorbid personality disorder. We were not able to determine if it met the inclusion criteria for the review on complex depression and consequently it was excluded from that review.
Nottinghamshire Healthcare NHS Foundation Trust	Full	671	General	In addition to some of the more restrictive recommendations simply not being in line with the evidence base there are a several other issues that support a more inclusive recommendation for the use of MBCT. These include: 1. The stipulation that MBCT can only be offered after other treatment options goes against not only the evidence for MBCT (there is an absence of any evidence of superiority of other treatments in preventing depressive relapse, and indeed that it is equal in effect to maintenance anti-depressant medication, Kuyken et al, 2015) but also against patient choice. There are numerous qualitative studies highlighting the popularity of MBCT with patients (e.g., Mason & Hargreaves, 2001; York, 2007) 2. There are an increasing number of people trained in MBCT within the NHS and Health Education England have committed to training more. There is consequently a growing capacity to deliver MBCT and a NHS	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. They noted that: • recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. • the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry

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				England and HEE commitment to enhancing that capacity. 3. There are substantial benefits of integrating MBCT into the workplace. As a consequence of staff training in MBCT there are mindfulness groups run for the wider staff group aimed at increasing staff's ability to manage stress and improve overall wellbeing. This is a consequence of integrating MBCT into clinical services. As a result approximately 500 Notts Healthcare staff have been through a MBCT programme in the past several years	commentary on the Kuyken et al (2016) meta-analysis). • In the majority of trials of MBCT (including those in Kuyken et al (2016) participants had been in receipt of, or continued to use antidepressants. • of the trials of MBCT which specified a previous number of episodes as an entry criteria, 7 out of the 9 trials considered as part of the guideline evidence review had 3 or more episodes as their entry criteria. When these factors are taken into account the committee considered that it was appropriate to include these qualifiers in the recommendations. Thank you for providing the information on capacity to deliver MBCT. However, making recommendations on integrating MBCT into the workplace is outside the scope of this guideline.
Royal College of Psychiatrists	Full	672	26-29	This is restrictive. What about all those situations in which ECT is an appropriate first-line treatment? When it is opted for by the patient or by their family, often because it worked so well before? When other treatments are relatively contraindicated or less preferable (e.g. in pregnancy, during breastfeeding, with co-morbid physical illness	Thank you for your comment. ECT was included as an intervention in the review questions on treating depression. Very little new evidence was identified and as stated in the 'evidence to recommendations' sections in the full guideline, the committee did not consider this new evidence was sufficient to warrant changing the recommendations

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				e.g. hyponatraemia)? When a rapid action is desired but life is not in danger (e.g. tormented by delusions, or postpartum with a need to feed and bond with baby)? These are all evidence-based indications yet this guidance denies treatment to these vulnerable groups of patients and puts their well-being and that of their families at risk. It is recommended that we must wait until "*multiple* pharmacological *and* psychological treatments" have failed. What does "multiple" mean here? What about a patient who thinks she is dead and believes she is in hell? The guidance may leave her in that pitiful state for many weeks on a ward while treatment after treatment fails to help her? This recommendation also lacks practical utility: engaging a highly agitated patient who can barely string a sentence together in CBT is not practical. The ECT Committee of the Royal College of Psychiatrists and indeed the RCPsych itself agreed with the recommendations of CG90 which stated "ECT should be considered for severe depression that is life-threatening, or where a rapid response is required or where other treatments have failed. ECT should not be used routinely in moderate depression but should be considered if there has been no response to multiple drug treatments and psychological treatment. If patients have not	made in the 2009 guideline.

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				responded well to ECT in the past, ECT should only be considered again after review of the adequacy of previous treatment, a consideration of other options and after discussion with the patient and their advocates or carers if appropriate." We are confident that no new evidence has emerged in the past 8 years to warrant any change in NICE's position. Indeed there has been a consolidation of data and information driven by some large well conducted RCTs.	
Royal College of Psychiatrists	Full	672	21-22	This recommendation does not have an evidence base and would be impractical and very difficult to standardise and implement. Considerable problems (e.g. learning effects) would ensue with repeating such tasks at such frequency There are no established measures for assessing "subjective memory impairment". See the following three papers for reviews of this area: - 1.Semkovska, M. & McLoughlin, D. M. (2013). Measuring retrograde autobiographical amnesia following electroconvulsive therapy: historical perspective and current issues. The Journal of ECT 29, 127-133. 2. Semkovska, M. & McLoughlin, D. M. (2014). Retrograde autobiographical amnesia after electroconvulsive therapy: on the difficulty of finding the baby and clearing murky bathwater. The Journal of ECT 30, 187-188. 3. Semkovska, M., Noone, M., Carton, M. &	Thank you for your comment. ECT was included as an intervention in the review questions on treating depression. Very little new evidence was identified and as stated in the 'evidence to recommendations' sections in the full guideline, the committee did not consider this new evidence was sufficient to warrant changing the recommendations made in the 2009 guideline. Semkovska et al. (2012, 2013, 2014) cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				McLoughlin, D. M. (2012). Measuring consistency of autobiographical memory recall in depression. Psychiatry Res 197, 41-48. We agree with the recommendations on lines 16-18 and 20 on this page (672) and consider those measures to be evidence based and practical.	
Royal College of Psychiatrists	Full	674	7-8	There should also be a recommendation for continuation ECT as an option to prevent relapse after successful ECT here. There is good RCT data in geriatric depression that additional ECT after remission (in the study operationalized as four continuation ECT treatments followed by further ECT only as needed) was beneficial in sustaining mood improvement for most patients and better than the venlafaxine plus lithium arm (Kellner et al, Am J Psychiat, 173, 1110-1118, 2016). Another RCT showed that continuation ECT combined with antidepressant prolonged survival time in elderly patients with psychotic unipolar depression who had remitted with ECT compared to the antidepressant alone. (Navarro et al, Am J Geriatr Psychiatry 16,498-505,2008)	Thank you for your comment. ECT was included as an intervention in the review questions on treating depression. Very little new evidence was identified and as stated in the 'evidence to recommendations' sections in the full guideline, the committee did not consider this new evidence was sufficient to warrant changing the recommendations made in the 2009 guideline. Navarro 2008 was excluded from the relapse prevention review as participants were not randomised to maintenance therapy. In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies

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					should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. Kellner 2016 could not be included as it was published after the search cut-off date (June 2016).
British Association for Counselling and Psychotherapy	Full	733	General	The economic analysis is based on the assumption that all psychological therapies are delivered in an equal number of sessions (16 sessions) but the draft guideline acknowledges that there is evidence that counselling may be delivered in fewer sessions (8 sessions). Changing the number of sessions of individual psychological interventions delivered would have an impact	Thank you for your comment. The resource use estimates in the guideline economic modelling aimed to reflect reported resource use in the RCTs included in the NMA, also considering optimal delivery of psychological interventions in the UK. Based on these principles, the number of counselling sessions in deterministic analysis was set at 16, although the reported number of

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				on the economic model. At the moment in the deterministic analysis all interventions are assumed to have 16 sessions of 1 hour in length. In the probabilistic sensitivity analysis versions for both models the number of sessions for individual psychological interventions can be varied randomly between a maximum of 16 and a minimum of 5, (with an 80% of being between 10 and 16 and a 20% change of being between 5 and 9). This assumes that the number of sessions provided by the interventions can genuinely vary randomly across interventions in this way. However if there is more of a systematic difference in the number of sessions offered for counselling specifically then the cost effectiveness rankings shown in the modelling are likely misleading.	sessions in the RCTs that informed the counselling effect in the NMAs varied widely, ranging from 6 to up to 30. The committee noted that a number of RCTs that informed the counselling class reported a lower number of sessions, between 6-12, and agreed that these scenarios may comprise variations of clinical practice in some settings; therefore a deterministic sensitivity analysis was conducted to test the impact of assuming 8 sessions of counselling on the results. Probabilistic analysis did acknowledge that, in reality, the number of sessions of any individual psychological intervention may vary, but the committee did not think that the number of sessions offered for counselling would or should systematically differ from the number of sessions offered for other individual psychological interventions, hence a lower number of sessions for counselling relative to other individual psychological interventions was not reflected in probabilistic analysis. Please note that RCTs of other individual psychological therapies included in the NMA also reported a range of number of sessions, with some studies assessing interventions delivered in fewer than 16 sessions. For short-term psychodynamic therapy individual the number of sessions in the RCTs ranged from

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					8 to 30. For IPT, it ranged from 6 to 20. For behavioural therapies, from 8 to 24. Regarding the CT/CBT individual class that was considered in the final guideline, a separate intervention of CBT (under 15 sessions) contributed to the class effect [and it was the class effect and not the individual intervention one that informed the final economic analysis]; the reported number of sessions in the studies assessing CBT individual under 15 sessions ranged from 6-12. Therefore, the sensitivity analysis assuming fewer counselling sessions tends to favour counselling over other interventions. In the full guideline it has been acknowledged that lowering the number of counselling sessions to 8 improves its cost effectiveness (top of page 824 of the consultation guideline draft) and this was taken into account when making recommendations (page 246 "The committee also noted that according to the guideline economic analysis the cost effectiveness of counselling improved when this was effectively delivered by therapists paid at Band 6 or when this was delivered in 8 sessions, and agreed that these scenarios tested in sensitivity analysis may comprise variations of clinical practice in some

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					settings."). These considerations were also made by the committee when finalising recommendations following guideline consultation.
British Association for Counselling and Psychotherapy	Full	823	General	**Inconsistency in reported rankings following sensitivity analysis in less severe depression model** In Chapter 14 there is a discussion of the impacts on relative cost effectiveness of varying the bands of psychological workers. Page 823 states that: "W*hen all psychological interventions were assumed to be delivered by a band 5 PWP, the intervention cost of individual high-intensity psychological interventions was reduced and their relative cost effectiveness increased, resulting in changes in ranking. According to this scenario, the order of interventions from the most to the least cost-effective in deterministic analysis was as follows: mirtazapine, CBT group, physical exercise programme, CBT individual, IPT combined with citalopram, BA, citalopram, psychoeducational group programme, cCBT with support, cCBT without or with minimal support, physical exercise programme combined with sertraline, coping with Depression course (group), counselling, IPT,*	Thank you for your comment and for spotting this error in the reporting of the results. The results have been updated following stakeholder consultation and consideration of additional evidence and also checked for accuracy. Given that this was a complex economic analysis that included 2 distinct populations (with less and more severe depression), 15 treatments, one additional probabilistic analysis (after bias adjustment) and at least 12 further scenarios tested in deterministic sensitivity analysis, we are reassured by the fact that only one error ('slightly different order') in the reporting of the results of one of the scenarios was identified. This strengthens our confidence in the analysis.

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				short term PDPT combined with citalopram, short term PDPT, clinical management, CBT individual combined with citalopram" As a check on the analysis, an independent researcher commissioned to review the economic analysis for BACP used the version of the economic model without bias correction for less severe depression and applied these adjustments and found a slightly different order, e.g. with Exercise ranked 4th instead of 3rd and Counselling ranked 10th instead of 13th: The full order would be Mirtazapine, CBT group, IPT + citalopram, Exercise, BA, CBT individual, Citalopram, Psychoeducational group programme, cCBT with support, Counselling, Exercise + sertraline, IPT, Coping with Depression course (group), cCBT, Short term psychodynamic psychotherapy +citalopram, Short term psychodynamic psychotherapy, clinical management, CBT individual + citalopram. This inconsistency should be checked before model and guidance are published. Such errors do not foster confidence in the analysis.	
University of Nottingham	Full	837	5	There seems to be some confusion over the definition of counselling and how it is applied	Thank you for your comment. The committee reviewed the evidence on the effectiveness

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				to the context of the delivery of evidence based therapies. There is an evidenced based therapy for depression that has in the title the term 'counselling'. We understand this might be confusing for the guideline reviewers because in fact the evidenced based form of counselling for depression is actually 'person-centred experiential' counselling for depression. It should be noted that this approach does not follow the definition and description given for counselling within the guideline. Where counselling is defined it makes reference to a more surface level and eclectic way of conducting therapy. This is NOT the 'counselling for depression' that IAPT has approved of and therefore the definition of counselling for depression should be amended and clearly marked out as a distinct form of therapy. We notice there is no abbreviation present for CfD (Counselling for Depression) indicating that it does not have any presence in the revised guideline. CfD was developed by the BACP (who do appear in the abbreviations p. 835) in collaboration with IAPT and Skills for Health. The approach is an evidence based therapy that draws on the humanistic competency framework and a group of randomised control trials that test the effectiveness of Person-Centred Experiential	of counselling but did not think the evidence supported recommending one particular version of counselling over another. No specific RCT evidence on PCE-CfD was identified and so no recommendation for the use of PCE-CfD was made. However, the committee have recommended counselling based on a model that is specifically developed for depression, which would be in line with the specific training programme for counselling developed as part of IAPT. Thank you for informing us about the ongoing PRaCTICED trial. We will forward this information to the NICE surveillance team for consideration.

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				Therapies. CfD needs to be named explicitly in order to describe precisely what it is i.e.: Person-Centred Experiential Counselling for Depression (PCE-CfD). This is important and will ensure the approach is identified directly, in the same way as IPT and CBT. Presently there is an RCT being conducted into person-centred experiential-CfD (PCE-CfD) called PRaCTICED being led by researchers at the University of Sheffield and is funded by BACP. It is a non-inferiority trial comparing PCE-CfD and CBT. The results are expected to be reported in early 2018. In regards to the abbreviation of the approach, for the purposes of this feedback we will use the abbreviation for Person-Centred Experiential Therapies (PCET) and specifically for PCE-CfD when referring to the approach as it is refined for working with clients diagnosed with depression.	
British Association for Counselling and Psychotherapy	Full	239; 831; 832; 834	General	The economic analysis is largely based on the network meta-analysis which is in itself based on a number of assumptions which may be flawed. The problems in the NMA are detailed in the comments above. In addition the fact that flaws in the NMA have repercussions for interpretation of the economic analysis is acknowledged at various points in the Guideline draft:	Thank you for your comment. The NMAs undertaken to inform review questions on the treatment of new episodes of depression comprised a particularly complex piece of work. As with every piece of work, they were characterised by limitations which have been transparently reported in the guideline and taken into account when interpreting the results and making recommendations.

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				Results [from the Guideline economic analysis] need to be interpreted with caution due to the limited evidence base characterising some of the interventions assessed in the models and methodological limitations characterising some of the NMAs that were used to populate the economic analyses. (p239) *The quality and limitations of RCTs considered in the NMAs have unavoidably impacted on the quality of the economic model clinical input parameters. For example, economic results may be have been affected by reporting and publication bias. (p831)* *In addition, two of the NMAs that informed the economic analysis, remission in completers in less severe depression and discontinuation in more severe depression, were characterised by inconsistency between direct and indirect evidence, and therefore their results should be interpreted with caution. The limitations characterising the data included in the NMAs and the NMA outputs informing the economic analyses should be considered when*	The fact that a limited evidence base characterised some classes and interventions has been highlighted in the 'Evidence to recommendations' sections, under 'Quality of evidence'. To address the problem of the limited evidence base for some classes and interventions, following consideration of the available evidence and of stakeholder comments, all classes that have been tested on fewer than 50 people across RCTs in any of the main outcomes that informed the economic analysis [i.e. discontinuation (any reason), response in completers, remission in completers] have now been removed from the economic analysis so that the final economic analysis includes only classes of interventions for which more robust evidence base exists. For counselling, the evidence base for less severe depression in the final guideline was widened, following inclusion of new studies, reclassification of some interventions and small data corrections. We agree that the evidence base for counselling is limited for more severe depression, as no remission in completers data are available. Based on the lack of data on remission in completers, counselling has been removed from the final economic analysis for people with more severe depression.

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				interpreting the cost effectiveness results. (p832) For counselling in particular the significant lack of data on which the analysis is based is highly problematic. For counselling, the data on response in completers for less severe depression comprised only N=73; for remission in completers N=59; and for more severe depression, the data on response in completers was based on N=101. And no remission in completers data was available for counselling, which borrowed data from IPT (N=62) (p832). In fact the chapter which summarises the economic modelling of cost effectiveness (chapter 14) ends with the statement: "Results need to be interpreted with caution due to the limited evidence base characterising some of the interventions assessed in the models and methodological limitations characterising some of the NMAs that were used to populate the economic analyses" (p834).	The fact that the quality and limitations of RCTs considered in the NMAs and the NMAs themselves, including reporting and publication bias, have impacted on the quality of the economic model clinical input parameters is true of any economic model informed by NMA or pairwise meta-analysis. There is no economic model without limitations; any economic modelling results should be interpreted following consideration of underlying limitations and this is what the committee did. In the updated NMAs, inconsistency was observed in SMD and response in those randomised, but in none of the NMAs that informed the economic analysis. Therefore, the updated economic analyses are not characterised by this limitation anymore. In any case, the inconsistency identified in these networks, which informed the clinical analysis, was taken into account by the committee when interpreting the results and forming the final recommendations.
Society for Psychotherapy Research (SPR) UK Chapter	Full & Short	General	General	**Evidence base** There is a systemic problem with the evidence base used in formulating the guidelines. These rely heavily on	Thank you for your comment. When making recommendations we used both clinical and cost-effectiveness data to assess the relative benefits of the relevant interventions. In doing so we were trying to determine the

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				Randomised Controlled Trials which predominantly feature Cognitive Behavioural Therapy. This is not to decry the efficacy of Cognitive Behavioural Therapy but to highlight its special place in the research spectrum. It is never going to be possible for all the psychotherapies to be tested in Randomised Controlled Trials. Or for the weight of efficacy evidence to equal that accumulated by Cognitive Behavioural Therapy through its special position in the clinical psychology practitioner-researcher model of training. Brand-based therapies tend to over-emphasise difference in content whereas therapeutic factors are common to all effective therapies (Lambert and Ogles 2004) and tend not to encompass the variable content of integrative and multimodal therapies. Furthermore, Randomised Controlled Trials by design minimise therapist effects which are important elements in improvement or deterioration. Therapy interventions are not particularly disorder specific, rather they contain actions of general application and benefit for psychological distress with varying degrees of utility in specific disorders. In summary, it needs to be borne in mind that absence of evidence is not evidence of ineffectiveness (Roth and Fonagy, 2004).	relative efficacy of different interventions compared against each other. RCT data is the best type of evidence to achieve this and hence our evidence reviews have focused on this data. When making recommendations, the committee interpret this evidence in light of their knowledge of the clinical context so that the 'reality' for people experiencing depression is taken into consideration and recommendations can be made that are relevant to the populations that clinicians typically encounter. The committee's discussions on this are documented in the evidence to recommendations sections of the full guideline. We agree that absence of evidence is not absence of effectiveness. However in developing the guideline we can only make recommendations for those interventions where there is evidence of their effectiveness. Barkham 2002, Lambert 2004, Roth 2004 and Wampold 2017 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				Complex meta-analysis may yield spurious results. What is needed is a different approach to level the playing field and avoid burying equally effective alternative therapies (Wampold et al., 2017). Given the nature of psychological therapies much more weight needs to be given to practice-based evidence (Barkham et al., 2002). At the end of the day, clinical effectiveness is what counts. If clinical practice delivers equivalence of outcome to the bench-mark therapies, a wider range of therapies should be supported in the guidelines. For practice-based evidence to work, there needs to be a range of agreed outcome measures including CORE-OM which are routinely collected in clinical practice. Mechanisms of change across therapies should be elucidated through qualitative studies. If the mechanisms of change are similar to those in the bench-mark therapies, this should be considered as another source of equivalence-evidence. **References:** Barkham, M., E. Guthrie, G. E. Hardy, F. Margison and D. A. Shapiro (2002). Evidence-based practice in psychodynamic-interpersonal therapy: A conversational model. London, Sage. Lambert, M. J. and B. M. Ogles (2004). The efficacy and effectiveness of psychotherapy.	

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				Handbook of Psychotherapy and Behavior Change. M. Lambert. New York, Wiley: 139-193. Roth, A. and P. Fonagy (2004). What works for whom? A critical review of psychotherapy research. New York, Guilford Publications. Wampold, B. E., C. Flueckiger, A. C. Del Re, N. E. Yulish, N. D. Frost, B. T. Pace, S. B. Goldberg, S. D. Miller, T. P. Baardseth, K. M. Laska and M. J. Hilsenroth (2017). "In pursuit of truth: A critical examination of meta-analyses of cognitive behavior therapy." Psychotherapy Research, 27(1), 4-32.	
Society for Psychotherapy Research (SPR) UK Chapter	Full & Short	General	General	**Call for a recall for consultation** As the above comments demonstrate, we have raised serious concerns about various important aspects of the draft guideline we hope a revision process will address. We would like to request and recommend that any revisions of the document should go out for further consultation.	Thank you for your comment. Section 10.3 of Developing NICE guidelines: the manual clarifies when a second consultation may be needed. This states that "In exceptional circumstances, NICE may consider the need for a further 4-week stakeholder consultation after the first consultation. This additional consultation may be needed if either: • information or data that would significantly alter the guideline were omitted from the first draft, or • evidence was misinterpreted in the first draft and the amended interpretation significantly alters the draft recommendations. NICE staff with responsibility for guideline quality assurance make the final decision on

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					whether to hold a second consultation." NICE judged that these criteria were not met, therefore no second consultation was conducted.
The British Psychological Society	Full / Short	General		The Society is concerned about the overall approach of the document and how the content of the draft guidance is worded entirely from that perspective that depression is to be identified and treated. The Society believes that an alternative, psychological, perspective should be adopted so that these guidelines would be focus on supporting a person who is experiencing depression, rather than just identifying and treating the illness. This does not mean challenging the evidence, rather refocussing the recommendations. The focus should not be identifying and treating depression but recognising and responding to the needs of the person. The Society believes that there is a broader issue which is not specific only to the needs of people with intellectual and learning disabilities, in that it is based on the diagnosis of depression which diagnosis itself has questionable reliability and validity. Inter-rater reliability in the 2015 field trials for DSM-V	Thank you for your comment. The scope of this guideline is to make recommendations on the treatment and management of depression in adults. Throughout the guideline there is a recognition of the limits of the current nosology of depression and an acknowledgement that the problems of depression need to be addressed in a wider personal and social context. However, the committee do not think this would be resolved simply by replacing diagnosis with formulation. In good medical practice a diagnosis can be an important part of the formulation of a persons' problems. Such an approach, which is consistent with the approach set out in this guideline, strongly stresses recognising and responding to the needs of a person. Therefore we have not changed the focus of the recommendations to be about formulation. Recovery approaches, personal narratives, psychological formulation and the importance of the social context are not referred to explicitly in the recommendations but they form part of assessment. As

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				showed kappa scores of 0.32 for Major Depressive Disorder, 0.06 for Mixed Anxiety Depression Disorder, 0.40 for Bipolar Disorder. There is little evidence to demonstrate that depression actually occurs in isolation of anxiety and a range of trauma-related conditions. There is evidence that the poor reliability seriously compromises research into 'antidepressant' medication (Lieblich et al, 2015). Therefore, we feel strongly that the guidance to this should take account of the Society's Division of Clinical Psychology guidance on use of language in relation to functional psychiatric diagnoses. (BPS Division of Clinical Psychology, 2011) See below. **Formulation** The Society recommends a strong reference to prioritising formulation over psychiatric functional diagnoses. The BPS, the Royal College of Psychiatrists (in their general guidance to practitioners) and Skills for Health all see formulation as a core skill for mental health professionals and core to service delivery (BPS Division of Clinical Psychology, 2011; Royal College of Psychiatrists, 2017). The Society recommends that 100% of care provided	specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to this section. The committee agreed that RCT evidence adequately addressed the question set out in the review protocols. The committee noted the reference to Pybis et al but were uncertain if the populations treated by counselling and CBT were in fact similar. A review of the IAPT national data sets (a large component of the services covered by the audit) suggest that this is not the case as significantly more people in receipt of CBT were stepped up to a more intensive intervention (i.e. having failed an initial low intensity intervention) prior to CBT whereas many service users seen by counsellors were not stepped up to a more intensive intervention. This indicates that the populations were likely to be different and it is not possible to draw direct comparisons between the 2 modalities.

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				under the auspices of NICE should follow a formulation. As Skills for Health have made clear, this formulation does not have to overwhelm the training and resources of junior or non-specialist staff (such as PWP workers or GPs). But all care should follow a formulation. Formulation should form the basis for a coordinated and team-based approach at all times, not just for complex or difficult cases (Skills for Health, 2014) Recovery approaches, personal narratives and psychological formulation are not referred to in its detailed form in the guidelines – these are important ways that people address mental health issues in general and depression in particular. Promoting formulation as a process of sharing understanding can help people consider the possible origins of their distress and options that may be open to them rather than medicalise their distress. For a good review, see The BPS Good Practice guidelines on the use of psychological formulation. Leicester: British Psychological Society. (British Psychological Society, 2011) The Society recommends that more emphasis is required on importance of social	

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				context –there is a great deal of evidence collected demonstrating that social context is relevant to why people become depressed. (Meltzer et al, 2010). It is also significant in terms of support and interventions needed for people when they are depressed (Castonguay & Beutler, 2005). The importance of healthy communities, workplaces and schools and the need for investment with a view to supporting communities to become and remain psychologically healthy should also be given more emphasis. The Society believes that the Practice-Based Evidence from the second round of the National Audit of Psychological Therapies (NAPT) in addition to the evidence from randomised controlled trials (RCTs) and Meta-Analyses of RCTs should be considered. The Society is concerned that the current version of the draft NICE Guidelines for Depression appears to neglect the Practiced-Based Evidence into the efficacy of counselling and CBT. Pybis and her colleagues (2017) looked at the outcomes of 33,243-patients across 103 Improving Access to Psychological Therapy (IAPT) Services (Pybis, Saxon, Hill & Barkham, 2017), who	

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				were treated for depression with either CBT or counselling. They concluded that the outcomes of counselling and CBT in the treatment of depression were comparable. Their data also suggested that counselling is more efficient than CBT for patients who required less than 8-sessions of therapy.	
Lundbeck Limited	Full and Short	General	General	**Lundbeck ("we) would like to make a number of general comments which we refer to below at the point(s) at which they appear in the short and/or full guidelines**: 1. **There is no mention of Technology Appraisal (TA) 367 (NICE, 2015), a current and extant piece of TA guidance, which is not yet due for review and which makes evidence-based recommendations about the use of vortioxetine which are highly relevant to this guideline update. The final scope for the guideline identified this TA as being closely related to the guideline and yet the TA367 (NICE, 2015) recommendations are not included in either the short or full guidelines.** • We are at a loss to understand why the Guideline Committee (GC) did not consider NICE TA367 a relevant piece of	Thank you for your comments. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on

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				evidence for the purpose of this guideline, particularly in view of the final scope for this guideline. • The final scope for this guideline (Appendix A) clearly states that the vortioxetine technology appraisal is "closely related to this guideline" and yet, despite being recommended, there is no mention of vortioxetine in the proposed care pathway (pharmacological treatment) at all. • There is no reference to TA367 or to vortioxetine in the short guideline at all, despite it being a highly relevant and current piece of TA guidance, which is directly relevant to the patient populations considered in the guideline. • There are only three mentions of vortioxetine in the draft full guideline and none in the guideline recommendations. • There is no reference to vortioxetine in any of the guideline appendices, with the exception of Appendix J5, which lists a vortioxetine Randomised Controlled Trial (RCT) as an excluded study, on the basis of it not being an intervention of	the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. The wording in the guideline has also been revised to remove reference to vortioxetine being a 'third-line' agent. We have reviewed the wording of the recommendations on collaborative care but do not think that anything in the wording implies that this will have to be done in secondary care. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care

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				interest. **2. Vortioxetine has inexplicably been excluded as an intervention of interest for the decision problem for all of the review questions considered by the Guideline Committee.** • Whilst we understand why vortioxetine was not included as an intervention of interest for chapter 7 where the decision problem was limited to interventions most likely to be used as first-line treatment, we can find no justification or explanation for why the GC did not consider vortioxetine a relevant intervention for further line treatment of depression [Chapter 8] or for chronic depression [Chapter 9]. These are the exact populations and treatment settings where NICE has recommended vortioxetine as a treatment option. • Vortioxetine is licensed for the treatment of major depressive episode (MDE) in adults, without restriction as to a particular line of therapy, and is the only antidepressant (AD) which has been the subject of a rigorous	services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				Single Technology Appraisal (STA) by NICE. Not only has vortioxetine been excluded from the decision problems completely, the GC has included interventions that are not even licensed for the treatment of MDE or depression. **3. As a consequence of being excluded from the decision problem in each case, vortioxetine was not included as a search term for the systematic literature review.** • Because of this flawed search strategy, the GC has omitted to consider relevant RCT and economic evidence relating to the use of vortioxetine as a clinically- and cost-effective treatment option in specific groups of adults with depression; for example, people who have failed to have an adequate response to initial treatments. **4. As a result of points 1-3 above, vortioxetine has been omitted from the proposed care pathway for adults with depression entirely, despite it being the only pharmacological treatment licensed for the treatment of**	

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				depression that has (current, extant, positive) NICE technology appraisal guidance. At the same time, unlicensed treatments (such as anti-psychotics) without the benefit of a NICE appraisal have been recommended for off-label use based on clinical and economic evidence, which the GC concluded was mainly of low or very low quality. • Not only will this be extremely confusing for mental health professionals and commissioners (who have been obliged to implement NICE TA367 and adhere to the funding direction for the last 18 months), but it effectively renders TA367 obsolete a full 15 months before it falls due for review. • This also gives rise to a somewhat counter-intuitive result, whereby unlicensed, off-label, drugs that are not approved by NICE are preferred over a licensed treatment which is recommended by NICE. **5. By not acknowledging in the guideline recommendations that TA367 (NICE, 2015) is a current piece of guidance,**	

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				which clinicians should take into account when making treatment decisions, and by omitting to include vortioxetine as an intervention of interest at any point in the treatment pathway, the GC leaves the reader with the clear impression that vortioxetine is no longer a relevant or appropriate treatment option for adult patients with depression at any point in the treatment pathway. • We believe this should be accurately reflected in the pharmacological treatment pathway recommendations in the updated NICE depression guideline to ensure consistency between the guideline recommendations and the Technology Appraisal guidance (TAG), and to reduce potential confusion for prescribers and healthcare organisations who are following the implementation mandate of this TA. **In addition:** **6. On the three occasions where vortioxetine is mentioned in the full guideline (on pages 35, 190 and 207**	

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				only out of a total of 851 pages), it is erroneously described as a third-line agent. This is not correct. • Vortioxetine is licensed by the European Medicines Agency for the treatment of MDE in adults, with no restriction as to line of therapy. • Following a STA in 2015, vortioxetine is recommended by NICE as a "clinically and cost-effective treatment option for treating MDE in adults whose condition has responded inadequately to 2 antidepressants within the current episode" (NICE, 2015). **7. There appears an important change of direction from that taken in the predecessor guideline, CG90, shifting the prescribing decision for all but first-line pharmacological options into secondary and specialist care, which we do not believe will be able to cope with the increased number of referrals.** • This runs counter to the direction of many Sustainability and Transformation Partnership (STP) plans, Mental Health Trust (MHT) plans, and Clinical Commissioning	

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				Group (CCG) commissioning strategy plans, where the focus is to deliver care in community settings closer to patients' homes, and to avoid unnecessary referrals and admissions to specialist and hospital settings. • We are particularly concerned that the collaborative care model put forward in this guideline update marginalises the role primary care plays in identifying and managing depression and promotes an over-reliance on specialist services. This risks over-demand for already stretched services, while also increasing the stigma associated with depression by referring people to specialist settings who may be more appropriately managed closer to home in primary care and community settings. 8. **So far as pharmacological interventions are concerned, the draft guideline takes a retrograde step from CG90, choosing to recommend older ADs with a high side-effect burden (such as mirtazapine, tricyclic ADs or moclobemide), as well as off-label**	

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				treatments, rather than newer generation ADs with a lower side-effect burden. • The GC notes that recommending off-label usage should be the exception rather than the rule, and then only where clearly supported by the evidence. • CG90 and the current NICE Pathway stress the importance of using agents with a lower side-effect burden, wherever possible. • However, it is apparent that a number of the recommendations for interventions in the updated draft guideline are based on low, or very low quality clinical and economic evidence. We are concerned that current recommendations and care pathways are being overridden by such poor quality evidence. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes (November 2015).	
Lundbeck Limited	Full and short	General	General	The lack of any substantive mention of vortioxetine (especially in Chapter 8 of the full guideline where recommendations for further line treatment are included) is also likely to	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). We

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				lead to confusion as health professionals and commissioners seek to navigate between the differences between Clinical Guidelines (best practice recommendations) and TA guidance (mandatory implementation). Without clear referencing and/or inclusion of TA367 (NICE, 2015), clinicians, healthcare organisations, commissioners and patients may be left uncertain as to whether the new guideline recommendations supersede, replace, include, or run parallel to the extant TA recommendations for vortioxetine. Clarity on this should be built into the final version of the updated guideline. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015.	have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Lundbeck Limited	Full and Short	General	General	Although Lundbeck is fully cognisant of the process and timelines for developing draft NICE clinical guidelines, Lundbeck feels that a longer consultation period should have been allowed for on this occasion, particularly as the 8-week consultation window fell nearly completely within the main UK summer vacation period. The appropriate management of 'Depression in Adults' is a hugely important topic, with hundreds of registered stakeholders. The draft guideline is sizable, comprising 851 pages for the full	Thank you for your comment. The standard consultation period for a draft guideline is 6 weeks. In recognition of the complexity of this guideline and the consultation period falling over the summer it was decided to increase the consultation period by 2 weeks to a total of 8 weeks, to allow stakeholders more time to respond to the consultation.

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				draft, multiple appendices and associated Excel models. Many registered NHS and other consultee organisations may be low on staff during this period. This may mean they miss the window, cannot fully review all the documentation in this time, or are not able seek the feedback of internal stakeholders who may be away in this vacation period.	
The Psychotherapy Foundation	Full and short	General	General	The document, although complex and detailed, lacks sophistication and accuracy in translating research evidence into usable practice guidelines. Methodology and structure is fragmented, and this is reflected in a lack of integration within the documents as a whole. It has the appearance of being underworked. It is possible that these guidelines have grown organically through several revisions and it is time for a complete rewriting.	Thank you for your comment. We hope that revisions made on the basis of comments received from stakeholders will improve the guideline.
The Psychotherapy Foundation	Full and short	General	General	In some ways this might be considered to be a useful discussion or background paper, with reservations. However it is not of a standard to be placed as a NICE Guideline.	Thank you for your comment. Both the full and short versions of the guideline were developed following an accredited process and have been subject to extensive quality assurance by NICE before they were issued for consultation. As such we think that they meet the required standards.
The Psychotherapy Foundation	Full and short	General	General	The production of the document is of a poor standard and quality with spelling and grammatical errors. It is poorly referenced in general, and sources need to be properly cited.	Thank you for your comment. Errors that have been identified during and after consultation have been corrected. Both the full and short versions of the guideline will be subject to extensive quality assurance by

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					NICE before final publication to meet the required standards.
The Psychotherapy Foundation	Full and short	General	General	A section on 'Recognition and assessment' (Section 6) fails to utilise a proper approach to differential diagnosis, and although mention is given to 'Depression with comorbidities' (Section 10), failing to recognise that dominant, evidence based models of psychological treatment require concurrent management of anxiety through treatment of the depressive disorder, and perhaps a more important diagnosis of comorbid depression and personality disorder is not properly addressed. Similarly sections on remission, recovery, treatment failure and treatment success rates are not properly described or differentiated. Treatment failure and data is obscured within remission. A failure to properly integrate evidence about assessment and diagnostics, including comorbidities, with data about remission, recovery, treatment failure and treatment success is a major weakness of the draft guidelines.	Thank you for your comment.The introduction to this section is not intended to be a review of the full range of comorbidities but to provide a context in which the research that follows can be placed. The integration of evidence about assessment and diagnostics to which you refer is a central task for the committee, who draw on their expertise when developing the recommendations. Their views on this are summarised in the 'evidence to recommendations' sections in the full guideline.
The Psychotherapy Foundation	Full and short	General	General	There are topics in this draft guideline that are asserted with authority but with inadequate review and analysis, or referenced evidence, eg chronicity. Other research evidence referenced in this document, and relied on in detail, in our view	Thank you for your comment. All studies included in the guideline were assessed for risk of bias and all analyses examined for heterogeneity and downgraded where this exists.

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				is overvalued and given greater hierarchical status than might be considered appropriate. There are few properly replicated studies, and few which are replicable given that the specification of patients, therapists, therapies and study methods is generally not of a high standard and often unreliable. These weakness are workable in reviewing individual studies for progression of understanding, but contribute to heterogeneity which is highly corrosive of reliable results in meta-analysis, and thoroughly undermining in more complex methods such as network meta-analysis.	
The Psychotherapy Foundation	Full and short	General	General	Despite a growing disquiet amongst knowledgeable users, researchers and senior clinicians over recent years about a use of the cover term 'cognitive behavioural therapy (CBT)' the documents present this uncritically throughout. It seems to us that there is little doubt that, within the domain announced by this cover term, there are many specific cognitive and behavioural treatments. Some of these specific treatments have an evidence base, usually restricted by setting and/or diagnosis, and some have little or no evidence base. As is discernible from the research referenced in the draft guidelines only a very small number of treatment	Thank you for your comment. We consider that cognitive behavioural therapy is a widely used term that will be understood by readers of the guideline Therefore we have kept this term in the guideline.

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				approaches within the domain 'cognitive behavioural therapy' are evidence based for the treatment of depression. The continued use of the cover term 'cognitive behavioural therapy' is misleading and obscures treatment development and research direction. We suggest that it is misleading for patients and users, clinicians, educators, researchers, providers, commissioners, and the public as a whole.	
The Psychotherapy Foundation	Full and short	General	General	In simplifying these draft guidelines, and improving their utility, it would be better to structure this as declarative of the limitations of our current knowledge and ability to intervene in depressive disorders: ▪ To declare there is one first line psychological treatment with adequate evidence for use. ▪ To be transparent that treatment failure is high. ▪ To acknowledge that second line treatments have yet to be properly researched and identified. ▪ That service organisation in providers is more than likely a large contributing factor to treatment success.	Thank you for your comment. Treatments for depression have limitations, as is the case in many other areas of medicine, but we do not think it would not be accurate to describe these as high, especially when there is significant natural remission (particularly in less severe cases of depression). We expect that a better understanding of the mechanisms underlying depressive problems is more likely to improve outcomes than re-structuring service providers.

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The Psychotherapy Foundation	Full and short	General	General	The 'Improving Access to Psychological Therapies' (IAPT) programme has been an important development in the treatment of depression. Some providers deliver good results within expected parameters, but many do not. Providers are often hampered by: ▪ Poor assessment and diagnostic procedures which fail to properly identify comorbidities, particularly involving personality disorder, which impede therapeutic progress and contribute to treatment failure – diagnosis. ▪ Poor processes for getting the right therapist, expert in the right therapy, in front the right patient with an amenable identified disorder – training and matching. ▪ Proper outcome monitoring, with follow-up rather than just last session – feedback and research The solutions to these issues are obscured in the current draft guidance. The document would be better structured:	Thank you for your comment. Making recommendations about the structure of the IAPT programme is not within the remit of this guideline. We did not think your suggested alternative structure was appropriate as the last 3 bullet points in our view would not be understood within the wider NHS community.

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				▪ Assessment and diagnosis ▪ First line treatment ▪ Inhibitors to treatment – comorbidity, complexity and severity ▪ Limitations to treatment – treatment resistance, treatment failure and chronicity ▪ Openness to second line treatments in structure evaluation, trails and research	
The Psychotherapy Foundation	Full and short	General	General	There are serious concerns about various important aspects of the draft guidelines. We propose a complete revision and rewriting process to address these concerns and to derive a suitable document for its time. We recommend that revisions and rewriting of the guidelines go out for further consultation.	Thank you for your comment. Section 10.3 of Developing NICE guidelines: the manual clarifies when a second consultation may be needed. This states that "In exceptional circumstances, NICE may consider the need for a further 4-week stakeholder consultation after the first consultation. This additional consultation may be needed if either: • information or data that would significantly alter the guideline were omitted from the first draft, or • evidence was misinterpreted in the first draft and the amended interpretation significantly alters the draft recommendations. NICE staff with responsibility for guideline quality assurance make the final decision on whether to hold a second consultation." NICE judged that these criteria were not met,

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					therefore no second consultation was conducted.
Luiz Dratcu, Maudsley Hospital	Full GL			The NICE guidance on the treatment and management of depression in adults is to be welcomed, as is its comprehensive discussion of psychosocial treatments, although it would benefit from further discussion about the role, choice and timing of this long list of psychotherapies. In marked contrast, the detail given on pharmacological and somatic treatments is scant. Nor do the guidelines provide meaningful guidance for clinicians regarding medications - they merely mention two SSRIs (sertraline and citalopram) and mirtazapine. Later, in the section on chronic depression, the document also mentions tricyclic antidepressants, moclobemide and amisulpiride. The evidence-base for these recommendations is unfamiliar to many of us, omits major research in the field and requires further scrutiny.	Thank you for your comment. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable.
Luiz Dratcu, Maudsley Hospital	Full GL			In terms of service provision, the recommendation to refer to a specialist for augmentation after the failure of one SSRI will overwhelm secondary services.	Thank you for your comment. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant

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					recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Luiz Dratcu, Maudsley Hospital	Full GL			Treating depression properly and early is vital to minimise disability and suicide. Medication is a key part of the treatment of depression for many people. To fail to treat depression adequately also has an economic cost. These guidelines, if followed in clinical practice, are likely to leave people suffering needlessly from inadequately treated depression; raise suicide rates; put unnecessary stress on secondary care services; increase sickness leave; and add to the costs of providing services.	Thank you for your comment. The purpose of the guideline is to provide prompt and effective treatment for people with depression, based on evidence of clinical and cost effectiveness. We have made recommendations on this basis.
Janssen	Full, short and appendices	General	General	We thank NICE for the opportunity to comment on the update of NICE Clinical Guideline 90: Depression in adults: recognition and management. We very much welcome NICE taking this opportunity to update the current clinical guideline with the latest evidence published in the disease area.	Thank you for your comment. We clarify in the recommendations that commissioners and providers of mental health services should consider using stepped care models for organising the delivery of care and treatment for people with depression. We have also made additional recommendations

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				However, we have several concerns regarding the update of both the short and full clinical guidelines, which we believe need to be addressed to ensure continued clarity of the guideline and to ensure the correct recommendations are made regarding the relative effectiveness of the interventions. We note the draft clinical guideline out for consultation has been significantly revised from the existing version. We do not believe that the new evidence identified in the update warrants a complete restructure of the clinical guideline. We are concerned that that the new recommendations could lead to confusion amongst HCPs and commissioners, which may impact on the quality of care that patients receive. We would strongly suggest that current structure and framework based on the stepped care model should be retained to ensure continuity of care and clarity of recommendations throughout the guideline. Furthermore, we have a couple of concerns regarding the robustness of the network meta-analyses (NMAs) that have been conducted to inform the relative effectiveness of interventions. We would urge caution in interpreting the results of the NMAs by the guideline committee (GC). Overall, we do not	to promote better integration between primary care and secondary care. The current structure of the guideline is such that lower intensity interventions are provided prior to more intensive interventions. We think this structure is logical and easy to follow and is not likely to lead to limited or restricted access to interventions. We have made a number of changes to the recommendations about first line treatment of more and less severe depression, in particular moving group CBT from the initial treatment for less severe depression to a position in the sequence that is more in line with a stepped care model. Regarding your concerns about the robustness and methodological challenges of the NMA, we have responded in detail where you raise specific concerns. Please be reassured that the committee have not used only the NMAs as the basis for making their recommendations. They have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues.

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				believe the NMAs should currently be used as the basis for making strong recommendations regarding the relative effectiveness of interventions, but only to inform a range of interventions to be recommended. In summary, we suggest that the following key points should be considered further by the GC: 1. Reconsider the need to change the existing guideline framework and structure based on the 'stepped care model.' The current model aside from its familiarity, provides greater clarity regarding how patients can move between effective interventions. The removal of the stepped care model could lead to confusion between HCPs and commissioners with regards to the most appropriate time to use interventions within the pathway. This could lead to limited or restricted access to effective interventions for patients. Some of the previous guideline recommendations for interventions have been split and appear throughout the document now. This has led to the guideline becoming disjointed in places and, in	We have considered conducting a NMA of interventions for people who have failed previous treatment. However, the study population is highly heterogeneous, comprising people who have not responded to specific pharmacological, psychological or combined interventions and therefore it was not appropriate to undertake a NMA. For example, it would not be appropriate to include in the same NMA people who have not responded to a SSRI (but may be treatment-naive to other drugs and psychological therapies) and people who have not responded to CBT (who may be treatment-naive to other psychological interventions and other drugs). The committee agreed it was appropriate to draw on the evidence for first line treatment of more severe depression when making recommendations for further line treatment. This was because, based on the expert knowledge and experience of the committee, if a person hadn't responded to treatment they would need a treatment that had been identified as being effective for the majority of people with more severe depression. This detail has been added to the 'evidence to recommendations' section.

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				our view, could lead to misinterpretation and consequent patient harm. 2. Address the methodological challenges and consequent uncertainty in the current NMAs to improve the robustness of the guideline recommendations and the relative effectiveness of the interventions. In addition, we are concerned that NMA evidence from a first line treatment population has been used to informed the relative effectiveness of later lines of therapies. We would strongly suggest that an additional NMA is conducted in the population that has had an inadequate response to treatment to ensure the guideline recommendations made in that population reflect the available relative effectiveness evidence. Overall, we urge the GC to address these concerns to enhance the clarity of the guideline and to ensure that the recommendations are implemented in an effective way by commissioners and healthcare professionals (HCPs). We are concerned that that the new recommendations could lead to confusion	

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				amongst HCPs and commissioners, which may impact on the quality of care that patients receive. Furthermore, we are concerned that the NMAs and recommendations based on them may impact the interventions patients receive, which may not be reflective of the effectiveness of those interventions in clinical practice. In addition, we have several more minor comments that we have outlined below regarding the content of the guideline.	
CHESS (Centre for Humanities Engaging Science and Society), Durham University	Full/Appendix J5	General P202 line 4 onwards		There are serious problems with the Draft Revision's method of dividing trial populations by categorising baseline severity simply as more severe or less severe. We are very concerned that it leads to misleading impressions and conclusions/recommendations in which potentially valuable treatment effects are ignored: **We suggest:** • The Revision identify and use categories and methods of analysis which are more appropriate as ways of determining the value of treatments than currently. • Use partial remission rates as well as full remission rates particularly where	Thank you for your comment. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations

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				• baseline severity is 'very severe' and/or where the prognosis is poor, for example, because of the complexity or chronicity/treatment resistance of the depressive disorder. • Specifically, in relation to, Fonagy et al (2015) which the Draft currently reports as 'Less severe' in J5 for baseline severity, when this trial employed the 17 item HAMD on which, as a matter of fact, the mean baseline score of the trial sample is in the 'severe' category. Please correct or alternatively demonstrate the greater reliability and validity of Draft Revision's algorithm over the 17-item HAMD's thresholds. **Justifications:** Summary: The Draft Revision uses a single reductive proxy estimate of severity, which depends on the unevidenced assumption that a valid, reliable equivalence algorithm combining different depression rating scales is established. Most of the component measures have their own range of severity categories, validated in the literature. The Draft Revision simply seems to have ignored these. The method developed for the Draft Revision does not seem to reflect their validated categories and therefore its reliability framing for the	of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee

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				analyses of treatments for new episode depression is questionable. Furthermore, the Draft is inconsistent even in its use of this categorisation. On this insecure basis: • Trials are then categorised in the Draft Revision by using mean patient scores rather than ranges of individual ones. As a result, trials can be assigned to "less severe" by being, for example, ≤ 1 point below the chosen threshold mean, while another is assigned to "more severe" merely by being ≥ 1 point above it. Several trials have essentially identical patient populations, with large overlaps of the baseline scores of individual patients, yet are subjected to different unequal standards of comparison. Furthermore, individual patient's symptom scores fluctuate greatly over time, yet the Draft Revision neglects follow-up and follow-along data. The single baseline severity score employed does not have a good correlation with the other important areas of disability that exist in depression. Yet after duly acknowledging their importance in preambles, the Draft Revision proceeds effectively to disregard	also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means

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				measures of social functioning and quality of life as part of a necessary basis for recommendations. • The Draft Revision does not always use its own measure of baseline severity consistently: in the "Further-line treatment" section it adopts instead another also dubious distinction, for example, that it draws between TRD and chronic depression. • For patient populations in whom baseline severity is 'very severe', the Revision needs to take more serious account of the implications of the evidence of the extreme difficulty for some users of achieving a target of 'full remission' (e.g. The STAR-D study). In the interests of these patients, it is essential that the Revision takes *partial remission rates* into account not just full ones. • Specifically, Fonagy et al (2015) is currently recorded in J5 as 'Less severe' for baseline severity. This trial used the 17 item HAMD. According to the latter's categories, the mean baseline score actually comes in the	of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression. It is not clear how partial remission rates could be used as an outcome for complexity or chronicity. We have used remission, response and symptom severity at end point. This latter outcome would take into account the impact of the intervention including those who had not remitted and was also a more commonly reported measure than partial remission, the definition of which may vary across studies. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2

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				'severe' band. We ask the GDG first to acknowledge this discrepancy and second to demonstrate exactly how the Revision's methodology is more valid and reliable than that of the source measure, or failing this to correct this misleading classification of the severity of this Study's patient population. • Of course, baseline severity must be considered when judging trial outcomes. However, this can be achieved without resorting to crude dichotomising cut-offs. In this context, please note that given the wide variation in outcomes and in baseline severity, the SMD alone, as listed in J5, is inadequate from several angles, including statistically. A method for determining Reliable and Clinically Significant Change (Jacobsen & Truaux, 1991) offers a better assessment of how changes on different measures considering baseline severity, might be interpreted. For example, IAPT data records an overall 'recovery' rate of 46.3% (HSCIC, 2016). Whereas, analysis of 'reliable improvement' (which considers baseline and end-	separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were

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				point severity, rather than only whether the case met 'clinical caseness' at either point) indicates a figure of 62.2%. Using 'reliable improvement' in the trials included in the guideline meta-analyses would offer a fuller picture; particularly important when trials have studied the treatment of markedly severe populations for whom currently there are few moderately well-evidenced treatments available. Failing to report both partial remission or the reliable improvement rates assessed in such trials ignores the potential of the benefits that have been found for more severe and complex populations than studied generally. Again, Fonagy et al (2015) is an important case in point. Health and Social Care Information Centre (2016) Psychological Therapies: Annual Report on the use of IAPT services, England, 2015-16.; Jacobson, N. S., & Truax, P. (1991). Clinical significance: A statistical approach to defining meaningful change in psychotherapy research. *Journal of Consulting and Clinical Psychology,* 59, 12-19. Trivedi, M.H; Rush, AJ; Wisniewski, SR, et al:	used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine which scale would be used to determine severity if 2 or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. The committee took into account not only the cut-offs suggested by developers but also data on the validity of the suggested cut-offs. For example, Fournier et al, 2010 JAMA. 6;303(1):47-53; which in a patient level meta-analysis identified 23 on the Hamilton DRS as the point at which the drugs were clinically significantly better than placebo. The committee took the view that such data provided better validation of the cut-offs developed by scale developers which were often not based on empirical data but on the expert opinion of scale developers. Another example which the

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				Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. American Journal of Psychiatry 163:28–40, 2006	committee took into account in developing their own cut offs is the PHQ-9 which classifies mild depression as a score between 5 and 9 when the PHQ-9 cut off for caseness in is a score of 10 or more. Unfortunately, the committee were not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small

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					difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of

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					severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the outputs of the NMA. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee

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					considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive symptoms'. Given the available data it was not possible to calculate Reliable and Clinically Significant Change. This would have required access to the original trial data. Also as we mention above the studies would need

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					to use the same definition of partial remission. Health and Social Care Information Centre 2016 and Jacobson 1991 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs). Trivedi 2006 could not be included as data were only reported for the group receiving citalopram.
Camden & Islington NHS Foundation Trust	general	general	general	As part of the development and continued provision with IAPT services there has been a hugely successful, incredibly well run and highly efficient programme of IPT training and supervision for IPT trainees, practitioner and supervisors across the country. This has involved a huge investment and has lead to a large increase in the number of well trained and highly skilled IPT practitioners within IAPT services carrying out very effective treatment for depression for patients presenting with moderate to severe depression. The success of this work is evidenced in the 2015-2016 IAPT Outcome date which shows IPT to have achieved a 54.3% recovery rate for patients treated for depression, outperforming CBT by 8.4%. Given the existing guidance of IPT being recommended for moderate - severe depression we can assume that the majority of these patients fall within the phq 15 and	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. IPT remains an option for the treatment of less severe depression. It has also been added to the treatment options for more severe depression.

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				above at baseline group. We consider it a waste of training resources and expertise for therapists to stop offering IPT to patients having consistently shown the efficacy of the treatment (above CBT) within IAPT services. We consider this a waste of valuable NHS resources.	
British Association for Counselling and Psychotherapy	General	General	General	**Recommendations for research** The draft guideline identifies a number of suggestions for research (e.g. p324). Based on the arguments made herein BACP would argue that what is necessary is: 1) RCTs which utilise CBT as a comparator; specifically RCTs on Humanistic Therapies focussed on both mild to moderate and severe depression. 2) Qualitative outcome studies with service users that focus on their experience of treatment of depression in primary care in the UK, in particular studies focussed on looking at experience of different therapeutic modalities; qualitative synthesis studies in the same area. 3) Research which seeks to systematically examine the differential impact of depression treatment for	Thank you for your comment and suggested areas of research. 1. There is a large trial which is nearing completion in this area so we did not prioritise recommending further research. 2. We would think that the proper place for this study to start would be an analysis of existing datasets to determine whether further primary research is needed. 3. We agree that this would be a good idea. A number of research recommendations for specific groups of people have been made in other NICE guidelines, for example Antenatal and perinatal mental health. 4. Therapist effects are outside the scope of the guideline, so we have not looked and the evidence and are not able to recommend further research.

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				different groups in the UK. 4) Studies which examine therapist effects. A related recommendation is that NICE should review their approach to guideline development in line with some of the criticisms made here.	
Mind	General			IAPT staff retention and satisfaction: Mind CHWF is an independent IAPT provider. We have found that we are able to better retain staff and maintain stronger staff morale of those involved in mindfulness interventions over those that practice purely cognitive behavioural therapy.	Thank you for your comment and providing this information on staff retention and satisfaction.
Mind	General			Clients are rarely offered a full menu of choice and the "care pathways" are rigid and unhelpful to some people who would like to try therapies other than CBT. If someone does try CBT and does not get on with it, they may be stepped over to counselling (and vice versa) but we fear there are many clients who drop out without knowing there was a choice.	Thank you for your comment. The recommendations in section 1.4 clarify that clinicians should provide people with information about the available treatment options, to assist them in making an informed choice.
The British Psychological Society	General			**References** Barker, E.D. (2011) *The contribution of prenatal and postnatal maternal anxiety and*	Thank you for your comment and for bringing these references to our attention. Unfortunately none of the studies referenced (Barker 2011, BPS 2011, Castonguay 2005, Coppock 2000, Cromby 2013, Drake 2004,

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				depression to child maladjustment, Wiley's Online, **28(8)**, 696–702, DOI: 10.1002/da.20856 BPS Division of Clinical Psychology (2011) *Good Practice Guidelines on the use of psychological formulation* http://www.bps.org.uk/system/files/Public%20files/DCP/cat-842.pdf Castonguay, L.G., Beutler, L.E. (2005). *Principles of Therapeutic Change*, Oxford University Press Coppock, V., Hopton, J. (2000) *Critical Perspectives on Mental Health*, Psychology Press Cromby, J., Harper, D., Reavey, P. (2013) *Psychology, Mental Health and Distress,* The Palgrave MacMillan. Drake, R.J., Pickles, A., Bentall, R.P., Kinderman, P., Haddock, G., Tarrier, N., Lewis, S.W. (2004) *The evolution of insight, paranoia and depression during early schizophrenia*, Psychol Med, **34(2)**, 285-92 Lieblich Samuel, M., Castle, D.J., Pantelis, C., Hopwood, M., Young, A.H., Everall, I.P. (2015) *High heterogeneity and low reliability*	Lieblich 2015, Meltzer 2010, Pybis 2017, Royal College of Psychiatrists 2017, Skills for Health 2014) could be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				in the diagnosis of major depression will impair the development of new drugs; BJPsych Open, **1**, e5–e7. doi: 10.1192/bjpo.bp.115.000786 http://bjpo.rcpsych.org/content/bjporcpsych/1/2/e5.full.pdf Meltzer, H., Bebbington, P., Brugha, T., Jenkins, R., McManus, S., Stansfeld, S. (2010) *Job insecurity, socio-economic circumstances and depression* *Psychological Medicine*, Volume 40, PMID: 19903366 DOI: 10.1017/S0033291709991802 Pybis, J., Saxon, D., Hill, A., Barkham, M. (2017) *The comparative effectiveness and efficiency of cognitive behaviour therapy and generic counselling in the treatment of depression*: evidence from the 2nd UK National Audit of psychological therapies. BMC Psychiatry, **17(1)** Royal College of Psychiatrists (2017) *Using formulation in general psychiatric care: good practice* http://www.rcpsych.ac.uk/files/pdfversion/OP103.pdf Skills for Health (2014) *UK Core Skills Training Framework: Subject Guide – Version*	

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				1.2 https://www.whatdotheyknow.com/request/242427/response/602988/attach/3/CSTF%20Subject%20Guide%20v1%202.pdf	
Department of health	General			I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
Royal College of	General			This is to inform you that the Royal College of Nursing has no comments to submit to inform on the Depression in adults: recognition and management: draft guidance consultation.	Thank you for your comment.
Institute of Health Visiting	General	Table 2	Table 2	Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. CBT 2-3 times per week is recommended however currently is only offered once per week and the waiting list is usually quite long. Perhaps a drive for more CBT practitioners may be helpful to ensure depressed adults get the intervention they need in a timely way. Antenatal visits are being conducted but not uniformly due to lack of capacity and staffing in certain areas. This will impact on the quality of services and future outcomes for our families and needs addressing and considering	Thank you for your comment. We recommend 2 sessions of CBT for the first 2-3 weeks. This is what is closest to what is recommended in the treatment manuals, involves no greater resource allocation and in our view is likely to produce better outcomes. We are unclear what your comment about antenatal visits refers to as we do not mention these in the recommendations.

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Institute of Health Visiting	General	Table 2	Table 2	Would implementation of any of the draft recommendations have significant cost implications? Cost effectiveness would generate from prevention of depression in the first place. The interventions are very much downstream and reactive. Pro-active prevention is the way forward. The role of the health visitor and school nurse is critical in this work. It is widely documented in the literature that Early help/early intervention makes for significant financial returns and equity long term (Allen, Tickell, Munro). Vitamin D supplementation during pregnancy and new birth of baby should be given as this would reduce depression long term and would be significantly cheaper than mental health services in future. The funding was removed for this and could prove to be expensive long term Vitamin d can only be obtained from the sun direct for 20 mins everyday and only 15% from food. This means we may all be deficient and is not an ethnic group problem anymore. All skin colours are at risk of vit d deficiency which can result in depression	Thank you for your comment. Prevention of depression is outside the scope of this guideline and we are not able to make recommendations on this issue.
Institute of Health Visiting	General	Table 2	Table 2	What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.	Thank you for your comment. The guideline includes a number of recommendations on assessment which are designed to ensure that a full assessment of need is undertaken

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				Vitamin D supplementation as above to support mood and accessible drop in exercise classes and social activities so reduce isolation resulting in depression. A 2 - way process is needed with service uses and health professionals working collaboratively in partnership. Considering the "actual diagnosis" and root cause of the depression so the underlying problems are addressed as opposed to masking the problems with medication which is only mean to be a short term solution anyway. Depression is most often treated blindly based on symptoms but can be chemical imbalance or overload of stress. Targeted baby massage for mothers with low mood but the antenatal visit is critical prior to this to identify risks before the low mood arises. Working closely with the psychology team is critical with IY baby incredible years and VIG video interactive guidance bonding and attachment so the foundations are good for later life which begins at conception the 1001 critical days and NBO training which is currently being rolled out across Manchester. Good bonding and attachment with mother na dbaby is crucial for later life mental health. Could we have a campaign and raise awareness re the critical importance of the early stages again perhaps?	and decisions on treatment are not made solely on the basis of a symptom count. Perinatal mental health is outside the scope of this guideline and we are not able to make recommendations on this issue.

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Institute of Health Visiting	General	Table 2	Table 2	NICE would also welcome views on the Equality Impact Assessment. Having read the equality impact assessment there appears to be no consideration towards hard to reach groups asylum seekers and protected characteristics including LBGT and pregnancy etc? These rae critical to include and consider within the mental health documentation as most likely to suffer with mental health issues	Thank you for your comment. Pregnant women are already covered by existing NICE guidance on Antenatal and perinatal mental health. LGBT groups are already explicitly mentioned in recommendation 1.3.5 as a group where pathways need to be in place to promote their access to mental health services. In light of your comment we have added asylum seekers to this recommendation.
Action on Smoking and Health (ASH)	Overall	General	General	The guidelines set out the important relationship between physical ill health and depression. However, it does not identify that higher smoking rates among people with depression and more broadly with mental health conditions play an important part in the increased incidence of many physical conditions. Among people with depression the best evidence we have of rates of smoking comes from 2007 Adult Psychiatric Morbidity Survey. While in 2007 22% of the adult population as whole smoked, 32% of those with depression and anxiety did. [McManus et al Cigarette smoking and mental health in England Data from the Adult Psychiatric Morbidity Survey 2007, 2010 https://pdfs.semanticscholar.org/5fec/d1dbe8c563684e3018c2283b92c2383427f0.pdf]	Thank you for your comment. This guideline is about the treatment and management of depression in adults. It is outside the scope to make recommendations on smoking.

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				There are concerns that this gap may be widening as smoking rates among the general population have fallen rapidly since 2007 and are now around 16% while there is evidence that smoking rates among people with the mental health condition have not made the same progress in this period. [Smoking and Mental Health. A joint report by the Royal College of Physicians and the Royal College of Psychiatrists. 2013 https://cdn.shopify.com/s/files/1/0924/4392/files/smoking_and_mental_health_-_full_report_web.pdf, Action on Smoking and Health, The Stolen Years, 2016 http://ash.org.uk/download/the-stolen-years-the-mental-health-and-smoking-action-report/] It is also worth noting that among groups where depression is more common smoking is also more likely to be prevalent for example among people with substance use issues, experience of homelessness, low incomes and prisoners. [ASH Brief; Health inequalities and smoking http://ash.org.uk/download/ash-briefing-health-inequalities-and-smoking/] Given the relationship between poor physical health, depression and smoking this is a	

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				highly relevant topic for this guidance.	
Parkinson's UK	Short	General	General	1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. For people affected by Parkinson's who commonly experience depression, some of the areas which will have the biggest impact on practice include: • 1.3.1 – pathways having multiple entry points and ways to access the service, including self-referral. We believe that Parkinson's services should be able to directly refer into mental health services where required. • 1.3.1- should be accessible and acceptable to people using the services. This is vital for people with Parkinson's who may have mobility issues. Therefore, it is vital that the delivery of care and treatment of individuals with depression is accessible for all. • 1.4.2 – taking into account any physical health problems. We believe it is vital that both mental and physical health problems are taken into account in equal measure and that possible interactions with any other medicines are considered. Only	Thank you for your comment. This guideline is about the treatment and management of depression in adults. People with depression and a chronic physical health problem, such as Parkinson's, are not within the scope of this guideline. Therefore it is not possible to make recommendations for people with Parkinson's in this guideline.

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				this approach will ensure person-centred treatment and care for the person experiencing depression. We believe it may be challenging to implement some of the recommendations around specialist care planning as research suggests that despite the commitment to deliver parity of esteem between physical and mental health, some mental health trusts are still struggling to fund services. Furthermore, the recent Care Quality Commission report (July 2017) *The state of care in mental health services 2014-2017* highlighted significant areas of concern including too much variation in both quality and access to services, including long waiting times, as well as poor recording and sharing of information. As the report suggests, there are serious concerns around growing demand, workforce gaps and funding difficulties which could directly impact the implementation of this vitally important NICE guideline.	
British Association for Psychopharmacology	Short	General	General	These guidelines are a very substantial revision of CG90 published in 2009. In particular there has been a very substantial increase in reference to psycho-social interventions. This is to be welcomed. In all 13 different interventions are described (CBT (individual and group), BA, IPT, STPT, BCT, MBCT, CBASP, self-help with support,	Thank you for your comment and support for our recommendations on psychosocial interventions. The IAPT programme has been central to then implementation of NICE recommendations on treatment of depression. This programme is currently

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				physical activity programmes and rehabilitation programmes). The concern with such a broad range of therapies included in the recommendations for routine care is a) the lack of awareness of the range of treatments and the difference between them (e.g. between BA and physical activity programmes, CBASP vs CBT and MBCT); b) the lack of availability of such a range across the country and c) the degree of fidelity to each of the specific model 'in the field'. The emphasis and detail around psychosocial interventions in the guideline is in stark contrast to the reduction in focus on pharmacotherapy in the draft guideline compared with CG90. The concern is that many of the generic statements and those specifically related to medication have been drafted by experts who do not have experience of prescribing. For example there is an interesting choice of words in the footnote on page 25 regarding combining an antipsychotic with an antidepressant: "The prescriber should follow relevant professional guidance…." We are unclear what "professional guidance" the committee are referring to. Similarly, there is a general recommendation in section 1.4.5 for all interventions to use "sessional outcome measures". We are unclear what this means	undergoing further expansion which should also enhance availability of interventions. In recognition of the current variation in the use of specific psychological interventions we have made recommendations about how they should be structured. The footnote you cite is standard text used in NICE guidelines when a recommendation is made for an off license use of an intervention. The wording was not constructed by the committee. The committee included a number of people with significant expertise and experience of prescribing medication. We have clarified that the use of sessional outcome measures should be considered as they do not currently apply to all interventions. In light of feedback from stakeholders the recommendation about medication management has been deleted as the committee agreed that it was no longer a widely used treatment option and so inclusion of the recommendation could lead to confusion. In light of your comment we have made a number of changes to our recommendations

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				in relation to the prescription of medication. Recommendation 1.4.22 also appears to have been written by somebody who does not prescribe medication. It states "Do not routinely provide medication management on its own as an intervention for people with depression." 'Medication management' is defined on page 34 as "giving a person advice on how to keep to a regime for the use of medication (for example, how to take it, when to take it and how often). The focus in such programmes is only on the management of medication and not on other aspects of depression." With such a definition, we are in agreement with recommendation 1.4.22. However, this definition of 'medication management' bears little resemblance to what actually happens in the clinic in practice. When considering the pharmacotherapy recommendations in isolation, for example in the situation where a patient refuses psychological interventions, or such interventions are not available within a time scale that is clinically appropriate, there is concern regarding a) the limited extend of the recommendations; b) the nature of the recommendations in particular how different these are in relation to the previous NICE guidelines (CG90), other respected UK	for medication. In particular we have included further detail on the monitoring of lithium and antipsychotics, the need to be aware of potential interactions between antidepressant medications and the relative position of medication compared to psychological interventions. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				guidance (e.g. British Association for Psychopharmacology – Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525) and current clinical practice with it being unclear what new evidence underpins such a radical departure from previous guidelines; c) the potential impact of the recommendations on service provision. This last point is a particular concern given how hard pressed specialist mental health services currently are. Following the draft guideline, if a patient chooses medication and are prescribed an SSRI at a standard starting dose and they don't respond over 3-4 weeks, and then they don't respond to a dose increase, switch or addition of a second medication over a further 3-4 weeks, then recommendation 1.9.8 states that the clinician should "consider consulting with, or referring the person to, a specialist service. In theory this means that within just 6 weeks of presenting to their GP and failing to respond to just one antidepressant (with dose optimisation) could end up in specialist care. While there is concern about patients being treated for far too long in primary care before referral to specialist services, given the evidence that duration of untreated depression is associated with poorer outcomes (De Diego-Adelino et al. 2010 J	

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				Affect Disorders 120:221 – 225), our concern is that the guidelines prompts referral too early and potentially un-necessarily in too many situations. Recommendation 1.14.4 recommends referring people to specialist services if the person has more severe depression and "….complicating problems, for example unemployment, poor housing or financial problems". This will account for a very significant proportion of such patients. Given how common depression is, lowering the threshold for referral to specialist care even just slightly runs the risk of services becoming swamped. As such, we believe that the guidelines as drafted potentially will lead to vast increases in costs to the NHS and potential destabilisation of services.	
Lundbeck Limited	Short	General	General	Lundbeck is very concerned to note that there is no mention of vortioxetine or TA367 (NICE, 2015) at all in the short version of the draft guideline. Following the rigorous clinical and health economic analysis conducted by NICE in 2015, NICE recommended vortioxetine as an "option for treating major depressive episodes in adults whose condition has responded inadequately to 2 antidepressants within the current episode." (NICE, 2015) The TAG was published in November 2015 and so does not fall due for review until	Thank you for your comment. In light of this and the other comments you have made we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.

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				November 2018. In the meantime, we believe that TA367 should be explicitly and accurately reflected in the pharmacological treatment pathway recommendations in this updated NICE depression guideline. This is necessary in order to ensure consistency between the guideline recommendations and the extant TAG, and to reduce potential confusion for prescribers and healthcare organisations who are following the implementation mandate/funding direction associated with this TAG. The short version of the guideline is likely to be the primary point of reference for most individuals and organisations and so this omission has the potential to result in NHS organisations and individuals overlooking TA367 (NICE, 2015) and the mandatory implementation requirements associated with it, when updating local guidelines and protocols. This may mean they inadvertently fail to offer patients access to a technology that has been found by NICE to be cost- and clinically-effective for adults with depression who have had an inadequate response to 2 ADs in their current depressive episode. Organisations updating their clinical pathways in line with the updated NICE guideline are likely to ignore TA367 (NICE,	

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				2015) if it is not clearly referenced in the recommendations contained within the short version of the guideline. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015.	
British Psychoanalytic Council	Short	General	General	<u>Patient Choice:</u> Despite increasing evidence that patients have improved treatment outcomes and completion rates if they can access a preferred choice of therapy, the recommendations do not support meaningful patient choice. Instead, Cognitive Behavioural Therapy (CBT) is proposed as the first treatment for patients, alone or with medication. Given this growing evidence for the efficacy of providing a range of treatments - appropriate treatments for all patients – we consider that limiting choice not only goes against the growing evidence but is also unethical and cost-ineffective. Limiting choice also undermines parity of esteem between physical and mental health, where it is common practice and considered	Thank you for your comment. Patient choice is a central element of the provision of effective healthcare. We have made recommendations in the general principles section which require those providing treatment and support for people with depression to set out the benefits and harms, and the requirements of individual interventions so as to enable people to make an informed choice. These recommendations and others throughout other sections of the guideline also make clear that an individual has a right to decline an offer of treatment. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person. NICE guidelines make recommendations for interventions where there is evidence that they are clinically and cost effective. When making the recommendations for specific interventions, the committee took into

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				cost-effective within treatment for physical health for example, to match patients to the most appropriate treatment for them individually (as recognised by NHS England in 2016). Evidence which needs to be considered includes: Lindhiem, O., Bennett, CB., Trentacosta, CJ., & McLear, C. (2014). Client preferences affect treatment satisfaction, completion, and clinical outcome: a meta-analysis. *Clinical Psychology Review*, *34*(6): 506–517. Lin, P., Campbell, DG., Chaney, EF., Lie, C., Heagerty, P., Felker, BL., Hendrick, SC. (2005) The influence of patient preference on depression treatment in primary care. *Annals of Behavioral Medicine*, 30(2):167–173.	account clinical and cost effectiveness and a variety of other factors including a person's previous experience of treatment and the outcome of treatment. This has led, in particular with first line treatment of less severe depression, to the development of a stepped care model in which interventions are recommended in a sequence (full details of the justification for this can be found in the 'evidence to recommendations' sections in the full guideline). The purpose of recommending such a sequence is not to remove patient choice, but rather to provide people with a choice from those interventions that have the greatest likelihood of being effective. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with

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					support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).

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					Lindhiem 2014 could not be included as the comparison of active choice condition relative to no involvement in shared decision making does not match the review protocol. Patient preference, choice and the principles of shared decision making were considered by the committee during the interpretation of evidence and making the recommendations. Lin 2005 could not be included as mediator/moderator analyses do not match the review protocol.
Nottinghamshire Healthcare NHS Foundation Trust	Short	General	general	**Project Summary** The Key Summary of this submission is that within Nottingham Healthcare NHS Foundation Trust Let's Talk Wellbeing IAPT Service Interpersonal Psychological Therapy (IPT) has proved to be an effective psychological therapy for the treatment of depression, with very positive patient recovery rates and experience feedback. Additionally, the IPT clinicians have reviewed the draft guidelines and enclosed is their considered opinions. The following summary will articulate the effectiveness of IPT for patients with a diagnosis of F32 and F33 diagnosis between 11/9/15 and 11/9/17, followed by patient	Thank you for your comment and the helpful description of the role of IPT in your service. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. IPT remains an option for the treatment of less severe depression. It has also been added to the treatment options for more severe depression.

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				experience feedback that the IPT clinicians have received from their patients, and concluded by Practitioner feedback regarding the draft NICE guidelines for depression. All data within the report is aggregated and anonymized, and conforms to NHS Information Governance expectations. Background: The service has six IPT clinicians working since the inception of Improving Access to Psychological Therapies initiative (IAPT). They have supported the service in delivering an effective IAPT service for patients experiencing depression and helped contribute to the Service achieving above an annual recovery rate of 50 % plus. This cohort is a long standing experienced workforce. This workforce works with predominantly moderate, moderate to severe and severe depression patient presentations that are encompassed within the following focus areas: dispute, grief, transition, and sensitivity. Current situation – The Let's Talk Wellbeing Service operates under an Any Qualified Provider contractual model with a PBr tariff based payment structure. The current IPT clinical governance model is that IPT will treat moderate up to severe depression ranging	

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				between cluster 3-4, within a 1-1 based treatment model. The practitioners receive monthly supervision from an accredited IPT UK supervisor and also receive peer supervision and caseload management. Subsequently, it is assumed there is high adherence to the IPT treatment protocols. The treatment model operates with an optimised approach with patients generally having between 4-16 therapy sessions though the mean average number of sessions for IPT is approximately 7-8 sessions. The IPT clinicians are on NHS payment band 6. **Effectiveness of IPT within Let's Talk Wellbeing for Depressive Disorders:** Total IPT pt included: 491 / Results derived from: / Data between range: 11/9/15 to 11/9/17 PHQ9 Score range 1 2 3 4 5 PHQ9- 0-4 / PHQ9- 5-9 / PHQ9 - 10-14 / PHQ9 - 15-19 / PHQ9 - 20-27 No. patient in sample: 5 / 21 / 115 / 169 / 181 IPT treatment only treatment — No. recovered with PHQ9 only: N/A / N/A / 89 / 90 / 83 2 or more IPT sessions only — No. recovered with PHQ and GAD: N/A / N/A / 81 / 80 / 65 F32 or 33 diagnosis — PHQ9 only recovery calculation: N/A / N/A / 77.39% / 53.25% / 45.80% Used typical IAPT recovery calculation — PHQ9 & GAD7 recovery calculation: N/A / N/A / 70.43% / 47.33% / 35.90% Key: 1 0-4 - Non; 2 5-9 Mild; 3 10-14 Moderate; 4 15-19 Moderate / Severe; 5 20-27 Severe Fig 1 Descriptive analysis of IPT recovery rate using IAPT recovery rate formula. **IPT Patient Experience Feedback from patients' with Depressive Disorders within Let's Talk Wellbeing:**	

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Patient Experience Feedback
Extremely helpful. X was excellent, she has taken me on a journey not yet completed but needed to go i want to go
I feel it's helped me to understand what is wrong. Addressing the difficulties will be a much longer process
X is excellent at her job.
I often found the call takers at the LT Main could be quite short & not overly helpful.
Big thank you to "X" for listening and her advice to help me make small steps moving forward.
X has helped me to live again. She is an outstanding therapist. Thank you is not enough!
Although I am still being treated for anxiety and depression, the sessions with X have helped me greatly to come to terms with my situation.
This service to me was a great help. It was good to be able to talk honestly to someone with whom I felt safe and at ease
X helped be enormously and I will be forever grateful for her help.
I can't thank X enough for what she done for me she is AMAZING!!!
X was a very good councellor. She listened at all times and made me have very confidence in her. She helped me arrive to many difficult decisions and helped me make my own choices for the first time in many years.
She understood my thought process and made me face my past to deal with it and move forward. X was impartial and guiding in every way. Thank You.

Fig 2 Sample of patient experience feedback for IPT clinicians.

IPT Let's Talk Wellbeing clinicians views of the Draft Depression NICE Guidelines

NICE 2017 Draft Depression Guidelines – Lets Talk Wellbeing IPT clinician feedback regarding the draft guidelines

Less Severe Depression	Severe
term less severe depression includes the traditional categories 16 of subthreshold symptoms, mild depression, and the lower half of moderate 17 depression.	term m depres traditio upper l depres depres

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						Or If a person has had no response or a limited response to initial treatment after assessing the issues in recommendation provide more support by increasing the number and length of appointments.	
				Conclusion / Feedback: Less Severe Depression Group intervention difficult for many with interpersonal issues in their depression Please consider the Cuijpers et al 2016; IPT for mental health problems, a meta analysis. Conclusions: IPT is effective in the acute treatment of depression and may be effective in the prevention of new depressive disorders and in preventing relapse. IPT may also be effective in the treatment of eating disorders and anxiety disorders and has shown promising effects in	Conclusion / Feedback: Severe Depression Consistent 50% + recovery rate; (Lets Talk Wellbeing) IAPT outcome data for 2015-16 54.3% recovery rate IPT for depression. Recommendations state client should be given choice and advised of outcomes.	Conclusion / Feedback: Limited response and treatment-resistant depression Table 47 of guidelines suggest good outcome of IPT with medication. Using IPT focus rather than increase number sessions in CBT will change focus from thoughts to emotions can be accessible to chronically depressed individuals with lot of negative symptoms 1.6.2 If a person with more severe depression does not want to take medication, offer:	Conclusion Chronic dep No feedbac work is not remit.

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				some other mental health disorders. 1.9.3 When changing treatment for a person with depression who has had no response or a limited response to initial medication, consider: • combining the medication with a psychological therapy (CBT, BA, or IPT), or • switching to a psychological therapy alone (CBT, BA, or IPT) if the person wants to stop taking medication. [new *Please specify that this can be for both more severe and less severe depression*	Many clients have difficulty with homework concept as present in CBT. Cheaper workforce Cause and effect of interpersonal issues on depression significant. 1.5.8 Offer CBT or BA if a person with less severe depression To include IPT as a choice for patients as a front line treatment for less severe depression as it has been shown to be at least as effective as CBT with a lower DNA rate and can be adapted to be offered with less sessions if required 1.5.9 Consider IPT if a person with less severe depression would like help for interpersonal difficulties that focus on role transitions, disputes or grief. Reconsider whether to	Group CBT or individual CBT/BA Consider including the choice of IPT in combination with an SSRI as the initial treatment for more severe depression. Although the evidence based outcomes are better for a combination of medication and IPT, IPT is also a successful treatment for severe depression when a person does not want to take medication 1.6.1 Offer individual CBT in combination with an SSRI as the initial treatment for more severe depression Consider including the choice of IPT in combination with an SSRI as the initial treatment for more severe depression. I believe this is currently the case and there seems no reason to exclude IPT as a choice for persons as an initial treatment in Primary Care	

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					include this statement at all or if including this statement to add that the focus of interpersonal problems is not always obvious and can be redefined / changed with further assessment or changed completely, for example in the light of further insight or if further interpersonal events occur.				
				Fig 3 Collated feedback from IPT clinicians within the Let's Talk Wellbeing Service regarding the draft guidelines in question. **SWOT analysis** **Strengths:** • IPT affords the opportunity for a service to provide a cost effective means of treating moderate to severe depression other than CBT.					

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				• IPT offers a different type of treatment for patient experiencing moderate to severe depression with either of the following: complicated, grief, adjustment to long term conditions and early attachment issues that are manifesting with a depressive disorder. **Weaknesses:** • Whilst there is limited high quality Quantitative controlled research presented in the current analysis of the full draft guidelines for depression. There has to be consideration of soft / less stringent research to support the effectiveness of IPT when working with depression. As IPT does not have the research infrastructure as other therapy modalities. • Subsequently, devaluing IPT to a second line of treatment runs the risk of disadvantaging patients of a highly effective intervention according to softer research design.	

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				Opportunities: • From the soft data presented in the current document it is clear to see the patient cohort with moderate depression experience a very significant recovery of 70% with both PHQ9 and GAD7. Though, for the patient cohort that experiences moderate to severe depression there is a recovery rate of 53% with just the PHQ9, and for the patient cohort with severe depression 45% achieved recovery with just the PHQ9. Additionally, as can be seen adjunct to the patient experience feedback – IPT contributes very significantly to the quality agenda for the Let's Talk Wellbeing IAPT Service. **Threats:** • With the proposed downgrading of IPT from a frontline intervention, there is the risk of IAPT services being unable to treat moderate to severe depression other than with CBT. This is particularly important when considering not all patients are suitable, or want CBT, which doesn't conform to a Patient choice or a	

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				Patient Centred approach and individualised care as promoted within the NHS. • With the proposed withdrawal of IPT to a second line intervention, patients could be, being denied an effective intervention that maybe guilty of having limited or poor research infrastructure, despite it originally, being included in the original NICE guidelines for depression. • Additionally, there is a financial risk to IAPT services, as with IPT being viewed as a second line of treatment, the cost effectiveness of treating depression could be effected as CBT is a more costly intervention.	
University of Nottingham	Short	general	general	Digitally delivered CBT interventions have been shown to be effective in RCTs and are now widely available. Why is there no specific mention or recommendation about these in the key recommendations?	Thank you for your comment. We have included digitally delivered CBT interventions in the supported self-help analysis.
Royal College of Psychiatrists	Short	General	General	These guidelines represent an extensive revision of CG90, with a substantial increase in guidance relating to psychosocial interventions. Many different psychosocial interventions are described (CBT, BA, IPT, STPT, BCT, MBCT, CBASP, self-help with	Thank you for your comment and support for our recommendations on psychosocial interventions. The IAPT programme has been central to then implementation of NICE

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				support, physical activity programmes and rehabilitation programmes), but most clinicians are unaware of this range and the differences between varying therapies, many are not currently available in standard clinical care settings, and some have not been tested in 'real world' clinical practice. By contrast, pharmacological treatments have received less attention, perhaps because many of the contributing experts have minimal experience of prescribing psychotropic drugs. For example, there is a general recommendation in section 1.4.5 for all interventions to use 'sessional outcome measures': but what this means in relation to prescription of medication is unclear. 'Medication management' is defined on page 34 as 'giving a person advice on how to keep to a regime for the use of medication (for example, how to take it, when to take it and how often). The focus in such programmes is only on the management of medication and not on other aspects of depression'. However, this definition of 'medication management' bears little resemblance to what actually happens in clinical practice. Medication interventions receive little consideration, it is unclear why comments on medication differ so substantially from those within previous NICE guidance or from the recommendations of other respected	recommendations on treatment of depression. This programme is currently undergoing further expansion which should also enhance availability of interventions. In recognition of the current variation in the use of specific psychological interventions we have made recommendations about how they should be structured. The footnote you cite is standard text used in NICE guidelines when a recommendation is made for an off license use of an intervention. The wording was not constructed by the committee. The committee included a number of people with significant expertise and experience of prescribing medication. We have clarified that the use of sessional outcome measures should be considered as they do not currently apply to all interventions. In light of feedback from stakeholders the recommendation about medication management has been deleted as the committee agreed that it was no longer a widely used treatment option and so inclusion of the recommendation could lead to confusion.

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				guidance (for example that produced by the British Association for Psychopharmacology [BAP]), and little thought appears to have been given to the potential impact of this new guidance on service provision in primary and secondary care. This last point represents a particular concern. In the draft guideline, if a patient chooses medication and is prescribed an SSRI at a standard starting dose but does not respond over 3-4 weeks, and then does not respond to a dose increase, switch or addition of a second medication over a further 3-4 weeks, recommendation 1.9.8 states that the clinician should 'consider consulting with, or referring the person to, a specialist service'. This implies that within just 6 weeks of presenting to their GP and failing to respond to just one antidepressant (with dose optimisation) a patient could enter specialist care, which is simply not feasible in practice. Furthermore, Recommendation 1.14.4 recommends referring people to specialist services if the person has more severe depression and '….complicating problems, for example unemployment, poor housing or financial problems'. Probably the majority of depressed patients have such difficulties. Lowering the threshold for referral to specialist care means limited services could easily become disarrayed and	In light of your comment we have made a number of changes to our recommendations for medication. In particular we have included further detail on the monitoring of lithium and antipsychotics, the need to be aware of potential interactions between antidepressant medications and the relative position of medication compared to psychological interventions. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				overwhelmed, and there could be a considerable increase in costs for the NHS.	
Leeds Community Healthcare Leeds IAPT	Short	General	General	We are concerned that counselling is not included in first line treatment for less severe depression without first offering CBT, BA, group, self-help or medication when counselling may be the most appropriate intervention for the client. We are concerned that counselling is still not recognised as an effective therapeutic approach in its own right despite client demand and continued positive outcome (measured by clients achieving clinical recovery). Nice recommend counselling as an alternative to "antidepressant, CBT, IPT, behavioural activation and behavioural couples therapy" which in our view devalues the approach and its effectiveness at treating depression. We are also concerned that DIT (Dynamic Interpersonal Therapy) and CfD (Counselling for Depression) are not specifically referenced as suitable interventions for the treatment of depression despite being recognised as IAPT compliant therapies.	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Counselling remains an option for people with less severe depression (and who would like help for significant psychosocial, relationship or employment problems) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication, individual CBT or BA or IPT) had not worked well in a previous episode of depression or in those who did not want the other recommended interventions. The committee made this a 'consider' recommendation because of the small benefit on the SMD outcome, the larger benefits on the other 2 clinical outcomes, and the lower cost effectiveness of counselling compared with other high intensity individual psychological

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					interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of counselling was likely to be higher in the sub-population in the recommendation compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). The committee reviewed the evidence on the effectiveness of counselling but did not think the evidence supported recommending one particular version of counselling over another. No specific RCT evidence on PCE-CfD or DIT was identified and so no recommendation for the use of these interventions was made. However, the committee have recommended counselling based on a model that is specifically developed for depression, which would be in line with the specific training programme for counselling developed as part of IAPT.
Leeds Community Healthcare	Short	General	General	We are concerned that being unable to offer IPT as a first line treatment for moderate to severe or severe depression would result in	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the

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Leeds IAPT				an increase of referrals being offered for CBT. Our service offers evidence based treatments that vary in its delivery. If we solely start to essentially offer one treatment (CBT) then this implies that other evidence based treatments are not effective, that patients are not capable of making informed choices when treatment and explanations and rationales are provided. IPT is a good fit for Depression triggered by certain life events. It is a pragmatic approach and meaningful to many patients. In addition if we start to offer CBT as a first line to everyone with Depression this will impact significantly on access to treatment as demand will outweigh capacity. This also may not be the most suited treatment and patients may have to go through a number of processes to get to the right treatment for them which is not a good patient experience. If the offer of IPT is reduced how are we able to increase the evidence base to demonstrate its effectiveness in comparison to CBT that has been a treatment that has had a longer period of research and investment? Within the LCH consortium from 1st June 2016 to 1st July 2017, 177 patients with either a depressive episode (F32) or recurrent depressive episode (F33) were treated with	treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both

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				IPT. Of these, 126 (71.2%) presented with more severe depression (PHQ9 score of 18+). Within LCH between 1st April 2017 and 31st August recovery rates were comparable between the different modalities offered as shown below (% discharged and in recovery); Guided Self Help (Step 2) including groups: 51.3% CBT (step 3) including groups: 48.4% IPT (step 3): 45.6% EMDR (step 3): 42.9 Counselling for Depression (step 3): 53.3% Dynamic Interpersonal Therapy (step 3): 47.6% Please note that the above rates will be a measurement of both anxiety and Depression scores.	types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
College of Mental Health Pharmacy (CMHP)	Short	general		In comparison with NICE CG90, the removal of relevant information on medication, particularly antidepressants is misleading in clinical practice. This draft guidance does not reflect current clinical evidence or give relevant advice about how to shift from current prescribing of antidepressants towards psychological therapies. In addition it does not offer a logical evidence based pathway for clinicians to follow from initial	Thank you for your comment. We have restructured the guideline according to first presentation, further line treatment, chronic depressive symptoms, complex depression, psychotic depression and relapse prevention. We have included recommendations on pharmacological treatments in each of these sections. We have also included many recommendations about general principles around the use of

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				therapy to second, third line and augmentation which reflects current clinical practice. There seems to be a big shift away from medication and greater focus on psychological therapies. The robust NICE-level evidence base for this is lacking, as almost all psychological therapy studies use waiting list controls, shown to be detrimental. Such evidence would not be acceptable to NICE were it applied to medicines (and certainly not in non-mental health Guidelines) so it is highly objectionable to approve such low levels of evidence to psychological therapies. At the European College of Neuropsychopharmacology meeting in September this year an internationally known Professor from the US stated that if you followed these guidelines in the US then it would be considered **malpractice** by an American Court of Law.	pharmacological interventions. We think this structure provides greater integration between pharmacological and psychological interventions. In relation to your comment about studies using wait list controls as a comparator, in the NMA for treatment of a new depressive episode these studies were included explicitly to allow for important comparisons to be made between psychological intervention and pill placebo. The effect sizes between psychological interventions and pill placebo have been central to decision making about which interventions to recommend for first line treatment.
College of Mental Health Pharmacy (CMHP)	Short	General		Even though section 1.4.10 mentions stopping treatment, the document gives no specific guidance on length of treatment if using an antidepressant which needs to be included.	Thank you for your comment. It will be for individual prescribers in discussion with the patient to decide on the length of treatment with an antidepressant.
College of Mental Health Pharmacy (CMHP)	Short	General		The documents reads as if psychological therapies are without adverse effects but all antidepressants will cause them. The quite substantial risks of psychodynamic therapies	Thank you for your comment. We have amended recommendation 1.4.6 to specify that the harms of pharmacological and psychological therapies should be

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				are not addressed. The document is unbalanced.	monitored.
Turning Point	Short	General	General	**Turning Point welcomes the new emphasis on groups** because it helps enable the greatest number of people to access treatment. A key challenge will be in helping to shift people's expectations of therapy. In publishing the guidance we would ask that NICE take the opportunity to start a national conversation (i.e. through media coverage) about group work. We feel the key messages that need to be conveyed are: • There is a good evidence base and the skills people learn in a group are same skills they will learn during 1:1 therapy • Groups are now 'the first line of defence', not a second place option • The vast majority of people are very positive about their experiences of group work and the group itself can foster learning and peer support which isn't possible in 1:1 sessions • The greater emphasis on groups will enable more people suffering from depression are able to access support	Thank you for your comment and support for the recommendation on group interventions. Your comments will be considered by NICE where relevant support activity is being planned.
Turning Point	Short	General	General	**Group work has benefits above and beyond increasing the numbers accessing treatment which we would like to see covered in future updates of the guidance**. Groups help people build connections in their	Thank you for your comment. Future updates of the guideline may look at evidence on group activities if this evidence is available and within the scope of the update.

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				community and strengthen their social networks. This is especially the case for targeted groups which are often more attractive for some people who may be more reluctant to take part in group work. For example, Turning Point run an older person's depression group with Age UK in Nottingham and in Wakefield we run groups in conjunction with Mesmac, which have been very well received by LGBT service users. Although participants are sometimes initially nervous to attend groups we have seen very close friendships develop on the back of these programmes which help sustain people's recovery and protect against relapse. We would like future updates to include an assessment of the evidence for targeted groups such as this.	
Turning Point	Short	General	General	**Groups and CCBT**. Turning Point are currently developing an online workshop people can access from home. There is potential to develop group CCBT e.g. a webinar where participants are able to receive information and engage in real time discussion with other members of the group without having to physically be in the same room. Future iterations of this guidance should consider this innovation in scope.	Thank you for your comment. Future updates of the guideline may look at evidence on group CCBT if this evidence is available and within the scope of the update.
Turning Point	Short	General	General	**Logistical challenges** .The main logistical challenge we anticipate in implementing the guidance is the follow-up gap, the space	Thank you for your comment and support for the recommendation on group interventions. Dealing with booking challenges will be a

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				between the last session in a block and the update session. There may be some booking/capacity challenges. However, this is unlikely to have significant resource implications.	matter for local implementation.
Sussex Partnership NHS Foundation Trust	Short	general		Many in our Trust are concerned about the introduction of new categories of more severe and less severe depression. This is not in line with the internationally recognised diagnostic systems or with how most trials are conducted. Most treatment trials are not restricted to one or other of these groups and nor do they typically include moderator analyses to allow differential treatment effects between groups to be examined. It will lead to confusion and difficulties in applying research findings to these categories and in education and training.	Thank you for your comment. The committee determined that the distinction between more and less severe depression was a better basis on which to develop recommendations than the mild to moderate and moderate to severe distinction adopted in the 2009 guideline as this was thought to be less ambiguous and have more clinical utility. The distinction between more and less severe builds on what is commonly used in clinical practice and was developed to support decision making in primary care. This distinction has also proven effective in supporting the development of specific service models such as IAPT.
Sussex Partnership NHS Foundation Trust	Short	general		We would welcome a statement on use of hormones in depression in women, post or premenopausal, or post natally. Patients often ask if HRT is useful and seek hormones from GPs.	Thank you for your comment. The committee did not consider HRT to be an intervention that is in regular clinical use for the treatment of depression. Also HRT preparations do not have a license to be used as treatments for depression**.** As such the evidence on this intervention has not been appraised and we are not able to make any recommendations on its use.
The British Psychological	Short		Secti	**Self – Help:** A focus on guided self-help is	Thank you for your comment and support for our recommendation on advance directives.

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Society			on 1.1.1 1.1.2 1.14 1.2 1.25 1.3	good, but there needs to be an emphasis on quality control, some things are likely to make people worse (for example, professional support for those in need of care). **Advance Directives**: This section is welcomed – it has good prominence and gives people real choices regarding treatments. **Cultural Sensitivity**: this is a good section, however the emphasis on using people's "preferred language" doesn't only apply to cultural issues, and it applies across the piece. **Assessment:** The Society welcomes this section. However, it is vital that this be looked at very carefully, and re-worded, to ensure that the emphasis is on the identification and assessment of a phenomenon or experience (one with very serious consequences), than an 'illness' or 'disorder'. See above note on formulation. For people with intellectual (or learning) disabilities (or other cognitive) impairment, care should be taken to attempt to gather assessment information directly from the individual, for example using appropriate language and accessible information or	**Self-help, cultural sensitivity, assessment** As specified in the scope, the patient experience and recognition, assessment and initial management sections from the 2009 guideline (sections 1.1 and 1.2) were not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, as the evidence in these areas has not been reviewed, we are not able to make the changes you suggest to the recommendations on self-help, cultural sensitivity or assessment. **Access to services** We have set out criteria which would support people in accessing services, the support they need to get the best out of a service. However it is important to emphasise this guideline is about the effective treatment of depression so this is the prime focus of the evidence that has been appraised. Where there is evidence of the effectiveness of interventions such as collaborative care and befriending, which provide support beyond specific treatment interventions, these have been recommended. However only limited evidence on these types of intervention have been identified which has limited the recommendations that could be made.

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			1.4 1.41 1.43/	assessment tools. While we recognise also the importance in seeking family member or carer perspectives, this should be complimentary to, and not at the expense of, attempts to seek information directly from the individual about any psychological distress. Although it is to be welcomed that the NICE Guidance (2016) Mental Health Problems in People with Learning Disabilities is also referenced here, the current 'shorthand' wording in the NICE 'Depression' Guidance raises a risk that the proxy accounts sought from carers or family members will be prioritised over taking time and making adaptations to ensure the perspectives of individuals with intellectual / learning disabilities are sought. **Access to Services:** The Society welcomes this section, but again focus should be on support of the person experiencing depression, not on treating depression. There needs to be much more emphasis on social responses, because there is huge evidence of social causes and NICE systematic review system tends to limit the use of this type of data. It would be appropriate to also consider here the needs of people with intellectual / learning disabilities and / or other cognitive	We have added people with learning disabilities and people with acquired cognitive impairment to recommendation 1.3.5 as you suggest. **General principles of care** As will be apparent from reading the guideline, particularly the recommendations on assessment and general principles, there is a strong theme throughout of collaborative decision making about care. We expect that this would influence the approach taken to treatment for each individual. The NICE guidance on Mental health problems in people with learning disabilities provides more detailed information on the needs of individuals with learning disabilities than it would be possible to include in this guideline on Depression. In line with NICE processes and to ensure continuity between different NICE guidance documents, we have inserted a cross reference to the guidance on Mental health problems in people with learning disabilities. We think that this will ensure the needs of individuals with learning disabilities will be addressed. **Service user preference** As will be apparent from reading the

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			1.4.4 1.4.5 1.4.9 1.4.10/1.4.11 1.5.5 1.9	impairment or communication or sensory difficulties as a group also at risk of exclusion from mental health services, as NICE seems to recognise on page 41 of the document when considering need for research into those who have additional difficulties in accessing services including those with disabilities. The Society recommends information about services be presented in an accessible, easy text to facilitate access. **General Principles of Care** As above, we would advocate that for all individuals, interventions should be based on assessment and a collaboratively developed formulation, which rather than being diagnosis based such as depression, allows an integration of multiple psychological / social / physical factors to lead to a individualised understanding of the person's distress, which can then lead to the development of a treatment plan. The Society is concerned regarding references to the needs of people with learning disabilities removed in several sections instead just referring to people with 'acquired cognitive impairment', which is of course not the same as a learning disabilities, the rationale being that there is now separate	guideline, particularly the recommendations on assessment and general principles, there is a strong theme throughout of collaborative decision making about care. We expect that this would influence the approach taken to treatment for each individual. However we have added another recommendation to section 1.4 to clarify the importance of decisions being made in collaboration with the person. **Manuals** We did consider whether providing references to specific manuals would be helpful but given the wide range of manuals available and the potential for this to be seen as NICE endorsing a particular manual, we decided not to do so. We agree that accreditation for the delivery of training is important but this is a matter for implementation. **Routine monitoring** We have amended the recommendation to specify that routine outcome monitoring should use validated measures to improve delivery. **Medication** The committee noted that whilst people will not become addicted to antidepressants,

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				NICE Guidance available on Mental Health Problems in People with Learning Disabilities. Although this is the case, it is still the case the people with mild or unidentified learning disabilities should present to mainstream mental health services, and as such, clinicians in those services may be more familiar with generic NICE guidance such as this Depression guidance. Therefore, The Society advocates that references to the needs of individuals with learning disabilities remain in the main body of this Guidance, whilst also referring professionals onto the learning disabilities specific guidance. In the sections on interventions, there should be explicit mention regarding the need to tailor psychological interventions to individuals' with intellectual / learning disabilities level of understanding, and strengths and needs. This may require use of accessible information and flexibility with length / duration / nature of the CBT or other psychological therapy techniques delivered. The Society recommends that reference should be made to the NICE Guidance (2016) Mental Health Problems in People with Learning Disabilities here. **Service User Preference** The Society welcomes this section but felt	they can experience discontinuation symptoms if they stop taking them. The committee agreed that concerns about 'addiction' may be a reason why people are reluctant to take antidepressants and thought it was important that the recommendations highlight that this is not the case. However, in light of comments received from stakeholders the committee have amended recommendation 1.4.8 to include discussion of patients concerns about stopping medication. **Medication withdrawal** We have amended recommendation 1.4.8 to clarify that support needs to be provided when stopping antidepressants. There may be a number of reasons for stopping or changing medication (for example lack of efficacy or tolerability, interactions with other prescribed drugs) and the plan for withdrawal would need to take these reasons into account. Therefore we do not think it would be appropriate to have this plan in place before starting antidepressants. **Activity** The evidence that was identified for the treatment of a new depressive episode was about the effectiveness of physical activity programmes specifically for depression. We
			1.10 1.10.4 1.11 1.13		

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				that it could be stronger. This section is phrased as if the person receiving care can influence the medical / disease model approach. There should be a stronger emphasis on alternative approaches, and on the obligation on services to respect the views of the user.	do not have any evidence about the effectiveness of activity more generally on which to make a recommendation. **Social factors** As will be apparent from reading the guideline, particularly the recommendations on assessment and general principles, there is a strong theme throughout of collaborative decision making about care. We expect that this would influence the approach taken to treatment for each individual to make it person centred.
			1.13.8	**Manuals** The Society believes that this could be stronger with, examples and reference to the accreditation systems. **Routine Monitoring** The Society welcomes this section, as there is evidence of the benefits for some individuals. However, it recommends that this requires better delivery in a clinic, again with choice for people.	**Chronic depression** As will be apparent from reading the guideline, particularly the recommendations on assessment and general principles, there is a strong theme throughout of collaborative decision making about care. We expect that this would influence the approach taken to treatment for each individual.
			1.14.4/1.14.5	**Medication** The Society is concerned regarding the suggestion that antidepressant medication is not addictive. The word addictive is used here in a very technical sense, as in requiring increasing doses to get effect. In lay language, addictive means what is listed, that there are profound withdrawal effects, discontinuation effects, chemical change to the body and brain. We believe that this should be revised to reflect this more clearly.	**Social Interventions** Social factors would be taken into account during initial assessment and when people are not benefiting from treatment. **Personality Disorder** The challenges in the diagnosis and treatment of personality disorder are

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				The Society is concerned that this runs the risk of being misinterpreted as meaning that the drugs have no harmful or dependence-inducing effects, and this is simply not true. The Society recommends that this needs to be re-worded to acutely reflect the comments made above. **Medication Withdrawal** The Society is concerned that this section needs significant revision. There is clear evidence of the harm of long-term antidepressant use (see BMA), of the problems of withdrawal, of the harms done by poorly-managed withdrawal, of the paucity of information, of support services. The Society would recommend that a plan for withdrawal before should be in place starting anti-depressants, agreed with the client and recorded. Services, locally and nationally, need a systematic network of withdrawal support (BMA report). **Activity** The Society recommends that this section needs strengthening – there is very good evidence for the benefits of activity, including on physical health, and should be emphasised.	discussed and acknowledged in other NICE guidance on that subject. Discussion of the validity of the constructs of personality disorder is outside the scope of this guideline. **ECT and cognitive impairment** Cognitive impairment is already covered in recommendations 1.13.3 and 1.3.6. Neuropsychological assessment has an important part to play in the assessment of individuals with identified cognitive impairment, who are being considered for or receiving ECT. In the formal psychiatric assessment for anyone being considered for ECT there will be an initial assessment of cognitive function and subsequent assessment of cognitive function during treatment. The committee were of the view that at this point a decision needs to be taken as to whether a more formal neuropsychological assessment is needed rather than the routine use of this for everyone who is considered for/receiving ECT. Such an approach would be unnecessary and not practical to deliver routinely. **Specialist care planning** Feedback was received from stakeholders that there would not be sufficient resources

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				Social Factors: The Society recognises the comments regarding addressing social factors are important, however it recommends that it is given greater emphasis with a 'person-centred' approach. The Society recommends that further consideration is needed of individuals' social circumstances and the acknowledgement of social stressors that are likely to have significant impact on development, maintenance and recurring difficulties with 'depression' and other elements of psychological distress. There are references of this throughout the document, but this section did not place sufficient emphasis on these important factors. More emphasis should be placed on social responses e.g. 'Commissioners and providers of mental health services should consider…' The Society recommends 'greater investment in supporting communities to address the social determinants of mental health and increase access to mental health support within communities', rather than seeking individualised pathologies. **Chronic Depression**	in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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				We believe that this is important and recognises that this will have funding implications, as does 1.10.3. However, Psychological formulation need to be considered here. The Society recommends that all people experiencing long term depression should be given the opportunity to develop a collaborative psychological formulation or understanding of their difficulties, strengths and needs to inform their plan to address their difficulties. The Society recommends a more collaborative approach e.g. rather than say 'giving them' suggest ' with them developing a formulation or collaborative understanding of their difficulties, needs and assets to inform plans' **Social Interventions** The Society recommends that this be given higher priority and emphasis and should include support to address social or vocational aspects of their plan informed by formulation. **Personality Disorder** As outlined earlier, The Society is concerned that the focus of the document considers personality Disorder is to be identified and treated, rather than supporting a personal experiencing personality disorder	

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				The Society is concerned that diagnoses, and especially diagnoses of so-called personality disorders, are essentially shorthand labels for complex behaviours. To say that someone's problems are consistent with a diagnosis of personality disorder and depression is synonymous with listing his or her observed difficulties such as self-harm, emotional instability, and both separating and concurrently linking, these. It is also important to note that most psychiatric diagnoses, and especially diagnoses of personality disorder, reflect social conventions and are subject to change over time. Indeed, there was considerable speculation in 2013, that DSM-5 would remove the category. (Barker, 2011; Bentall, 2004; BPS, 2011; Coppock & Hopton, 2000) The current classification systems are less controversial for conditions with an identified biological aetiology such as in the fields of neuropsychology, dementias, and moderate to severe learning disability. The Society is concerned regarding the increasing medicalisation of distress and behaviour in both adults and children (BPS, 2011). The functional diagnoses, for which there is substantial evidence for psychosocial factors	

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				in aetiology, and very limited support for a disease model, give rise to a wider range of views and positions. This position should not be read as a denial of the role of biology in mediating and enabling all forms of human experience, behaviour and distress (Cromby, Harper & Reavey, 2013), as is demonstrated, for example, in emerging epigenetic research. It recognises the complexity of the relationship between social, psychological and biological factors. In relation to the experiences that give rise to a functional psychiatric diagnosis, it calls for an approach that fully acknowledges the growing amount of evidence for psychosocial causal factors, but which does not assign an un-evidenced role for biology as a primary cause, and that is transparent about the very limited support for the 'disease' model in such conditions. Such an approach would need to be multi-factorial, to contextualise distress and behaviour, and to acknowledge the complexity of the interactions involved, in keeping with the core principles of formulation. **ECT and Cognitive Impairment** The Society is concerned that there is no clear recognition of the need to stop treating	

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				if there is evidence of cognitive impairment. The Society recommends that a thorough neuropsychologist assessment should also precede ECT and that this should be clearly stated in the guidance. **Specialist Care Planning** The recommendations are to "refer people to specialist mental health services for a programme of coordinated multidisciplinary care". The Society recommends that this should be available for all. It also recommends a more collaborative approach, for example, rather than say 'giving them' The Society recommends 'with them developing a formulation or collaborative understanding of their difficulties, needs and assets to inform plans'.	
Southern Health & Social Care Trust	Short	General	General	We are concerned that the level of psychological therapies suggested given the paucity of psychological therapies available - which whilst we continue to try and develop this area in Mental Health, there is a severe shortage of trained staff.	Thank you for your comment. Training of staff to deliver the interventions recommended in this guideline will be a matter for implementation.
Southern Health & Social Care Trust	short	General	General	We are concerned at the level of robust research put forward in relation to anti-depressant medications but there is little evidence mentioned in relation to the psychological approaches recommended	Thank you for your comment. The RCT evidence identified for the review questions has been documented in the guideline along with an assessment of the quality for each outcome (using GRADE). Evidence was

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					found for a variety of both pharmacological and psychological interventions. When making recommendations, the committee considered both the quality and amount of evidence available on the different interventions, and worded their recommendations accordingly. Their rationale for making the recommendations is documented in the 'evidence to recommendations' sections in the full guideline
Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	general		We are concerned about the way that treatment resistant, complex and chronic depression are defined separately in this guideline as we are not aware of any current assessment tools that can reliably differentiate these overlapping presentations, and with the introduction of PbR we are concerned that service users with one or more of these diagnoses will fall through the cracks of each separate category. It will be very difficult for services as they are currently configured to implement a pathway that treats these patient groups separately and it would make more sense to offer a common pathway across all 3 of these classifications with a range of options for the pathway. Given that our members (medical psychotherapists, consultant clinical psychologists) have leading roles in running many such services that currently provide	Thank you for your comment. A number of stakeholders commented on the utility of the term 'treatment resistant depression' (TRD) and 'no or limited response'. In this guideline TRD followed the accepted conventional definition which is no or limited response to 2 or more adequate antidepressant treatments. Other studies adopted a somewhat different definition, for example inadequate response in a population with longer term problems. The committee considered the feedback from stakeholders and decided that the term TRD had somewhat different definitions in different studies and was potentially open to misinterpretation. Therefore it would be more appropriate to use the term 'no or limited response after initial treatment' in the guideline. The committee thought this term would have more clinical utility as many

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				therapy to these patient groups we would be willing to work with the GDG and NICE to ensure evidence of effectiveness from these services can be reflected appropriately in the guideline.	patients, (typically more than 50%) have a limited response to initial treatment. In addition, the populations included in these trials often had a number of previous episodes of depression and significant prior (potentially relatively recent) experience of treatment. Another factor the committee considered in coming to this decision was that in the currently available data, outcomes of treatment for people with TRD or no/limited response were broadly the same. A number of stakeholders argued that TRD and chronic depression were essentially similar. The committee took the view that this is consequence of a misunderstanding of the current definition of TRD. In addition to this misunderstanding, the data on the populations in chronic depression revealed considerable heterogeneity in populations, for example trials may include participants with dysthymia, double depression, and chronic depression. Given the heterogeneity of populations and consequent uncertainty about the evidence the committee were not able to generate specific recommendations for groups such as those with dysthymia, double depression, or chronic depression and therefore thought it appropriate to change the overall term from 'chronic depression' to 'chronic depressive

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					symptoms'. The committee considered a number of comments on the use of the term 'complex depression' in this guideline. In the guideline 'complex depression' was limited to depression that was co-morbid with a personality disorder. A number of stakeholders pointed out that other factors such as other mental health co-morbidities, drug and alcohol misuse, social and environmental factors and a history of poor response to treatment can also contribute to a diagnosis of complex depression. The committee considered these factors and noted that co-morbidity with a range of other mental disorders also occurred in participants in studies for first line treatment, TRD and chronic depression. The committee therefore considered that co-morbidity alone would not be useful in describing complex depression. The focus on depression that was co-morbid with personality disorder was because of the committee's knowledge and experience that it can complicate the treatment of depression (see for example the meta-analysis by Newton-Howes et al (2006) Personality disorder and the outcome of depression: meta-analysis of published studies. British Journal of Psychiatry, 188, 13-20)). The committee therefore decided to

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					stay with the current definition of complex depression used in the guideline as alternative suggested definitions did not clarify the issue. However they acknowledge there are limitations with this definition of complex depression.
Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	general		We welcome the explicit recommendation to improve provision to under-represented population groups. We are concerned that this will not happen because the range of interventions that is being commissioned is becoming narrower and more restricted to the detriment of the diverse needs of whole populations. The impact of IAPT has been to restrict investment in CBT only. Other evidence-based therapies are progressively being eradicated from the NHS both from primary and secondary care and from specialist services. This is detrimental to local health populations and is having the unintended consequence that more and more people are being forced onto long-term anti-depressant treatment, which they do not want, because they have tried CBT and it didn't work. The GDG needs to consider whether a similar consequence will occur following this guideline and whether existing inequity of provision will be made worse. The current workforce plans for IAPT continue to expand CBT and widen inequity.	Thank you for your comment. Based on evidence of clinical and cost effectiveness, the guideline makes recommendations for a range of different psychological therapies, not only CBT, and also for pharmacological interventions. As part of implementing this guideline, commissioners will need to ensure that the interventions recommended in the guideline are made available. As you will be aware, the current IAPT programme has existing national commissioning guidance and the funding for a range of training programmes for counselling, IPT, STPT and couples therapy which clearly support the development of a broad range of psychological therapies within the IAPT programme.
Association for	short	gener	gene	We would like to point out that the use of an	Thank you for your comment. This guideline

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Family Therapy and Systemic Practice		al	ral	individualistic 'disease' model of depression is a particular perspective which encourages focus on individual intrapsychic factors and encourages less consideration of the relational, social, cultural, economic and other contextual factors which are likely to be an important part of the person's experience of what is being labelled as depression. This model is highly influenced by western individualised cultural assumptions and locates 'what is wrong' within the individual and suggests that the most appropriate 'treatment' is a treatment of the individual (with therapy or medication) to 'fix' this problem. We appreciate that in this revision there has been more inclusion of factors outside of the individual, and more mention of relationships. But the model of 'something wrong' with the individual remains, and influences the way that evidence is understood and communicated, obscuring the relevance of social, cultural and economic injustices and inequalities. For example, in the past, when society was unaccepting of homosexuality, therapy or medication were employed to 'fix' these individuals who did not fit into society's norms, obstructing the issue that greater acceptance in society was the more relevant issue. Likewise if people are experiencing distress from other societal causes (discrimination, marginalisation,	operates within a diagnostic/problem framework within ICD-10. However, the committee took into account a broad range of societal and contextual factors when making their recommendations. Section 1.2 of the short guideline provides recommendations on the recognition and assessment of depression.

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				violence, abuse, poverty, etc.) labelling these experiences as 'depression' obscures the need for societal change.	
Talking Mental Health Derbyshire	Short	General		We are concerned that the High intensity treatment recommendations give an absolute number for the sessions recommended, without the qualifier "up to" that is in the current guideline. In addition the removal of the statement in the existing guidelines that duration of treatment may be reduced if remission has been achieved or increased if progress is being made is also of concern. Whilst we appreciate the likely intention is to ensure patients get sufficient dose, the new guidelines mean that the NICE guidelines no longer support clinical judgements that may need to be applied in the best interests of the person to curtail treatment. This weakens the guidelines.	Thank you for your comment. We have amended the recommendation to clarify that it is 'up to' 16 sessions as you suggest.
Talking Mental Health Derbyshire	Short	General		We have gathered clinical data to illustrate the effectiveness of IPT for severe depression. Please would NICE consider calling for research in this area as the quality of studies in this area was of low quality and the available sample size with IAPT offering IPT is growing.	Thank you for your comment. The committee prioritised recommending research into the mechanisms of action of effective psychological interventions for acute episodes of depression. It is possible that IPT will be included in such future research.
RCGP	SHORT	General	General	Really welcome to have increased focus on psychological treatments but disappointing lack of information and sometimes contradictory information around prescribing.	Thank you for your comment. We have revised the recommendations about medication to make them clearer.
RCGP	SHORT	Gener	Gen	There needs to be much greater clarity	Thank you for your comment. Feedback was

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		al	eral	around roles and responsibilities between primary care and secondary care, especially round starting, changing and discontinuing medication and the monitoring of medication.	received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Association for Family Therapy and Systemic Practice	short		1.14.9	'make the full range of recommended psychotherapies (group CBT, CBT or BA) available' – this is not the full range included in the rest of the recommendations and this should be consistent.	Thank you for your comment. We have clarified that the psychological therapies recommended in this guideline should be made available.
Relate	Short	44-48		As we note above, again here in the recommendations, we are concerned that couples therapy for depression is missing from the interventions recommended for the treatment of less severe depression – despite the fact that in the full guidelines, couples	Thank you for your comment. We have clarified in the short version of the guideline that the recommendations on behavioural couples therapy apply to both more and less severe depression.

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				therapy is recommended for treatment of both more severe and less severe depression. We urge NICE to remedy this discrepancy by including couples therapy within the recommendations for less severe depression	
British Association for Psychopharmacology	short	23-26	18, page 23 to line 10, page 26	**Limited response and treatment-resistant depression (section 1.9)** However it is the recommendations for second line pharmacotherapy described in section 1.9 that cause greatest concern. As they stand we believe that they are fundamentally dangerous, not supported by the evidence base, will have a detrimental impact on provision of services and do not provide the breadth or depth of recommendations that clinicians need. If a person treated with an SSRI or mirtazapine first line has no, or only a limited, response, recommendation 1.9.2 includes the options of combining the medication with a psychological therapy or "changing to a combination of 2 different classes of medication, in specialist settings or after consulting a specialist". This is very out of kilter with current practice where patients tend to have trials of two or more antidepressants before referral into specialist care. Given that only around 50-60% of patients respond to the first antidepressant	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration

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				they try (Papakostas & Fava Eur Neuropsychopharmacol 2009;19:34-40; Rush et al. Am J Psychiatry 2006;163:1905), if the 40-50% not responding are referred into specialist care, or even if specialist care are just consultant about them, then services will be swamped. Section 1.9.5 detailing the nature of the medication combinations recommended causes great concern. Firstly, there is the recommendation "adding an antidepressant of a different class to their initial medication, for example an SSRI with mirtazapine". There are many problems with this recommendation from both a safety and evidence based perspective. These include: a) Critical to the recommendation is what constitutes a 'class' of antidepressant. Commonly antidepressants are described by both a mixture of their pharmacological action (e.g. selective serotonergic reuptake inhibitors – SSRIs) and their chemical structure (e.g. tricyclic antidepressants – TCAs), while many do not fall neatly into any grouping (e.g. vortixetine, agomelatine, bupropion). This has been highlighted as a potential cause for clinical confusion (Zohar et al. Eur Neuropsychopharmacol. 2015 Dec;25(12):2318-25). It is therefore unclear how clinicians will interpret the NICE recommendation.	between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression. Whilst we note that antidepressants can be described by their pharmacological action or their chemical structure, we think that the recommendations are clear about what antidepressants to use and will not be misunderstood. We note that combining antidepressants is potentially complex which is why we have recommended consulting with specialist care. We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations of medication which should be avoided. The footnote is only intended to highlight where an intervention has been recommended off license. In light of your comment we have amended the wording in the footnote to clarify that not all antipsychotics are licensed for the treatment of depression and remove reference to specific drugs as this was confusing. As documented in the 'evidence to recommendations' section in the full

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				b) Combining antidepressants is a potentially complex and dangerous thing to do. Some combinations are not pharmacologically logical, for example combining an SNRI, such as venlafaxine, with an SSRI, given that the former is a potent inhibitor of serotonin re-uptake in its own right and it is questionable whether it is possible to increase the degree of blockade any further with an SSRI. Of more concern is that several combinations of antidepressants are potentially dangerous. Historically TCAs have been combined with MAOIs though this is potentially dangerous combination (Ponto et al. Am J Hosp Pharm. 1977 Sep;34(9):954-61.) and other guidelines have specifically recommended that the combination of MAOIs and TCAs, SSRIs or SNRIs should not be used (Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85; Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525). Another dangerous combination is that of SSRIs and TCAs (something that is not uncommon in clinical practice). The issue is that SSRIs, particularly fluoxetine and paroxetine, inhibit the metabolism of TCAs potentially leading to dangerous plasma levels of the TCA (Vandel et al. Pharmacol Res. 1995 Jun;31(6):347-53). The guidelines, as they stand, could be used to defend using such combinations.	guideline combinations with an antidepressant of a different class, antipsychotics (aripiprazole, risperidone, quetiapine, olanzapine) and lithium were all identified in the reviews undertaken for this guideline as effective (i.e. they resulted in improved rates of remission or response and in depressive symptoms) in the treatment of no or limited response to initial treatment. Therefore the committee decided to recommend them. We have added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram. The guideline sets out a range of therapeutic options for the management of depression that has no/limited response. There was no evidence to support making recommendations for further lines of treatment with thyroid hormone or modafinil. Ketamine was not prioritised for investigation by this guideline as it is not a currently available first line intervention for depression, it is not licensed for use in depression and it is a widely abused drug. In these circumstance the committee did not think it was appropriate to review it. As stated above, we have revised the ordering of the recommendations on further line treatment. In doing so we have clarified

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				c) While there is data from small RCTs suggesting efficacy of some combinations of antidepressants, the largest study to date, the Co-MED study (Rush et al. Am J Psychiatry. 2011 Jul;168(7):689-701) was negative. The second element of the recommendations of section 1.9.5 is similarly unclear and potentially hazardous. This is "combining an antidepressant with an antipsychotic….". A foot note then states "At the time of consultation (July 2017) antipsychotics (with the exception of quetiapine and flupenthixol) did not have a UK marketing authorisation for this indication". It is unclear if this means that the NICE Guideline Committee are therefore recommending quetiapine and flupenthixol ahead of all other antipsychotics, or simply recommending all antipsychotics. If the latter, then the major concern with this is that there is a complete lack of evidence for most antipsychotics in combination with antidepressants for the treatment of depression. This is particularly the case for first generation antipsychotics and indeed there are two small negative studies (Anderson Adv Psychiatr Treat 2003 9: 11–20). The data for flupenthixol is old and questionable and hence it is not included as a recommended treatment in either UK (Cleare et al. J Psychopharmacol. 2015	that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. Thank you for bringing these references to our attention. Papakostas 2009, Rush 2006, Zohar 2015, Vandel 1995, Anderson 2003, Cleare 2015, Bauer 2013 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs) Rush 2011 was excluded from the chronic depression review as the study included a mixed population (<80% of the sample met inclusion criteria). Aronson 1996 and Papakostas 2008 systematic reviews were searched for relevant references but no additional studies that met the inclusion criteria were identified. Goss 2013, Han 2016 and Thase 2016 could not be included as the interventions were outside the review protocols (modafinil,

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				May;29(5):459-525) or international (Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85) guidelines, despite its UK licence. Conversely the evidence base around quetiapine is much stronger. However, it is disappointing that the NICE Guideline Committee has made no comment regarding whether or not quetiapine can be safely combined with citalopram or escitalopram due to QTc prolongation concerns of both medications. The evidence base supporting other antipsychotics (e.g. aripiprazole which is considered a first line augmentation strategy by both the British Association for Psychopharmacology (Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525) and the World Federation for Societies of Biological Psychiatry (Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85) has not even been considered. Lithium is included as an option to combine with an antidepressant. This is to be welcomed and is in line with the evidence base and other guidelines (Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525; Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85). However, it is a concern that no other options have been described beyond second line treatment. Unfortunately a significant minority of patients fail to	ketamine, and vortioxetine respectively). Jakubovski 2016 systematic review was searched for relevant references. One additional RCT was identified and added to NMA of treatment of a new depressive episode. Thanks for bringing this review to our attention. Adli 2005 systematic review was searched for relevant references. Two additional RCTs were identified and added to the further-line treatment review. Thanks for bringing this review to our attention. Thase 2006 was considered for the further-line treatment review but could not be included as the comparison (switching to different dosages of the same intervention) was outside the protocol for this review. Gaynes 2012 was considered for the further-line treatment review but could not be included as it was a secondary analysis of study that was already included (STAR*D [Rush 2006; Trivedi 2006]) Corya 2006 and Shelton 2005 were included in the further-line treatment review. Cipriani 2011 could not be included as the

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				respond to first and second line treatments. NHS clinicians are in need of advice with regards to what treatment options such be considered in such circumstances. There is an evidence base for a number of options including thyroid hormone (Aronson et al. Arch Gen Psychiatry 1996 53: 842–848) and modafinil (Goss et al. J Clin Psychiatry 2013 74:1101–1107. These and other options are included in other guidelines (Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525; Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85) and are conspicuous by their absence in these NICE guidelines. There is also growing evidence for the use of ketamine for MDD with published meta-analyses (e.g. Han et al. Neuropsychiatr Dis Treat. 2016 Nov 3;12:2859-2867) and, indeed, a growing number of centres in the UK providing this. We are unclear why NICE has chosen not to mention this at all in the guideline. Section 1.9.7 describes alternatives to using two medications (for a person refusing psychological therapies or in whom psychological therapies may not be appropriate). These include increasing the dose of the antidepressant or switching. There is a footnote saying "There is limited evidence to support routine increases in dose of antidepressants or switching in people who	population were outside scope (treatment of acute mania).

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				have not responded to initial treatment". We dispute this particular contention as well as placing this option after using drug combinations on the following grounds: a) It is the case that there is limited evidence of a dose response relationship with SSRIs, though there is some (Jakubovski et al. Am J Psychiatry. 2016 173(2): 174–183). This does not appear to have been considered by the committee. There is more evidence around a dose response relationship for other antidepressants (e.g. TCAs (Adli et al. Eur Arch Psychiatry Clin Neurosci 2005 255: 387–400), venlafaxine (Thase et al. J Clin Psychopharmacol. 2006 Jun;26(3):250-8.) and vortioxetine (Thase et al. Eur Neuropsychopharmacol. 2016 Jun;26(6):979-93)). b) While remission rates with first line treatment with an SSRI are around 30-40%, remission rates of patients who have failed one SSRI are 24% if switched to another SSRI and 28% if switched to a drug from a different class (Papakostas et al. Biol Psychiatry. 2008 Apr 1;63(7):699-704). Given the decreasing response and remission rates seen with any treatment after each successive treatment failure (Rush et al. Am J Psychiatry 2006;163:1905), such remission rates following switching antidepressants are not to be ignored.	

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				c) There is limited evidence comparing increasing dose or switching with combining two drugs. However a study of olanzapine plus fluoxetine versus switching to venlafaxine in SSRI non-responders found no difference (Corya et al. Depress Anxiety. 2006;23(6):364-72), with a similar finding when the comparative antidepressant was the TCA nortriptyline (Shelton et al. J Clin Psychiatry. 2005 Oct;66(10):1289-97). Similarly there was no significant difference in response or remission rates or time to response or remission, between patients who switched antidepressant versus those who had their antidepressant augmented in the Star*D study (Gaynes et al. J Clin Psychopharmacol. 2012 Feb;32(1):114-9). Increasing the dose of an antidepressant (in a patient who is tolerating the medication), or switching to another antidepressant are both likely to be safer than combining two medications together, are associated with fewer side effects and are also well within the capacity of primary care, removing the need for referral to specialist services or obtaining specialist advice for a vast number of patients. It is therefore most likely that such options are more cost-effective second line pharmacological options than those recommended in the draft guidelines. In relation to these discussions around	

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				switching antidepressants, it is a concern that there has been no mention of drugs such as venlafaxine which may have slightly greater efficacy compared to other modern antidepressants (e.g. Cipriani et al. Lancet. 2011 Oct 8;378(9799):1306-15) or vortixoetine which NICE has recommended as a potential third line option (TA367). It is very unclear how such a recommendation fits into the recommendations of the draft Guidelines.	
College of Mental Health Pharmacy (CMHP)	Short	17-18		There are 86 lines devoted to psychological therapies, and 5 lines on antidepressants. This is embarrassingly inappropriate and unbalanced.	Thank you for your comment. We agree that there is greater detail on psychological interventions in the guideline. We thought this reflected the necessary complexity in adequately describing the range of interventions and their appropriate place in the care pathway. We have also made changes to the recommendations for medication and believe we now have a balanced set of recommendations which properly reflect the evidence reviewed.
Sussex Partnership NHS Foundation Trust	Short	12-13		1.4.7-1.4.9 We think it is this amount of information is highly unlikely to all be taken in on first assessment / prescribing. There needs to be an on-going process of discussing this information as the patient improves and /or at the appropriate time in treatment process. We think there should also be mention of possible length of treatment, and the effect of antidepressants	Thank you for your comment. The recommendations give guidance on what information people need to have in relation to taking antidepressant medication. They do not specify when this information should be provided. This will depend on the individual and the current wording of the recommendation allows for this flexibility.

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				on other medication that may be taken.	
Sussex Partnership NHS Foundation Trust	Short	18-19		1.5 and 1.6 – we think that consideration should be given to recommending MBCT as a first-line treatment for both less severe and more severe depression in order to increase patient choice. This is based on a meta-analysis of randomised controlled trials (Strauss, Cavanagh, Oliver, & Pettman, 2014). Only one of the included trials was restricted to people with more severe depression.	Thank you for your comment. Whilst 2 studies of MBCT were included in the NMA for treatment of a new depressive episode, the committee did not consider that the evidence was strong enough to support recommending this intervention, which was primarily developed for relapse prevention, for first line treatment. Strauss 2014 systematic review has been checked for relevant studies. Only one study meets our criteria for inclusion and that had already been included.
Sussex Partnership NHS Foundation Trust	Short	26-27		1.10.3 – We expected that lithium might be mentioned as a possible adjunctive treatment. We think the choice of amisulpiride as the anti-psychotic is odd. We would usually use quetiapine or aripiprazole. We are not aware of the use of amisulpride in depression and could only find limited studies referring to it, where it seems to have no benefits over other antipsychotics, including the licensed quetiapine.	Thank you for your comment. As documented in the 'evidence to recommendations' section in the full guideline, there was some evidence for benefits of tricyclic antidepressants, moclobemide and amisulpride in people with chronic depression where an SSRI was not appropriate. The committee therefore agreed that these should be given as examples of pharmacological interventions that could be considered in these circumstances.
Association for Family Therapy and Systemic Practice	short	39-40		The research recommendation here is focused on identifying effective 'mechanisms of action' to 'isolate the most effective components'. This way of thinking may not necessarily apply to the complexities of therpay as this always happens in a relational	Thank you for your comment. A focus on mechanisms of action should not be confused with specific therapeutic techniques. Different techniques, including those taking account of relational context, may nevertheless operate through the same

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				context. Isolating techniques can encourage neglect of the important relationship and collaborative aspects of therapy, as well as the inclusion of important wider relationship and wider societal experiences within the therapeutic conversation.	underlying psychological mechanism.
Lundbeck Limited	Short	24-25	1-29;1-23	We are surprised by the recommendations for second- or further-line options for treating chronic depression (i.e. where insufficient response has been achieved with an SSRI) for two reasons. (i) The draft guideline recommends trying classes of AD that are known to be associated with a high side-effect burden (tricyclic ADs, moclobemide) and which should only be prescribed by specialist mental health professionals (in secondary or tertiary care), or off-label treatment (amisulpride); (ii) The draft guideline makes no mention of vortioxetine, which is extremely relevant to this treatment setting. Vortioxetine is a NICE-recommended treatment option for people with depression who have failed two or more ADs *within the current episode*, i.e. those who have chronic depression. It is inconceivable that the GC prefers to recommend treatments which are	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication.

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				off-label and/or older classes of drugs known to be associated with a high side effect burden over a newer generation AD which NICE recommended as a clinically- and cost-effective treatment option in 2015. **Reference:** NICE Technology Appraisal 367: Vortioxetine for treating major depressive episodes. November 2015.	
Camden & Islington NHS Foundation Trust	Short	19-20	1-18	We are concerned about the recommendations regarding IPT for different severity of presenting depression. We note that less severe refers to a baseline phq score of 10-17 and more severe to a baseline phq of 18 and above. We are concerned that the consultation document places IPT only as a second line intervention for patients presenting with less severe depression and that it does not recommend it as a treatment for those presenting with more severe depression. Within our service we provide a successful and expanding IPT service for patients resenting with depression. Over the past 5 years we have consistently achieved recovery rates well above 50%. Our data from January 2012 up to July 2017 shows a 58% recovery rate for patients receiving IPT within our IAPT clinic (sample size of 91	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The caveats for the application of IPT in less severe depression are based on the committee's consideration that the effectiveness and cost effectiveness of these interventions was likely to be higher in the sub-population specified in the recommendation, compared with the 'general' population with less severe depression that was the focus of the

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				patients). Of those, we achieved a recovery rate of 44% with patients presenting with a baseline phq score of 18 and above, with 77% showing reliable change. **Were the new guidelines to be implemented IPT would only be offered to a very small proportion of these patients who's baseline phq score fell between 15 and 17 and therefore would not be offered to the majority of these patients for whom IPT has been shown to be highly effective.** Given the above as well as the issue of patient choice we feel very strongly that IPT should be offered as an option for first line treatment for patients presenting with more severe depression. The current recommendations would not involve patients being given the choice of IPT as a treatment option. This feels very limiting - meaning that people presenting with with relational issues and depression will not have a treatment that fits with their experience readily available, especially within the NHS in primary care. Many patients present to us with an understanding of their depression within an interpersonal context, and/or are find the model makes sense as is of great help to them. For these patients presenting for treatment for depression we believe that it	guideline economic analysis. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).

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				should be offered as a first line option for treatment	
Dorset HealthCare University NHS Foundation Trust	Short	45 - 46	11	We are concerned that this recommendation implies that Interpersonal Psychotherapy (IPT) is unsuitable for patients with more severe depression. This recommendation will be a challenging change in practice has cost implications as Dorset healthcare University Foundation NHS Trust has been providing IPT for Depression in primary care since 2010; and, since 2015, has invested in training and supervision so that patients who suffer with depression in the severe range can be offered IPT as a treatment option, in line with the 2009 NICE Guidelines. This has been particularly important for patients who are unable to make use of CBT; who have recurrent depression and /or repeating Interpersonal patterns of difficulty. Of those offered IPT a greater proportion, specifically 86%, has been delivered to patients in the more severe range (PHQ18+) compared with those in the less severe range, specifically 14%. From a clinical point of view this recommendation will be difficult to implement as the delivery of IPT for depression relies on each patient's awareness and experience of their depression symptoms pre, post and during treatment so that they can see the impact that their improved Interpersonal	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment

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				functioning has on their depression. In other words, they learn what the specific interpersonal changes have on their depression, thereby improving both their chances of recovery and maintenance of the same. Those who enter treatment in the less severe range (PHQ9 10-17) are less aware of their symptom experience and find it harder to notice the specific links with their interpersonal functioning; in other words, they are less aware of their symptom experience and impact that their interpersonal changes have on their depression. From 3rd March 2015 – end August 2017 of those patients that entered treatment in our service who only received IPT : - 75% in the severe range (PHQ9 18+) showed clinically reliable improvement. - 60% in the less severe range (PHQ9 10-17) showed clinically reliable improvement.	of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Dorset HealthCare University NHS Foundation Trust	Short	45 - 46	11	Our Trust has experience of implementing Interpersonal Psychotherapy (IPT) and would be willing to submit its experiences to the NICE shared learning database.	Thank you for your comment. We will pass this information to our local practice collection team. More information on local practice can be found here https://www.nice.org.uk/about/what-we-do/into-practice/local-practice-case-studies

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British Association for Psychopharmacology	short	12-13	13, page 12 to line 4, page 13	This recommendation includes a large number of issues that patients should be given information about when prescribed an antidepressant. In general, we agree with this recommendation. However the extent of the information is such that it is totally unrealistic to expect all of this to be imparted at a single consultation, especially in primary care and especially to patients suffering from depression. We would suggest that the recommendation be amended to suggest that this information is imparted over a number of consultations. The third bullet point states "how treatment might need to be carried on even after remission". We do not agree with the tenor of this recommendations, for the reasons detailed above regarding section 1.8. While there MAY possibly be equal efficacy in relapse prevention between MBCT alone and antidepressants alone, this is based on one study with a major flaw. Conversely, there is a wealth of data demonstrating that antidepressant continuation after the point of remission significantly decreases relapse rates with a large effect size. As a result, we argue that the expectation should be that antidepressants will continue after remission, unless there is a good reason not to do so.	Thank you for your comment. The recommendations give guidance on what information people need to have in relation to taking antidepressant medication. They do not specify when this information should be provided. This will depend on the individual and the current wording of the recommendation allows for this flexibility. We have amended recommendation 1.4.9 to clarify that patients should receive information on how the need for treatment to carry on after remission will be assessed.
British Association for	short	13-14	18, page	These sections relate to discontinuing medication and discontinuation syndromes.	Thank you for your comment. We have added another recommendation to clarify

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Psychopharmacology			13 to line 15, page 14	This is valuable guidance. We are unclear why details of specifically risky medication (venlafaxine and paroxetine), that were mentioned in CG90, have been removed.	that paroxetine and venlafaxine are more likely to be associated with discontinuation symptoms.
British Association for Psychopharmacology	short	21 - 22	18, page 21 to line 24	**Relapse prevention (section 1.8)** There is a myriad of data demonstrating efficacy of antidepressants for relapse data given that such data is a requirement for a drug to be licensed in Europe. Meta-analysis demonstrates the large effect size of medication versus placebo in placebo controlled studies (e.g. Geddes et al. Lancet. 2003 Feb 22;361(9358):653-61). We are therefore somewhat surprised that the first option listed in recommendation 1.8.3 for patients who have recovered on medication is CBT, even if continuing medication is listed immediately afterwards. For people with severe depression who have recovered with medication, recommendation 1.8.4 is MBCT or group CBT with medication or MBCT or group CBT alone. We presume that the recommendation for the combination of medication plus MBCT is based on the Huijbers et al 2016 study (B J Psych 208 (4) 366-373). However, support for MBCT without antidepressants for relapse prevention is less clear. There is a study that has compared MBCT versus antidepressant	Thank you for your comment. We have reversed the bullet points in recommendation 1.8.3 so that continuing with medication is now the first option. The committee were aware of the effectiveness of antidepressants for relapse prevention but also considered the fact that a number of the studies had relatively short term outcomes (up to 6 months), in contrast to those studies reviewed by Geddes 2003 which were typically of 12 months or greater. The committee considered a combination of psychological intervention and medication to be the preferred option for relapse prevention, but noted that some people do not want to continue with medication. In those circumstances, having considered all the evidence, the committee agreed it was appropriate to recommend psychological interventions alone. Geddes 2003 systematic review was searched for relevant references but no additional studies that met the inclusion

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				in preventing relapse (Kuyken et al. 2015). In this study there was no significant difference between arms. We presume that this is the finding that has influenced NICE recommendations. However, it should be noted that 30% of the patients in the MBCT arm of this study continued on antidepressants, somewhat bringing into question whether MBCT alone really is as effective as continuing antidepressants. Conversely, the Huijbers et al. 2016 study clearly demonstrated that MBCT alone is inferior to the combination of MBCT with antidepressants. We feel that this information needs to be emphasised in the guidelines, ensuring that patients are aware of this before deciding on what treatment they might prefer.	criteria were identified Huijbers 2016 and Kuyken 2015 are included in the relapse prevention review.
British Association for Psychopharmacology	short	26-27	11, page 26 to line 15 page 27	We have a number of concerns regarding this section. Chronic depression is defined in the guideline as "….when a person continually meets criteria for the diagnosis of a major depressive episode for at least two years." However, much of the evidence that has been used to support the recommendations made in section 1.10 actually relate to dysthymia. As the Committee will be aware, dysthymia is defined as the presence of depressive symptoms NOT meeting criteria for MDD. An additional issue is that the population with 'chronic depression' overlaps	Thank you for your comment. In analysing the data we found that a number of the populations in the trials met a range of diagnostic criteria including chronic depression, double depression and persistent residual symptoms. After discussion the committee agreed the most productive way to address this properly was to formulate recommendations for chronic depressive symptoms which would encompass the range of problems referred to in your comment. We have adjusted the title and wording of the recommendations

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				substantially with the population of patients with 'treatment resistant depression' (TRD). This means that the pharmacological recommendation of using an SSRI as the first line pharmacological agent is in many cases irrelevant. The biggest concern we have with regards to this section is the recommendations for medication options if an SSRI fails to lead to remission. Given the overlap of chronic depression with TRD and the definition of chronic depression used in the guidelines, it is unclear why the medication options recommended in section 1.9 are not included here. Indeed many of the patients included in the studies used to support the use of combinations of medications have an episode duration of over 2 years. The medication options recommended are somewhat perplexing. A switch to a TCA or moclobemide is recommended, despite the statements in section 1.9 that there is little value in switching antidepressants. The rationale for the recommendation for TCAs is not clear. We assume the rationale for the recommendation of moclobemide or amisulpride is on the basis of the network meta-analysis of Kriston et al. 2014 (Depress Anxiety 31: 621–630). This suggested an advantage of moclodemide and amisulpride over fluoxetine in patients with persistent	accordingly. A number of studies that are categorised in further-line treatment would also meet criteria for chronic depression. The distinction was made on the basis of the treatment strategy. For studies where participants were randomised at the point of non-response and treatment strategies included increasing dose, augmenting or switching, the study was allocated to the further-line treatment review (even if participants would also meet criteria for chronic depression). If a study included participants with chronic depression and treatment was first-line (or it was not clear from the paper that a further-line treatment strategy was being tested), the study would be allocated to the chronic depression review. As documented in the 'evidence to recommendations' section, the committee considered that although the balance of the evidence was in favour of an SSRI over alternative pharmacological interventions, some people may not be able to tolerate an SSRI or have failed to respond to previous treatment with an SSRI, and for these people an alternative pharmacological intervention would be needed. There was some evidence

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				depression as defined by DSM-5. There are at least two concerns about the extrapolation of these findings to the recommendations made for 'chronic depression' as defined in the NICE guideline. Firstly, the studies included in this network analysis were predominantly of patients with dysthymia rather than patients with chronic MDD. Of the studies including amisupride, Amore 2001 was of patients with dysthymia +/- MDD, Smeraldi 1998 was of patients with dysthymia or MDD in partial remission, while the studies of Leon 1994, Boyer 1996, Belino 1997, Bogetto 1997, Ravizza 1999 and Rocca 2002 entirely consisted of patients with dysthymia. The second issue we have with regards to the extrapolation from this study to recommend moclobemide or amisulpride for Chronic MDD is that these two drugs were only superior to fluoxetine. They were not superior to paroxetine, sertraline or imipramine. As for non-chronic depression, the second line treatments (after a single trial of an SSRI) are recommended for use in specialist care or with specialist advice. As we have argued above, such a recommendation will lead to a dramatic increase in demand on specialist services and it is unclear that there are not more cost-effective approaches that could be employed at a primary care level.	for benefits of tricyclic antidepressants, moclobemide and amisulpride, and the committee agreed that these should be given as examples of pharmacological interventions that could be considered in circumstances where an SSRI was not appropriate. However, due to concerns around the tolerability of these drugs and potential drug interactions the committee agreed that these should only be prescribed in a specialist setting or after consultation with a specialist. The rationale for the recommendation of moclobemide or amisulpride is based on the pairwise analysis and network analysis in the current guideline and not on the network meta-analysis of Kriston 2014. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social

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					functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Royal College of Psychiatrists	Short	Sections 1.5-1.6		The only specific reference to pharmacotherapy is 'an SSRI or mirtazapine': there is no guidance on how to choose between an SSRI and mirtazapine, and grouping SSRIs in this way neglects their rather diverse pharmacological properties. Important pharmacokinetic differences are neglected, but paroxetine, fluvoxamine and fluoxetine have the propensity for pharmacokinetic interactions with other medication. When considering discontinuation symptoms (sections 1.4.9 to 1.4.13), there is no mention of drugs that are more likely to cause such symptoms (e.g. the SSRI paroxetine and SNRI venlafaxine). Furthermore, general practitioners are often uncertain whether the SSRIs citalopram or escitalopram should still be used, given the evidence for a dose-related increase in QTc in the ECG, but this aspect of treatment is not mentioned.	Thank you for your comment. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with the patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable. We have added another recommendation in section 1.4 to clarify that paroxetine and venlafaxine are more likely to be associated with discontinuation symptoms. In recommendation 1.4.11 we have also noted that the pharmacokinetic profile needs to be taken into account when stopping antidepressant medication. We have also added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram.

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Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	1.4.1 pages 10-11	29-30 1-7	We welcome the recommendation that a person's preferences should be elicited routinely and that choice of intervention type and gender of therapist should be offered, and that options should be considered if the initial intervention is not helpful. We are concerned that this will not be implemented, however, or will be implemented unevenly. We would make the following suggestions to strengthen this recommendation: 1. The 2nd national audit of psychological therapies for depression reported evidence about service user priorities for preference and this should be referred to so that it is clear this recommendation is supported by evidence 2. Elsewhere (in the Full guideline) there is a statement attributed to the service user / carer members of the GDG that appears to downgrade the need for choice of treatment type, which is contradicted by the evidence, and contradictory to this recommendation. This statement of opinion is not helpful, not justified by the evidence, and should be removed from the Full guideline so there is consistency. 3. In order to support clinicians and providers this recommendation should point to a user-friendly tool for	Thank you for your comment and support for the recommendations. 1. We have not reviewed the 2nd national audit of psychological therapies for depression as part of the evidence base, so we are not able to make reference to it. 2. We have reviewed this text and agree that it is confusing. It has been amended to make it clear that patient choice is important. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person. 3. We have not looked at the evidence on the effectiveness of different tools for establishing patient preference. Therefore we are not able to make any recommendations about this. 4. We are aware that IAPT has programmes specifically aimed at reducing waiting times and increasing choice. It will be a matter for national and local implementation to address the issues you raise in our comment. 5. We have not reviewed the evidence on recovery rates in relation to treatment preferences and are not able to make and

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				establishing preference such as the IAPT patient choice questions at assessment, and this should be routinely reported along with other routine data so that pathways can be continually adjusted to meet preferences / demand 4. This recommendation should include a specific requirement on commissioners to monitor and respond to patterns of demand by ensuring their local providers have capacity to offer choice within the access standards (waiting times) that currently apply to IAPT services 5. There is evidence to show that recovery rates improve when people are offered their treatment preference and this should be emphasised in the recommendation	recommendations on this issue. This evidence may be considered by future updates of the guideline.
NHS England National IAPT Team	Short	1		Given developments to broaden characteristics and competencies in the NHS healthcare workforce, does consideration need to be given to try to capture such increased diversity in the targeting of this guidance. In mental healthcare, as part of the IAPT programme, a new Step 2 workforce, Psychological Wellbeing Practitioner, has been developed that has been proposed to represent a 'practitioner' level, 'paraprofessional' workforce. Potentially	Thank you for your comment. All NHS staff are part of the target audience for this guideline. How the recommendations in the guideline are put into practice will be a matter for local implementation.

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				recognising a wider workforce as targets of this guidance may help to broaden guidance reach and enhance the representativeness of the guidance.	
Association for Family Therapy and Systemic Practice	short	1		The term 'further line treatment' is an unusual phrase. Perhaps 'further treatment' would be more understandable?	Thank you for your comment. We have made your suggested change.
Royal College of Psychiatrists	Short	Section 1.10		'Chronic depression' is defined in the guideline as '….when a person continually meets criteria for the diagnosis of a major depressive episode for at least two years'. However, much of the evidence used to support the recommendations relates to dysthymia, which has been defined as the presence of persistent depressive symptoms that do not meet diagnostic criteria for MDD. Furthermore, the population with 'chronic depression' overlaps substantially with the population of patients with 'treatment resistant depression', so the recommendation of using an SSRI as first line pharmacological agent is often irrelevant. There are major flaws in the recommendations for medication options if an SSRI fails to lead to remission. It is unclear why medication options recommended in section 1.9 are not included here, and the suggested options are rather strange. A switch to a TCA or moclobemide is	Thank you for your comment. In analysing the data we found that a number of the populations in the trials met a range of diagnostic criteria including chronic depression, double depression and persistent residual symptoms. After discussion the committee agreed the most productive way to address this properly was to formulate recommendations for chronic depressive symptoms which would encompass the range of problems referred to in your comment. We have adjusted the title and wording of the recommendations accordingly. A number of studies that are categorised in further-line treatment would also meet criteria for chronic depression. The distinction was made on the basis of the treatment strategy. For studies where participants were randomised at the point of non-response and treatment strategies

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				recommended, despite the statements in section 1.9 that there is little value in switching antidepressants. The rationale for recommending a TCA is not clear. The reason for recommending moclobemide (or amisulpride) is presumably derived from the network meta-analysis of Kriston et al. 2014 (Depress Anxiety 31: 621–630), which suggested an advantage of moclobemide or amisulpride over fluoxetine in patients with persistent depression: however, the studies included in this analysis were predominantly in patients with dysthymia, and moclobemide or amisulpride were only found superior to fluoxetine, with no superiority over paroxetine, sertraline or imipramine.	included increasing dose, augmenting or switching, the study was allocated to the further-line treatment review (even if participants would also meet criteria for chronic depression). If a study included participants with chronic depression and treatment was first-line (or it was not clear from the paper that a further-line treatment strategy was being tested), the study would be allocated to the chronic depression review. As documented in the 'evidence to recommendations' section, the committee considered that although the balance of the evidence was in favour of an SSRI over alternative pharmacological interventions, some people may not be able to tolerate an SSRI or have failed to respond to previous treatment with an SSRI, and for these people an alternative pharmacological intervention would be needed. There was some evidence for benefits of tricyclic antidepressants, moclobemide and amisulpride, and the committee agreed that these should be given as examples of pharmacological interventions that could be considered in circumstances where an SSRI was not appropriate. However, due to concerns around the tolerability of these drugs and potential drug interactions the committee

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					agreed that these should only be prescribed in a specialist setting or after consultation with a specialist. The rationale for the recommendation of moclobemide or amisulpride is based on the pairwise analysis and network analysis in the current guideline and not on the network meta-analysis of Kriston 2014. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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Royal College of Psychiatrists	Short	1.4.10 .		This makes recommendations about the period over which to withdraw medication, depending on the length of treatment with the antidepressant. There are some data suggesting length of treatment is a factor in deciding the duration over which withdrawal should occur (Schatzberg et al. J Clin Psychiatry. 2006; 67 Suppl 4: 27-30), but the basis for the recommendations seems unclear. The guideline should probably state that the duration of withdrawal should also depend on the pharmacokinetic properties of the antidepressant.	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.10 to ensure that when stopping medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms. In recommendation 1.4.11 they have also noted that the pharmacokinetic profile needs to be taken into account when stopping antidepressant medication. Schatzberg 2006 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs).
Association for Psychoanalytic Psychotherapy	short	1.4.1 to 1.4.6	29-30 1-25	We welcome the specification of use of outcome monitoring, treatment manuals, training competence, review and supervision	Thank you for your comment. We agree these are important issues but these will be matters for local implementation of the

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in the NHS (APP)		pages 10-12	1-5	of effective delivery of interventions and audit. Again, we have concerns that this will be implemented unevenly, as was found by the 2 national audits for psychological therapies for depression. The 1st audit found that adherence and use of the above quality criteria was widely variable. The 2nd audit found that whereas CBT had improved in standard, and that training and supervision of CBT therapists was now close to 100%, in the other therapies being delivered there was evidence of untrained, unsupervised practice continuing. To strengthen this recommendation, therefore, we suggest the following: 1. Commissioners should be asked to reflect these standards in their specifications for providers 2. Reference to the evidence from the national audits should be made, and specific reference to the gaps that were found in skills, training and supervision should be highlighted 3. Providers should be encouraged to draw up, carry out and report on the outcome of regular local audit to ensure these recommendations are fully implemented	guideline. We have not reviewed the national audits of psychological therapies for depression as part of the evidence base, so we are not able to make reference to them.
Association for Psychoanalytic Psychotherapy	short	1.5.1 1.5.3 1.5.5	20-28 1-22	We are not aware of any evidence that supports group CBT as more effective than other interventions and we are concerned	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the

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in the NHS (APP)		pages 16-17		that providers will adopt a rigid stepped care model where in practice people will be forced to have a psychological intervention in a format they do not feel safe in (e.g. vulnerable individuals in a group setting who are harmed by exposure to negative interactions with other group members). It is very difficult to prevent this without thorough assessment and selection procedures, but these are not specified in the draft. Likewise, whilst 1.5.3 and 1.5.5 both state that these options should be offered to people "who do not want" group CBT, we are concerned that this will not be implemented and that current very high levels of attrition (people not taking up treatment offers in IAPT services) will increase even further as a result of this recommendation. To mitigate this harm, we suggest: 1. The offer of group CBT should be made on an opt-in basis and a preference for group CBT should be stated by the service user 2. Before taking up the offer of group CBT, a second option preference should be elicited as the fall-back plan if group CBT does not help 3. The full range of options should be explained in user-friendly language and people should be offered their first preference treatment, if they have	treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5).

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				one, as this is supported by the evidence 4. Where service users do not have a preference the stepped care model should be followed with a review following the initial intervention	
Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	1.5.14 page 19	13-20	Whilst we welcome the way that STPT is indicated as suitable for specific presentations and consider this a marked improvement on previous guidelines we are concerned based on the evidence from previous guidelines that a recommendation of what is effectively a 3rd or 4th line option will simply not be commissioned and that there is no justification for differentiating STPT from CBT given the evidence of equivalence / non-inferiority in the RCTs that have been included in the review. In whatever way that this guideline recommends CBT is offered, STPT should be offered similarly. Following the 2009 guidance the availability of access to STPT was reduced. It will be reduced even further when this guideline is published if the current draft is not amended. We suggest that the recommendations make it clear that: 1. CBT, BA, IPT, Counselling and STPT should all be provided as treatment options as there will be some service users for whom any one of these is best matched to their individual needs.	Thank you for your comment. We do not agree that STPT will not be commissioned based on the recommendations made in the guideline. As you may be aware there is an existing training programme for STPT delivered through the IAPT programme. This is supported by policy guidance which sets out the need for choice in IAPT services, including STPT and counselling. In developing the guideline we can only make recommendations for those interventions where there is evidence of their effectiveness. The evidence examined does not support equivalence between STPT and CBT. Therefore we have not made your suggested changes to the recommendations. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost

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				2. The evidence supports treatment selection amongst the above options being guided by service user preference, previous treatment history, and indicators for suitability based on the match between the specific treatment mechanism and the precipitating factors – elsewhere in the guidance this is what is recommended. 3. There is no evidence for greater clinical effectiveness, cost effectiveness or reliability of CBT, BA or IPT compared with STPT. The current 'sequenced model' at high intensity will have the effect in practice of denying access to STPT for those patients for whom STPT is indicated. 4. Alternatively, the guideline could refer to experience from the previous guideline which showed that STPT was not offered and that access to STPT was reduced as a result of commissioners only investing in CBT. If a specific recommendation is made to commissioners to ensure that access to STPT increases (based on current levels) this may mitigate the harm from a sequenced approach. 5. There was no economic modelling to support the sequencing of CBT and	effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues.

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				BA, followed by IPT, followed by Counselling and STPT and that it may be equally or more cost effective to reverse this sequencing and monitor the impact locally. The evidence from the IAPT data suggests that CBT should be offered last as it has the lowest recovery rates for depression at high intensity for the past 2 years.	
Royal College of Psychiatrists	Short	Section 1.8		Antidepressants have proven efficacy in the prevention of relapse, meta-analysis demonstrating the large effect size of medication versus placebo in placebo-controlled studies (e.g. Geddes et al. Lancet. 2003; 361: 653-661). Given the wealth of data relating to efficacy of antidepressants, why is CBT the first option listed in recommendation 1.8.3 for patients who have recovered on medication? For people with severe depression who have recovered with medication, recommendation 1.8.4 is for MBCT or group CBT with medication or MBCT or group CBT alone. However, the support for the efficacy of MBCT without antidepressants for relapse prevention is limited: a study compared MBCT versus antidepressant in preventing relapse (Kuyken et al. 2015), and there was no significant difference between treatment arms. However, in this study 30% of patients in the 'MBCT' arm continued antidepressants, which raises	Thank you for your comment. We have reversed the bullet points in recommendation 1.8.3 so that continuing with medication is now the first option. The committee were aware of the effectiveness of antidepressants for relapse prevention but also considered the fact that a number of the studies had relatively short term outcomes (up to 6 months), in contrast to those studies reviewed by Geddes 2003 which were typically of 12 months or greater. The committee considered a combination of psychological intervention and medication to be the preferred option for relapse prevention, but noted that some people do not want to continue with medication. In those circumstances, having considered all the evidence, the committee agreed it was appropriate to recommend psychological interventions alone.

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				the question of whether MBCT given alone really is as effective as continuing antidepressants. By contrast, another study (Huijbers et al. Br J Psychiatry 2016; 208: 366-373) demonstrated MBCT given alone was inferior to the combination of MBCT with antidepressants.	Geddes 2003 systematic review was searched for relevant references but no additional studies that met the inclusion criteria were identified Huijbers 2016 and Kuyken 2015 are included in the relapse prevention review.
Royal College of Psychiatrists	Short	Section 1.9		The recommendations for second line pharmacotherapy described in section 1.9 have major flaws. They are not supported by the evidence base, would have a deleterious impact on clinical services, and could be hazardous for patient safety. If a person treated with an SSRI or mirtazapine first line has no response, or only a limited response, recommendation 1.9.2 includes the options of combining the medication with a psychological therapy or 'changing to a combination of 2 different classes of medication, in specialist settings or after consulting a specialist'. This does not reflect current practice, where primary care patients tend to have trials of two or more antidepressants before referral. Only 50-60% of patients respond to the first antidepressant (Papakostas & Fava. Eur Neuropsychopharmacol 2009;19:34-40; Rush et al. Am J Psychiatry 2006;163:1905), so if 40-50% of patients are referred to specialist services, those services will be overwhelmed.	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3

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				Section 1.9.5 recommends 'adding an antidepressant of a different class to their initial medication, for example an SSRI with mirtazapine', but there are considerable problems with this recommendation. First, no guidance is provided on what constitutes a different 'class'. Second, combining antidepressants is potentially complex and dangerous (for example combining an MAOI with an SSRI). Third, there are limited data on the efficacy of combinations of antidepressants, and the largest study (Rush et al. Am J Psychiatry 2011; 168: 689-701) was negative. Section 1.9.5 also comments on combinations of an antidepressant with an antipsychotic. A footnote states 'At the time of consultation (July 2017) antipsychotics (with the exception of quetiapine and flupentixol) did not have a UK marketing authorisation for this indication', so it is unclear whether this means that the guidance therefore recommends quetiapine or flupentixol ahead of all other antipsychotics, or is simply recommending all antipsychotics. If the latter, there is a lack of evidence for most antipsychotics in combination with antidepressants for treating depression. Furthermore, the data for flupentixol is old and questionable and not included as a recommended treatment in either UK (Cleare	(short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression. We note that combining antidepressants is potentially complex which is why we have recommended consulting with specialist care. We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations of medication which should be avoided. The footnote is only intended to highlight where an intervention has been recommended off license. In light of your comment we have amended the wording in the footnote to clarify that not all antipsychotics are licensed for the treatment of depression and remove reference to specific drugs as this was confusing. As documented in the 'evidence to recommendations' section in the full guideline combinations with an antidepressant of a different class, antipsychotics (aripiprazole, risperidone, quetiapine, olanzapine) and lithium were all identified in the reviews undertaken for this

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				et al. J Psychopharmacol. 2015; 29: 459-525) or international (Bauer et al. World J Biol Psychiatry. 2013; 14: 334-85) guidelines. By contrast, the evidence base for quetiapine is much stronger, but there is no guidance on whether quetiapine can be safely combined with citalopram or escitalopram due to QTc prolongation concerns of both medications (see above). In addition, the evidence base supporting other antipsychotics (e.g. aripiprazole which is considered a first line augmentation strategy by both the BAP and the World Federation for Societies of Biological Psychiatry is not considered. Lithium is included as an option to combine with an antidepressant, which is appropriate. However, no other options are described for steps beyond second line treatment. Many patients do not respond to first and second line treatments, and NHS clinicians are in great need of clear advice about what treatment options such be considered in such circumstances. There is an evidence base for a number of options including thyroid hormone (Aronson et al. Arch Gen Psychiatry 1996 53: 842–848), modafinil (Goss et al. J Clin Psychiatry 2013 74:1101–1107) and ketamine (Han et al. Neuropsychiatr Dis Treat. 2016; 12: 2859-2867) but these potential options are not mentioned. Section 1.9.7 describes alternatives to using	guideline as effective (i.e. they resulted in improved rates of remission or response and in depressive symptoms) in the treatment of no or limited response to initial treatment. Therefore the committee decided to recommend them. We have added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram. The guideline sets out a range of therapeutic options for the management of depression that has no/limited response. There was no evidence to support making recommendations for further lines of treatment with thyroid hormone. As stated above, we have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. Thank you for bringing these references to our attention. Cleare 2015, Bauer 2013,

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				two medications (for a person refusing psychological therapies or in whom psychological therapies may not be appropriate). These include increasing the dose of the antidepressant or switching, a footnote commenting 'There is limited evidence to support routine increases in dose of antidepressants or switching in people who have not responded to initial treatment'. We dispute both this contention as well as placing this option after using drug combinations, on three grounds. First, there is some evidence for a dose-response relationship with SSRIs (Jakubovski et al. Am J Psychiatry. 2016; 173(2): 174–183) and for some other antidepressants [e.g. TCAs (Adli et al. Eur Arch Psychiatry Clin Neurosci 2005 255: 387–400), venlafaxine (Thase et al. J Clin Psychopharmacol. 2006; 26: 250-258), and vortioxetine (Thase et al. Eur Neuropsychopharmacol. 2016; 26: 979-993)]. Second, remission rates of patients who have not responded to an SSRI are 24% if switched to another SSRI and 28% if switched to a drug from a different class (Papakostas et al. Biol Psychiatry. 2008; 63: 699-704). Given the decreasing response and remission rates seen with any treatment after each successive treatment failure (Rush et al. Am J Psychiatry 2006;163:1905), such remission rates following switching	Rush 2006 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs) Aronson 1996 and Papakostas 2008 systematic reviews were searched for relevant references but no additional studies that met the inclusion criteria were identified. Goss 2013, Han 2016 and Thase 2016 could not be included as the interventions were outside the review protocols (modafinil, ketamine, and vortioxetine respectively) Corya 2006 and Shelton 2005 were included in the further-line treatment review. Gaynes 2012 was considered for the further-line treatment review but could not be included as secondary analysis of study already included (STAR*D [Rush 2006; Trivedi 2006]). Cipriani 2011 could not be included as the population were outside the scope (treatment of acute mania).

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				antidepressants should not be ignored. Third, whilst there is limited evidence comparing increasing dose or switching with combining two drugs, a study of olanzapine plus fluoxetine versus switching to venlafaxine in SSRI non-responders found no difference (Corya et al. Depress Anxiety. 2006; 23: 364-372), with a similar finding when the comparator antidepressant was the TCA nortriptyline (Shelton et al. J Clin Psychiatry. 2005; 66: 1289-97). In addition, the Star*D study found no significant difference in response or remission rates between patients who switched antidepressant versus those who had an antidepressant augmented (Gaynes et al. J Clin Psychopharmacol. 2012; 32:114-119). Increasing the dose of an antidepressant (in a patient who is tolerating the medication), or switching to another antidepressant are both likely to be safer than combining two medications together. Both strategies are associated with fewer side effects and within the capability of primary care, so limiting the need for referral to specialist services for a vast number of patients. It is therefore most likely that such options are more cost-effective second line pharmacological options than those recommended in the draft guidelines. In statements relating to switching	

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				antidepressants, it is surprising that neither venlafaxine (which may have slightly greater efficacy compared to other modern antidepressants - e.g. Cipriani et al. Lancet. 2011; 8; 378: 1306-1315) nor vortixoetine (which NICE recommends as a potential third line option in TA367) is recommended. It is unclear how the latter recommendation accords with draft guidance.	
Royal College of Psychiatrists	Short	1.4.8.		The extent of the information to be given to patients in a single consultation seems unrealistic, especially in primary care and for patients with depression who find it hard to attend for long periods. Perhaps it would be better if the information is provided over a number of consultations. The third bullet point states 'how treatment might need to be carried on even after remission", but it would be better to state that antidepressants should be continued beyond remission, unless there is a good reason not to do so.	Thank you for your comment. The recommendations give guidance on what information people need to have in relation to taking antidepressant medication. They do not specify when this information should be provided. This will depend on the individual and the current wording of the recommendation allows for this flexibility. Regarding the third bullet point, these are recommendations about general principles of care for people who take antidepressants. Recommendations on when specifically to use antidepressants are covered in other sections of the guideline.
Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	1.10.1 1.10.2 1.11.2		We are concerned that CBASP and CBT are recommended here for chronic depression and CBT for complex depression but psychoanalytic psychotherapy has not been recommended, when there is good evidence from the Tavistock Adult Depression trail to	Thank you for your comment. Fonagy 2015 ('Pragmatic randomized controlled trial of long-term psychoanalytic psychotherapy for treatment-resistant depression: the Tavistock Adult Depression Study [TADS]') is included in the review for further-line treatment as the

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				support this as an option, given the limited options available for this patient group. We think the GDG should reconsider including this option.	study cites their inclusion criteria as "at least two failed treatment attempts (elicited at interview and verified from medical records), one of which must have included treatment with an antidepressant medication, and the other with either an antidepressant medication or a psychological intervention". Fonagy et al 2015 was not included in the review questions for chronic depression or complex depression as it did not meet the inclusion criteria. Therefore we do not have any evidence on LTPP in either of these reviews and have not make recommendations about this intervention.
Royal College of Psychiatrists	Short	1.4.10 – 1.4.13.		Details of medications with higher risk of discontinuation symptoms (venlafaxine and paroxetine), that were mentioned in CG90, have been removed.	Thank you for your comment. We have added another recommendation to clarify that paroxetine and venlafaxine are more likely to be associated with discontinuation symptoms.
Royal College of Psychiatrists	Short	Monitoring of medication – sections 1.4.17 –		It is unclear why there is no mention of, for example, ECG monitoring of medication such as citalopram, escitalopram and TCAs, all of which can increase QTc intervals in a dose related way, or of blood pressure monitoring of venlafaxine at higher doses.	Thank you for your comment. We have added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram.

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		1.4.19			
Northumberland Tyne and Wear NHS Foundation Trust	Short	4	7-15	Good that advance planning and directives are included.	Thank you for your comment and your support.
Northumberland Tyne and Wear NHS Foundation Trust	Short	4	4-5	Enable people to engage with self-help and community resources that suit them, through informed and supported signposting. This needs to be more that awareness raising.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to the recommendation you cite.
Northumberland Tyne and Wear NHS Foundation Trust	Short	4 5	16-17 1-11	Good emphasis on family involvement but this can be more about sharing an understanding of what family or social pressures might by influencing and perpetuating the person's experience of depression and predicated on family meetings rather than on managing symptoms.	Thank you for your comment. As specified in the scope, the experience of care section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on experience of care has not been reviewed and we are not able to make any changes to the recommendations you cite.
Royal College of Speech and Language Therapists	short	4	10	The RCSLT welcome the focus on informed consent and reference to the Mental Capacity Act. However, 1-3% of the UK population has communication difficulties arising from pervasive developmental difficulties or	Thank you for your comment. The management of communication difficulties in people with depression was not prioritised for inclusion in this update. The evidence in this area has not been reviewed and we were unable to make recommendations on

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				acquired brain dysfunction (including chemical dysfunctions associated with some mental health conditions). In addition there is evidence for comorbidity between mental health disorders and physical health disorders. Possible mechanisms for this may be that mental health disorders affect the rate of other health conditions, e.g. mental health problems are associated with risk factors for chronic diseases such as smoking and obesity (de Leon *et al.* 2002), and conditions such as depression affect serotonin metabolism and inflammatory processes which are associated with cardiovascular disease and cancer (Zorrilla *et al.* 2001). Alternatively, some chronic health conditions create a psychological burden which increases the risk of mental health problems. In addition, some comorbid mental health problems affect treatment and outcomes for other health conditions (Robson and Gray 2007). Therefore speech, language and communication difficulties are relatively common and these difficulties will affect the validity of all verbally mediated assessment and treatment. We suggest that a short additional section is added to the guidelines referring to 'managing people with depression who have communication difficulties'. This	this issue.

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				would substantially add to the value of the guidelines and would be of particular value to clinicians who work within a multi-disciplinary team that does not include a speech and language therapist (very common). RCSLT would be happy to assist NICE in writing and evidencing this additional section.	
Northumberland Tyne and Wear NHS Foundation Trust	Short	5	12-22	Cultural sensitivity is important and includes understanding issues from the service user's perspective which needs to allow for the consideration of experiences of discrimination or racism.	Thank you for your comment and providing this information.
RCGP	SHORT	5	9	Confidentiality should refer to information sharing consensus document recommended by DH and GMC: http://iapdeathsincustody.independent.gov.uk/wp-content/uploads/2015/08/Information-sharing-and-suicide-prevention-—-Consensus-statement.pdf	Thank you for your comment. As specified in the scope, the patient experience section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on patient experience has not been reviewed and we are not able to make any changes to this section.
Northumberland Tyne and Wear NHS Foundation Trust	Short	6	27-28	The importance of holistic assessments is well made.	Thank you for your comment and your support.
Royal College of Speech and Language	short	6	16	There is reference to involving a family member if a person has a significant communication difficulty. This may be helpful,	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009

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Therapists				but some people will not wish to be represented by a family member, the family member may have a different view to the person and issues such as a child questioned about a parent can lead to ethical issues and a poor standard of care. A speech and language therapist, would be able to assist the clinical team in ascertaining what form of support for communication would best assist the person with significant communication	guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to the recommendations you cite.
Royal College of Speech and Language Therapists	short	6	22	There is a welcome reference to a comprehensive assessment for suspected depression. This is welcome, however, as above; this assessment will be highly verbally mediated creating a validity issue for people with speech, language and communication difficulties.	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to the recommendations you cite.
Royal College of Speech and Language Therapists	short	7	14	There is a reference to consulting with 'a relevant specialist' when developing treatment plans. This is welcome, but where a person has speech, language or communication difficulties, there needs to be explicit reference to involving a speech and language therapist to ensure that accurate communication is achieved. Ultimately this will speed up agreement on treatment and will maximise the likelihood of verbally	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to the

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				mediated interventions such as cognitive behavioural therapy (CBT) being effective if communication difficulties are recognised and the treatment plan is modified to ameliorate these added difficulties.	recommendations you cite.
Northumberland Tyne and Wear NHS Foundation Trust	Short	8	20-24	Also need to initiate discussion and share advice to the service user and family about what helps mood and maintains safety, eg lifestyle issues such as sleeping patterns, eating, gently paced activity and low demand stimulation, how friends can help.	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to the recommendations you cite.
Royal College of Speech and Language Therapists	short	8	25	It is well recognised that risk assessment may be more difficult to achieve where a person has speech, language and communication difficulties. Risk assessment itself largely relies on verbally mediated questioning and the person giving an account of their feelings. Missing any signals of distress through communication difficulty will particularly affect assessment of suicide potential. Again a speech and language therapist will be able to advise the multi-disciplinary team on how to ensure effective communication or to use alternative non-verbal strategies.	Thank you for your comment. As specified in the scope, the recognition, assessment and initial management section from the 2009 guideline was not included in this update. In line with NICE processes, the 2009 content has been carried across to this updated guideline. However, the evidence on recognition, assessment and initial management has not been reviewed and we are not able to make any changes to the recommendations you cite.
Northumberlan	Short	9	15-	More emphasis on social responses	Thank you for your comment. These are

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d Tyne and Wear NHS Foundation Trust			27	appropriate and the discussion of access to potential support eg support from friends, communities, exercise on referral, arts on referral.	recommendations on how services should be configured to provide care for people with depression. As such we do not think you changes are appropriate here. However, exercise and befriending are supported by evidence and have been referred to in the recommendations in later sections. No evidence on arts on referral was identified so we have not made recommendations on this.
Tavistock Relationships	Short	9	15	We believe that the following bullet point should be added to the list (under 'Stepped care pathways should:') – "allow entry at different steps according to assessment of clinical need rather than always requiring patients to have been through lower steps". We make this suggestion (which is in keeping with the reference to 'multiple entry points' in point 1.3.1 of the short guideline) because patients who are assessed as needing a particular therapy should not have to go through, say, a Step 2 level treatment before being referred to a Step 3 one if assessment suggests that the Step 3 intervention is most clinically appropriate.	Thank you for your comment. We have clarified in recommendation 1.3.1 that stepped care pathways should have clear criteria for entry to all levels of the service.
The Pituitary Foundation	Short	9	28	When accompanied by other long-term health conditions it is important for depression to be evaluated regularly as a patient's life story	Thank you for your comment. There is separate NICE guidance on Depression in adults with a chronic physical health problem

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				progresses- taking into account a change in physical /health circumstances.	so we have not made any changes to our recommendations as a result of your comment. However, we have included a list of related NICE guidance in the full version for information.
Action on Smoking and Health (ASH)	Short	10	Relating to general principles of care	Addressing smoking can have a positive impact on depression and anxiety in particular. A systematic review and meta-analysis published in 2014 found that smoking cessation was associated with reduced depression, anxiety and stress, and improved positive mood and quality of life compared with continuing to smoke. The effect size was as large for people with psychiatric disorders as those without. The effect sizes were equal or larger than those of antidepressant treatment for mood and anxiety disorders. [Taylor G, Change in mental health after smoking cessation: systematic review and meta-analysis, BMJ 2014 https://www.ncbi.nlm.nih.gov/pubmed/24524926] One of the concerns of staff working in mental health can be that addressing smoking while a person is seeking to manage their mental health condition could be detrimental to that person's mental health outcomes. However, the evidence points to the opposite outcome and that supporting	Thank you for your comment. This guideline is about the treatment and management of depression in adults. It is outside the scope to make recommendations on smoking cessations. For this reason, Taylor 2014 could not be included in the guideline. As you mention in your comment, this guidance already exists in Smoking: acute, maternity and mental health services and Smoking: brief interventions and referrals. We have included a list of related NICE guidance in the full version which cites these documents.

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				people who have co-morbid complex needs such as substance use to quit can improve likelihood of improved outcomes elsewhere in their lives. [Smoking and Mental Health. A joint report by the Royal College of Physicians and the Royal College of Psychiatrists. 2013 https://cdn.shopify.com/s/files/1/0924/4392/files/smoking_and_mental_health_-_full_report_web.pdf, Action on Smoking and Health, The Stolen Years, 2016 http://ash.org.uk/download/the-stolen-years-the-mental-health-and-smoking-action-report/] A standard response to all smokers with depression is needed by healthcare professionals involved in their care. This should be in line with NICE PH48 and NICE PH1. Health professionals should be confident in providing brief advice and referral to stop smoking services and advising people with depressions about alternatives to smoking such as using nicotine replacement therapy or another nicotine delivery device such as an e-cigarette.	
Northumberland Tyne and Wear NHS Foundation	Short	10 11	27-30 1-7	Suggest a more collaborative approach e.g. rather than say 'giving them' suggest ' with them developing a formulation or collaborative understanding of their	Thank you for your comment. This is a recommendation for prescribers to follow, specifying what information they need to give people about antidepressant medication. It

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Trust				difficulties, needs and assets to inform plans	has been worded in this way to ensure that prescribers give this information to people as this will enable the person to make an informed choice about their treatment. Therefore we think the term 'giving' is appropriate. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person.
NHS England National IAPT Team	Short	10	1-2	A feature of the depression pathway is to 'promote easy access to, and uptake of, interventions in the pathway' which is to be applauded and promoted. However, as Points (5, 11, 14) will establish below, the recommendation that Group CBT for depression should represent the first treatment offered on its own, could be seen to contradict the promotion of easy access and intervention uptake. Group delivery requires patients to travel to access, requiring travel demands and costs. The literature also highlights that group delivery may not represent an acceptable treatment option for all patients, especially with regards to depression, the presenting symptomatology may reduce desire to engage. Later Points, will therefore highlight concerns regarding the way in which the recommendation to initially offer groups for 'milder' forms of depression	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the

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				may contradict the stated features of a depression pathway.	committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5).
Association for Family Therapy and Systemic Practice	short	10	16-17	Whilst we welcome the inclusion of information being provided in a non-stigmatising way, using age and culturally-appropriate language and format, we would again point out that provision of a pathway heavily influenced by an individualised 'disease' model in itself may be culturally inappropriate, particularly for people used to being part of more collectivist cultures. Flexibility with ways to engage with people and ways to collaborate with them is also very important, and this may include engaging with different ways of understanding what has been labelled as 'depression' here.	Thank you for your comment. We agree that a number of factors, such as cultural factors, can impact the process of assessment, engagement and treatment. The recommendations in section 1.2 of the short guideline draw attention to this.
Tavistock Relationships	Short	10	3	Bullet point should read as follows: 'allow for prompt assessment of adults with depression, including assessment of severity and risk, as well as any relational factors involved' We make this because our experience of training PWPs, as well as the extremely low levels of delivery of Behavioural Couples Therapy in IAPT services, tells us that IAPT	Thank you for your comment. These are recommendations on how services should be configured to provide care for people with depression. As such we do not think your suggested change is appropriate. Assessment is covered in section 1.2 of the guideline.

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				services are very poor at assessing for relational factors which may be implicated in patients' depression. Given that the full draft guideline (page 37-38) includes some valuable and welcome material on the links between depression and relationship difficulties, it behoves the actual guideline to do what it can to ensure that such relational factors are routinely and properly assessed for.	
Parkinson's UK	Short	10	7	It would be extremely valuable for the recommendation to explicitly link to the 'Depression with a chronic physical health problem' clinical guideline. In order for pathways to fully deliver coordination and continuity of care as recommended under 1.3.2, treatment and support must take into account co-existing physical health problems. There should be a clear recommendation that where there is a physical health condition that professionals who are delivering mental health treatment and care, liaise directly with the professionals providing care for the physical health condition.	Thank you for your comment. We have inserted a list of related NICE guidance in the full version of the guideline. Making reference to each of these in the recommendations would not be practical as there are many NICE guidelines that contain recommendations that are potentially relevant to people with depression.
The Pituitary Foundation	Short	10	7	Coordination of care should always between mental health professionals and physical health practitioners/specialists where relevant if/when other health issues need treatment.	Thank you for your comment. We agree that where needed there should be coordination of care between mental health professionals and physical health practitioners. The current wording of the recommendation would enable this to happen.

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Tavistock Relationships	Short	10	8	We welcome the inclusion that pathways should now include routine data collection on outcomes, and hope that NICE will include this data as evidence when it next updates this guidance. This is an important development which we hope will mean that, in time, data from clinical settings will be used to inform the development of this and other NICE guidelines.	Thank you for your comment and your support.
Tavistock Relationships	Short	10	14	We know that some people are unable to access Behavioural Couples Therapy because their IAPT service does not offer this treatment outside of normal working hours. We would suggest then that 'and couples' is added to the list in brackets, as this is a group which needs to be explicitly identified in order to promote access and increase uptake of BCT. We don't feel that the inclusion of the final bullet point (see comment 5 below) is sufficient.	Thank you for your comment. Providing access to behavioural couples therapy will be a matter for implementation of the guideline.
Parkinson's UK	Short	10	26	We are concerned that carers have been left off the list of people that should be involved by commissioners and providers of mental health services as it currently only lists family/partner. We recommend that people receiving treatment and care should have the option of involving a range of people, including a family member, a carer, a partner, friend or advocate.	Thank you for your comment. We have added 'carers' to the recommendation as you suggest.

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The Pituitary Foundation	Short	10	26	This is welcomed and particularly important for family members/carers of patients with long-term condition- help to reduce stigma around which still remains	Thank you for your comment and your support.
Tavistock Relationships	Short	10	26	It is unclear what 'involvement of families/partners' means in this context (i.e. the current wording doesn't make sense). We would suggest instead that this bullet point reads: 'information which encourages the involvement of families/partners'	Thank you for your comment. We have amended the recommendation to clarify that there should be procedures to support the active involvement of families, partners and carers.
Association for Family Therapy and Systemic Practice	short	10	26	Here the guidance says 'involvement of families / partners', where elsewhere it is modified with where appropriate and in accordance with the person's wishes. Whilst relational issues are often very important in this area of experience, they are also complex, since relationships may be experienced as many different variations of supportive or coercive. Proper consultation and collaboration with the person concerned is important, as a guide to what will be most helpful. Where there are conflicts or disputes or controlling behaviour in relationships it is important that the person responsible for co-ordinating the involvement of families or partners has sufficient skills and experience in working with families or couples in therapy.	Thank you for your comment. These are recommendations on how services should be configured to provide care for people with depression. As such we do not think your suggested change is appropriate.
Janssen	Short	11	8-15	We welcome the addition of recommendation 1.4.2 in the short clinical guideline, especially as this outlines the routine use of outcome monitoring and follow up of interventions.	Thank you for your comment and support of this recommendation. We have not recommended a particular outcome measure or rating scale but we have clarified that

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				Recommendation 1.4.2 states: Provide interventions for people with depression in a framework. This should include: • an assessment of need • the development of a treatment plan • taking into account any physical health problems • regular liaison between healthcare professionals in specialist and non-specialist settings • routine outcome monitoring and follow-up. [new 2017] In current clinical practice routine outcome monitoring and follow up is not regularly done and so this is a welcome step in terms of understanding whether people have responded and whether they should be switched to alternative interventions. We suggest that the recommendation should go further and recommend an outcomes measure or rating scale that could measure response to treatments, as has been suggested in recommendation 1.8.7 for relapse prevention.	routine outcome monitoring should use validated measures. Reference to the PHQ-9 scale in the recommendations on relapse prevention has been removed in response to stakeholder feedback.
British Association of Art Therapists	Short	11	16-21	The use of treatment manuals would at the present time exclude many people from group and individual art therapy who might	Thank you for your comment. Art therapy was not prioritised for investigation in the review questions for this guideline.

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				benefit from it. Group art therapy, in particular, is likely to be cost-effective and is accessible in many places and there is an emerging evidence base for its efficacy with a range of groups of people who experience depression, including older people and those with serious physical conditions [Uttley, L. et al. (2015) The clinical and cost effectiveness of group art therapy for people with non-psychotic mental health disorders: A systematic review and cost-effectiveness analysis. *BMC Psychiatry*, 15: 151 DOI 10.1186/s12888-015-0528-4; Nan, J.K.M., and Ho, R.T.H. (2017) Effects of clay art therapy on adults outpatients with major depressive disorder: A randomized controlled trial. *Journal of Affective Disorders,* 217, pp. 237-245. DOI 10.1016/j.jad.2017.04.014]. A manual for art therapy for depression is likely to emerge in time, but in the interim, users should ensure that art therapists are qualified and HCPC registered and have regular supervision from an appropriately qualified person. Routine outcome measures are welcomed, along with additional scales the art therapist or service users may deem appropriate, such as the Rosenberg Self-Esteem scale, or PSYCHLOPS (http://www.psychlops.org.uk/), a self-report scale that allows patients to decide their own outcome goals and rate them, and which has	Consequently the papers that you cite by Uttley et al. (2015) and Nan & Ho 2017 did not meet the inclusion criteria and have not been appraised in the guideline. As the evidence on art therapy has not been appraised we have not made any recommendations on the use of this intervention.

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				good psychometric properties. A measure of alexithymia may also be considered.	
Tavistock Relationships	Short	11	1	We strongly suggest that this bullet point be amended such that people are supported to decide on their preferences having had information about the range of therapies recommended by NICE and not just those particular therapies which their local provider happens to provide (which are, for the most part, CBT and counselling). We suggest therefore that this bullet point is amended to read: 'information on what the full range of interventions recommended by NICE are, and the expected outcomes'	Thank you for your comment. We have amended the recommendation to make it clearer that it refers to information on interventions that may be provided.
Tavistock Relationships	Short	11	3	As per comment 6, we strongly suggest that this bullet point is amended to read: 'choice on the intervention type (the patient having been given information on the full range of therapies recommended by NICE)'	Thank you for your comment. We have clarified in the recommendation that there is choice of the interventions recommended in this guideline.
Tavistock Relationships	Short	11	12	We note the omission in the short guideline of any mention of relational factors. We feel this is a major oversight, particularly given the inclusion on pages 37-38 of the full guideline of helpful material regarding the links between depression and couple relationship difficulties. We urge the GC to include 'taking into account any relationship factors' in this list of bullet points	Thank you for your comment. We recognise the importance of relational factors in informing the choice of intervention and think that they would be considered as part of assessment. Recommendations on assessment are made in section 1.2. As specified in the scope, the evidence on assessment has not been reviewed and we are not able to make any changes to these recommendations.

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Association for Family Therapy and Systemic Practice	short	11	16	We recognise that there can be a tension between the use of treatment manuals and being able to work flexibly and effectively in the presence of complex contextual, relational and societal factors. This is another example of how a 'disease' model focuses understanding upon the 'effective ingredients' of the 'treatment'. Whilst this model may work well with respect to isolating effective chemical components of pharmacological treatments, for therapy it encourages focus on therapeutic 'techniques' where these are unlikely to be the most effective parts of therapy. (See 'The Great Psychotherapy Debate: The Evidence for What Makes Psychotherapy Work' By Bruce E. Wampold, Zac E. Imel (2015)).	Thank you for your comment. We recognise that non-specific factors are an important component of treatment but a consideration of mechanisms of action of different treatments is outside the scope of this guideline. The recommendations in this guideline are intended to guide healthcare professional on the appropriate treatments and management for depression. However individual treatment will vary depending on the specific needs of the individual which will be a matter for clinical judgement.
Association for Family Therapy and Systemic Practice	short	11	18	This is a similar issue to the above point. Effective supervision is not merely about adherence to manuals / protocols. Therapy supervision is important for therapists to have a 'safe space' to think and challenge / expand their understanding, and to review ways to improve the collaboration in therapy.	Thank you for your comment. We recognise that non-specific factors are an important component of treatment but a consideration of mechanisms of action of different treatments is outside the scope of this guideline. The recommendations in this guideline are intended to guide healthcare professional on the appropriate treatments and management for depression. However individual treatment will vary depending on the specific needs of the individual which will be a matter for clinical judgement.
Association for Family	Short	11	22	In 1.4.5 we would suggest that the use of sessional relationship measures additionally	Thank you for your comment. Relationship measures are not an agreed primary

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Therapy and Systemic Practice				is also important to give therapists effective feedback on the person's experience of the session.	outcome for depression. Individual therapists may wish to use these measures as part of their own practice but the committee did not consider that there was sufficient evidence to support recommending their use at the present time.
The Pituitary Foundation	Short	11	24	Our patient community describe examples of this not occurring- rather primary care practitioners are dismissive and/or uninformed of physical symptoms relating to some pituitary disorders and (continue to) prescribe anti- depressants.	Thank you for your comment. Implementation of the recommendations in this guideline should address the issue that you highlight.
Tavistock Relationships	Short	11	24	We suggest that the second bullet point of 1.4.5 is amended to read: "review how well the treatment is working with the person, couple or family" We make this suggestion because we believe that the inclusion of 'couple or family' would be more congruent with the statements included in page 37-38 of the full guideline on the links between depression and family and couple stress.	Thank you for your comment. We think that in this recommendation the focus should be how well the treatment is working for the person. Therefore we have not made your suggested change.
Association for Family Therapy and Systemic Practice	short	11	25	The phrase 'monitor and evaluate treatment adherence' can encourage explanations of poor outcomes in terms of poor adherence to treatment. Again, whilst this conceptualisation may be a good fit for the use of medications, it is more complex in the field of therapy,	Thank you for your comment. There are a number of factors that contribute to poorer outcomes in treatment. The nature of these is for individual therapists to consider, and where possible address. However, without a good understanding of treatment adherence

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				since when a therapist is thinking in these ways, it may adversely affect the therapeutic relationship by, locating blame within the individual and obscuring what the therapist might be doing (or not doing) which might be leading to the therapy being less acceptable or engaging to the person; for example if the person has not felt heard or where the focus of therapy feels irrelevant or unimportant to the person..	it may not be possible to effectively address these issues. Therefore we think it is important that adherence is monitored and evaluated.
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	12 13	13-29 1-4	1.4.8 This recommendation includes a large number of issues that patients should be given information about when prescribed an antidepressant. In general, we agree with this recommendation. However the extent of the information is such that it is totally unrealistic to expect all of this to be imparted at a single consultation, especially in primary care and especially to patients suffering from depression. We would suggest that the recommendation be amended to suggest that this information is imparted over a number of consultations. The third bullet point states "how treatment might need to be carried on even after remission". We do not agree with the tenor of this recommendations, for the reasons detailed above regarding section 1.8. While there MAY possibly be equal efficacy in	Thank you for your comment. The recommendations give guidance on what information people need to have in relation to taking antidepressant medication. They do not specify when this information should be provided. This will depend on the individual and the current wording of the recommendation allows for this flexibility. We have amended recommendation 1.4.9 to clarify that patients should receive information on how the need for treatment to carry on after remission will be assessed.

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				relapse prevention between MBCT alone and antidepressants alone, this is based on one study with a major flaw. Conversely, there is a wealth of data demonstrating that antidepressant continuation after the point of remission significantly decreases relapse rates with a large effect size. As a result, we argue that the expectation should be that antidepressants will continue after remission, unless there is a good reason not to do so.	
College of Mental Health Pharmacy (CMHP)	Short	12	6-17	1.4.7,8&9: Agreed this is all good, but reads as if this should all be given at the point of prescribing, ie on first prescription. That would not be appropriate and many people cannot concentrate properly when depressed. So phrasing needs amending to reflect that. Emphasising that information will often need reiterating on repeated occasions. Not just once and certainly not all at the onset of prescribing.	Thank you for your comment. The recommendations give guidance on what information people need to have in relation to taking antidepressant medication. They do not specify when this information should be provided. This will depend on the individual and the current wording of the recommendation allows for this flexibility.
Janssen	Short	12	13-15	We believe that part of recommendation 1.4.8 maybe be confusing to HCPs and patients because of the stated timelines regarding when patients begin to start to feel better conflicts with timelines to assess a response to antidepressant medication. We suggest a further recommendation should be added which outlines when a patient should return to the HCP to seek an adjustment to their medication. Recommendation1.4.8 currently states:	Thank you for your comment. Recommendation 1.4.9 (formerly 1.4.8) and 1.9.1 have been amended to clarify that the timeframe for a response is typically within 3 weeks for an antidepressant. We have also added to recommendation 1.4.9 that people should seek a review with their prescriber if there has been no improvement in 3-4 weeks. The current structure of the guideline is such

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				1.4.8 When prescribing antidepressant medication, give people information about: • how long it takes (typically 2–4 weeks) to begin to start to feel better • how important it is to follow the instructions on when to take antidepressant medication • how treatment might need to carry on even after remission • how they may be affected when they first start taking antidepressant medication, and what these effects might be • how they may be affected if they have to take antidepressant medication for a long time and what these effects might be,especially in people over 65 • how taking antidepressant medication might affect their sense of resilience (how strong they feel and how well they can get over problems) and being able to cope • how taking antidepressant medication might affect any other medicines they are taking • how they may be affected when they stop taking antidepressant medication, and how these effects can be minimised • the fact that they cannot get addicted	that lower intensity interventions are provided prior to more intensive interventions. We think this structure is logical and easy to follow and is unlikely to be misunderstood.

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				to antidepressant medication We believe that the 2-4-week time frame could currently be interpreted incorrectly as the timeframe to assess a response to antidepressant medication, which is contained in a separate later recommendation in section 1.9.1. The recommendations states: 1.9.1 If a person with depression has had no response or a limited response to initial treatment (within 3–4 weeks for antidepressant medication or 4–6 weeks for psychological therapy or combined medication and psychological therapy), assess: • whether there are any personal or social factors that might explain why the treatment isn't working • whether the person has not been adhering to the treatment plan, including any adverse effects of medication. As stated above, we believe that recommendations regarding the pharmacological interventions should be grouped together to ensure that there is no misunderstanding from reading separate parts of the guideline. In addition, we believe	

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				that recommendation 1.4.8 should add a further recommendation that states 'How people should return to their HCP if they do not feel better within 4-6 weeks.' We believe that this additional recommendation will ensure that people understand the need to return to their HCP to receive appropriate follow up treatment if they have not initially responded to their antidepressant medication.	
British Association of Art Therapists	Short	12	4-5	If the absence of competency monitoring with audio were to result in poor CQC rating, this could also potentially prevent people accessing art therapy, since there are not currently therapist competencies in the form that could be reliably rated systematically to satisfy audit of competency. This might be sensible for trainee art therapists but may not be practical or reasonable for experienced ones. Nevertheless, good patient outcomes could mitigate concerns about difficulty rating therapist competencies, so validated outcome measures (e.g. as above) should be used.	Thank you for your comment. Art therapy was not prioritised for investigation in the review questions for this guideline. As the evidence on art therapy has not been appraised we have not made any recommendations on the use of this intervention.
College of Mental Health Pharmacy (CMHP)	Short	12	15-16	Lines 15-16 state antidepressants take typically 2-4 weeks to start working. This is incorrect and perpetuates an ancient myth. While it may take 2-4 weeks to statistically prove that a medicine treatment group separates from placebo, the speed of	Thank you for your comment. The committee have considered this and have amended the recommendation to clarify that people will start to feel better typically within 3 weeks. Zilcha-Mano 2017 and Pasternak 2005 could

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				response in responders is actually much quicker and separates from placebo more rapidly (e.g. Zilcha-Mano et al, Am J Geriatr Psychiatry 2017; 25: 654-61 Medline28318797), with over 50% of the effect occurring in the first two weeks (e.g. s=47, n=8500, d/b, p/c, Pasternak and Zimmerman, J Clin Psych 2005, 66, 148-58). NICE should be attempting to address this misperception (which results in people inappropriately discontinuing antidepressants when responding in the first two weeks, thinking it must be for another reason) rather than perpetuating it.	not be included in the guideline as the outcome was outside protocol (speed of recovery).
College of Mental Health Pharmacy (CMHP)	Short	12	13-14	Different antidepressants have different side effects so this should be commented on. To devote two pages essentially to side effects and discontinuation effects is unbalanced.	Thank you for your comment. We think that providing information on the side effects of antidepressants are adequately covered by the existing bullet points 3-5. Providing information on the different side effect profiles between antidepressants would be encompassed by recommendation 1.4.9. The committee's rationale for providing these detailed recommendations on antidepressants is documented in the 'evidence to recommendations' section in the full guideline.
Association for Family Therapy and Systemic Practice	Short	12	1.4.6	We would argue that 'high quality supervision' is very important but high quality is more than adherence to treatment manuals (1.4.4). In terms of monitoring and evaluation of therapist competence we would argue it is	Thank you for your comment. The recommendation about supervision does not restrict this to use of treatment manuals. Incorporating the perspectives of people receiving therapy into the evaluation and

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				also important to include the perspectives of the people receiving therapy, here (this could include outcome and relational scales but also other ways of asking for regular feedback).	monitoring of competence would be encompassed within the parameters of the current recommendation.
University of Nottingham	Short	12	9	There is a recommendation that risks and benefits are discussed when offering a person antidepressant medication, but throughout the guideline there is very little consideration of risks associated with different antidepressants. Increased risks of serious adverse outcomes such as fractures and upper gastrointestinal bleeding have been shown to be associated with SSRIs. These may be of particular concern to certain individuals (e.g. with specific risk factors or history of these events) and other antidepressants such as TCAs might be preferable, especially since these were found to be more effective than SSRIs and mirtazapine in people with more severe depression (Full guideline, page 281).	Thank you for your comment. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable.
Association for Family Therapy and Systemic Practice	Short	12	19 and 22	The use of the terms 'how treatment may need to carry on' and 'if they have to take antidepressant medication for a long time' does not indicate a collaborative approach to decisions about medication, since it locates the decision to continue with medication externally to the person, and phrases it as unavoidable and necessary. If this is based	Thank you for your comment. This is a recommendation for prescribers to follow, specifying what information they need to give people about antidepressant medication. It has been worded in this way to ensure that prescribers provide this information to people as this will enable the person to make an informed choice about their treatment. It is

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				on an evidence-based recommendation about continuation of medication it should be phrased as 'how treatment may be recommended to carry on' / 'if they are recommended to take antidepressant medication for a long time'. If this is not based on a strong research recommendation then we would suggest more collaborative phrasing, such as 'discussions should take place about the positive and negative effects of continuing medication during remission, and over a longer timescale, to enable the person to make an informed choice in collaboration with the healthcare professional.	not intended to imply that the person does not have a choice about whether to continue with medication. We have also added a recommendation to section 1.4 to highlight the importance of decisions about treatment being made in discussion with the person.
Northumberland Tyne and Wear NHS Foundation Trust	Short	13	5-17	A very important point about withdrawal effects and the challenges of coming off/reducing anti-depressants (this can be understandably be interpreted as "addictive" by service users and their families who need to fully understand the range of effects) This needs thorough discussion of the pros and cons and honesty about the downsides of medication. It would be worth recommending any appropriate websites that offer information and support.	Thank you for your comment and support for our recommendation. We are not able to signpost to any websites in the guideline as this could be viewed as NICE endorsing the content of that website.
College of Mental Health Pharmacy (CMHP)	Short	13	5-17	It is not appropriate to put all antidepressants together. Some antidepressants e.g paroxetine and venlafaxine may cause more problems when doses are missed and on discontinuation.	Thank you for your comment. The recommendations have been revised to highlight particular drugs that are more likely to be associated with discontinuation symptoms.

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Northumberland Tyne and Wear NHS Foundation Trust	SHORT	13 14	18-28 1-15	1.4.10 – 1.4.13 These sections relate to discontinuing medication and discontinuation syndromes. This is valuable guidance. We are unclear why details of specifically risky medication (venlafaxine and paroxetine), that were mentioned in CG90, have been removed.	Thank you for your comment. The recommendations have been revised to highlight particular drugs that are more likely to be associated with discontinuation symptoms.
British Association for Psychopharmacology	short	Page 13	Lines 18-24	This makes a series of recommendations regarding the length of time over which to withdraw medication, depending on the length of treatment with the antidepressant. While we agree that there is data that suggests length of treatment is a factor in deciding the duration over which withdrawal should occur (Schatzberg et al. J Clin Psychiatry. 2006;67 Suppl 4:27-30), we are unclear on what basis the committee has come up with the specific numbers quoted in the recommendation. We also strongly recommend that the guideline should state that the duration of withdrawal should also depend on the pharmacokinetics of the antidepressant. Examples (such as fluoxetine vs paroxetine) could also usefully be added (as they were in CG90).	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.11 (formerly 1.4.10) to ensure that when stopping medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms. In recommendation 1.4.11 they have also noted that the pharmacokinetic profile needs to be taken into account when stopping antidepressant medication.

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					Schatzberg 2006 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs).
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	13	18-24	1.4.10 This makes a series of recommendations regarding the length of time over which to withdraw medication, depending on the length of treatment with the antidepressant. While we agree that there is data that suggests length of treatment is a factor in deciding the duration over which withdrawal should occur (Schatzberg et al. J Clin Psychiatry. 2006;67 Suppl 4:27-30), we are unclear on what basis the committee has come up with the specific numbers quoted in the recommendation. We also strongly recommend that the guideline should state that the duration of withdrawal should also depend on the pharmacokinetics of the antidepressant. Examples (such as fluoxetine vs paroxetine) could also usefully be added (as they were in CG90).	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.11 (formerly 1.4.10) to ensure that when stopping medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms. In recommendation 1.4.11 they have also noted that the pharmacokinetic profile needs to be taken into account when stopping antidepressant medication. Schatzberg 2006 cannot be included in the

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					review as it does not meet the study design criteria (not an RCT or systematic review of RCTs).
Northumberland Tyne and Wear NHS Foundation Trust	Short	13	18-24	The addition of the mention of "discontinuation symptoms" is important in order to prepare the service user and their supporters before and throughout their treatment.	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.11 (formerly 1.4.10) to ensure that when stopping medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms.
College of Mental Health Pharmacy (CMHP)	Short	13	18-20	This seems to be the only section that covers stopping antidepressants. It would be helpful to at least refer to differences in antidepressant pharmacokinetics. Refer to/ seek advice from pharmacist on reducing / stopping doses given differences in pharmacokinetics of different antidepressants. For example, statement	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.11 (formerly 1.4.10) to ensure that when stopping

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				"slowly reduce the dose based on how long the person has been taking it" and "over several days if the person has been taking it for 2–8 weeks" is not appropriate for fluoxetine at the standard dose of 20mg daily. This would just be stopped. In contrast, the approach to reducing and stopping paroxetine would be very different because of its short half-life.	medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms. In recommendation 1.4.11 they have also noted that the pharmacokinetic profile needs to be taken into account when stopping antidepressant medication.
British Association of Art Therapists	Short	13	3-4	It could be misleading to tell people they cannot get addicted to antidepressants, given the increasing evidence of serious difficulties that many people have coming off them, especially after taking them for long periods. One could argue the precise technicalities of what constitutes addiction, but most service users would not understand this, and would be misled by a clinician telling them they cannot become addicted. This does not really seem acceptable in NICE guidelines. To have a guideline that people should be given this message presents the following challenges: More people taking antidepressants who don't need them, more people having	Thank you for your comment. The committee noted that whilst people will not become addicted to antidepressants, they can experience discontinuation symptoms if they stop taking them. The committee agreed that concerns about 'addiction' may be a reason why people are reluctant to take antidepressants and thought it was important that the recommendations highlight that this is not the case. However, in light of comments received from stakeholders the committee have amended recommendation 1.4.8 to include discussion of patients concerns about stopping medication.

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				'discontinuation effects' and therefore having to stay on them beyond needing them, costing money for more medication or the cost of treatment required due to stopping. It also makes antidepressants appear to be a more benign option than they really are, perhaps reducing the incentive for services to make alternative approaches (especially psychological therapies) available, or for service users to consider alternatives.	
Sussex Partnership NHS Foundation Trust	Short	13	18	1.4.10 We think this may not be entirely correct as it is often dependant on dose and the drug half-life. Some clarification or nuancing of this would be welcome.	Thank you for your comment. The committee were aware that there is information from patient experience that when stopping antidepressants, if the dose is reduced too quickly the person may experience discontinuation symptoms. They therefore made recommendation 1.4.11 (formerly 1.4.10) to ensure that when stopping medication the dose would be reduced gradually. In light of feedback from stakeholders, the committee agreed that the timings given in the recommendation were too prescriptive and potentially confusing. They have amended the recommendation to reflect that the dose should be reduced at a rate proportionate to the duration of treatment. They have also highlighted particular drugs that are more likely to be associated with discontinuation symptoms. In recommendation 1.4.11 they have also noted that the pharmacokinetic profile needs

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					to be taken into account when stopping antidepressant medication.
University of Nottingham	Short	14	16-20	The same care recommended when starting an antidepressant because of the risk of self-harm and suicide should also be applied when changing or stopping an antidepressant, as rates of suicide and self-harm are increased at these times (Coupland C, Hill T, Morriss R, Arthur A, Moore M, Hippisley-Cox J. Antidepressant use and risk of suicide and attempted suicide or self harm in people aged 20 to 64: cohort study using a primary care database. BMJ. 2015;350:h517).	Thank you for your comment. We agree and think that existing recommendations cover these aspects of care. Coupland 2015 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs).
Association for Family Therapy and Systemic Practice	short	14	1.4.14	This recommendation is not clear. Putting together those under 30 with those who are thought to be at increased risk of suicide makes it unclear whether these are put together because there is a population risk of suicide with antidepressive medication for those under 30, which may not be picked up in assessment, and this is why they are seen 1 week after starting. It is not clear whether the frequent reviews should also apply to under 30's or only those where an increased risk of suicide is assessed. This phrasing needs clarification.	Thank you for your comment. There is a population risk of suicide with antidepressant medication in those under 30. However increased risk of suicide is not restricted to only those under 30 and so we have mentioned both groups in the recommendation. We think the use of the word 'or' in the stem makes it clear that the recommendations about review apply to both groups.
College of Mental Health Pharmacy	Short	14	20	"Review them frequently until the risk of suicide is reduced." This is too vague and non-specific. Reduced to what? We cannot	Thank you for your comment. We have amended the recommendation to give greater clarity on the frequency of review

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(CMHP)				see how this will be achievable.	and what this should be based on.
Sussex Partnership NHS Foundation Trust	Short	14	20	1.4.14 – How frequently is frequently?!	Thank you for your comment. We have amended the recommendation to give greater clarity on the frequency of review.
College of Mental Health Pharmacy (CMHP)	Short	14	26	To exclude venlafaxine from the treatment of depression is absurd. Whilst there may be some evidence of greater risk of overdose death with venlafaxine this is accepted as being because venlafaxine is an antidepressant with a dose-related response and frequently used in treatment-resistant depression, which by definition has a higher risk of overdose.	Thank you for your comment. This recommendation does not say that venlafaxine should not be used in the treatment of depression. It highlights the greater risk of death from overdose associated with venlafaxine as something to be aware of when prescribing antidepressants for people at significant risk of suicide.
British Association for Psychopharmacology	short	15	7-21	These sections are useful. However, we are unclear why there is no mention of, for example, ECG monitoring of medication such as citalopram, escitalopram and TCAs that can increase QTc intervals in a dose related way, or blood pressure monitoring of venlafaxine especially at higher doses?	Thank you for your comment. We have added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram.
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	15	7-21	Monitoring of medication – sections 1.4.17 – 1.4.19 These sections are useful. However, we are unclear why there is no mention of, for example, ECG monitoring of medication such as citalopram, escitalopram and TCAs that can increase QTc intervals in a dose related way, or blood pressure monitoring of venlafaxine especially at higher doses?	Thank you for your comment. We have added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram.

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Sussex Partnership NHS Foundation Trust	Short	15	7-14	1.4.17 & 1.4.18 – We think that this doesn't agree with BPAD guidelines for monitoring of lithium. It also doesn't state where lithium fits within treatment.	Thank you for your comment. Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. These are now more consistent with what is in the NICE guidance on Bipolar disorder, however there are still some differences because this is guidance for the use of antipsychotics in depression. Recommendations on the use of lithium appear in section 1.9 of the guideline.
Parkinson's UK	Short	15	4-5	While we agree that when prescribing antidepressant medication for older people that the person's general physical health and interactions with other medications should be taken into account, we are concerned that this recommendation may imply that it is only important for older people. Pharmacological treatment for depression may also not be appropriate for young people if there is the risk of interaction with medications prescribed to address physical symptoms, especially in the context of neurological conditions. (Fernie BA, et al, Cognitive behavioural interventions for depression in chronic neurological conditions: A systematic review, J Psychosom Res (2015).	Thank you for your comment. The committee agreed that this consideration was particularly important for older people and needed to be highlighted in the recommendation. Recommendation 1.4.9 covers these issues for younger people. The recommendations in section 1.3 specify how services should be organised to ensure effective and integrated delivery of care. This guideline is about the treatment and management of depression in adults. People with depression and a chronic physical health problem, such as Parkinson's, are not within the scope of this guideline. Therefore it is not possible to make recommendations for people with Parkinson's in this guideline.

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				Although the majority of people with Parkinson's develop symptoms after the age of 65, thousands of working age people are also affected (Pringsheim, Tamara, et al. "The prevalence of Parkinson's disease" *Movement Disorders* 29.13 (2014): 1583-1590). Therefore, the recommendation around taking other medications into account when prescribing antidepressants should be extended beyond older people due to the complex medication regime. It is also important that there is recognition of the importance of a direct and continued relationship between healthcare professionals involved in a person's care, to ensure that any side effects and interactions between medications are fully addressed. We would therefore recommend that this is explicitly highlighted.	People with depression and a chronic physical health problem, are covered in CG91.
College of Mental Health Pharmacy (CMHP)	Short	15	11-12	Lithium level monitoring. Safety advice needs to be consistent regardless of diagnosis. Recently updated NICE Bipolar Affective Disorder CG185 guidance says monitor every 6 months after the first year, not 3, but we approve of the recommendation to keep it at 3 months. The Bipolar Guidelines panel had no explanation or rationale for changing the frequency to 6-months and would not engage in conversation about the change, especially as they had been made aware of recent	Thank you for your comment. Additional detail has been included in the recommendations about monitoring patients who are taking lithium or antipsychotics as the committee agreed that more detail was required due to the increased side effect burden with these drugs and a coroner's report on lithium toxicity. These are now more consistent with what is in the NICE guidance on Bipolar disorder, however there are still some differences because this is

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				evidence ("One lithium level >1.0mmol/L causes an acute decline in eGFR: findings from a retrospective analysis of a monitoring database". Kirkham, Skinner, Anderson, Bazire, Twigg and Desborough, BMJ Open 2014;4:e006020) that less frequent monitoring is likely to lead to development of toxic levels, toxic effects and renal damage. Also need to include target lithium plasma levels for depression.	guidance for the use of antipsychotics in depression. We have clarified in the recommendations about lithium monitoring that the plasma lithium levels should not exceed 1.0 mmol/L. Kirkham 2014 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs).
College of Mental Health Pharmacy (CMHP)	Short	15	13-14	Should also advise an ECG in patients prescribed lithium who already HAVE cardiovascular disease	Thank you for your comment. We have included an ECG for people taking lithium who have cardiovascular disease, as you suggest.
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	16 17 18 19 20	15-28 1-29 1-27 1-27 1-18	First line pharmacotherapy (sections 1.5 and 1.6) First line pharmacotherapy is described in sections 1.5 and 1.6 of the guideline. The only reference to the specifics of the therapy is "an SSRI or mirtazapine". There is no guidance given with regards to the choice between an SSRI and mirtazapine might be made. Lumping all SSRIs together is rather dismissive of the diverse pharmacology of the 1-27SSRIs. For example, is the Guideline Committee equally happy to recommend paroxetine, fluvoxamine and fluoxetine along with the other SSRIs for patients on other medication given the propensity for the	Thank you for your comment. The committee considered the evidence from the NMA on the effectiveness of different SSRIs. No particular drugs within this class were shown to be more effective, so the committee were unable to recommend specific drugs. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable.

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				former to have pharmacokinetic interactions with other medication, since description of this in CG90 has now been removed? Similar, while risk of discontinuation symptoms is included in the guideline (sections 1.4.9 to 1.4.13) there is no mention of drugs more likely to lead to this as there was in CG90 (e.g. the SSRI paroxetine). One of the most common questions that GPs ask during educational sessions regarding the use of antidepressants is whether SSRIs citalopram or escitalopram should still be used given the evidence for a dose related increase in QTc in the ECG, and if they are used, what should the monitoring requirements be. This is not mentioned at all in the guideline.	We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations which should be avoided. We have also added another recommendation in section 1.4 to clarify that paroxetine and venlafaxine are more likely to be associated with discontinuation symptoms. We have also added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram.
The Mindfulness Initiative	Short Short	16 19	15 25	We suggest that the evidence for MBCT as a first-line intervention for depression warrants its inclusion in 1.6 & 1.7 as an option to increase patient choice. The meta-analysis of RCTs carried out by Strauss, Cavanagh, Oliver, & Pettman (2014) found that MBCT for people treated with a *current episode* of depression showed significant effects on depressive symptom severity. The included trials included people experiencing less severe and more severe depression. Research has shown that having choice in treatment increases patient motivation and	Thank you for your comment. Whilst 2 studies of MBCT were included in the NMA for treatment of a new depressive episode, the committee did not consider that the evidence was strong enough to support recommending this intervention, which was primarily developed for relapse prevention, for first line treatment. Strauss 2014 systematic review has been checked for relevant studies. Only one study meets our criteria for inclusion and that had already been included.

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				often leads to better outcomes and adherence (Alfonsson, S., Olsson, E., & Hursti, T., 2016).	
Sussex Partnership NHS Foundation Trust	Short	16	20	1.5.1 – The elevation of group CBT as the initial treatment for people with less severe depression, and sequencing it before individual self-help, may cause implementation difficulties and costs in our IAPT services. Our experience of offering groups is that attrition is high, and certainly higher than in RCTs. In addition, the implications of prioritising a 9 session CBT based group over 12-16 weeks would significantly disrupt the current IAPT model. A group based CBT intervention of that length and intensity would require high intensity therapist delivery. It undermines the stepped care model of IAPT. Effective use of a stepped model or care is linked with better recovery rates in IAPT. Low intensity interventions as treatment of least burden form the backbone of the IAPT model and underpin the concept of stepping up to high intensity groups or one to one work should further more intensive input for that patient be required. Hence, we think that there are likely to be significant costs to the implementation of the recommendations as they currently stand and	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5).

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				we wish to ensure that these have been fully considered in the guidelines and in particular in the assumptions that underpin the economic modelling. Our questions are: Is the level of attrition from group treatment taken in to account? Is this from RCTs or also from studies in routine care? Is the banding level of the therapists accounted for? Guided self-help in IAPT is provided by low intensity workers (psychological well-being practitioners) at NHS AfC Bands 4 and 5, whereas CBT groups are more typically provided by high intensity therapists (or equivalent) at AfC Bands 6, 7 and 8, and therefore CBT groups may not represent a cost saving in comparison to guided self-help. Are the likely training implications of these recommendations costed? The recommendation for group CBT as the initial treatment would mean a large-scale restructuring of IAPT High Intensity training courses, with more HI's than PWPs needing to be trained, and associated higher salary costs. We also have found that individual guided self-help is more flexible and accessible for people than attendance at fixed time and place groups. We wonder if there is any data	

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				available on service user choice and acceptability of different interventions. Overall, for reasons of practical implementation and concerns around costs underlying the existing recommendations, we suggest that the recommendation should be to offer either individual guided self-help or group CBT as an initial intervention. For service-related reasons we suggest that low intensity interventions in a stepped care model should initially be prioritised. If after a low intensity intervention, recovery has not been achieved, the patient should be stepped up to access one to one evidence based high intensity interventions or group CBT intervention.	
NHS England National IAPT Team	Short	16	20	Professor Tony Roth's comments on the recommendation that group CBT should be the first line intervention for mild to moderate depression. These comments relate to recommendations concerning group CBT; these appear in many of the sections detailing treatment options for both less and more severe depression. To summarise what follows, this recommendation is based on a small set of studies of group CBT and a questionable health economic analysis. The interpolation	Thank you for your comment. Group CBT was previously included in the class of cognitive and cognitive behavioural therapies. So, although a few group CBT studies were included in the NMAs for less and more severe depression, group CBT 'borrowed' treatment effect from this class. Following careful consideration of stakeholder comments and of the likely impact of the mode of delivery on the intervention effect, group CBT, and all other cognitive / cognitive behavioural group interventions, were removed from the

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				of group CBT in guideline recommendations disrupts the stepped-care model that structured earlier versions of the guideline and the pattern of service delivery within IAPT. A critical corollary is that service reorganisation to accommodate this new guidance would have its own – considerable – costs, though these are not modelled in the health economic analysis. In more detail: **Group-CBT studies included in the review and the Network Meta-Analysis** Seven group-CBT studies were included in the review and analysis (Table 1; extracted from Appendix J3). A number of separate Network Meta-Analyses (NMA) were conducted, focused on different outcomes. Different combinations of the seven studies were included in different analyses: Table 2 identifies which contributed to which analyses (and indicates that the NMAs were based on few studies (between two and five) with small sample sizes (ranging from 50 - 284)). **Health economic model** The economic model asserts that group CBT is cost-effective when the following parameters apply:	cognitive and cognitive behavioural therapies class. These were put together with behavioural group therapies, which were removed from the behavioural therapies class, to form a new class of 'behavioural, cognitive, and cognitive behavioural group therapies'. The number of group CBT studies included in each analysis depended on the availability of appropriate data in each study [i.e. discontinuation data, ITT or completers' continuous symptom data, response data, remission data]. Data for group CBT were limited, in particular for more severe depression, and this has been taken into account in the interpretation of the results of clinical and economic analyses and when revising recommendations. Please note that Hvennegaard (submitted) has been removed from the clinical analyses as the systematic review and NMAs included only studies published until June 2016, as this was the systematic search cut-off point (the study had thus been included in error in the consultation guideline draft). Cramer 2011 has been included in the analysis. The fact that it is a feasibility and pilot study did not affect its inclusion in the

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				• 9 sessions; 90 minutes duration • 2 therapists (Band 5 PWPs) • 12 participants per group This yields a total cost per client of £93 (group CBT) + £36 (1x GP consultation). The model is based on effect sizes from three of the network meta-analyses: (i) discontinuation, (ii) response in those completing treatment, and (iii) remission in those completing treatment (see Table 3). However, it is unclear where there odds ratio for 'remission in completers' came from, as this is not included in the network meta-analysis in Appendix 17. **Less severe depression** Based on the health-economic model, group CBT was classed as the second most cost-effective intervention for less severe depression, after Mirtazapine. Cross-referencing Table 3 with Table 2 shows that odds-ratio for 'response in completers' was based on only 2 studies, with a sample size of 105. These are Hvennegaard (submitted) and Cramer (2011). It is not possible to review the Hvennegaard paper as it is not yet published, but the trial protocol is available	NMA, as the uncertainty in the relative effects is taken into account in the NMA and therefore it does not matter if a study was underpowered. In fact, the purpose of meta-analysis (pairwise or network) is often to get more power by putting together many such studies. Note that in the guideline NMA we did not focus on statistical significance; the aim was to quantify the relative effects of one treatment compared to another and the uncertainty around this effect. This uncertainty was also reflected in the economic modelling results (since NMA data informed effectiveness in the guideline models). Manicavasgar 2011 compares 2 forms of group therapy; the study does not contribute to the estimation of the relative effect of group CBT versus another (active or inactive) intervention, but is still included in the NMA as it contributes to the estimation of the variance around the (behavioural, cognitive, and cognitive behavioural group) class effect. The active intervention in Ekkers 2011 has been included in the behavioural, cognitive, and cognitive behavioural group class and has contributed to the class effect.

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				(Hvennegaard et al. 2015). This outlines a comparison of rumination-focused group-CBT to 'standard' group-CBT. If these are the treatment reported in the submitted study, it is not clear how it has been included in the NMA. For an indirect comparison to be made between the 'standard' CBT arm and pill placebo, it would need to be 'connected' via a study which compares rumination-focused CBT to placebo. However, no studies with this design appear to be included. However, Appendix J3 identifies the treatment comparison as group CBT versus Behavioural Activation – either there is a third arm not reported in the trial protocol, or a significant error has taken place. Cramer et al. (2011) is suitable for inclusion in the NMA, as it compares a group-CBT intervention to treatment as usual. However, it is described by the authors as 'feasibility and pilot study', not a full-trial of group-CBT. It has a small sample, with n=48 in the intervention arm and n=19 in the TAU arm. Further, the study fails to find a significant effect for group CBT, either in terms of (i) continuous PHQ-9 scores, (ii) response-rate or (iii) remission rate). It describes a trend towards significance for response and remission at 3 months, though notes that this (non-significant) effect appears to have	Beutler 1991 and Chiang 2015 were included in the NMAs because they met inclusion criteria. Covi 1987 compared 3 interventions: short-term psychodynamic therapy group (n=24), group CBT (n=32), and combination of group CBT with imipramine (n=34). There were more than 10 participants in each arm, otherwise the study would not have met criteria for inclusion in the NMA. In total, across less and more severe depression and different NMAs, there were 13 studies assessing group CBT (one of which compared group CBT with 3rd-wave cognitive therapy group), 5 studies assessing coping with depression course group, one study assessing rational emotive behaviour therapy group, and another 3 studies assessing 3rd-wave cognitive therapy group (in total 22 RCTs assessing behavioural, cognitive, and cognitive behavioural group therapies were considered). It is true that most interventions within the class have been compared indirectly with most other active treatments, such as individual CBT or SSRIs, mostly via TAU, due to lack of head-to-head comparisons in RCTs. However, the benefit of performing a NMA in such situations is

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				diminished by six months. It does report large odds-ratios for the group CBT intervention, though these have extremely wide 95% confidence intervals (*response*: OR=4.21, 95% CI=0.83-21.23; *remission*: OR=3.12; 95% CI=1.00-9.72). **More severe depression** Group CBT was estimated to be the fourth most cost-effective treatment for more severe depression, behind (i) individual CBT + Sertraline, (ii) BA, and (iii) short term psychodynamic psychotherapy. Again, cross-referencing Table 3 with Table 2 shows that evidence for the efficacy of group CBT for MSD was based on only *one* study of group CBT with a sample of 26 (Manicavasgar 2011). The other effect size feeding into the model (remission in completers) was 'borrowed' from individual CBT. The Manicavasgar study was a small-scale RCT comparing Mindfulness-based cognitive therapy group (MBCT; n=19) to group CBT (n=26). It reported a significant main effect of time (i.e. both groups improved), but no main effect of group. The CBT group showed a 13-point drop in BDI score, from 36 to 23. This study suggests that group-CBT is as effective as MBCT; it does not compare group CBT to a relevant comparison (e.g. TAU, individual	that it allows making these indirect comparisons and drawing conclusions about their relative effects when interventions in a network have not been compared in a head-to-head trial. Results of the NMAs (both those constituting the clinical analyses and those informing the economic analyses) have been considered by the committee after taking into account the numbers of participants tested on each class, and also have been judged for their plausibility. Analyses with extreme/ implausible results have been considered with great caution. The committee considered further the issue of some interventions/classes having been tested on a small number of participants. Following this consideration, the updated economic analyses included only classes that were tested on at least 50 participants on each of the main outcomes of interest, i.e. treatment discontinuation, response in those completing treatment and remission in those completing treatment. Following consultation with stakeholders and after re-checking the resource use reporting in the respective RCTs included in the NMAs, we also revised the resource use

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				CBT, medication). **Details of other studies reporting a group-CBT intervention** Do the other studies included in the systematic review (but not the relevant meta-analyses) provide evidence for the efficacy of group CBT? **Ekkers (2011)** This study compares "transdiagnostic training for worrying and rumination", named Competitive Memory Training (COMET) + TAU, to TAU. The intervention aims to change the 'amount of involvement' with negative thoughts and emotions, promoting 'acceptance' and 'indifference' to these thoughts. As such it appears to be a 'third wave' form of CBT, akin to ACT or meta-cognitive therapy. The intervention consisted of seven manualised sessions of 90min each, in groups of 6-8 patients, run by 'trained therapists'. The intervention group consisted of N=49 subjects, the TAU group N=20. Participants were older adults (mean age=71.8 years). A significant effect of CBT group vs TAU was	assumptions for group CBT in the economic analysis: in the updated analysis, group CBT is provided in 12 sessions lasting 2 hours each, provided by one Band 7 (clinical psychologist) and one Band 6 (clinical psychologist trainee) therapist to groups of 8 participants and also includes an individual orientation meeting lasting one hour with a Band 7 therapist. The updated intervention cost is £664 (group CBT) + £36 (1 GP consultation). Please note that the model does account for attrition, as discontinuation has been included in the model structure and numbers of people discontinuing each treatment have been informed by the respective NMAs. The economic model assumed that people who discontinued a group treatment moved to a less effective treatment option (clinical management or no treatment) and still incurred "the full cost of therapy, since participants in a group intervention are not replaced in the group if they discontinue and therefore the full cost of therapy per participant is incurred, whether the participant attends the full course or not" (see page 805 of the consultation guideline draft). The odds ratio for 'remission in completers' came from a separate NMA done to inform this parameter. You are correct that Chapter

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				found in the intent to treat analysis (effect sizes of d=0.54 (GDS) and d=0.66 (QIDS-SR)) and completer analysis (effect sizes of d=0.8 (GDS) and d=1.1 (QIDS-SR)). This suggests a third-wave CBT group has benefit when contrasted to TAU. **Beutler (1991)** This study was designed to analyse patient predictors of change, namely 'coping' and 'resistance potential'. It compared these variables across three interventions: (i) Group Cognitive Therapy (n=21), (ii) 'Experiential therapy' (n=22), and (iii) self-directed therapy (n=20). The CBT group consisted of 21 participants, who underwent therapy in groups of 5-10; it is not clear how many therapists ran each group (?4). A significant main effect of time was found, (indicating that all groups improved), but no significant interaction between group and time (indicating that no group was superior to another).. **Chiang (2011)** This study compared sample of 30 patients who attended a CBT group (n=30) to a TAU group (n=32) in a single-blind RCT. The intervention group consisted of 12 weeks of group CBT delivered by a doctoral student	17 in the guideline consultation draft does not include the results of this analysis, as originally we planned to use the results of 'remission in those responding' NMA to inform the economic analysis. However, as we explain on page 778 of the consultation full guideline draft (lines 31-39), "It needs to be noted that originally, the outcome of interest in order to populate the economic model with numbers of people remitting was remission conditional on response (i.e. probability of remission in those responding to treatment). However, the network constructed for this outcome in people with more severe depression was disconnected, and therefore relative effects between interventions of interest for this outcome were not possible to estimate for all comparisons. Moreover, the network constructed for this outcome in people with less severe depression was sparse and covered a limited number of interventions. For this reason, remission in those completing treatment was selected as an outcome instead, to allow, in combination with data on response in those completing treatment, calculation of numbers of people who responded and remitted. When running the probabilistic analysis, the number of people reaching remission was not allowed to exceed the number of people responding

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				with eight years' experience of CBT. An unusually large effect was reported: For the experimental group BDI-II scores reduced from 40.30 to 9.09, and remained low at 12-month follow-up (12.10). By contrast, the control group showed no change (pre-test=37.59, post=37.75, 12 month=37.97). This study must be an outlier, given the magnitude of the reduction in symptoms for the intervention group, and the lack of improvement in the control group. **Covi (1987***)* It was not possible to retrieve this article. From the abstract and the guideline appendix this was a two-arm contrast of group CBT versus group CBT + imipramine. There were 6-8 patients per group, and the groups ran for 15 sessions; in addition each member had two 1-hour individual CBT sessions. **Discussion** For less severe depression, evidence of the efficacy of group CBT appears to be based on only two studies (n=105); one of which is unpublished and compared two types of group CBT, the other of which was a pilot study and found no significant effect for group	to treatment. In iterations where the probability of remission exceeded the probability of response, the number of people in remission was forced to equal that of people in response (so that all people who responded also remitted in those iterations)." The analyses of 'remission in treatment completers' have now been updated and included in Appendix N1 (Chapter 17 in the consultation draft), replacing the analyses of 'remission in responders'. Following the changes above regarding the classification of group CBT, the inclusion in the economic analysis of classes that had been tested on at least 50 people on each of the main outcomes of the economic model, and the associated resource use updated estimates, the results of the clinical and economic analyses were as follows: Less severe depression: group CBT was shown to be less effective than before in the clinical analysis (in particular on the SMD outcome, which was the main clinical outcome examined by the committee), and the 6th best intervention in terms of cost effectiveness. More severe depression: clinical data for group CBT were very limited and, where

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				CBT compared to TAU. Evidence for the efficacy of group CBT with more severely depressed individuals is based on one study, which showed group CBT to have a comparable effect to MBCT. Even taking together all the studies included in the review (but not necessarily the economic analysis) the evidence is fairly weak. It consists of: • One study which examined the effect of adding imipramine to a group-CBT intervention (Covi, 1987). • Two studies which compared a third-wave CBT group to a traditional CBT group (Manicavasgar, 2011; Hvennegaard (submitted). • One study which compared a CBT group to other forms of group therapy (Beutler, 1991). • One study which compared a third-wave CBT group to TAU (Ekkers, 2011). • Two studies which compared a CBT group to TAU (Chiang, 2011; Cramer, 2011). Of these studies comparing group CBT to a different type of group therapy, neither found that group CBT was superior. Of the three studies comparing group CBT to TAU, two	available, rather implausible. Behavioural, cognitive and cognitive behavioural therapies as a class were not represented on the SMD analysis; they were also not represented in the economic analyses, as they had been tested on less than 50 people on one or more main outcomes utilised in the economic analysis. The related recommendations have been updated and/or removed in the light of the updated clinical and economic results described above. Group CBT for first line treatment has now been classified as a high intensity treatment and has a more restricted position in the recommendations for less severe depression behind both low intensity interventions, medication and individual interventions such as IPT, BA and CBT.

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				found that group CBT was more effective (one of which was a third-wave intervention). One of these studies (Chiang et al.) is an outlier, in that the effect size was unusually large. The other study found no effect for CBT vs TAU. It seems reasonable to conclude that: • Group CBT is as effective as other group therapy interventions • There is some evidence that group CBT is better than TAU • There is no direct evidence of the efficacy of group CBT contrasted to individual CBT or SSRIs Turning to the guideline recommendations, the health economic model makes a number of questionable assumptions, all of which yield a lower costing than is likely to be the case in real-world application: a) the recommended group size is significantly larger than that employed in research studies and in most clinical settings, where 6-8 is normative b) it is predicated on delivery by therapists who are less well-trained (and hence employed at a lower band) than is the case when	

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				delivering CBT on an individual basis c) in relation to preparation for the group it identifies a single GP consultation as the only additional cost; in practice most groups will be prefaced by at least one initial meeting with each group member to screen for suitability, adding a considerable (but potentially 'hidden') cost d) the model does not account for attrition, a predictable feature of all groups, and one that inevitably reduces the therapist-client ratio **Implications for IAPT service delivery** Group CBT is not a low-intensity intervention and interpolating this into the guidance for the management of low-severity depression represents a significant departure from a stepped-care model. Implementing this aspect of the guideline would involve significant service reorganisation, with attendant costs. This would be appropriate if the evidence-base was strong and the health economic model robust, conditions which (as above) do not apply. **Conclusion** The evidence-base for group CBT is not	

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<tr><td></td><td></td><td></td><td></td><td>strong, and the health-economic case is based on assumptions which are unlikely to be echoed in clinical practice. There is insufficient justification to assert that group CBT should be a first-line intervention for individuals with low-severity depression and a second-line intervention for more server depression.

Table 1: Group-CBT studies included in systematic review
<table>
<tr><th>Study ID</th><th>Arm 1 intervent 'n</th><th>Arm 2 intervent 'n</th><th>Arm 3 interve 'n</th></tr>
<tr><td>Covi (1987)</td><td>CBT group</td><td>CBT group + imipramin e</td><td>-</td></tr>
<tr><td>Cramer (2011)</td><td>CBT group (under 15 sessions)</td><td>TAU</td><td>-</td></tr>
<tr><td>Ekkers (2011)</td><td>CBT group (under 15 sessions)</td><td>TAU</td><td>-</td></tr>
<tr><td>Hvennega ard (submitted)</td><td>Ruminati on focused</td><td>CBT group*</td><td>-</td></tr>
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<tr><td></td><td>CBT group (under 15 sessions)</td><td></td><td></td><td></td><td></td><td>then 11 x 3 hour groups</td><td>7 years' experience</td><td></td><td></td></tr>
<tr><td>Beutler (1991)</td><td>CBT group (over 15 sessions)</td><td>Short-term psychodynamic therapy</td><td>Non-directive counselling</td><td></td><td>5-10</td><td>20</td><td>4?</td><td>76</td><td>30</td></tr>
<tr><td>Chiang (2015)</td><td>CBT group (under 15 sessions)</td><td>TAU</td><td>-</td><td></td><td>Not reported</td><td>12 x 2 hour</td><td>1 x doctoral student with 8 years CBT experience</td><td>81</td><td>62</td></tr>
<tr><td>Manicavasgar (2011)</td><td>CBT group (under 15 sessions)</td><td>Third-wave CBT group</td><td>-</td><td></td><td>6-8</td><td>8 x 2–2½ hours</td><td>2 therapists (at least 1 clinical psychologist)</td><td>69</td><td>45</td></tr>
</table>
* Note this arm erroneously listed as 'Behavioural Activation ' in Appendix J3 and analysed as such in NMAs</td><td colspan="2"></td></tr>
<tr><td>University of Nottingham</td><td>Short</td><td>16</td><td>26</td><td colspan="9">A minimum group size should be stated for CBT groups as they have been for other types of groups e.g. for physical exercise. It can be intimidating and overwhelming for patients to be in a group with only one remaining person yet two therapists. Minimum group size should be 8 for all</td><td colspan="2">Thank you for your comment. Recommendation 1.5.10 specifies that the number of participants for group CBT should be 6-8. This is a formal psychological intervention delivered at a high intensity level and the recommended number of participants takes this into account.</td></tr>
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				groups as recommended for physical exercise and for similar reasons. It is important to be consistent.	
Leeds Community Healthcare Leeds IAPT	Short	16	26	We are concerned that limiting the number of group participants to 12 would add additional pressures to services as additional groups would be needed to meet service demands. Currently group numbers at step 2 LI range from approximately 15 to 35 participants. Our GSH recovery rate (which includes depression recovery group) is 51.3% and this course is a 6 week course and of up to 35 participants if at full capacity.	Thank you for your comment. Recommendation 1.5.10 specifies that the number of participants for group CBT should be 6-8. This is a formal psychological intervention delivered at a high intensity level and the recommended number of participants takes this into account.
Association for Family Therapy and Systemic Practice	short	16	13 and 14	We welcome the recommendation to not routinely provide medication management on its own as an intervention for people with depression.	Thank you for your comment. In light of feedback from stakeholders the recommendation about medication management has been deleted as the committee agreed that it was no longer a widely used treatment option and so inclusion of the recommendation could lead to confusion.
Northumberland Tyne and Wear NHS Foundation Trust	Short	17	3-12	Group CBT and self-help based on CBT principles is a pragmatic as well as a well evidenced approach that can be adapted to individuals.	Thank you for your comment and your support.
Lundbeck Limited	Short	17	24-29	We are surprised that mirtazapine is recommended as a first line treatment option and would query whether it is an appropriate first line pharmacological intervention for a	Thank you for your comment. Based on feedback from stakeholders, the analyses of the clinically and cost effective treatments for a new depressive episode have been

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				person with "less severe" depression. The mirtazapine Summary of Product Characteristics (SPC) lists a large number of potential drug-to-drug interactions with mirtazapine, including a large number of widely-prescribed drugs including hypertensives and diabetes treatments. The SPC advises caution when using mirtazapine in combination with an SSRI, because of the potential for serotonin syndrome. Mirtazapine can affect alertness and driving, no alcohol should be consumed while on mirtazapine treatment, and the treatment effects of increase in appetite and weight gain affect more than 1 in 10 people treated with mirtazapine (MSD Limited, 2017). Given this profile, we are concerned that mirtazapine is not a suitable or appropriate first-line pharmacological option for the vast majority of people with depression. **Reference:** MSD Ltd. 30 mg mirtazapine Summary of Product Characteristics. http://www.medicines.org.uk/emc/medicine/21573. February 2017.	revised. The committee have carefully considered the updated data and as a result the recommendations for treatment of less severe depression have been amended. In light of feedback from stakeholders about the limited nature of the data on mirtazapine and the lack of SMD data, the committee have removed this intervention from the recommendations for less severe depression.
British Association of Art Therapists	Short	17	24-29	If group psychotherapy has not helped and the person does not want medication, consider group art therapy before medication,	Thank you for your comment. Art therapy was not prioritised for investigation in the review questions for this guideline. As the

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				for the reasons in point 4 above.	evidence on art therapy has not been appraised we have not made any recommendations on the use of this intervention.
College of Mental Health Pharmacy (CMHP)	Short	17	24-29	It displays a lack of knowledge to consider SSRIs as if they are just one drug. Considerations such as chemical structures, receptor affinities, risk of QT prolongation with citalopram/escitalopram, discontinuation problems with paroxetine, interactions with other medications because of effects on liver enzymes etc make them all quite distinctly different. Perhaps the Guidelines panel would like to explain how all this will be available, and provide the evidence for psychological therapies effectiveness in different cultures. England is multicultural and there are many non-English speakers with mental health problems (especially PTSD and similar consequences of persecution in other countries). Is the panel suggesting that they should have second line treatment as default	Thank you for your comment. We have added another recommendation in section 1.4 to clarify that paroxetine and venlafaxine are more likely to be associated with discontinuation symptoms. We have also added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram. We recognise the importance of enabling people from different cultural backgrounds to access appropriate psychological therapies. The guideline makes specific recommendations about assessment and choice which would support the adaptation of the delivery of psychological interventions to take into account cultural factors.
Northumberland Tyne and Wear NHS Foundation Trust	Short	17	13-15	A physical activity programme a well evidenced suggestion and needs greater emphasis. Service users may need very active support to access physical activity but this is likely to be highly effective.	Thank you for your comment and support of the recommendation on physical activity programmes.
Parkinson's UK	Short	17	10	Parkinson's UK welcomes the flexible approach adopted in this particular	Thank you for your comment. This guideline is about the treatment and management of

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				recommendation, with the option of face-to-face, telephone, or online Cognitive Behavioural Therapy (CBT) sessions. Mohr et al found that significantly fewer participants dropped out of telephone delivered CBT than face-to-face. (Mohr DC, Ho J, Duffecy J, et al. Effect of telephone-administered vs face-to-face cognitive behavioural therapy on adherence to therapy and depression outcomes among primary care patients: A randomized trial. JAMA 2012;307(21):2278–85) In the context of Parkinson's, with a condition that is fluctuating and on/off periods from hour to hour and day to day, along with mobility issues, accessibility of CBT sessions is of vital importance. However, we have some concerns around the recommendation that the sessions must take place over 9-12 weeks, including follow-up. Many people with Parkinson's may experience mobility issues that could make it more difficult for participants to attend regular therapy sessions. Parkinson's is a fluctuating condition and "on/off" responses to medication cause fluctuations from hour to hour and day to day. Someone is "on" when their medication is working. But when someone is "off", they can barely move and may become acutely anxious. Some people cycle between painful cramps (dystonia)	depression in adults. People with depression and a chronic physical health problem, such as Parkinson's, are not within the scope of this guideline. Therefore it is not possible to make recommendations for people with Parkinson's in this guideline. Mohr 2011 was included in the NMA of treatment of a new depressive episode.

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				when "off" and involuntary movements (dyskinesia) that can cause injury to themselves or others when they are "on". "On/off" fluctuations can be unpredictable. Some people become reluctant to leave familiar surroundings in case they "switch off" and are unable to move or communicate, which could leave them in a vulnerable or even dangerous situation. Others are "off" for hours at a time, and become confined to their bed or chair. Therefore, while we believe sessions should be offered in a timely manner by providers, we believe that there should be flexibility for people who may not be able to attend sessions within an arbitrary timeframe due to their physical condition. We recommend that this is taken into account so people are not unfairly penalised.	
Association for Family Therapy and Systemic Practice	short	17	13	Since physical activity is likely to be helpful to most people experiencing what is labelled depression should this be offered to everyone, rather than only as a substitute for other low intensity interventions?	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less

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					severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5).
British Association of Art Therapists	Short	17	23	For people who do not want medication or group CBT, consider group art therapy if available, with the provisions suggested in point 1 above for outcome measurement. This would mean more options available, especially of psychological therapies, which are largely preferred to medication as documented in the full draft guidelines. Art therapy can be especially attractive to people who would find it difficult to talk right from the start, and art-making or mark-making can be a way into beginning to explore difficult or confusing thoughts and feelings and later verbalise them.	Thank you for your comment. Art therapy was not prioritised for investigation in the review questions for this guideline. As the evidence on art therapy has not been appraised we have not made any recommendations on the use of this intervention.
University of Nottingham	Short	17	25	Throughout the recommendation sections on pharmacological treatment, SSRIs or mirtazapine are advocated as first-line pharmacological treatments. There is	Thank you for your comment. Based on feedback from stakeholders, the analyses of the clinically and cost effective treatments for a new depressive episode have been

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				evidence in several papers including a study of FDA Summary Basis of Approval RCTs that mirtazapine is associated with increased mortality, suicide attempts and in some analyses suicides (Khan A, Faucett J, Morrison S, Brown WA. Comparative mortality risk in adult patients with schizophrenia, depression, bipolar disorder, anxiety disorders, and attention-deficit/hyperactivity disorder participating in psychopharmacology clinical trials. JAMA Psychiatry. 2013;70(10):1091-9. Coupland C, Dhiman P, Morriss R, Arthur A, Barton G, Hippisley-Cox J. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. BMJ. 2011;343:d4551. Coupland C, Hill T, Morriss R, Arthur A, Moore M, Hippisley-Cox J. Antidepressant use and risk of suicide and attempted suicide or self harm in people aged 20 to 64: cohort study using a primary care database. BMJ. 2015;350:h517. Danielsson B, Collin J, Jonasdottir Bergman G, Borg N, Salmi P, Fastbom J. Antidepressants and antipsychotics classified with torsades de pointes arrhythmia risk and mortality in older adults - a Swedish nationwide study. Br J Clin Pharmacol. 2016;81(4):773-83.) We are concerned that mirtazapine is recommended as a first-line drug in less severe depression when it has a risk profile for death and	revised. The committee have carefully considered the updated data and as a result the recommendations for treatment of less severe depression have been amended. In light of feedback from stakeholders about the limited nature of the data on mirtazapine and the lack of SMD data, the committee have removed this intervention from the recommendations for less severe depression. Khan 2013, Coupland 2011, Coupland 2015 and Danielsson 2016 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).

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				suicide attempts/self-harm like this and the evidence on effectiveness was limited (Full guideline section 7.4.1).	
Relate	Short	16, section 1.5		We are concerned that couples therapy for depression is missing from the recommendations for first-line treatments for less severe depression – despite the fact that in the full guideline (section 7.9.4, p324), couples therapy for depression is recommended (rightly, we believe) for 'a person with more severe and less severe depression who has problems in the relationship with their partner'. The short version of the guidelines appears to neglect couple therapy as a treatment for less severe depression, against the full guidelines' recommendation that it be considered as a treatment for *both* more severe *and* less severe depression.	Thank you for your comment. We have clarified in the short version of the guideline that the recommendations on behavioural couples therapy apply to both more and less severe depression.
Leeds Community Healthcare Leeds IAPT	Short	18	General	We are concerned that IPT and counselling are not included in first line treatment for less severe depression without first offering CBT or BA when IPT or counselling may be the most appropriate intervention for the client (for example if the patient is presenting with clear a triggers and relationship issues).	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

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					The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. IPT and counselling are recommended after other high intensity psychological interventions because of their small benefit on the SMD outcome (compared with other interventions), the larger benefits on the other 2 clinical outcomes, and their lower cost effectiveness compared with other high intensity individual psychological interventions as well as clinical management.
Northumberland Tyne and Wear NHS	Short	18	1-8	Need to emphasise potential perpetuating factors such as difficult relationships, history of adversity, ongoing pressures that make	Thank you for your comment. These factors are highlighted in the recommendations in section 1.4. Therefore we have not specified

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Foundation Trust				recovery difficult.	them again here.
Mind	Short	18	19-21	This recommendation will be a challenging change in practice because it does not stipulate the criteria for offering this as opposed to the previous recommendations.	Thank you for your comment. Recommendations 1.5.5 and 1.5.6 detail who should receive CBT, BA and IPT. The stipulation of delivery of treatment in these recommendations is in line with current practice so we do not think these recommendations will be challenging to implement.
Leeds Community healthcare Trust, Child and adolescent mental health service	Short	18	2	We are concerned that IPT and counselling are not included in first line treatment for less severe depression without first offering CBT or BA when IPT or counselling may be the most appropriate intervention for the client (for example if the patient is presenting with clear a triggers and relationship issues).	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically

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					effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. IPT and counselling are recommended after other high intensity psychological interventions because of their small benefit on the SMD outcome (compared with other interventions), the larger benefits on the other 2 clinical outcomes, and their lower cost effectiveness compared with other high intensity individual psychological interventions as well as clinical management.
Association for Family Therapy and Systemic Practice	short	18	1.5.9	IPT is not the only approach effective for interpersonal issues. Systemic psychotherapy could also be considered here.	Thank you for your comment. We did not find any evidence on systemic psychotherapy and are not able to make any recommendations for its use.
Camden & Islington NHS Foundation Trust	short	18	11	We are concerned about the recommendations regarding IPT for different severity of presenting depression. We note that less severe refers to a baseline phq score of 10-17 and more severe to a baseline phq of 18 and above. We are concerned that the consultation document places IPT only as	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the

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				a second line intervention for patients presenting with less severe depression and that it does not recommend it as a treatment for those presenting with more severe depression. Within our service we provide a successful and expanding IPT service for patients resenting with depression. Over the past 5 years we have consistently achieved recovery rates well above 50%. Our data from January 2012 up to July 2017 shows a 58% recovery rate for patients receiving IPT within our IAPT clinic (sample size of 91 patients). Within the less severe group we achieved an impressive recovery rate of 66% and no deterioration for any patients. **Were the new guidance to be implemented this group would only be offered IPT if they did not benefit from of declined group CBT or individual self- help**. We think that it would be an oversight to fail to offer IPT as a first line treatment option for these patients given the efficacy of this treatment. Given the above as well as the issue of patient choice we feel very strongly that IPT should be offered as an option for first line treatment for patients presenting with less	NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. IPT is recommended after other high intensity psychological interventions because of the small benefit on the SMD outcome (compared with other interventions), the larger benefits on the other 2 clinical outcomes, and the lower cost effectiveness compared with other high intensity individual psychological interventions as well as clinical

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				severe depression. The current recommendations would not involve patients being given the choice of IPT as an initial treatment option. This feels very limiting - meaning that people presenting with relational issues and depression will not have a treatment that fits with their experience readily available, especially within the NHS in primary care. Many patients present to us with an understanding of their depression within an interpersonal context, and/or are find the model makes sense as is of great help to them. For these patients presenting for treatment for depression we believe that it should be offered as a first line option for treatment	management. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Sussex Partnership NHS Foundation Trust	Short	18	11	1.5.9 – We think that the recommendation that IPT only be offered to people with less severe depression is unnecessarily restrictive, not in line with the evidence reviewed and will cause specific difficulties in implementing in routine care. The treatment trials did not exclude people with more severe depression by the criteria these guidelines use. Current IPT training	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for

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				guidelines suggest that the treatment should be offered to people with a PHQ >14. If people with severe depression (PHQ > 17) are not to receive IPT then this leaves a very narrow band of people for whom IPT would be applied. Many people who currently benefit from IPT in routine clinical services would now fall outside the guideline. We suggest that IPT might also be recommended for people with more severe depression as well.	treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Norfolk & Suffolk Foundation Trust	Short	18	22	The guide talks about giving twice weekly sessions and maintenance but unclear rationale for this in the short or full guideline. This will have major implications for services in terms of delivery and therefore the rationale for this is important.	Thank you for your comment. This specification was taken from what was used in the trials that were included in the clinical evidence review and economic analysis. These recommendations were shown to be clinically and cost effective.
Leeds Community	Short	18	23	We are concerned about the practicality of offering 2 sessions per week due to current	Thank you for your comment. This specification was taken from what was used

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Healthcare Leeds IAPT				service demand	in the trials that were included in the clinical evidence review and economic analysis. These recommendations were shown to be clinically and cost effective.
Leeds Community Healthcare Leeds IAPT	Short	18	23	We are concerned about the practicality of offering multiple follow up appointments due to service demand.	Thank you for your comment. This will be a matter for local implementation.
Mind	Short	19	13 - 15	We are unsure why the focus is still only on psychodynamic therapy (STPT) if a person with less severe depression would like help for emotional and developmental difficulties in relationships. The new Counselling for Depression (CfD) treatment is being offered and all Personal Wellbeing Practitioners are being trained in this- it's an approach that is part EFT and part Person-Centred so why isn't this recommended more explicitly?	Thank you for your comment. The expert opinion of the committee was that it was correct to focus STPT on developmental (historical) difficulties in relationships. This emphasis on historical developmental issues was in the view of the committee the important differentiator from counselling.
British Association of Art Therapists	Short	19	1	Consider group art therapy for people with less severe depression if they find it hard to express their difficulties in words, expressing emotions, are feeling isolated or have difficulty with their sense of who they are.	Thank you for your comment. Art therapy was not prioritised for investigation in the review questions for this guideline. As the evidence on art therapy has not been appraised we have not made any recommendations on the use of this intervention. We will forward your comment to the NICE surveillance team for consideration.
British Association of	Short	19	1	If employment problems, Individual Placement and Support has good evidence	Thank you for your comment and for bringing these references to our attention. Baksheev

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Art Therapists				from randomised trials conducted in other English-speaking countries, with even severe mental health conditions. The Centre for Mental Health is expanding its provision of this to more places. [Baksheev, G.N., Allott, K., Jackson, H.J., McGorry, P.D. and Killackey, E. (2012), "Predictors of vocational recovery among young people with first-episode psychosis: findings from a randomized controlled trial", Psychiatric Rehabilitation Journal, Vol. 35 No. 6, pp. 421-7; Bond, G.R. and Drake, R.E. (2008), "Predictors of competitive employment among patients with schizophrenia", Current Opinion in Psychiatry, Vol. 21, pp. 362-9.]	2012 and Bond 2008 could not be included because these were not depression populations. Consequently we do not have any evidence on these interventions and are not able to make any recommendations about them.
Association for Family Therapy and Systemic Practice	short	19	1.5.12	'counselling' is not well defined here and the qualifications of counsellors can vary widely. This recommendation suggests this would be a 'stepped care' step up from individual CBT / BA where in fact it may not add more expertise / experience unless the level of counselling is better defined.	Thank you for your comment. We have specified in the recommendation that this should be counselling based on a model developed specifically for depression.
Association for Family Therapy and Systemic Practice	short	19	1.5.14	Short term psychodynamic psychotherapy is not the only approach effective for difficulties in relationship. Systemic psychotherapy could also be considered, here.	Thank you for your comment. We did not find any evidence on systemic psychotherapy and are not able to make any recommendations for its use.
Association for Family Therapy and Systemic	short	19	1.7	Which we welcome the inclusion of interventions for couples, behavioural couples therapy is not the only effective therapy for couples where one person may	Thank you for your comment. We did not find any evidence on systemic psychotherapy and are not able to make any recommendations for its use.

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Practice				be experiencing what is labelled 'depression'. Other forms of Systemic psychotherapy could also be considered here.	
Dorset HealthCare University NHS Foundation Trust	Short	19	9	We are concerned that this recommendation implies that many experienced counsellors who currently deliver brief counselling, in 6-8 session, for mild to moderate depression will be unable to continue to provide this modality. This has significant cost implications for our Trust; given counselling's cost-effectiveness. Furthermore this implies that generic counselling is not effective for these patients. In my locality alone the evidence supports Generic Counselling as, of those entering counselling with PHQ9 10-27 the following numbers, on average, have reached recovery (PHQ9 = 9 or less): - 54.7 % in 2014 – 15 - 54.5% in 2015 – 16 - 55.5% in 2016 - 17	Thank you for your comment. The recommendations were based on the committee's consideration of the evidence of clinical and cost effectiveness for counselling. The model of counselling used in the clinical trials in the evidence was typically for 16 sessions. We did not find any high quality evidence to support the use of briefer numbers of counselling sessions. However, it may be the case that a number of individuals who are offered counselling for depression, recover in less than the suggested 16 sessions, as of course is also the case for other high intensity psychological interventions. This view is supported by the data from NHS-D, which reports on the IAPT programme, although the means reported within it will include those who have left treatment earlier than the originally agreed number of treatment sessions.
Mind	Short	19	10	We are concerned that this recommendation may imply that only models already stipulated within the guidelines will be considered by practitioners. It would be helpful if a list or a link to a list of models specifically developed to deal with depression was mentioned here	Thank you for your comment. The evidence suggests interventions developed specifically for a disorder tend to be more effective and so the committee have recommended these are used. We have not identified evidence for any specific models and so are not able

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				specifically highlighting direct alternatives to CBT and psychodynamic approaches such as Counselling for Depression (CfD).	to name them in the recommendations.
NHS Sheffield CCG	Short	19	1 & 9	With particular reference to counselling, the CCG would like to reiterate that counselling is indeed a valuable intervention and agrees that it should form part of a stepped model of care	Thank you for your comment and your support.
Mind	Short	19	12	This recommendation will be a challenging change in practice because it means if a client is given 16 sessions and attends weekly then there is no spread out follow-up opportunity like that which is offered on page 18, lines 25 – 27. We would advise offering the same opportunity for follow-ups over another 16 week period on top of the 16 weeks initially offered.	Thank you for your comment. When developing the suggested structure for the number and duration of sessions, the committee based their recommendations on the models of delivery used within the clinical trials.
British Psychoanalytic Council	Short	19	13	With regard to short-term psychodynamic psychotherapy (STPT) being recommended only after other recommended interventions (group CBT, physical activity programme, facilitated self-help, pharmacological interventions, individual CBT or BA) had not worked well in a previous episode of depression or in those who did not want the other recommended interventions and who would like help for emotional and developmental difficulties in relationships: We are greatly concerned that, in practice,	Thank you for your comment. As you have identified STPT is one of the interventions provided through the IAPT programme. We are confident that if other psychotherapy services wish to make use of IAPT material on STPT then this could be made available to them. This would be a matter for local implementation.

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				this will deplete the availability of STPT nationally. Little information is currently given to patients on therapy types recommended by NICE (as opposed to information provided to patients about the types of therapy available at their local IAPT). Given the above mentioned dataset which shows equivalent recovery rates between STPT and CBT is NICE content to publish a set of guidelines which will likely lead to STPT being less available as a treatment option for patients?	
British Psychoanalytic Council	Short	19	13	Re: In cases of less severe depression, Short-term Psychodynamic Psychotherapy (STPT) being offered only where CBT, exercise, facilitated self-help or medication did not work for an earlier episode of depression or are not wanted, and a person requests help with emotional and developmental difficulties in relationships: This is also problematical because it goes against evidence, which shows that, for example, only 6.6% of patients identify developmental difficulties as the cause of their depression, where 68.6% of patients identify existing life stressors as the key reason for their depression. Evidence also	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Short-term psychodynamic therapy remains an option for people with less severe depression (who would like help for emotional and developmental difficulties in relationships) for whom other recommended

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				shows that patients with depression caused largely by developmental difficulties are more likely to have difficulties in their current relationships. The above recommendation therefore suggests that many persons who would benefit from STPT will not do so, largely down to focusing overwhelmingly on their current relationship difficulties in the first instance. Please take into consideration the following study: Hansson, M., Chotai, J., & Bodlund, O. (2010). Patients' beliefs about the cause of their depression, *Journal of Affective Disorders*, 124 (1-2): 54-9.	interventions (self-help with support, physical activity programme, antidepressant medication, individual CBT or BA or IPT) have not worked well in a previous episode of depression or in those who did not want the other recommended interventions. The committee made this a 'consider' recommendation because of the moderate benefit on the SMD outcome and the lower cost effectiveness of short-term psychodynamic therapy compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of short-term psychodynamic therapy was likely to be higher in the sub-population in the recommendation compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). Hansson 2010 could not be included in this review as the aetiology of depression and experience of care are excluded from the scope of this update.

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United Kingdom Council for Psychotherapy	Short	19	13	**Overly restrictive criteria for recommending STPT for less severe depression** While the draft guidance includes Short-Term Psychodynamic Psychotherapy (STPT) as a recommended treatment for depression, we are concerned that it is only recommended in unjustifiability limited circumstances. Therefore this recommendation is problematic for both practitioners and patients. The guidance indicates that in cases of less severe depression, short-term psychodynamic psychotherapy (STPT) can be offered only in cases where CBT, exercise or facilitated self-help, or medication did not work for an earlier episode of depression or are not wanted, *and* a person requests help with emotional and developmental difficulties in relationships. The requirement that a person asks for help with '*emotional and developmental difficulties in relationships'* is problematic on a number of grounds. Firstly, the experimental evidence does not justify this requirement. A recent meta-analysis comparing STPT to CBT showed	Thank you for your comment. We would expect that in any assessment undertaken of an individual's needs, early experience and developmental factors would be taken into account. In discussion with a therapist, this may inform the choice of treatment. Steinert 2017 systematic review was searched for relevant references but no additional studies that met the inclusion criteria were identified. Bifluco 2006 cannot be included in the review as it does not meet the study design criteria (not an RCT or systematic review of RCTs)

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				comparable effects for *all* cases of depression (Steinert et al, 2017). Secondly, even if client's depression has a developmental origin, it may be manifesting in a different way at the time they present for treatment. Clients may not make the conscious link between their past experiences and their current difficulties. Evidence indicates that as few as 6.6% of patients identify developmental, childhood difficulties as the cause of their depression when they present in primary care compared with 68.6% who identify current life stressors as the precipitating factor in their depression (Hansson et al, 2010). While developmental difficulties do indeed contribute to the cause of depression, patients with such factors are also more likely to experience difficulties in their *current relationships* (Bifluco et al, 2006) and it is current life stressors that they are far more likely to present with at assessment (Hansson et al, 2010). The guidance makes assumptions about the sophistication of patients' understanding of complex, developmental aetiological models of depression when the evidence suggests that this is not likely to be the case. Such patients with childhood difficulties may benefit	

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				from STPT but would miss the opportunity to receive this psychological intervention given their more likely presentation of current stressors rather than developmental issues. Thirdly, the guidance further assumes that patients are always willing to disclose highly sensitive information about their historic experience during initial assessment, including childhood abuse and neglect. This is not the case, as guidance from the Royal College of General Practitioners and the National Society for the Prevention of Child Cruelty suggests: '*Knowing and understanding a patient's history is key to providing appropriate support and management but many patients find it hard to disclose a history of abuse and GPs may become frustrated by a seeming inability to help a patient attending frequently with apparently inexplicable symptoms or unsolvable problems'* (RCGP/NSPCC, 2014, p.108). As a result, practitioners would have little opportunity to recommend STPT for patients' depression, even though it has been established as an efficacious treatment for depression and may represent the choice of the patient. While we welcome the acknowledgement of developmental causes of depression within the guidance, the guidance is problematic for patients who are	

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				not likely to receive STPT but for whom it may be the most appropriate form of treatment.	
United Kingdom Council for Psychotherapy	Short	19	13	**Restrictive criteria for STPT** The provision of STPT throughout the guidance should not rest solely on the patient's own identification of causal developmental factors at assessment that may be contributing to their depression. We suggest that treatments should be recommended in line with patient choice and matching, as described above.	Thank you for your comment. Short-term psychodynamic therapy is an option for people with less severe depression (who would like help for emotional and developmental difficulties in relationships) for whom other recommended interventions (self-help with support, physical activity programme, antidepressant medication, individual CBT or BA or IPT) have not worked well in a previous episode of depression or in those who did not want the other recommended interventions. The committee made this a 'consider' recommendation because of the moderate benefit on the SMD outcome and the lower cost effectiveness of short-term psychodynamic therapy compared with other high intensity individual psychological interventions as well as clinical management. They also agreed that the effectiveness and cost effectiveness of short-term psychodynamic therapy was likely to be higher in the sub-population in the recommendation compared with the 'general' population with less severe depression that was the focus of the guideline economic analysis. Full details of the committee's

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					rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5).
College of Mental Health Pharmacy (CMHP)	Short	19	13	Short term psychodynamic therapy is not something the majority of people will be familiar with. A link is needed here.	Thank you for your comment. We are confident that short term psychodynamic therapy is an intervention that practitioners will be aware of.
Leeds Community healthcare Trust, Child and adolescent mental health service	Short	20		We are concerned that being unable to offer IPT as a first line treatment for moderate to severe or severe depression would result in an increase of referrals being offered for CBT. Our service offers evidence based treatments that vary in its delivery. If we solely start to essentially offer one treatment (CBT) then this implies that other evidence based treatments are not effective, that patients are not capable of making informed choices when treatment and explanations and rationales are provided. IPT is a good fit for Depression triggered by certain life events. It is a pragmatic approach and meaningful to many patients. In addition if we start to offer CBT as a first line to everyone with Depression this will impact significantly on access to treatment as demand will outweigh capacity. This also may not be the most suited treatment and patient's may have to go	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic

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				through a number of processes to get to the right treatment for them which is not a good patient experience. If the offer of IPT is reduced how are we able to increase the evidence base to demonstrate its effectiveness in comparison to CBT that has been a treatment that has had a longer period of research and investment	analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Leeds Community healthcare Trust, Child and adolescent mental health service	short	20		Within the LCH consortium from 1st June 2016 to 1st July 2017, 177 patients with either a depressive episode (F32) or recurrent depressive episode (F33) were treated with IPT. Of these, 126 (71.2%) presented with more severe depression (PHQ9 score of 18+). Within LCH between 1st April 2017 and 31st August recovery rates were comparable between the different modalities offered as shown below (% discharged and in recovery); Guided Self Help (Step 2) including groups: 51.3% CBT (step 3) including groups: 48.4% IPT (step 3): 45.6% EMDR (step 3): 42.9 Counselling for Depression (step 3): 53.3% Dynamic Interpersonal Therapy (step 3): 47.6%	Thank you for your comment and for providing data on the interventions provided by the LCH consortium.

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				Please note that the above rates will be a measurement of both anxiety and Depression scores.	
Northumberland Tyne and Wear NHS Foundation Trust	Short	20	10-18	Consider choice of relational therapies in addition to STPT eg Cognitive Analytic Therapy. Compassion Focussed Therapy.	Thank you for your comment. No evidence was identified to support making a recommendation for these interventions.
Leeds Community healthcare Trust, Child and adolescent mental health service	Short	20	1-7	We are concerned that IPT has been removed from the recommendations for first line treatment of more severe depression	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic

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					analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Leeds Community Healthcare Leeds IAPT	Short	20	1-7	We are concerned that IPT has been removed from the recommendations for first line treatment of more severe depression.	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic

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					analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
University of Nottingham	Short	20	1	We have the same concerns about recommendations of mirtazapine as a first-line treatment for more severe depression based on its safety profile.	Thank you for your comment. In the NMA for more severe depression, there was evidence (n=272) of a small improvement on the SMD outcome in favour of mirtazapine compared to pill placebo. Mirtazapine was also shown to be a cost effective option. As the effect shown by the NMA is in line with evidence from head to head comparisons, the committee agreed that the results from the NMAs and economic analysis were realistic and reliable and so made a recommendation for this intervention. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Sussex Partnership NHS	Short	20	1	1.6.1 – We think that consideration should be given to Behavioural Activation as a first line treatment for more severe depression. There	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the

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Foundation Trust				is evidence from a definitive RCT that BA may outperform cognitive therapy for people with more severe depression (Dimidjian et al, 2006). Hence we believe the first line recommendation could be 'CBT or BA plus SSRI or MIrtazepine'.	treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
United Kingdom Council for	Short	20	10	**Overly restrictive criteria for recommending STPT for severe depression**	Thank you for your comment. Based on feedback from stakeholders, the data in the NMAs and economic models for the

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Psychotherapy				Consistent with our comments above regarding less severe depression, for the treatment of severe depression we do not think it is appropriate for STPT to be offered only in cases where CBT, exercise or facilitated self-help, or medication did not work for an earlier episode of depression or are not wanted, *and* patients have identified for themselves aetiological developmental factors and are willing to disclose their emotional and developmental relationship difficulties at assessment. Instead STPT should be available as part of a broader spectrum of patient choice given the evidence of its efficacy.	treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. The committee considered the results of the clinical analysis (using the SMD as the main clinical outcome and response and remission in those randomised as secondary outcomes), in order to identify clinically effective treatment options. Subsequently, the results of economic modelling (cost effectiveness) were used to identify cost-effective options among the clinically effective ones. The committee have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. Short-term psychodynamic therapy, alone or in combination with an SSRI or mirtazapine, remains an option for people with more severe depression (who would like help for

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					emotional and developmental difficulties in relationships) who do not want to have or who have had poor response to individual CBT, IPT or BA alone, antidepressant medication alone or combined CBT, IPT or BA with antidepressants for a previous episode of depression. The committee made this a 'consider' recommendation after considering the equal effects of short term psychodynamic therapy with pill placebo on the SMD and response in those randomised outcomes and the fact that pill placebo has an established, large effect in depression but it is not a realistic treatment option. The committee also considered that making this recommendation would improve patient choice. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7).
Tavistock Relationships	Short	20	20	We suggest that the words 'less severe or more severe' are added to 1.7.1. so that it reads as follows: "Consider behavioural couples therapy for a person with depression (less severe or more severe) who has problems in the relationship with their partner if:'"	Thank you for your comment. We have clarified in the short version of the guideline that the recommendations on behavioural couples therapy apply to both more and less severe depression.

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				We make this suggestions because the full guideline (p324) recommends that behavioural couples therapy should be considered "for a person with more severe and less severe depression who has problems in the relationship with their partner", and we feel that this needs to be made clearer in the short guideline (i.e. that the recommendation applies to the treatment of both less severe and more severe depression).	
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	21 22 23	1-29 1-28 1-17	Relapse prevention (section 1.8) There is a myriad of data demonstrating efficacy of antidepressants for relapse data given that such data is a requirement for a drug to be licensed in Europe. Meta-analysis demonstrates the large effect size of medication versus placebo in placebo controlled studies (e.g. Geddes et al. Lancet. 2003 Feb 22;361(9358):653-61). We are therefore somewhat surprised that the first option listed in recommendation 1.8.3 for patients who have recovered on medication is CBT, even if continuing medication is listed immediately afterwards. For people with severe depression who have recovered with medication, recommendation 1.8.4 is MBCT or group CBT with medication or MBCT or group CBT alone. We presume that the	Thank you for your comment. We have reversed the bullet points in recommendation 1.8.3 so that continuing with medication is now the first option. The committee were aware of the effectiveness of antidepressants for relapse prevention but also considered the fact that a number of the studies had relatively short term outcomes (up to 6 months), in contrast to those studies reviewed by Geddes 2003 which were typically of 12 months or greater. The committee considered a combination of psychological intervention and medication to be the preferred option for relapse prevention, but noted that some people do not want to continue with medication. In

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				recommendation for the combination of medication plus MBCT is based on the Huijbers et al 2016 study (B J Psych 208 (4) 366-373). However, support for MBCT without antidepressants for relapse prevention is less clear. There is a study that has compared MBCT versus antidepressant in preventing relapse (Kuyken et al. 2015). In this study there was no significant difference between arms. We presume that this is the finding that has influenced NICE recommendations. However, it should be noted that 30% of the patients in the MBCT arm of this study continued on antidepressants, somewhat bringing into question whether MBCT alone really is as effective as continuing antidepressants. Conversely, the Huijbers et al. 2016 study clearly demonstrated that MBCT alone is inferior to the combination of MBCT with antidepressants. We feel that this information needs to be emphasised in the guidelines, ensuring that patients are aware of this before deciding on what treatment they might prefer.	those circumstances, having considered all the evidence, the committee agreed it was appropriate to recommend psychological interventions alone. Geddes 2003 systematic review was searched for relevant references but no additional studies that met the inclusion criteria were identified Huijbers 2016 and Kuyken 2015 are included in the relapse prevention review.
The Mindfulness Initiative	Short	21	18	We are concerned that the exclusion of MBCT from 1.8.3 is not evidence-based and will lead to an unhelpful restriction in patient choice for those seeking treatment for relapse prevention following less severe depression. The recent meta-analysis by	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence.

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				Kuyken et al. (2016) found that MBCT significantly reduced risk of relapse in studies that included patients who were recovering from less severe depression. Further, Kuyken and colleagues found a significant reduction in between-group risk of depressive relapse when comparing MBCT to anti-depressant medication. Restricting relapse prevention options for those recovering from less severe depression to medication and CBT also restricts staff choice. Allowing NHS staff a choice of psychological therapies to train in and deliver will help to keep them engaged and less likely to leave their role. As mindfulness-based approaches are popular, non-stigmatising and have mainstream appeal, the option to train and deliver MBCT courses appears to have a particular impact on job satisfaction for NHS staff (Marx, Strauss, & Williamson, 2013; Rycroft-Malone et al., 2017). In addition, the requirement to develop a personal mindfulness practice through MBCT teacher training delivers benefits for staff as well as patients, reducing staff stress (Virgili, 2013) and potentially reducing turnover. Staff recruitment and retention is becoming a	One of these factors was that recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. Another factor was that the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). Marx 2013 and Rycroft-Malone 2017 could not be included as the outcome (job satisfaction of NHS staff) was outside of the review protocol inclusion criteria. Consequently the committee agreed to recommend MBCT for people with more severe depression. The considerations made by the committee are documented in section 11.7 of the full guideline.

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				serious problem in the NHS. Figures from the Health and Social Care Information Centre indicate that nearly 67,000 clinical staff left the NHS entirely in 2015/16 – 9,000 more than in 2010/11 – whilst agency spending has seen major increases.	Interventions are recommended in NICE guidelines primarily based on evidence of their clinical and cost effectiveness. Enabling NHS staff to have a choice of which psychological therapy to train in is therefore not a primary consideration when making recommendations.
Tees Esk and Wear Valleys NHS Foundation Trust	short	21	18	The guidance between page 21 line 18 and page 22 line 7 (ie sections 18.3 – 18.5) and between page 22 line 25 and page 23 line 7 (ie sections 1,8.9 – 1.8.10) deals with subgroups of recovered patients and advice about relapse prevention intervention for these subgroups. However it only gives advice for people who have recovered from previous episodes with the help of either medication or psychological therapy (or a combination of the two).It does not give any guidance for people who have recovered without treatment from professionals. Many people with depression don't receive professional intervention during their depressive episodes but would nevertheless benefit from a relapse prevention intervention. As things stand this important and sizeable group of people is apparently left out of the guidance altogether. A group that is hard to reach (for a variety of reasons) with regards to treatment should really not be	Thank you for your comment. No evidence was found that directly addresses the group you highlight so the committee did not make a specific recommendation for them. The expectation would be that an individual would draw on existing guidance to inform judgement about which relapse prevention strategy would be most effective.

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				neglected when it comes to relapse prevention.	
Tees Esk and Wear Valleys NHS Foundation Trust	short	21	18	The guidance between page 21 line 18 and page 22 line 7 (ie sections 18.3 – 18.5) and between page 22 line 25 and page 23 line 7 (ie sections 1,8.9 – 1.8.10) deals with subgroups of recovered patients and advice about relapse prevention intervention for these subgroups. The approach is logical but may lead the reader to believe that these are distinct and discrete subgroups and convey the idea that there is clarity about the best relapse prevention approach for each subgroup. It seems to me that the evidence is currently limited and unclear and that the guidance should adopt an approach that is more in keeping with this reality. As a clinician with an interest in relapse prevention, I find this part of the guidance unconvincing and unhelpful. I know that I personally would find it very difficult to successfully commit to memory the details of the subgroups and the recommendations applied to each. It is respectfully suggested that these sections are re-written with a simpler structure so that the guidance contained is clearer and more helpful to the reader and therefore more likely to have a beneficial impact on patient care. An approach that leaves more room for patient preference and clinician judgement (informed	Thank you for your comment. We have made revisions to simplify the structure of the recommendations in section 1.8. However it should be remembered that in all cases these recommendations are meant to supplement clinical judgement not to be used as protocols to be followed independently of the factors you refer to in your comment.

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				by a biopsychosocial formulation regarding mechanisms of relapse amongst other things) would be very appropriate in my view.	
Tees Esk and Wear Valleys NHS Foundation Trust	short	21	22	MBCT is not included in this list of interventions (1.8.3) for people who have recovered from less severe depression with the help of medication. MBCT is included in the following section (1.8.4) which deals with people who have recovered from more severe depression with the help of medication. The evidence for MBCT as a relapse prevention intervention does not point to a clear difference in effectiveness between those with more severe depression and those with less severe depression. Numerous RCTs of MBCT for depressive relapse prevention demonstrate reduced rates regardless of level of depression during episode.	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. One of these factors was that recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. Another factor was that the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). Consequently the committee agreed to

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					recommend MBCT for people with more severe depression. The considerations made by the committee are documented in section 11.7 of the full guideline.
Sussex Partnership NHS Foundation Trust	Short	21	25	1.8.4 – We are unclear of the basis for recommending MBCT for relapse prevention only for those who have recovered from more severe depression and not also for people who have recovered from less severe depression (1.8.3). It is also unclear why MBCT is recommended for people who have recovered following treatment with medication. A recent meta-analysis of MBCT for relapse prevention (Kuyken et al, 2016) includes trials with people who had had recovered from both less severe and more severe depression, and people who had recovered without any form of previous treatment (either medication or psychological therapy).	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. One of these factors was that recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. Another factor was that the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). Consequently the

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					committee agreed to recommend MBCT for people with more severe depression. The considerations made by the committee are documented in section 11.7 of the full guideline. Another factor was that in the majority of trials of MBCT (including those in Kuyken et al 2016) participants either had a history of antidepressant treatment or were continuing to use antidepressants at enrolment. Consequently the committee agreed that MBCT should be recommended for people who have recovered following treatment with medication.
Tees Esk and Wear Valleys NHS Foundation Trust	short	21	28	The evidence for group CBT as a relapse prevention intervention is considerably less robust than the evidence for MBCT as a relapse prevention intervention.	Thank you for your comment. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness.
Janssen	Short	22	11-20	We welcome the inclusion of the formal validated scale, PHQ-9 to assess mood and monitor potential relapse of depressive symptoms in recommendation 1.8.7, which states: For people continuing with medication to prevent relapse, hold reviews at 3, 6 and 12	Thank you for your comment and support for the use of validated scales in ongoing monitoring.

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				months after maintenance treatment has started. At each review: • monitor mood state using a formal validated rating scale, for example the PHQ-9 • review side effects • review any personal, social and environmental factors that may impact on the risk of relapse • agree the timescale for further review (no more than 12 months). [new 2017] We believe that ongoing monitoring to prevent relapse is extremely important consideration, in order, to ensure continued response to treatment and we agree with the recommendation to use a validated scale, such as the PHQ-9.	
Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	1.6.4 page 20	10-18	We welcome the inclusion of STPT for people with more severe depression. Our concern is that commissioners and providers will not be able to consider this offer unless the recommendation is strengthened. We suggest: 1. A recommendation is made to commissioners that they should ensure providers can provide STPT as an option for those people with more severe depression for whom STPT is their first preference, or	Thank you for your comment and suggestions. 1. We do not agree that STPT will not be commissioned based on the recommendations made in the guideline. As you may be aware there is an existing training programme for STPT delivered through the IAPT programme. This is supported by policy guidance which sets out the need for choice in IAPT services, including STPT and counselling.

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				where the clinician considers the service user's difficulties, treatment history and suitability makes STPT the first-choice offer. 2. The suggested sequencing should be monitored and changed, varied, according to whether a different sequencing produces higher overall recovery rates. The evidence from IAPT suggests that offering STPT, IPT and BA as first line options, and CBT, group CBT as second line options, would achieve the best overall recovery rates. 3. Likewise, as there was no economic modelling done to test different sequencing options, and as all providers will need to adopt payment by results in 2018, there should be a recommendation that local commissioners should monitor recovery rates by type of intervention and promote those with highest recovery rates via local flexing of their PbR framework.	2. There is no good evidence from properly constructed randomised studies on sequencing of psychological interventions. If it were possible to ensure proper scientific rigour, your suggestion for IAPT as a test bed for better understanding the sequencing of psychological interventions is to be welcomed. 3. We agree that routine monitoring of services by local commissioners is an excellent idea. Of course it will be important when drawing conclusions about differential effectiveness of different psychological treatments to ensure that the populations on which the comparisons are being made are equivalent. For example have patients who have not benefitted from a previous treatment been compared with those who are in receipt of their first treatment, clearly this is potentially a misleading comparison.
Tees Esk and Wear Valleys NHS Foundation Trust	short	22	25 - 27	This is potentially unclear. It might be understood as referring to the subgroup who satisfy both conditions: they are at higher risk of relapse *and* recovered with medication and wish to stop taking it. Or it might refer to the two subgroups: the subgroup who are at	Thank you for your comment. We have amended the recommendations in section 1.8 to improve clarity.

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				higher risk of relapse and the subgroup recovered with medication and wish to stop taking it.	
Tees Esk and Wear Valleys NHS Foundation Trust	short	22	1	The evidence for group CBT as a relapse prevention intervention is considerably less robust than the evidence for MBCT as a relapse prevention intervention.	Thank you for your comment. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness.
Tees Esk and Wear Valleys NHS Foundation Trust	short	22	7	Typo: I think 1.8.93 should read 1.8.9	Thank you for your comment. We have corrected the typo.
Tavistock Relationships	Short	22	17	We would like to see the word 'relational' included so that the bullet point reads: "review any personal, relational, social and environmental factors that may impact on the risk of relapse". We are suggesting this change because we know that many people undertaking assessments and reviewing cases in IAPT services either do not know about Behavioural Couples Therapy or have very little understanding about the impact of relational factors on depression. This amendment would act as a 'belt and braces' prompt to those reviewing cases that they need to explore the relational factors that may be implicated, as many practitioners	Thank you for your comment. We do not think this level of detail is required in the recommendation.

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				may not understand the need to look at the relational aspect from the words 'personal, social or environmental'.	
Mental Health Foundation	Short	22	25	The guidance places unnecessary limits on the applications of Mindfulness Based Cognitive Therapy (MBCT). Within these guidelines, the role of MBCT is restricted to those at high-risk of relapse (those who have had three or more previous episodes), and who have already received pharmaceutical/psychological interventions. We would advocate that MBCT and indeed Mindfulness Based Stress Reduction (MBSR) are effective as preventative and protective measures. A systematic review and meta-analysis conducted by Gu et al in 2015 evaluated mechanisms of action underlying both MBCT and MBSR. Inclusion criteria meant that studies were included if their outcome variables assessed mental health and well-being, rather than specifically for Major Depressive Disorder. In addition, studies were included even if they used adapted versions of MBCT or MBSR. For inclusion, studies must also have included MBCT or MBSR in a mediation analysis. These two mindfulness-based approaches were collapsed into one intervention category. A	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. Recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. Also the majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). Consequently the committee agreed to recommend MBCT for people with more severe depression. The considerations made by the committee are documented in

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				total of 20 studies were included in this review, and of these only nine included depressive symptoms as an outcome variable. Other outcomes included anxiety, stress, mood state, quality of life, and anger expression. The results of the narrative review showed strong and consistent evidence for cognitive and emotional reactivity, moderate and consistent evidence for mindfulness and repetitive negative thought, and preliminary but insufficient evidence for self-compassion and psychological flexibility as mechanisms of change within mindfulness-based interventions for clinical and nonclinical outcomes. The results of the two modelling analyses showed that both mindfulness and repetitive negative thought were significant mediators of the effect of MBCT/MBSR on mental health outcomes, including anxiety, depressive symptoms, general psychopathology, stress, and negative affect. These findings provide evidence that mindfulness is likely an influential factor in the effectiveness of MBCT for psychopathology. Indeed, the stipulation that MBCT can only be offered after other interventions runs contrary to the stated NHS goals of enabling patients to have more options in their treatment. This	section 11.7 of the full guideline. The committee also noted that of the trials of MBCT which specified a previous number of episodes as an entry criteria, 7 out of the 9 trials considered as part of the guideline evidence review had 3 or more episodes as their entry criteria. Consequently they specified this in their recommendations. The committee also noted that in the majority of trials of MBCT (including those in Kuyken et al, 2016) participants either had a history of antidepressant treatment or were continuing to use antidepressants at enrolment. Consequently the committee agreed that MBCT should be recommended for people who have recovered following treatment with medication. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. Gu 2015 could not be included in this review as mediator/moderator analysis are outside the protocol of this review

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				has been at the forefront of the patient choice agenda set out by the Secretary of State and the Department of Health, and is particularly pertinent where patients have strong aversions to other forms of psychological therapy or medication. Patients, of course, can only choose from what is available. It is crucial to broaden professional skillsets of staff so that MBCT can be offered more widely. Currently, the guidance offers MBCT on a par with CBT and the proposed change bears a risk that NHS Trusts will limit their offering to the latter because this is the modality where they have existing services. MBCT is a popular specialism for health professionals, and allowing staff to train to extend their portfolio of expertise could help tackle challenges around recruitment and retention.	
Tees Esk and Wear Valleys NHS Foundation Trust	short	22	25	The evidence for group CBT as a relapse prevention intervention is considerably less robust than the evidence for MBCT as a relapse prevention intervention.	Thank you for your comment. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness.
Sussex Partnership NHS	Short	22	25	1.8.9 – We are unclear why the specifier of three or more previous episodes of depression remains. The Kuyken et al (2016)	Thank you for your comment. When developing the recommendations for the prevention of relapse the committee took into

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Foundation Trust				meta-analysis showed the number of previous episodes was not a moderator of relapse prevention outcome. There is also the clinical consideration that it is often difficult to determine whether a period of depression is a single 'episode', more than one episode, or a fluctuating pattern of low mood that sometimes reaches a specific threshold. By removing the episode specifier it will be clearer to all what can be offered for relapse prevention without the additional assessment difficulty of identifying discrete episodes.	account a number of factors reported in the evidence. One of these factors was that of the trials of MBCT which specified a previous number of episodes as an entry criteria, 7 out of the 9 trials considered as part of the guideline evidence review had 3 or more episodes as their entry criteria. You raise the possibility that the lack of a finding of number of relapses as a mediator supports the dropping of this qualifier from the recommendation. However, Kuyken et al note the low heterogeneity of the populations in the included trials may well impact on the analysis of any mediators. They also report in some analyses an association between the number of episodes and relapse. When these factors were taken into account the committee considered that it was appropriate to include this qualifier in the recommendations.
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	23 24 25 26	18-28 1-29 1-23 1-10	Limited response and treatment-resistant depression (section 1.9) However it is the recommendations for second line pharmacotherapy described in section 1.9 that cause greatest concern. As they stand we believe that they are fundamentally dangerous, not supported by the evidence base, will have a detrimental	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications.

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				impact on provision of services and do not provide the breadth or depth of recommendations that clinicians need. If a person treated with an SSRI or mirtazapine first line has no, or only a limited, response, recommendation 1.9.2 includes the options of combining the medication with a psychological therapy or "changing to a combination of 2 different classes of medication, in specialist settings or after consulting a specialist". This is very out of kilter with current practice where patients tend to have trials of two or more antidepressants before referral into specialist care. Given that only around 50-60% of patients respond to the first antidepressant they try (Papakostas & Fava Eur Neuropsychopharmacol 2009;19:34-40; Rush et al. Am J Psychiatry 2006;163:1905), if the 40-50% not responding are referred into specialist care, or even if specialist care are just consultant about them, then services will be swamped. Section 1.9.5 detailing the nature of the medication combinations recommended causes great concern. Firstly, there is the recommendation "adding an antidepressant of a different class to their initial medication, for example an SSRI with mirtazapine".	Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression. Whilst we note that antidepressants can be described by their pharmacological action or their chemical structure, we think that the recommendations are clear about what antidepressants to use and will not be misunderstood. We note that combining antidepressants is potentially complex which is why we have recommended consulting with specialist

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				There are many problems with this recommendation from both a safety and evidence based perspective. These include: a) Critical to the recommendation is what constitutes a 'class' of antidepressant. Commonly antidepressants are described by both a mixture of their pharmacological action (e.g. selective serotonergic reuptake inhibitors – SSRIs) and their chemical structure (e.g. tricyclic antidepressants – TCAs), while many do not fall neatly into any grouping (e.g. vortixetine, agomelatine, bupropion). This has been highlighted as a potential cause for clinical confusion (Zohar et al. Eur Neuropsychopharmacol. 2015 Dec;25(12):2318-25). It is therefore unclear how clinicians will interpret the NICE recommendation. b) Combining antidepressants is a potentially complex and dangerous thing to do. Some combinations are not pharmacologically logical, for example combining an SNRI, such as venlafaxine, with an SSRI, given that the former is a potent inhibitor of serotonin re-uptake in its own right and it is questionable whether it is possible to increase the degree of blockade any further with an SSRI. Of more concern is that several combinations of antidepressants are potentially dangerous. Historically TCAs have been combined with MAOIs though this is potentially dangerous	care. We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations of medication which should be avoided. The footnote is only intended to highlight where an intervention has been recommended off license. In light of your comment we have amended the wording in the footnote to clarify that not all antipsychotics are licensed for the treatment of depression and remove reference to specific drugs as this was confusing. As documented in the 'evidence to recommendations' section in the full guideline combinations with an antidepressant of a different class, antipsychotics (aripiprazole, risperidone, quetiapine, olanzapine) and lithium were all identified in the reviews undertaken for this guideline as effective (i.e. they resulted in improved rates of remission or response and in depressive symptoms) in the treatment of no or limited response to initial treatment. Therefore the committee decided to recommend them. We have added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram. The guideline sets out a range of therapeutic

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				combination (Ponto et al. Am J Hosp Pharm. 1977 Sep;34(9):954-61.) and other guidelines have specifically recommended that the combination of MAOIs and TCAs, SSRIs or SNRIs should not be used (Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85; Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525). Another dangerous combination is that of SSRIs and TCAs (something that is not uncommon in clinical practice). The issue is that SSRIs, particularly fluoxetine and paroxetine, inhibit the metabolism of TCAs potentially leading to dangerous plasma levels of the TCA (Vandel et al. Pharmacol Res. 1995 Jun;31(6):347-53). The guidelines, as they stand, could be used to defend using such combinations. c) While there is data from small RCTs suggesting efficacy of some combinations of antidepressants, the largest study to date, the Co-MED study (Rush et al. Am J Psychiatry. 2011 Jul;168(7):689-701) was negative. The second element of the recommendations of section 1.9.5 is similarly unclear and potentially hazardous. This is "combining an antidepressant with an antipsychotic….". A foot note then states "At the time of consultation (July 2017) antipsychotics (with the exception of quetiapine and flupenthixol) did not have a UK marketing authorisation for this indication". It is unclear if this means that	options for the management of depression that has no/limited response. There was no evidence to support making recommendations for further lines of treatment with thyroid hormone or modafinil. Ketamine was not prioritised for investigation by this guideline as it is not a currently available first line intervention for depression, it is not licensed for use in depression and it is an abused drug. In these circumstance the committee did not think it was appropriate to review it. As stated above, we have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications**.** We have also added a cross reference to TA367 on the use of vortioxetine, to show this is an option before changing to a combination of 2 different classes of medication. Thank you for bringing these references to our attention. Papakostas 2009, Rush 2006, Zohar 2015, Vandel 1995, Anderson 2003, Cleare 2015,

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				the NICE Guideline Committee are therefore recommending quetiapine and flupenthixol ahead of all other antipsychotics, or simply recommending all antipsychotics. If the latter, then the major concern with this is that there is a complete lack of evidence for most antipsychotics in combination with antidepressants for the treatment of depression. This is particularly the case for first generation antipsychotics and indeed there are two small negative studies (Anderson Adv Psychiatr Treat 2003 9: 11–20). The data for flupenthixol is old and questionable and hence it is not included as a recommended treatment in either UK (Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525) or international (Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85) guidelines, despite its UK licence. Conversely the evidence base around quetiapine is much stronger. However, it is disappointing that the NICE Guideline Committee has made no comment regarding whether or not quetiapine can be safely combined with citalopram or escitalopram due to QTc prolongation concerns of both medications. The evidence base supporting other antipsychotics (e.g. aripiprazole which is considered a first line augmentation strategy by both the British Association for Psychopharmacology (Cleare	Bauer 2013 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs) Rush 2011 was excluded from the chronic depression review as the study included a mixed population (<80% of the sample met inclusion criteria). Aronson 1996 and Papakostas 2008 systematic reviews were searched for relevant references but no additional studies that met the inclusion criteria were identified. Goss 2013, Han 2016 and Thase 2016 could not be included as the interventions were outside the review protocols (modafinil, ketamine, and vortioxetine respectively). Jakubovski 2016 systematic review was searched for relevant references. One additional RCT was identified and added to NMA of treatment of a new depressive episode. Thanks for bringing this review to our attention. Adli 2005 systematic review was searched for relevant references. Two additional RCTs were identified and added to the further-line treatment review. Thanks for bringing this review to our attention.

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				et al. J Psychopharmacol. 2015 May;29(5):459-525) and the World Federation for Societies of Biological Psychiatry (Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85) has not even been considered. Lithium is included as an option to combine with an antidepressant. This is to be welcomed and is in line with the evidence base and other guidelines (Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525; Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85). However, it is a concern that no other options have been described beyond second line treatment. Unfortunately a significant minority of patients fail to respond to first and second line treatments. NHS clinicians are in need of advice with regards to what treatment options such be considered in such circumstances. There is an evidence base for a number of options including thyroid hormone (Aronson et al. Arch Gen Psychiatry 1996 53: 842–848) and modafinil (Goss et al. J Clin Psychiatry 2013 74:1101–1107. These and other options are included in other guidelines (Cleare et al. J Psychopharmacol. 2015 May;29(5):459-525; Bauer et al. World J Biol Psychiatry. 2013 Jul;14(5):334-85) and are conspicuous by their absence in these NICE guidelines. There is also growing evidence for the use of	Thase 2006 was considered for the further-line treatment review but could not be included as the comparison (switching to different dosages of the same intervention) was outside the protocol for this review. Gaynes 2012 was considered for the further-line treatment review but could not be included as it was a secondary analysis of study that was already included (STAR*D [Rush 2006; Trivedi 2006]) Corya 2006 and Shelton 2005 were included in the further-line treatment review. Cipriani 2011 could not be included as the population were outside scope (treatment of acute mania).

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				ketamine for MDD with published meta-analyses (e.g. Han et al. Neuropsychiatr Dis Treat. 2016 Nov 3;12:2859-2867) and, indeed, a growing number of centres in the UK providing this. We are unclear why NICE has chosen not to mention this at all in the guideline. Section 1.9.7 describes alternatives to using two medications (for a person refusing psychological therapies or in whom psychological therapies may not be appropriate). These include increasing the dose of the antidepressant or switching. There is a footnote saying "There is limited evidence to support routine increases in dose of antidepressants or switching in people who have not responded to initial treatment". We dispute this particular contention as well as placing this option after using drug combinations on the following grounds: a) It is the case that there is limited evidence of a dose response relationship with SSRIs, though there is some (Jakubovski et al. Am J Psychiatry. 2016 173(2): 174–183). This does not appear to have been considered by the committee. There is more evidence around a dose response relationship for other antidepressants (e.g. TCAs (Adli et al. Eur Arch Psychiatry Clin Neurosci 2005 255: 387–400), venlafaxine (Thase et al. J Clin Psychopharmacol. 2006 Jun;26(3):250-8.)	

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				and vortioxetine (Thase et al. Eur Neuropsychopharmacol. 2016 Jun;26(6):979-93)). b) While remission rates with first line treatment with an SSRI are around 30-40%, remission rates of patients who have failed one SSRI are 24% if switched to another SSRI and 28% if switched to a drug from a different class (Papakostas et al. Biol Psychiatry. 2008 Apr 1;63(7):699-704). Given the decreasing response and remission rates seen with any treatment after each successive treatment failure (Rush et al. Am J Psychiatry 2006;163:1905), such remission rates following switching antidepressants are not to be ignored. c) There is limited evidence comparing increasing dose or switching with combining two drugs. However a study of olanzapine plus fluoxetine versus switching to venlafaxine in SSRI non-responders found no difference (Corya et al. Depress Anxiety. 2006;23(6):364-72), with a similar finding when the comparative antidepressant was the TCA nortriptyline (Shelton et al. J Clin Psychiatry. 2005 Oct;66(10):1289-97). Similarly there was no significant difference in response or remission rates or time to response or remission, between patients who switched antidepressant versus those who had their antidepressant augmented in the	

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				Star*D study (Gaynes et al. J Clin Psychopharmacol. 2012 Feb;32(1):114-9). Increasing the dose of an antidepressant (in a patient who is tolerating the medication), or switching to another antidepressant are both likely to be safer than combining two medications together, are associated with fewer side effects and are also well within the capacity of primary care, removing the need for referral to specialist services or obtaining specialist advice for a vast number of patients. It is therefore most likely that such options are more cost-effective second line pharmacological options than those recommended in the draft guidelines. In relation to these discussions around switching antidepressants, it is a concern that there has been no mention of drugs such as venlafaxine which may have slightly greater efficacy compared to other modern antidepressants (e.g. Cipriani et al. Lancet. 2011 Oct 8;378(9799):1306-15) or vortixoetine which NICE has recommended as a potential third line option (TA367). It is very unclear how such a recommendation fits into the recommendations of the draft Guidelines.	
Northumberland Tyne and Wear NHS Foundation	Short	23	18-28	Point well made about checking for personal or social factors being linked with continued difficulties. Important to check for background factors too, especially histories of childhood	Thank you for your comment. We do not think background factors need to be specified in the recommendation as most clinicians would view these as being

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Trust				trauma and adversity. There is evidence that mental health and other staff do not sufficiently enquire about background experiences and how they impact on current functioning.	synonymous with what is already in the recommendation.
Tees Esk and Wear Valleys NHS Foundation Trust	short	23	1-7	Section 1.8.10 is complicated and potentially confusing. I am not sure about the evidence behind it. An approach that leaves more room for patient preference and clinician judgement would be much more appropriate in my view.	Thank you for your comment. The committee considered both the clinical and cost effectiveness data on relapse prevention and the possibility that some psychological treatments may already have components to promote relapse prevention. Where this was the case the committee decided to recommend an extension of that treatment in order to solidify strategies and techniques to reduce the risk of relapse.
Sussex Partnership NHS Foundation Trust	Short	23	1	1.8.10 - The point in section 1.8.10 that MBCT should be offered only "if initial psychological therapy had no explicit relapse prevention component" does not appear to be evidence-based. This assumes that explicit relapse prevention components in initial psychological therapy are as effective as MBCT in preventing relapse and it is not clear that this has been demonstrated in randomised controlled trials.	Thank you for your comment. The committee considered both the clinical and cost effectiveness data on relapse prevention and the possibility that some psychological treatments may already have components to promote relapse prevention. Where this was the case the committee decided to recommend an extension of that treatment in order to solidify strategies and techniques to reduce the risk of relapse.
Tees Esk and Wear Valleys NHS Foundation Trust	short	23	5	The evidence for group CBT as a relapse prevention intervention is considerably less robust than the evidence for MBCT as a relapse prevention intervention.	Thank you for your comment. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. After

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					considering the cost-effectiveness analyses the committee decided to recommend group CBT over individual CBT.
Sussex Partnership NHS Foundation Trust	Short	23	5	1.8.10 – We do not think that the evidence for group CBT for relapse prevention has as strong evidence as MBCT and do not think they should be listed in the same recommendation here. There is only one definitive RCT reviewed by the committee of group CBT showing effects on relapse prevention (Bockting et al, 2005), which the other pilot RCT fails to support (Wilkinson et al). A stronger recommendation should be made for MBCT than group CBT.	Thank you for your comment. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. After considering the cost-effectiveness analyses the committee decided to recommend group CBT over individual CBT.
Mental Health Foundation	Short	23	11	The guidelines refer to Mindfulness Based Cognitive Therapy (MBCT) as being delivered in a group setting of up to 15 participants. This neglects the fact that this modality can be highly effective when applied as an online training module. There is growing evidence (Stjernswärd 2016, Krusche et al 2013, Morledge et al 2013, Monshat 2012, Gluck et al 2011, Wolever et al 2012) for well-structured online mindfulness courses being as effective as other face-to-face interventions and online courses for stress, even without a therapeutic alliance. Studies are finding that online mindfulness courses can be beneficial for	Thank you for your comment and for bringing these references to our attention. Please see below for details of what has happened to each reference that you have provided. • Gluck 2011: Depression scale is not within the protocol for this review (added to excluded list) • Krusche 2013: Not an RCT • Monshat 2012: Not an RCT or systematic review • Morledge 2013: Intervention targeted at stress not depression. In developing recommendations for a NICE guideline it is necessary that there are robust

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				depression in samples with IBS and epilepsy and anxiety symptoms in a non-clinical sample comparing a 3-week mindfulness course with positive psychology interventions and treatment as usual. Online courses are not restricted by access issues in the same way as face-to-face approaches, and can be a preferred option for those who do not find face-to-face therapy appealing. We recommend that NICE amending the guidelines to reflect the availability of online MBCT training, in addition to face-to-face options.	and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. Stjernswärd 2016 was published after the date cut-off of June 2016 so cannot be included. Consequently we have not reviewed any

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					evidence about online delivery of MBCT and are therefore not able to make any recommendations about this.
Sussex Partnership NHS Foundation Trust	Short	23	11	1.8.12 – It would be helpful to have some guidance as to the nature of follow up sessions. We suggest that this could entail drop in sessions, day MBCT retreats, or a variety of other delivery formats, rather than the same original group re-forming. In Sussex Partnership, we have been successfully providing follow-up sessions to graduates from MBCT groups for several years in the form of monthly drop-in group sessions and regular all day retreats. In our experience, clarifying this recommendation would also make it more likely that they can occur in routine practice.	Thank you for your comment. The committee followed the manual for delivery of MBCT when developing these recommendations. We do not have any evidence to support recommending the approach you describe for follow up sessions.
Sussex Partnership NHS Foundation Trust	Short	24		1.9 Treatment resistant depression. We wonder why long term psychodynamic psychotherapy is not included in this series of recommendations following the Fonagy et al (2015) trial. This should be able to be offered to service users following inadequate response to other pharmacological and psychological therapy treatments.	Thank you for your comment. The committee decided not to recommend LTPP for further-line treatment as there was only data from a single study and the effects on both remission and depression symptomatology were not statistically significant. Stakeholders have commented that the guideline only considered endpoint and not follow-up data. However, if you consider 2-year follow-up data for Fonagy 2015, the effect on remission (HAMD≤8 [outcome measure consistent with other studies]) is not statistically significant, although effects on depression symptomatology are

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					statistically significant at this time point. Even with more consistent effects, the committee would be unlikely to make a recommendation on the basis of a single study.
Sussex Partnership NHS Foundation Trust	Short	24		1.9.2 & 1.9.4 – These sections talks of combining 2 different classes of medications. We wonder why it does not also mention the option of a change of antidepressant class.	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications.
College of Mental Health Pharmacy (CMHP)	Short	24	1-13 and 20-24	Both sections seem to recommend that if someone partially or doesn't respond in 3-4 weeks of their first SSRI or mirtazapine, then they should be given a second additional medication. This in not in line with evidence (STAR-D study). Current evidence is to change to a different antidepressant if the first one fails rather than combining antidepressants straight away. Switching classes is only slightly more likely to be successful than switching SSRIs, a further illustration that SSRIs are not identical. According to these draft guidelines combining a tricyclic and an MAOI would be an appropriate second line treatment. This is a combination we would seldom recommend in	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations of medication which should be avoided. Feedback was received from stakeholders that there would not be sufficient resources

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				clinical practice because toxic and sometimes fatal reactions (serotonin syndrome or similar) have been reported in patients taking MAOIs or RIMAs (e.g. moclobemide) with tricyclic antidepressants and related drugs (Stockleys drug interactions, [online]). In addition, adding another medication to one that has already not led to a response is not in line with the principles of good prescribing- why continue a medicine that is not working? And why increase the side-effect burden for the patient by combining the side-effect profiles of two different medications? Furthermore, this section is advising referral to secondary care after the failure with just one antidepressant. This is very heavy handed care pathway and completely impractical and unnecessary. We need to try to support patients in primary care wherever possible. In reality many GPs would try at least 2 different antidepressants as mono-therapy before referring to specialists. If future practice is going to be guided by this pathway, then there is a concern about a high rate of referrals to secondary care which the services may not be able to absorb and would result in delays in completely unnecessary treatment for a treatable and highly distressing condition.	in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
The Pituitary Foundation	Short	24	1	Primary care practitioners should also 'think outside the box' and investigate significant	Thank you for your comment. Physical health conditions have been added to

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				hormonal imbalances which are known to cause depression e.g. Cushing's Disease/Syndrome.	recommendation 1.9.1 as a potential reason that could explain why the treatment is not working.
Sussex Partnership NHS Foundation Trust	Short	24	5	1.9.2 We think the psychological therapies that might be used to augment antidepressants should be stated.	Thank you for your comment. We have clarified that the psychological therapies are CBT, BA or IPT.
Southern Health & Social Care Trust	Short	24	9	We are concerned that this will imply that all those individual who fail on one antidepressant will be referred to secondary care services and there will not be capacity to manage this recommendation. This statement has come as this is NEW for 2017 and appears out with current prescribing guidelines and based on meta analysis undertaken for this review.	Thank you for your comment. We have revised the ordering of the recommendations on further line treatment. In doing so we have clarified that increasing the dose, switching medication or changing to a combination of psychological therapy plus medication are options to consider before combining 2 medications. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3

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					(short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Janssen	Short	25	20-23	There are inconsistencies with the time to assess response to antidepressant medications in the guideline and we believe these should be clarified to avoid confusion. As above, in section 1.9.1, a timeframe of 3-4 weeks is given to assess whether the person has had no response or a limited response to initial treatment. However, we noted that in section 1.9.8. The recommendation states: 1.9.8 If a person's symptoms do not respond to a dose increase or switching to another antidepressant after 2–4 weeks, review the need for care and treatment and consider consulting with, or referring the person to, a specialist service. [new 2017] We believe that a consistent use of timeframe should be used to assess response to antidepressant therapy to ensure that patients have a chance to benefit from the antidepressant. We would suggest that at least 4 weeks is required and that further time (up to 12 weeks) may be required to reach remission. We suggest that consistency in	Thank you for your comment. Recommendation 1.9.1 has been amended to clarify that the timeframe is typically within 3 weeks. Recommendation 1.9.8 has been amended to clarify that the timeframe is a further 2-4 weeks.

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				time to response should be used and that should be at least 3-4 weeks rather than 2-4 weeks as specified in recommendation 1.9.8. If the 2-week timeframe is referencing the response to a dose increase, then this should be separated from assessing the response to another antidepressant to avoid confusion.	
College of Mental Health Pharmacy (CMHP)	Short	25	18-19	It would not be advisable to switch within antidepressant class if the first wasn't tolerated, as predictably the same intolerable side effects would be likely to occur. This would not be in the patients' best interest.	Thank you for your comment. We appreciate that within classes the broad range of side effects are common. However there are some variations between drugs for example in terms of drug interactions, weight gain and anxiety that may inform the choice of a particular drug within the same class.
College of Mental Health Pharmacy (CMHP)	Short	25	1	Surely the guidance should make a recommendation of the products licensed for this use in the main body of the document rather than just as a footnote	Thank you for your comment. It is standard NICE process to highlight any off-license use of interventions in the format of a footnote.
Southern Health & Social Care Trust	Short	25	17	We are concerned that the guideline suggests second line pharmacological therapy could be interpreted as a tricyclic or a MAOI being equally appropriate at this stage.	Thank you for your comment. We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations which should be avoided.
Sussex Partnership NHS Foundation Trust	Short	25	18	1.9.7 – We wonder why the recommendation is a switch to a medication of the same class if tolerability was the problem – surely another class would be preferable?	Thank you for your comment. We appreciate that within classes the broad range of side effects are common. However there are some variations between drugs for example in terms of drug interactions, weight gain and anxiety that may inform the choice of a particular drug within the same class.

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Sussex Partnership NHS Foundation Trust	Short	25	20	1.9.8 – We think there should be clarification that should read 'After a further 2-4 weeks of that antidepressant.'	Thank you for your comment. We have made your suggested amendment.
College of Mental Health Pharmacy (CMHP)	Short	25	21	Needs to say "after a FURTHER 2-4 weeks..."	Thank you for your comment. We have made your suggested amendment.
Northumberland Tyne and Wear NHS Foundation Trust	SHORT	26 27	11-28 1-15	Treating chronic depression (section 1.10) We have a number of concerns regarding this section. Chronic depression is defined in the guideline as "….when a person continually meets criteria for the diagnosis of a major depressive episode for at least two years." However, much of the evidence that has been used to support the recommendations made in section 1.10 actually relate to dysthymia. As the Committee will be aware, dysthymia is defined as the presence of depressive symptoms NOT meeting criteria for MDD. An additional issue is that the population with 'chronic depression' overlaps substantially with the population of patients with 'treatment resistant depression' (TRD). This means that the pharmacological recommendation of using an SSRI as the first line pharmacological agent is in many cases irrelevant. The biggest concern we have with regards to this section is the recommendations for	Thank you for your comment. In analysing the data we found that a number of the populations in the trials met a range of diagnostic criteria including chronic depression, double depression and persistent residual symptoms. After discussion the committee agreed the most productive way to address this properly was to formulate recommendations for chronic depressive symptoms which would encompass the range of problems referred to in your comment. We have adjusted the title and wording of the recommendations accordingly. A number of studies that are categorised in further-line treatment would also meet criteria for chronic depression. The distinction was made on the basis of the treatment strategy. For studies where participants were randomised at the point of non-response and treatment strategies

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				medication options if an SSRI fails to lead to remission. Given the overlap of chronic depression with TRD and the definition of chronic depression used in the guidelines, it is unclear why the medication options recommended in section 1.9 are not included here. Indeed many of the patients included in the studies used to support the use of combinations of medications have an episode duration of over 2 years. The medication options recommended are somewhat perplexing. A switch to a TCA or moclobemide is recommended, despite the statements in section 1.9 that there is little value in switching antidepressants. The rationale for the recommendation for TCAs is not clear. We assume the rationale for the recommendation of moclobemide or amisulpride is on the basis of the network meta-analysis of Kriston et al. 2014 (Depress Anxiety 31: 621–630). This suggested an advantage of moclodemide and amisulpride over fluoxetine in patients with persistent depression as defined by DSM-5. There are at least two concerns about the extrapolation of these findings to the recommendations made for 'chronic depression' as defined in the NICE guideline. Firstly, the studies included in this network analysis were predominantly of patients with dysthymia rather than patients with chronic MDD. Of	included increasing dose, augmenting or switching, the study was allocated to the further-line treatment review (even if participants would also meet criteria for chronic depression). If a study included participants with chronic depression and treatment was first-line (or it was not clear from the paper that a further-line treatment strategy was being tested), the study would be allocated to the chronic depression review. As documented in the 'evidence to recommendations' section, the committee considered that although the balance of the evidence was in favour of an SSRI over alternative pharmacological interventions, some people may not be able to tolerate an SSRI or have failed to respond to previous treatment with an SSRI, and for these people an alternative pharmacological intervention would be needed. There was some evidence for benefits of tricyclic antidepressants, moclobemide and amisulpride, and the committee agreed that these should be given as examples of pharmacological interventions that could be considered in circumstances where an SSRI was not appropriate. However, due to concerns around the tolerability of these drugs and potential drug interactions the committee

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				the studies including amisupride, Amore 2001 was of patients with dysthymia +/- MDD, Smeraldi 1998 was of patients with dysthymia or MDD in partial remission, while the studies of Leon 1994, Boyer 1996, Belino 1997, Bogetto 1997, Ravizza 1999 and Rocca 2002 entirely consisted of patients with dysthymia. The second issue we have with regards to the extrapolation from this study to recommend moclobemide or amisulpride for Chronic MDD is that these two drugs were only superior to fluoxetine. They were not superior to paroxetine, sertraline or imipramine. As for non-chronic depression, the second line treatments (after a single trial of an SSRI) are recommended for use in specialist care or with specialist advice. As we have argued above, such a recommendation will lead to a dramatic increase in demand on specialist services and it is unclear that there are not more cost-effective approaches that could be employed at a primary care level.	agreed that these should only be prescribed in a specialist setting or after consultation with a specialist. The rationale for the recommendation of moclobemide or amisulpride is based on the pairwise analysis and network analysis in the current guideline and not on the network meta-analysis of Kriston 2014. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.

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Lundbeck Limited	Short	26	11-27	It is not clear how "chronic" depression differs from "less severe" and "more severe" depression, or whether the three categories are mutually exclusive for the purposes of treatment and management recommendations contained in this draft guideline. We are concerned that this could prove confusing to healthcare professionals, patients and commissioners alike.	Thank you for your comment. A number of studies that are categorised in further-line treatment would also meet criteria for chronic depression. The distinction was made on the basis of the treatment strategy. For studies where participants were randomised at the point of non-response and treatment strategies included increasing dose, augmenting or switching, the study was allocated to the further-line treatment review (even if participants would also meet criteria for chronic depression). If a study included participants with chronic depression and treatment was first-line (or it was not clear from the paper that a further-line treatment strategy was being tested), the study would be allocated to the chronic depression review. Consequently there is some degree of overlap. We would expect people to exercise clinical judgement based on a proper assessment of the clinical course of the depressive symptoms.
Northumberland Tyne and Wear NHS Foundation Trust	Short	26	11-19	Psychological formulation should be considered here. All people experiencing long term depression should be given the opportunity to develop a collaborative psychological formulation or understanding of their difficulties, strengths and needs to	Thank you for your comment. As will be apparent from reading the guideline, particularly the recommendations on assessment and general principles, there is a strong theme throughout of collaborative decision making about care. We expect that

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				inform their plan to address their difficulties	this would influence the approach taken to treatment for each individual.
College of Mental Health Pharmacy (CMHP)	Short	26 and 27	24-28 1-2	This is the only section that seems to address second and third line treatments, but does so in such a way that fails the requirements of an evidence-based guideline. There is no mention either way if Lithium is recommended or not. Yet we were told that we may be using it in 1.4.17&18. This document needs to read consistently. Why are SNRIs e.g. venlafaxine not mentioned here? Surely vortioxetine should be included as a NICE TAG says it should be an option when 2 antidepressants have failed. T3 augmentation is not mentioned but was used in the STAR*D study.	Thank you for your comment. Recommendations on the use of lithium appear in section 1.9 of the guideline. We did not find any evidence to support making recommendations on the use of lithium in people with chronic depressive symptoms. We did not find any evidence to support making a recommendation on SNRIs for chronic depression. We have added a cross-reference to TA 367 to section 1.9 to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
College of Mental Health Pharmacy (CMHP)	Short	26	8-10	This is vague. The antidepressants considered suitable so far are only SSRIs and mirtazapine that have been mentioned. It could be suitable to try an SNRI	Thank you for your comment. We have clarified in recommendation 1.9.4 that where switching to a different class occurs this can include a range of different drugs (for example SSRIs, SNRIs, TCAs or MAOIs).
Sussex Partnership NHS Foundation Trust	Short	26	11	1.10 - We suggest that MBCT could be considered as a treatment for chronic depression in order to increase patient choice due to evidence from two pilot trials which show significant effects of MBCT (or its close variant Person-Based Cognitive Therapy) on depressive symptom severity in people with chronic depression (Barnhofer et al., 2009; Strauss, Hayward, & Chadwick, 2012).	Thank you for your comment. We do not have any evidence to support recommending MBCT for chronic depression.

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Association for Psychoanalytic Psychotherapy in the NHS (APP)	short	1.9.3 page 24	14-19	We welcome the offer of psychological therapy where medication has not helped but this should not be restricted to CBT, BA and IPT for the reasons that STPT is recommended as an option e.g. at 1.6.4. STPT should be added as an option for consideration where medication has not helped and where CBT, BA and IPT have been tried before and not helped or where the patient or clinician thinks STPT is the best option for them. There is good evidence that psychoanalytic psychotherapy – both brief and longer term - is effective for people with a poor response to previous treatment offers. We think the GDG should reconsider including this option.	Thank you for your comment. When considering what psychological therapies to recommend for people who had no or limited response, the committee drew on the evidence base for first line treatment of more severe depression. This was because the committee agreed that if a person hadn't responded to treatment they would need a treatment that had been identified as being effective for the majority of people with more severe depression. These were CBT, BA and IPT.
Northumberland Tyne and Wear NHS Foundation Trust	Short	27	3-11	Extra support with vocational issues is highly relevant and should be further emphasised as a preventative as well as a rehabilitative approach and throughout the Guidance.	Thank you for your comment. Prevention of depression is outside the scope of this guideline and we are not able to make recommendations on this issue.
Northumberland Tyne and Wear NHS Foundation Trust	Short	27	16-21	For complex depression, for example for service users with histories of trauma, it is important to consider a programme of coordinated multi-disciplinary care, which includes access to social and psychological interventions based on their aims, preferences and goals that are collaboratively agreed. These services may refer to specialist personality disorder services but this depends on the service user's identified	Thank you for your comment. This guideline defines complex depression as depression that is co-morbid with personality disorder. Evidence on people with histories of trauma would not have matched the review protocol for this question and would not have been appraised. Consequently we are not able to make recommendations for this group.

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				needs. Access to group support for skills building in distress tolerance and emotional stabilisation in Team settings is essential. This may be used in conjunction with individual psychological therapy.	
Lundbeck Limited	Short	27	2	What is the evidence base for recommending amisulpride as a suitable treatment option over proven, established generic ADs, and branded ADs recommended by NICE (i.e. vortioxetine)?	Thank you for your comment. As documented in the 'evidence to recommendations' section in the full guideline, there was some evidence for benefits of tricyclic antidepressants, moclobemide and amisulpride in people with chronic depression where an SSRI was not appropriate. The committee therefore agreed that these should be given as examples of pharmacological interventions that could be considered in these circumstances.
College of Mental Health Pharmacy (CMHP)	Short	27	2	This recommends amisulpride (there is no reference) which is unlicensed (but not noted in the text), but doesn't comment on the use of the licensed quetiapine. Such omissions in advice lead to confusion. And if you are not recommending quetiapine for an active reason, then more clarity is needed. The evidence for moclobemide as an antidepressant is poor and we are not aware of any evidence for moclobemide as an adjunct.	Thank you for your comment. The lack of a license for amisulpride is mentioned in the footnote. It is standard NICE process to highlight any off-license use of interventions in the format of a footnote. As documented in the 'evidence to recommendations' section in the full guideline, there was some evidence for benefits of tricyclic antidepressants, moclobemide and amisulpride in people with chronic depression where an SSRI was not appropriate. The committee therefore agreed that these should be given as examples of pharmacological interventions that could be

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					considered in these circumstances. There was direct data on the efficacy of amisulpride in chronic depression. However there was no data on the use of quetiapine. Hence a recommendation was made about amisulpride.
Sussex Partnership NHS Foundation Trust	Short	28		1.13 – ECT – this should state for use in secondary care services only. We also think it should state that a wider use of adjunctive treatment with other drugs e.g. lithium, antipsychotics should be considered and discussed before use of ECT.	Thank you for your comment. The nature of the administration of ECT means that it is already delivered in the way you describe so we do not think any changes are needed to the recommendations.
Northumberland Tyne and Wear NHS Foundation Trust	Short	28	8-15	A multidisciplinary approach is well recommended here for depression and psychosis and can include group work as in 1.11.1	Thank you for your comment and your support.
College of Mental Health Pharmacy (CMHP)	Short	28 to 30	16 to 27	If you are going to address in detail over 3 pages, the use of ECT, a very last line treatment only ever delivered by very specialist tertiary services, then you need to give greater advice about the far more routine second line treatments. Currently this is very imbalanced.	Thank you for your comment. These recommendations have been carried over from the 2009 guideline as there was no new evidence identified that warranted changes to be made. The committee agreed that the specialist nature of ECT treatment meant it was advisable to include this level of detail in the recommendations.
Northumberland Tyne and Wear NHS Foundation Trust	Short	29	1-9	The risks of cognitive impairment and what that means should not be underestimated and it is important to give service users and their supporters examples of how memory and functioning can be affected.	Thank you for your comment. The purpose of the recommendation is to ensure that people having ECT are fully informed of the risks and benefits, including risks to cognitive impairment. Giving examples of how

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					memory and functioning could be affected would form part of the discussion between the person and clinician and we do not think this needs to be specified in the recommendation.
Northumberland Tyne and Wear NHS Foundation Trust	Short	31	1	Reference to stepped care in multidisciplinary team settings is well made. The routine undertaking of collaborative formulations with service users needs adding as this enhances engagement and shared decision-making about goals and appropriate ways forward.	Thank you for your comment. Collaborative formulations are covered in section 1.2 on assessment.
Diabetes UK	Short	31	3	Specialist care planning 1.14.1 We would welcome a stronger recommendation to refer people with 'significant coexisting conditions' to specialist mental health services for a programme of coordinated multidisciplinary care (rather than just 'consider referring'). We know from Diabetes UK 2015 care survey that three-quarters of people who needed it were not offered emotional or psychological support from a specialist healthcare professional or service, so there is a way to go to make sure these referrals happen. However, the 2009 guidance included a point about 'providing collaborative care if depression is in the context of a chronic physical health problem'. This new wording of 'significant coexisting conditions' is less clear, and might lose an important implication that	Thank you for your comment. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of

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				depression in the context of diabetes might be quite different to other kinds of depression. We suggest the wording be changed to 'significant coexisting conditions, including if the depression is in the context of a chronic physical health problem' (such as diabetes).	people with depression. There is existing NICE guidance for people with Depression and a chronic physical health problem. Making your suggested change to the recommendation would be outside the scope of this guideline.
Parkinson's UK	Short	31	25	Specialist mental health services should explicitly be considered for people with neurological conditions, such as Parkinson's. We recommend that this is highlighted in this guideline. GP survey data shows that people with neurological conditions experience the highest levels of difficulty with depression and have the highest comorbidity with mental health conditions out of all long-term conditions (Neurological Alliance, Parity of esteem for people affected by Neurological Conditions, July 2017). We are, however, concerned that there could be challenges referring people to specialist mental health services, as work carried out by the Neurological Alliance (of which Parkinson's UK is a member), indicates that there are gaps in the availability of, and access to, specialist neuropsychological and neuropsychiatric support within multidisciplinary teams.	Thank you for your comment. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression. Making recommendations for people with

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					neurological conditions is outside the scope of this guideline.
Royal College of Psychiatrists	Short	31	25	If significant coexisting conditions includes substance misuse (as it should) it will be a significant service/resource challenge to meet the recommendation to refer to specialist mental health services for a programme of coordinated multidisciplinary care	Thank you for your comment. Feedback was received from stakeholders that there would not be sufficient resources in secondary care to support the implementation of the recommendations made in the draft guideline to refer to or consult with specialist mental health services. The committee reviewed the recommendations in light of these comments and amended the relevant recommendations to make clear that they relate to a more restricted group of people whose symptoms significantly impair their personal and social functioning. The committee also made additional recommendations in section 1.3 (short guideline) to ensure that structures are in place to promote greater integration between primary and secondary care services and thereby encourage more efficient and effective collaboration and management of people with depression.
Diabetes UK	Short	31	26	Multidisciplinary care plans 1.14.5 We support the need for multidisciplinary care plans and fits with what Diabetes UK says about collaborative care,	Thank you for your comment and your support.
Royal College of Speech and Language Therapists	short	31	27	We welcome the commitment to multidisciplinary care plans for people with co-existing or complicating problems. It is well recognised that depression may also be	Thank you for your comment. People with depression and a chronic physical health problem, are covered in CG91. We have therefore not emphasised the role of speech

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				associated with chronic health conditions. Mudge *et al.* (2011) screened continuous hospital admissions for one year and showed that in older people with chronic disease co-morbidities, weight loss associated with poor nutritional status and depression were the key risks for re-admission to hospital. Depression may be encountered within speech and language therapy services more often when it arises in conjunction with other conditions. Code and Hermann (2003) showed that depression is a common reaction to acquired communication impairment. Whilst there may be an interaction between depression and communication difficulty, the link is not inevitable and the interaction may be bidirectional (Miller *et al.* 2008). Further research is needed to understand the nature of this interaction. Wilkinson *et al.* (1997) showed that 36% of stroke patients followed up in the community, presented with depression. Emotional, social and psychological difficulties arising in people with aphasia are well recognised (Cruice *et al.* 2011). Again access to specialist speech and language therapy support for people presenting with both depression and communication difficulties is vital, both for the	and language therapy services in these recommendations.

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				person and their family, and to ensure that the care team can determine effective and accessible care.	
Northumberland Tyne and Wear NHS Foundation Trust	Short	32	16-23	More appropriate to talk about safety planning and positive risk taking.	Thank you for your comment. Safety planning and positive risk taking will need to be operationalised at a local level when implementing the recommendations in this guideline.
Parkinson's UK	Short	32	24	Parkinson's UK believes that for teams providing crisis resolution and home treatment to fully support people with depression, they must take into account any physical health conditions that the individual has. People must be able to access appropriate and timely treatment to manage their physical health condition. There are cases where people with Parkinson's have reached crisis point and inpatient treatment has been considered, however, lack of joined up care around the physical symptoms has resulted in their Parkinson's symptoms worsening. A family member of someone with Parkinson's explains "*as a mental health in-patient she wasn't getting her medication when she actually needed it, instead it was whenever the wards rounds were, and that's when she got her tablets. She also didn't have her regular physiotherapy appointments*	Thank you for your comment. This guideline is about the treatment and management of depression in adults. People with depression and a chronic physical health problem, such as Parkinson's, are not within the scope of this guideline. Therefore it is not possible to make recommendations for people with Parkinson's in this guideline. CG91 on 'Depression in adults with a chronic physical health problem' covers identifying, treating and managing depression in people aged 18 and over who also have a chronic physical health problem such as cancer, heart disease or diabetes. We will pass your feedback to the NICE surveillance team so that people with Parkinson's who are experiencing depression can be considered for inclusion in future updates of CG91.

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				which were important for her mobility. I didn't feel like it was joined-up". As crisis care isn't covered in-depth within 'Depression with a chronic physical health problem', we recommend that the importance of ensuring people can still access physical health services whilst under the management of crisis care is included in this NICE guideline.	
British Association of Art Therapists	Short	33	5-7	Regarding psychological therapies in inpatient facilities, art therapy is available in many of these, and offers the possibility of therapy without pressure to talk from the start. If talking is difficult, then individual or group art therapy should be offered – possibly starting with individual to draw the person out.	Thank you for your comment. Art therapy was not prioritised for investigation in the review questions for this guideline. As the evidence on art therapy has not been appraised we have not made any recommendations on the use of this intervention.
Tavistock Relationships	Short	36	16	We suggest that this sentence be extended to conclude with the phrase "including which of the therapies recommended in this guideline are not currently available in your service".	Thank you for your comment. This is standard text that is used in all short versions and we are not able to change it.
Society for Psychotherapy Research (SPR) UK Chapter	Short	37	12 - 29	We are concerned about this paragraph as it does not include the reference(s) where the data was taken from. We are furthermore concerned that the wording of the *Context* section as a whole is not sensitive to individuals and communities with lived experience of depression. We recommend a revision of this section to that effect, including	Thank you for your comment. The style for context sections in the short versions of NICE guidelines is not to cite references. The purpose of the context section is to give a brief background to the condition to illustrate why NICE guidance is required in this area. As such, we think that the current text is appropriate as is.

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				adequate citation of the supporting evidence.	
British Association for Psychopharmacology	Short	17 and 20	Lines 24-29 on page 17 Lines 1-18 on page 20	**First line pharmacotherapy (sections 1.5 and 1.6)** First line pharmacotherapy is described in sections 1.5 and 1.6 of the guideline. The only reference to the specifics of the therapy is "an SSRI or mirtazapine". There is no guidance given with regards to the choice between an SSRI and mirtazapine might be made. Lumping all SSRIs together is rather dismissive of the diverse pharmacology of the SSRIs. For example, is the Guideline Committee equally happy to recommend paroxetine, fluvoxamine and fluoxetine along with the other SSRIs for patients on other medication given the propensity for the former to have pharmacokinetic interactions with other medication, since description of this in CG90 has now been removed? Similar, while risk of discontinuation symptoms is included in the guideline (sections 1.4.9 to 1.4.13) there is no mention of drugs more likely to lead to this as there was in CG90 (e.g. the SSRI paroxetine). One of the most common questions that GPs ask during educational sessions regarding the use of antidepressants is whether SSRIs citalopram or escitalopram should still be used given the evidence for a dose related increase in QTc in the ECG, and if they are	Thank you for your comment. The committee considered the evidence from the NMA on the effectiveness of different SSRIs. No particular drugs within this class were shown to be more effective, so the committee were unable to recommend specific drugs. We have given advice on classes of antidepressants, their sequencing, their interactions and their combinations with other drugs. It will be for individual prescribers, in discussion with patient and taking into account specific side effects and drug interactions, to determine which particular antidepressant is most suitable. We have clarified in recommendation 1.9.9 that there are some potentially dangerous combinations which should be avoided. We have also added another recommendation in section 1.4 to clarify that paroxetine and venlafaxine are more likely to be associated with discontinuation symptoms. We have also added to recommendation 1.9.9 about potential QTc prolongation with citalopram or escitalopram.

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				used, what should the monitoring requirements be. This is not mentioned at all in the guideline.	
Lundbeck Ltd	Short	38		One of the purposes of the CG90 review is to identify evidence that might change the recommendations for pharmacological interventions for moderate to severe depression. Therefore, the omission of TA367 and the decision to exclude vortioxetine from the decision problems for the guideline review questions is particularly surprising.	Thank you for your comment. As you mention, there is existing NICE guidance on the use of vortioxetine in treating major depressive episodes in adults (TA 367). NICE processes on linking to published technology appraisals within NICE guidelines are documented in Developing NICE guidelines: the manual and specify the five approaches that can be taken. Because the Depression update was not intending to update TA 367 within the guideline, the evidence on vortioxetine was intentionally not searched for or appraised by this guideline. However, in light of your comment we have added a cross reference to TA 367 into the guideline to highlight that there is relevant, published NICE guidance on the use of vortioxetine.
Diabetes UK	Short	39	4	Research recommendation 1- Peer Support We are supportive of recommendation 1 on peer support. Diabetes UK has recently gathered evidence though our investigation into the Future of Diabetes report that peer support would be acceptable to some people with diabetes who would like additional	Thank you for your comment and your support.

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				emotional and psychological support. We are in support of future research that examines the effectiveness of peer support for people with depression as well as chronic physical health conditions such as diabetes to further develop this evidence base.	
Relate	Short	41		Recommendation for research number 5 (Increased access to services) rightly recognises that certain populations are under-represented in treatments for depression, and access can still be difficult. We would also draw to NICE's attention the need to increase access, across all populations, to *choice* of therapy. At present, although couple therapy for depression is the most effective therapy within the Improving Access to Psychological Therapies (IAPT) programme (at 58.8% recovery), it accounts for just 0.4% of IAPT sessions, and in many areas is not available. We would encourage NICE to include within the research recommendations research into who accesses (and does not access) couple therapy for depression, and barriers to access – including the significant barrier of this therapy not being available. Such research could also examine the numbers of people who could benefit from couples therapy and would like to access this yet are currently unable to do so due to this treatment not being available – and any	Thank you for your comment. The guideline makes recommendations for the use of behavioural couples therapy so we do not think further research is required in this area. Providing access to behavioural couples therapy will be a matter for implementation of the guideline.

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				impact of this on depression prevalence and recovery rates in local areas where couples therapy is not available.	
Society for Psychotherapy Research (SPR) UK Chapter	Short & Full	General	General	**The nature of depression** Although we welcome the draft guideline's acknowledgment and emphasis (full version, section 2.1., p. 30, l. 15) that there are considerable problems when attempting to classify depression into categories, we are concerned about the classification system utilized. The definition of depression is descriptive and symptom based, rather than explanatory. In this, it is disorder focused. It uses a practical severity classification of mild through moderate to severe which determines the step on which the person is placed at entry into the care system. Essentially, the classification runs from internal distress to distress discernible by people in that person's relationship circle and obvious and profound loss of ability to function. Symptom based definitions of depression are a practical way of categorizing disorder with benefits in communication, research and service provision. However, symptoms may have meaning and can be signposts to what	Thank you for your comment. The committee determined that the distinction between more and less severe depression was a better basis on which to develop recommendations than the mild to moderate and moderate to severe distinction adopted in the 2009 guideline as this was thought to be less ambiguous and have more clinical utility. The distinction between more and less severe builds on what is commonly used in clinical practice and was developed to support decision making in primary care. This distinction has also proven effective in supporting the development of specific service models such as IAPT. There is general agreement that severity of depression is a prognostic indicator for response to treatment. It is less certain how this operates for different sub-types of depression and how severity interacts with other factors such as the chronicity of the problem, the presence of comorbid mental and physical health problems and external social and environmental factors. Severity is often defined (mistakenly) simply by a symptom count but a proper

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	Short Short Short	20 27 31	1-2 3-11 23	is wrong in a person's life and might be open to change. Depression is not just an imposed disorder but frequently is part of that person's life narrative: the relationship with genetic and cultural inheritance, the interaction with their growing up and life, the quality and supportiveness of personal relationships, their ability to work and love and the opportunities open to them to have either or both, and the meaning they take and impose on their world. We have serious concerns regarding the adopted methodology of dividing the trial populations by categorizing baseline severity merely as *less severe* and more *severe.* There is no evidence of the validity of this dichotomy, and the method used to derive at this distinction in itself has not been validated and might thus not reflect a reliable methodology. We are particularly concerned as it might lead to misleading recommendations, which ignore potentially valuable treatment effects. Since depression is often an extension of or inextricably linked to the person's personality, assessment should take account of that aspect of a person's being. Walton and Presley's (1973) classification provides a mild, moderate and severe rating of severity	assessment of severity has to take into account the duration of symptoms and the degree of social and functional impairment. The committee were aware of the limitations of relying solely on symptom counts but were also aware of the need to support the development of recommendations that were practical in 3 senses. Firstly, they needed to support the development of recommendations which had practical utility, especially in primary care where the majority of people with depression and almost all first line presentations of depression are managed. Secondly, they needed to support effective clinical decision making and be aligned with how GPs and other primary care staff, in particular, conceptualise depression and use this to guide clinical decisions. Thirdly, they improved on the current NICE classification of mild to moderate and moderate to severe depression which although adopted quite widely was seen by the committee as not entirely satisfactory and was leading to some confusion about the management of moderate severity depression. The committee were also aware of the need to have a relatively homogeneous population to enable a network meta-analysis and were

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				similar to that used for depression in the draft guidelines as well as a categorical classification. Clinically, it is highly desirable for the affected person to give consent for interventions. In more severe forms of depression, insight in the sense of the person knowing that they are ill and that this is a quantitative alteration from normal may be impaired and in the most severe forms, almost by definition, be absent. Informed consent is not always possible. Another important clinical feature which is missing in the draft guideline is the increased risk of suicide during the recovery phase from severe and especially from retarded depression. This omission should be corrected. Section 1.6.1 deals with moderate to severe depression. Concurrent pharmacological and psychological treatments is to be considered for Cognitive Behavioural Therapy but why not for other forms of recommended psychological therapy? It is also important to consider the sequential use of antidepressants or other psychotropic medication in certain individuals to elevate their functional level to the point where they are able to participate actively in psychological treatments.	of the view that although the network was restricted to the treatment of a new depressive episode, to include depression of all levels of severity would result in too heterogeneous a population. The committee also excluded participants with comorbid physical health problems, chronic and complex depression, perinatal depression and psychotic depression from the NMAs of treatment of a new depressive episode. This contrasts with a number of other NMAs which were more inclusive in terms of different levels of severity and types of depression. The committee considered a number of ways by which severity of first presentations of a new episode of depression might be best characterised. In doing so they took into account a number of factors including what other factors had been considered important in determining severity, the need to maintain a distinction between first presentation and other types of depression covered in the guideline (for example chronic depression, treatment resistant depression) and what data on participant populations was common to the studies under review which could then be used to inform a decision on the severity of the population in the study. This latter factor was the key determinant of the choice

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				In section 1.10.4 befriending by another is singled out as a discrete intervention. Surely elements of befriending are part of long-term support. While we welcome the reference made to multiple complicating problems in section 1.14.4, little reference is made across the draft guideline as a whole to assessing the person in the context of their life, personality and situation. Where is the stress on formulation (Aveline, 1999) and where is the emphasis on psycho-social-biological assessment? Such assessments should be universal. **References**: Aveline, M. (1999). The advantages of formulation over categorical diagnosis in explorative psychotherapy and psychodynamic management. European Journal of Psychotherapy, Counselling and Health, 2(2), 199-216. Walton, H. J. and A. S. Presly (1973). Use of a category system in the diagnosis of abnormal personality. British Journal of Psychiatry, 122, 259-368.	of a symptom severity score as the determinant as it was the only common factor across all studies. After considering these factors, the committee concluded that baseline severity was the only viable means of obtaining an indication of severity in the studies of the first line population included in the reviews. When developing recommendations, the committee took into account the limitations arising from relying on symptom severity as an indicator of the overall severity of depression. The committee were also aware of a number of concerns about how the distinction between more and less severe depression would be used in routine practice Consequently they revised the guidance on 'classification' of depression that was published as an Appendix to the 2009 NICE guideline. As the 2 population groups needed to be analysed separately in order to reduce heterogeneity it was agreed to have 2 separate networks. This meant that the committee required a reliable and consistent way to classify studies to determine whether or not they were in the less severe or more severe network. The committee considered a number of factors including symptom

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					severity (the most commonly adopted classification in the analysis of studies), duration of disorder and functional impairment. They also considered other methods that had been used to classify the severity of depression. The committee reviewed existing studies that were being considered for inclusion within the networks and concluded that only base-line symptom severity scales were available across the majority of studies. Other factors, such as duration of disorder or functional impairment were not reported in a sufficiently consistent manner for them to be of use in determining severity. Having decided to use base-line symptom severity as the means of classifying populations in the studies as more or less severe, the committee needed a method which allowed for a 'read-across' between the different symptom severity scales that were used in different studies. The committee identified the scales that were used in all potentially included studies, that is the MADRS, HAMD, QIDS, PHQ-9, CGI-I, CES-D, BDI, HADS-D, and the HADS. The committee also decided to have a pre-agreed hierarchy of the scales in the order given in the previous sentence to determine

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					which scale would be used to determine severity if 2 or more scales were reported in an individual study. The committee then reviewed relevant studies which provided data on cut-offs for individual scales (for example mild, moderate and severe depression). They also reviewed relevant literature which provided 'read-across' for different scales and additional material which could provide information to validate the specific cut-offs or depression severity ratings. Unfortunately, the committee were not able to identify data to support a 'read-across' for all the included scales for either caseness for depression or indications of severity. Therefore the committee developed a method to do this, the details of which are described in section 7.2 of the full guideline. This method was then applied to all included studies and used to allocate studies either to the more or less severe network, depending on the base-line severity score of an individual study. The committee considered whether it was appropriate to allocate studies solely on the basis of a mean base-line severity score. Consideration was given to whether the variance within the population in each study could inform allocation to either of the 2 networks. However, after reviewing a number of studies it was agreed that the availability of published data on

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					variance in study populations did not provide sufficient information to support allocation to either the more or less severe network. As allocation was by base-line severity score, this inevitably meant that a small difference of a single point could determine which network a study went in to. However, the committee were also aware that depression severity is distributed on a continuum and that the purpose of the distinction between more and less severe depression was to develop more homogeneous networks and support decision making in clinical settings. Therefore, when developing their recommendations the committee took into account the essentially arbitrary nature of the cut-off and considered the outcomes of both networks when developing recommendations. The data for the more severe network also had fewer included studies, particularly for some psychological interventions and the committee took this into account when developing the recommendations. The committee also considered a number of suggestions from stakeholders about further refinement of the classification of more and less severe depression including algorithms for the classification of depression severity which

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					often required significant additional information. However, when the committee reviewed the included studies it was not possible, in a consistent and systematic way, to extract the information from these studies to develop a more complex classification of severity. The limitations of the classification of depression at point of entry into the study were borne in mind by the committee when interpreting the evidence. Recommendations in the guideline stress the importance of developing treatment programmes in conjunction with the person. The requirement to obtain consent to treatment is covered by statute and is therefore outside the scope of this guideline. Suicide risk is covered by recommendations 1.2.11 - 1.2.15 in the short version of the guideline. Involvement of the person in decision making should be part of standard clinical practice. However we have added a new recommendation in section 1.4 to highlight the importance of the person being involved in decision making. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode

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					have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). Regarding your point about the elevation of functional level we could find no evidence to support this assertion. The precise mechanisms by which combined treatments

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					operate is not well understood. Befriending has been developed and tested in formal trials as a discreet intervention and this is why it is identified separately in the recommendations. We consider that the issues you have raised are already covered by the recommendations made in section 1.2 of the short version about assessment. We do recommend assessment which includes looking at a range of psychosocial stressors. Aveline 1999 and Walton 1973 cannot be included in the review as they do not meet the study design criteria (not an RCT or systematic review of RCTs).
NHS England National IAPT Team	Short & Full	General	General	This response is prepared by NHS England's IAPT National Team following extensive discussion of the draft guideline within the team, with members of the IAPT Education and Training Committee, and with IAPT's national advisors (Clinical, Informatics and Education). The broad view is that: 1) the draft contains many new recommendations that helpfully clarify how treatments should be delivered and how outcomes should be measured, and 2) the draft also contains some	Thank you for your comment. The recommendation for group CBT for relapse prevention was based on a review of a number of individual and group CBT interventions aimed at preventing relapse. The reviews considered the clinical effectiveness of these interventions and then the cost-effectiveness. Two trials of group CBT were considered Bockting et al and Wilkinson et al 2009. Group CBT was evaluated as more cost-effective. The model for the delivery of group CBT was built on the Bockting model which is a large trial of

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				recommendations that may be difficult and/or expensive for IAPT to implement. For the latter recommendations, we would like the panel to review their decisions, carefully consider the strength of the evidence, and take into account our comments about problems with implementation. If the panel decides to stick with the recommendations, we would ask that these are more clearly justified and that any problems with implementation are explicitly addressed. Before listing our comments, we thought it might be helpful if we briefly summarized the current status of the IAPT programme as this will help panel members understand the context for our comments. **The IAPT Context** The Improving Access to Psychological Therapies (IAPT) programme was established to provide people in England with improved access to NICE recommended psychological therapies for depression and all the anxiety disorders. At the time that the programme was established (2008) NICE strongly recommended stepped care for patients with mild to moderate depression and for many of the anxiety disorders. The low intensity intervention that was dominant	group CBT specifically developed for relapse prevention. Taking the overall effectiveness of CBT interventions for relapse prevention together with the cost-effectiveness of group interventions the committee deemed it appropriate to recommended group CBT for relapse prevention. It should also be noted that the committee made recommendations for maintenance and relapse prevention with CBT and MBCT respectively. Based on feedback from stakeholders, the data in the NMAs and economic models for the treatment of a new depressive episode have been updated and the analyses have been re-run. The committee have carefully considered the updated results of both the NMAs and the economic models and amended the recommendations for treatment of less and more severe depression in line with the new results. Group CBT is no longer recommended as the initial treatment for people with less severe depression. Instead, self-help with support and physical activity programmes are recommended as possible initial options. A variety of other interventions including individual CBT or BA, IPT, group CBT, counselling, STPT and SSRIs have also

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	Short Short Short Short Short	10 11 11 12 17 & 18	8 15 and 23 16, 18,25 4	was guided self-help, often delivered by telephone (the core intervention in the Doncaster pilot). The high intensity interventions are various forms of face-to-face therapy (CBT, IPT, counselling, brief psychodynamic therapy), depending on NICE guidance. As CBT has the broadest indication, it forms the largest part of the workforce. Two distinct professional groups who are paid on different scales and have different prior experience and training were established to support stepped care. Psychological Well-Being Practitioners (paid on AfC 4 or 5) deliver guided self-help and other low intensity interventions (such as psychoeducation groups and exercise interventions). These practitioners are NOT trained to deliver normal CBT. High intensity therapists have more extensive mental health experience, are paid on AfC 6, 7 or 8, and are trained to deliver face-to-face CBT or other therapy modalities. From small beginnings in 2008, the IAPT programme has grown to a point where it now sees around 950,000 people each year. Some receive an assessment, advice and signposting. Around 60% (560,000 per year) go on to receive a course of treatment (defined as two or more sessions prior to discharge). A session-by-session outcome	been recommended. Full details of the committee's rationale for making the recommendations for treatment of a new, less severe, depressive episode are documented in the 'evidence to recommendations' section (7.4.5). An individual high intensity psychological intervention (CBT, BA, IPT), antidepressant medication (SSRIs or mirtazapine or a TCA in case of history of poor response to SSRIs or mirtazapine) or combinations of the 2 are now options for the treatment of more severe depression. This was decided because both types of interventions showed a better effect and higher cost effectiveness than pill placebo, but the limitations of the economic analysis did not allow the committee to make firm conclusions on the relative cost effectiveness between psychological interventions and antidepressant medication. Full details of the committee's rationale for making the recommendations for treatment of a new, more severe, depressive episode are documented in the 'evidence to recommendations' section (7.7). The committee considered that STPT potentially had an important role for people with severe depression who had emotional and developmental difficulties in

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	Short Short Short Short	18 & 19 19 23 16	10 3-7 20	monitoring system ensures that pre- and post-treatment measures of depression (PHQ-9) and anxiety (GAD-7 or other disorder specific measures) are obtained on a remarkable 98.5% of the people who have a course of treatment. For people who are clinical cases (score above 9 on the PHQ and/or above 7 on the GAD at intake) the pre-post effect sizes are large (1.5 & 1.4 respectively). The latest data show that 51% recover (drop below the clinical threshold on BOTH measures) and 67% show reliable improvement. These results are considered to be in line with expectation from research studies and would appear to provide good support for NICE's stepped care recommendations, especially as national analyses generally indicate that outcomes are worse when services deviate from NICE guidance. Panel members might wish to note that the IAPT outcomes quoted above relate to a full course of treatment within the stepped care model. For many people that course of treatment involves several interventions. No IAPT data is available that tracks a full cohort of patients from the start to the end of any single intervention (such as guided self-help, CBT, IPT, brief psychodynamic therapy etc). NHS Digital's most recent annual IAPT report	relationships. The committee were aware of the very limited evidence for STPT (only one study in the severe network) but they decided to extrapolate from data from less severe depression and make a recommendation for STPT as they agreed that the concentration of STPT on developmental and relationship issues may contribute to the effective treatment for some people with more severe depression. Thank you for bringing these references to our attention. Elkin 1989, Blom 2007 ('Combination Treatment for Acute Depression Is Superior Only when Psychotherapy Is Added to Medication'), Marshall 2008, Luty 2007, Schulberg 1996, Van Schaik 2006, Schramm 2007, Swartz 2008, and Swartz 2016 were included in the NMA of treatment of a new depressive episode. Schramm 2008 was included in the chronic depression review. Thank you for highlighting the Barth 2013 systematic review. This review has been checked for relevant studies and an additional 14 RCTs have been added to the NMA for treatment of a new depressive episode through this process.

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				(October 2016) shows that 23% of patients treated in 2015/16 had depression coded as their main problem and 22% had a mixed anxiety and depression code, which suggests that depression was a significant problem for 45%. Outcomes for this group were in line with the average so it seems reasonable to assume that the current depression outcomes are as specified above (i.e approx. 50% recovery and 66% reliable improvement). Looking at the components of stepped care, 37% of patients only had low intensity interventions from PWPs, 29% only had high intensity interventions from Hi therapists and 34% had both. This means that 71% were seen by a PWP at some time during their course of treatment and 63% were seen by a high intensity therapist sometime in the course of treatment. The IAPT pilot sites showed that the PWP workforce is critical for constraining costs as PWPs seen many more patient than Hi therapists and cost much less. **New recommendations that are uncontroversial and helpful** IAPT has shown that it is possible to collect more or less complete data on access to, uptake of, and outcomes of interventions in a depression pathway. It is good to see the	Cuijpers 2016 ('Interpersonal Psychotherapy for Mental Health Problems: A Comprehensive Meta-Analysis') was searched for studies relevant to the guideline. No additional studies matching our inclusion criteria were identified beyond those that have already been added through other means (for example through stakeholder comments). The following studies did not meet our inclusion criteria: • Elkin 1995: Secondary analysis of Elkin 1989 and no relevant outcomes reported. • Blom 2007 ('Severity and duration of depression, not personality factors, predict short term outcome in the treatment of major depression'): Secondary analysis of an RCT that was already included. • Reynolds 1999: Completion data <50% (>50% left treatment early). • Frank 2007 is not included in the NMA because it is not first-line treatment. It also does not meet the inclusion criteria for the relapse prevention review as the comparison is not of interest (weekly versus twice-monthly versus monthly IPT).

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				guideline recommends this more broadly. IAPT has shown that it is possible to get outcome data on essentially everyone (>98%) treated as long as one uses a session-by-session monitoring system. The revised guideline appears to recommend this system for all services. This seems entirely appropriate. However, it could be more clearly stated as this point is split between two recommendations (1.4.2 and 1.4.5). The recommendations that therapists should use treatment manuals, use competency frameworks and monitor treatment adherence are very welcome. They are at the heart of the IAPT model but are not always followed. Including them in the new Guidance should improve compliance. IAPT recommends that competence in delivering NICE recommended psychological therapies should be monitored and evaluated using video and audio tapes. While this is the norm on IAPT training courses, it is less common in IAPT services. The new recommendation will hopefully help ensure services assess competence more consistently. It is helpful to see post-treatment follow-ups	As outlined in the review protocol the objective of this review was to compare interventions against other active interventions or control arm(s) but different intensities of the same intervention was beyond the aims and objectives of this review. • Ekeblad 2016 is not included in the NMA because it is not first-line treatment (68% were receiving antidepressants at baseline). It also does not meet the inclusion criteria for further-line treatment as participants were not randomised at the point of non-response as a history of non-response were not eligibility criteria for this study. • Toth 2013: It was not possible to extract continuous data as only means with no measure of variance was reported. Given the size of the evidence base it was not possible to contact all authors for missing data. • Power 2012: Data cannot be extracted (available for <50% of those randomised and disaggregated data threatens randomisation). • Koszycki 2012: Trial specifically recruited participants with a physical health condition in addition to depression.

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	Short Short	 18 20	 11 10-18	being recommended as a routine activity. Commissioners of IAPT services have been reluctant to fund follow-ups but they are likely to be helpful for detecting any early signs of relapse and for taking appropriate preventative action. The new clarity about the number of sessions of therapy that would be reasonable for each treatment is very welcome. Some IAPT services "under-dose" and the recommendations will hopefully help reduce this phenomenon. It is helpful to see the recommendation that any counselling used for treating mild-moderate depression should be "based on a model specifically developed for depression". It would be helpful if this could be more clearly defined. IAPT has developed a specific counselling for depression training. It is similarly helpful to see that short-term psychodynamic therapy (STPT) should be based on a model developed specifically for depression. IAPT has a national training curriculum based on Fonagy's Dynamic Interpersonal Therapy (DIT) which is in line with this recommendation. We welcome the statement that therapy	• Driessen 2013 could not be included in acute treatment NMA as it is not first-line treatment (>25% have duration of current episode >2 years, >20% had received previous treatment for this episode). In developing recommendations for a NICE guideline it is necessary that there are robust and transparent methods for the identification of included studies that can be understood by users of the guideline. One important element of this is to have a clear cut-off date for any search strategy (see Developing NICE guidelines: the manual), lack of clarity in this area can lead to problems in determining which studies should be included. A search cut-off date of June 2016 was chosen by NICE for this guideline and documented in the methods section in the full guideline. This was expected to have been sufficiently close to publication of the guideline that all but a few studies published immediately prior to the publication date would have been included in the guideline analyses. Unfortunately, the complexity of the NMA for treatment of a new depressive episode meant that the final analyses were not completed until April 2017. The committee in collaboration with NICE considered whether a further search

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				should continue beyond recovery to ensure sufficient relapse prevention work had been done. As far as we aware, the only studies that have shown reduced rates of relapse after psychological therapy are all ones in which explicit relapse prevention work was included. However, we would question the recommendation to use group CBT for relapse prevention. We know of no studies that have shown that group CBT (as opposed to individual CBT) reduces relapse. It seems that the panel assumed that group CBT would reduce relapse in the same way to individual CBT but this really needs to be demonstrated. Clinically, one can think of many arguments (such as less individualized therapy) for saying that group treatment is less likely to have relapse prevention properties. **New recommendations that are more controversial and/or may be difficult/expensive to implement.** *Recommendation to offer group CBT as the initial treatment for people with mild to moderate depression.* This is a major change from the 2009 NICE guideline. Nobody in the NHS England IAPT National Team and Committees thought it was a good idea. We are all concerned that it will increase costs,	should be undertaken but decided that the work involved with this would lead to further delay in the publication of the guideline and therefore decided to keep the cut-off date of June 2016. During the consultation period it was identified that 12 studies had been included in the guideline that were published after the search cut-off date; June 2016. These were studies that had been identified by guideline committee members, rather than the searches. It was therefore necessary to remove the studies that had been erroneously included as we could not ensure systematic identification of all potentially relevant studies after this date. Gibbons 2016 was one of the studies that was removed from the guideline. A review of the outputs of all affected analyses suggested that the removal of the studies did not substantially affect the results of those analyses.

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				reduce convenience for patients, and fail to deliver improved outcomes. Currently IAPT implements the 2009 depression guideline. Most patients with mild to moderate depression start with a low intensity intervention given by PWPs with the vast majority receiving guided self-help, with therapist support often delivered over the telephone. This means that patients have substantial choice about when they can have their PWP support and don't have to waste valuable time travelling to appointments. The network meta-analysis (page 216 of the full guide) for less severe depression finds that guided self-help has the highest SMD compared to placebo of all the psychological treatments for depression. However, group CBT, which has a smaller SMD, is recommended above guided self-help on the basis of an economic analysis. Inspection of that economic analysis suggests that it is based on a series of incorrect assumptions that would tend to favour group CBT. Firstly, guided self-help is delivered by PWPs paid on AfC4 or 5. The economic analysis assumes that group CBT would be delivered by the same workforce. However, it is the unanimous view of the IAPT Education and Training Committee that group CBT can only	

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	Short Short	19 20	13 10	be delivered effectively by individuals who have been properly trained in individual CBT and have had some further training in group processes (i.e. Hi therapists paid on AfC 6,7,8). This view is in accord with the group CBT studies that the panel looked at to establish the efficacy of group CBT. Most (Ekkers et al, 2011;Chiang et al, 2005; Hvenegaard et al, 2015; Manicavasgar et al, 2011) used highly experienced therapists who had previously trained in individual CBT. For example, in Hvenegaard et al (2015) the therapists were "trained cognitive behaviour therapists with at least 7 years of experience in CBT". The only study that used a more junior, lower paid workforce is the Cramer et al (2011) study that can hardly be considered impressive evidence for group CBT as it was not significantly different from a minimal intervention "usual care" control condition and the trial was badly confounded by allowing patients to *start* anti-depressant medication during the group CBT intervention. Secondly, the economic analysis is over-optimistic about the number of people who will attend a group. Group size is assumed to be 12 but the studies of group CBT seen by the panel often have smaller numbers of people.	

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				In addition to concerns about the validity of the economic analysis, we would like to point out several limitations of group CBT that do not seem to have been taken into account by the panel. 1) Compared to guided self-help over the telephone, Group CBT greatly reduces patient choice about when and where therapy can occur. This will undermine the efficiency of IAPT services and convenience for patients. 2) Some IAPT services have experimented with group CBT. Reports back to the national team suggest that the drop-out rate can be high and that even when patients do not drop out they may be infrequent attenders because of the inflexible timing of groups. 3) The guideline recommends individual CBT for people that have failed to respond to group CBT. Of all the psychological therapies recommended for depression, individual CBT has the greatest support as a short-term intervention and as a treatment that reduces relapse. However, it seems very unlikely that individuals who have failed to respond to group CBT will want to have another course of what appears to be the same treatment but in individual format. A transition to individual	

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				CBT would be much more likely to be accepted if the first treatment was guided self-help. Perversely, making group CBT first choice could reduce the effective availability of individual CBT despite it generally being considered to be the gold standard psychological treatment for depression. The network meta-analysis supports the view that this would be a problematic change as the confidence interval for the SMD of group CBT versus placebo includes zero (i.e no difference) whereas the confidence interval for individual CBT versus placebo does not (see Figure 5 , page 218 of the Full Guide). We would also like to point out that moving to having group CBT as the first line intervention for mild to moderate depression would require major changes to the IAPT workforce and training programmes. IAPT services would require many less PWPs and many more high intensity therapists. This shift would be very expensive and a major challenge to commissioners, especially when they are also being asked to fund a substantial expansion of the IAPT programme by 2021. It would also fundamentally undermine the stepped care principle on which IAPT is based. As the principle has served the programme very well, we feel we would need compelling	

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				evidence before dropping it. If the guideline recommendation for group CBT were implemented there would be a marked reduction in the proportion of people who receive either guided self-help or individual CBT. This would be acceptable if group CBT was as clinically effective. However, it is not clear that this is the case. As far as we can see, the panel did not see any RCTs that directly compare the gold standard of individual CBT against group CBT. We are therefore concerned that following the new recommendation would put the hard won IAPT recovery rate of 50% or more at risk. We have wondered why the NICE panel classified group CBT as a low intensity intervention and assumed it would be delivered by PWPs for the sake of the economic model. It occurs to us that the panel may have confused psychoeducation groups (which are part of the PWP intervention set) with group CBT (which is a high intensity therapist activity). Close reading of the studies that NICE looked at to generate the new recommendation for group CBT indicate that they were not IAPT style psychoeducation groups but instead were mostly true group CBT interventions based	

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				on Beckian cognitive therapy and delivered by people who were trained in that high intensity modality. Our comments above about group CBT are partly based on a thorough analysis conducted by Professor Tony Roth and colleagues at UCL. For completeness we have pasted their full report into row two below. *Consider IPT for mild-moderate depression but NOT for moderate to severe depression*. In the 2009 Depression guideline IPT was recommended for the full range of depression severity (in combination with medication for the more severe cases). IAPT has been honouring this recommendation in services that have capacity to offer IPT and there are plans to further expand this capacity. We are unclear why the draft revised guideline has withdrawn the recommendation for IPT in moderate to severe depression and would appreciate clarification. Inspection of the Full Guide has not helped us understand the reasons for the change and we note that there are a substantial number of controlled trials of IPT that don't seem to be mentioned in the draft revised guide. We are unclear whether these have been missed or whether they were included in the network meta-	

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				analysis and economic analysis but not mentioned in the document. Our IPT experts have provided a comprehensive list of the studies they feel may have been omitted. The list is given below. IPT Studies Set One a. Elkin I, Shea MT, Watkins JT, Imber SD, Sotsky SM, Collins JF, et al. NIMH treatment of depression collaborative research program. General effectiveness of treatments. Archives of General Psychiatry. 1989; 46:971–82. PMID b. Elkin I, Gibbons RD, Shea MT, Sotsky SM, Watkins JT, Pilkonis PA, et al. Initial severity and differential treatment outcome in the National Institute of Mental Health Treatment of Depression Collaborative Research Program. J Consult Clin Psychol. 1995; 63(5):841–7 c. Blom MB, Spinhoven P, Hoffman T, Jonker K,	

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				Hoencamp E, Haffmans PMJ, van Dyck R. (2007) Severity and duration of depression, not personality factors, predict short term outcome in the treatment of major depression. J Affect Disord. 104: 119-126. d. Blom et al (2007) Combination Treatment for Acute Depression Is Superior Only when Psychotherapy Is Added to Medication Psychotherapy and Psychosomatics, 76, 289-297 e. Marshall C, Zuroff DC, McBride C, Bagby RM. (2008) Self-Criticism Predicts Differential Response to Treatment for Major Depression. J Clin Psychol; 64:231-244. f. Luty et al (2007) Randomised controlled trial of interpersonal psychotherapy and cognitive behavioural therapy for depression BJPsych 190, 496-502 g. Schulberg, HC et al (1996) Treating major depression in primary care practice. Eight-month clinical outcomes. Arch	

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				Gen Psychiatry. 1996 Oct;53(10):913-9 h. Reynolds, CF 3rd et al (1999) Nortriptyline plus interpersonal psychotherapy was effective in major depression in older adults. JAMA 1999 Jan 6;281:39–45. i. van Scheik et al (2006) Interpersonal psychotherapy for elderly patients in primary care. Am J Geriatr Psychiatry. 2006 Sep;14(9):777-86. j. Schramm, E., Schneider, D., Zobel, I., et al. (2008) Efficacy of interpersonal psychotherapy plus pharmacotherapy in chronically depressed inpatients. Journal of Affective Disorders, 109, 65-73. k. Schramm, E., Van Calker, D., Dykierek, P., Lieb, K., et al. (2007) An intensive treatment program of interpersonal psychotherapy plus pharmacotherapy for depressed inpatients: Acute and long-term results. American Journal of Psychiatry, 164 (5), 768-777.	

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				l. Swartz, H.A., Frank, E., Zuckoff, A., et al. (2008) Brief interpersonal psychotherapy for depressed mothers whose children are receiving psychiatric treatment. American Journal of Psychiatry, 165 (90), 1155-1162. m. Frank, E., Kupfer, D.J., Buysse, D.J., et al. (2007) Randomized trial of weekly, twice-monthly, and monthly interpersonal psychotherapy as maintenance treatment for women with recurrent depression. American Journal of Psychiatry, 164, 761-767. IPT Studies Set Two a. Cuijpers et al (2016) Interpersonal Psychotherapy for Mental Health Problems: A Comprehensive Meta-Analysis. Am J Psychiatry 2016; 173:680–687. b. Ekeblad et al (2016) Randomised trial of Interpersonal Psychotherapy	

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				and Cognitive Behavioural Therapy for Major Depressive Disorder in a Community Based Psychiatric Outpatient Clinic. Depression and Anxiety, 33 1090-1098 c. Toth, S.L. et al (2013) The efficacy of interpersonal psychotherapy for depression among economically disadvantaged mothers. Development and Psychopathology, 25, 1065-1078 n.b. the author makes clear this is not a perinatal depression study d. Power M.J. & Freeman, C (2012) A Randomized controlled trial of IPT Versus CBT in Primary Care: With some cautionary notes about handling missing values. Clinical Psychology & Psychotherapy, 19, 159-169 e. Koszycki, D. et al (2012) Interpersonal psychotherapy versus brief supportive therapy for depressed infertile women: first pilot study randomized controlled trial. Archives of Womens Mental Health, 15:	

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				193-201 f. Swartz, H. A et al (2016) Brief Psychotherapy for Maternal Depression: Impact on Mothers and Children. J Am Acad Child Adolesc Psychiatry 2016;55(6):495–503 n.b. the children in this study are teenager not infants. g. Barth et al (2013) Comparative Efficacy of Seven Psychotherapeutic Interventions for Patients with Depression: A Network Meta-Analysis PLOS Medicine, May, Vol 10, Iss 5, e1001454 *Consider short –term psychodynamic treatment (STPT) for people with BOTH less severe and more severe depression who would like help with emotional and developmental difficulties in relationships*. The 2009 Depression guideline recommended STPT for people with less severe depression but NOT for people with more severe depression. The revised guideline has upgraded the STPT recommendation so that it also applies to	

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				more severe depression. The IAPT programme has recently created a revised and extended training curriculum for STPT based on dynamic interpersonal therapy so it can respond to the revised recommendation by developing an appropriate workforce. As we already have the intention of expanding STPT this is straightforward at the training level. However, commissioners will want to be confident that the evidence for using STPT in more severe depression is clear. The Education and Training Committee felt that the text for the full guideline falls short in this respect. We assume that the main reason for the change is the publication of two studies (Driessen et al, 2013; Gibbons et al. 2016) that compared CBT with STPT, failed to find any significant differences and, for some measures, established non-inferiority. This is important evidence. However, we note that in both studies the clinical outcomes for both treatments are poor and well below expectation for IAPT (response rates are around 20% in Gibbons et al and recovery/remission is around 23% in Driessen et al). The absence of a control condition (such as placebo or TAU) means it difficult to know if the treatments in these studies are being equally effective or equally	

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				non-ineffective. To address this question one needs to look at the network meta-analysis findings as these allow for comparisons against placebo and TAU and use many more studies. Looking at the results of the network meta-analysis (Table 50 and Figure 13 in the Full Guide) we see that CBT is listed as being superior to pill placebo whereas the SMD for STPT places it below pill placebo. Similarly, if one looks at the confidence intervals for the SMDs against TAU one sees that they include zero (no difference) for the contrast with STPT but not for the contrast with CBT. At first glance this pattern of results would not seem to be particularly good evidence for the use of STPT in more severe depression. Clarification of the panel's thinking as it endeavoured to synthesize multiple sets of information would therefore be appreciated.	
Janssen	Short and Full	General	General	1. **Reinstating the existing guideline framework and structure based on the 'stepped care model' to ensure greater clarity regarding how patients can move between effective interventions.** We are concerned that with the restructure of the short guideline based on severity of the disease as opposed to a 'stepped care model' approach has led to recommendations	Thank you for your comment. We clarify in the recommendations that commissioners and providers of mental health services should consider using stepped care models for organising the delivery of care and treatment for people with depression. We have also made additional recommendation to promote better integration between primary care and secondary care. The current structure of the guideline is such

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				being presented in a confusing way. We believe that the removal of the existing recommendation on the stepped care model, recommendation 1.2, (and subsequent related recommendations 1.3, 1.4, 1.5 and 1.6), in the new clinical guideline has reduced the clarity in terms of which interventions should be offered and how patients should be transitioned through interventions. We believe this is most confusing in section 1.9 of the new draft guideline where various interventions and combinations of interventions are recommended based on previous (first line) treatments received. We believe the stepped care model provides a pragmatic framework to outline the various treatment options depending on the previous treatments tried and severity of disease. The stepped care model, as defined in the previous guideline, 'is a system for delivering and monitoring treatment with the explicit aim of providing the most effective yet least burdensome treatment to the patient first, and which has a self-correcting mechanism built in (that is, if a person does not benefit from an initial intervention they are 'stepped up' to a more complex intervention).' 'In addition, consideration should be given to not only the degree of restrictiveness associated with a treatment and its costs and effectiveness, but	that lower intensity interventions are provided prior to more intensive interventions. We think this structure is logical and easy to follow and is not likely to lead to limited or restricted access to interventions. We have made a number of changes to the recommendations about first line treatment of more and less severe depression, in particular moving group CBT from the initial treatment for less severe depression to a position in the sequence that is more in line with a stepped care model.

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				also the likelihood of its uptake by a patient and the likely impact that an unsuccessful intervention will have on the probability of other interventions being taken up.' We believe this is not only an appropriate framework to offer interventions in depression when there are choices to be made regarding pharmacological and physiological interventions, but also in settings where many psychological interventions may not be available at a local level, because of the requirement to have specialists running the services and the costs to deliver these services. The removal of this framework has impacted the overall clarity of how patients should be moved through different interventions. We believe that stepped care model provided a useful framework of moving between interventions and captured the pharmacological and psychological therapies that are used interchangeably depending on severity and previous treatments tried. We note that has been replaced in the new guideline by recommendation 1.3.1; 'commissioners and providers of mental health services should consider using stepped care models for organising the delivery of care and treatment of individuals with depression'. We are concerned that	

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				removal of the explicit use of a stepped care model in the clinical guideline means that patients may not be transitioned through appropriate interventions and that this may also create significant variation at a local level. This could lead to situations where people with depression are needlessly cycled through the same ineffectual treatments without being referred to a specialist or denied access to alternative interventions. Therefore, we would encourage the CDG to strengthen the recommendations around a stepped care pathway and ideally revert to structure in the current clinical guideline. Furthermore, we feel that the new structure for the recommendations for the classes of interventions is disjointed and may be confusing to HCPs and commissioners. The recommendations for interventions have been spread across the guideline, which do not necessarily correspond to the patient's severity of depression or the previous interventions that they have tried. For example, the recommendations for interventions on antidepressants are now in the following sections, recommendations 1.4.7 to 1.4.22 are in section 1.4 '*General principles of care'*, recommendation 1.5.7 is in section 1.5 *First Line treatment for less severe depression*, recommendation 1.9.1 to	

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				1.9.10 are in section 1.9 *Limited response and treatment-resistant depression*. The equivalent recommendations in the current guideline for antidepressants are all in one section 1.5 (1.5.2.1 to 1.5.2.31) in section *Step 3: recognised depression in primary care and general hospital settings – persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions, and moderate and severe depression.* From our reading of the new clinical guideline, it is difficult to follow the flow of the recommendations for the interventions and there is the real possibility that recommendations for interventions could be missed or incorrectly implemented. We strongly suggest that recommendations for pharmacological interventions should be grouped together to ensure that all recommendations for the pharmacological interventions are in one place and implemented correctly. We strongly urge the NICE GC to retain the existing structure of the guideline around the stepped care model and simply update the recommendations for each step of care. We believe this approach would provide an overall framework, which is clear and ensures that patients are transitioned to the next	

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				available effective treatment appropriately improving the chances of the recommendations being implemented correctly.	
Janssen	Short and Full	General	General	**2. Address the methodological challenges and consequent uncertainty in the current network meta-analysis (NMAs) to improve the robustness of the guideline recommendations around the relative effectiveness of interventions in line with clinical practice. The NMA as it stands currently is unreliable and may not reflective of actual effectiveness of interventions.** We have concerns with regards to how the NMAs has been conducted. We would therefore urge caution in terms of how the evidence from these NMAs is interpreted and used as the basis for making recommendations regarding specific interventions within the revised guidelines. We note that two NMAs were conducted by the guideline development group (GDG) for 'adults with a new episode of less severe depression' and 'adults with a new episode of more severe depression.' We understand the difficulties in synthesising such a wide-	Thank you for your comment. Regarding your concerns about how the NMAs have been conducted, we have responded in detail where you raise specific concerns. Please be reassured that the committee have not used only the NMAs as the basis for making their recommendations. They have recommended a range of interventions, after considering the results of the NMA and the economic analysis, the quality and the breadth of the evidence base, the plausibility of the results and the limitations of the analysis, patient characteristics and preferences, and implementation issues. The NMAs controlled for a large part of heterogeneity by splitting populations with less and more severe depression; using detailed treatment definitions [including treatment intensity and mode of delivery for psychological interventions] and categorising them using a class random effects model; examining for model fit and checking for inconsistency between direct and indirect evidence. Other potential effect modifiers, such as age and setting (outpatient versus inpatient) were assessed in sub-analyses,

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				ranging disease area, however, we suggest that the following tasks are undertaken to ensure the results of the NMA are reliable for decision making: • To include several relevant interventions that are used in clinical practice which were excluded in the current NMA, thus providing a more complete network of evidence, most notably SNRIs. (comment 4). • To further explore separate evidence networks given the significant heterogeneity in, but not limited to, the trial design, outcomes, populations and follow up of these studies (comment 5). Furthermore, we note that no NMA has been conducted in adults whose depression has either not responded or there has been limited response to previous treatment(s) for the current episode. We are concerned that the GC have therefore extrapolated the relative effectiveness results from a population receiving first line treatment to a population that has failed treatment. We strongly suggest that a NMA is conducted to ensure that appropriate effectiveness data is used to formulate recommendations in this population.	using pairwise meta-analysis. We considered a wide range of outcomes, including SMD, response in those randomised and remission in those randomised, which were the main clinical outcomes. Each analysis was informed by studies reporting relevant data. Before conducting the NMAs, the committee considered the heterogeneity in populations participating in the RCTs. They noted that participants in pharmacological and psychological trials may differ to the extent that some participants find different interventions more or less acceptable in light of their personal circumstances and preferences (so that they might be willing to participate in a pharmacological trial but not a psychological one and vice versa). Similarly, self-help trials may recruit participants who would not seek or accept face-to-face interventions. However, a number of trials included in the NMA have successfully recruited participants who are willing to be randomised to either pharmacological or psychological intervention and to either self-help or face-to-face treatment. The NMAs have assumed that service users are willing to accept any of the interventions included in the analyses; in

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				Overall, we have concerns regarding how the NMAs that have been conducted to inform the relative effectiveness of interventions. We would urge GC to re-run the network meta-analysis to address the ongoing concerns of its robustness and conduct a further NMA in a population that have had an inadequate response to existing treatments. This in our view will add further rigour to the recommendations for the short and full clinical guidelines.	practice, treatment decisions may be influenced by individual values and goals, and people's preferences for different types of interventions. These factors were taken into account when formulating recommendations. These considerations have been reported in the full guideline (see 7.1.4.3 under 'Indirectness'). Regarding the length of follow-up, all data were obtained at treatment endpoints, regardless of duration of treatment. This has now been clarified in the full guideline. The committee was of the view that it is relevant and appropriate to compare interventions at treatment endpoints, following completion of a full course of treatment, in order to compare the effects of treatments as they would be provided in optimal clinical practice. The duration / intensity of treatments was captured in the economic analysis, in the estimation of intervention costs. We acknowledge the difference in treatment course duration between pharmacological and psychological interventions, but course duration is inherent in the type of intervention rather than an effect modifier. Model fit, between-study heterogeneity, and inconsistency were formally assessed for

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					each network; results of this assessment were taken into account when interpreting the results of the NMA and making recommendations. The NMA enabled use of all available evidence and improved precision by allowing combination of direct and indirect comparisons. Moreover, the NMA enabled the use of a class model, where the effects of individual interventions were pooled into a more robust and precise class effect, while interventions retained their own intervention effect. The uncertainty of the relative effects informed by few or small studies was reflected in the uncertainty (Credible Intervals) around the relative effects. Some interventions that were represented by very few and small studies demonstrated extreme, implausible effects in the primary studies, which were subsequently 'transferred' in the NMA, but these extreme results would also have been obtained if pairwise meta-analysis had been attempted. This is a flaw of the primary studies, not of the NMA per se. Nevertheless, the committee took into account the results of the NMA in the context of the available evidence. Results on classes and interventions tested on a small number of people were treated with great caution and

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					the total number of people randomised to each class/ intervention across the NMA studies was taken into account when making recommendations. All NMA results were assessed for their plausibility, using the committee's expert judgement. We have considered conducting a NMA of interventions for people who have failed previous treatment. However, the study population is highly heterogeneous, comprising people who have not responded to specific pharmacological, psychological or combined interventions and therefore it was not appropriate to undertake a NMA. For example, it would not be appropriate to include in the same NMA people who have not responded to a SSRI (but may be treatment-naive to other drugs and psychological therapies) and people who have not responded to CBT (who may be treatment-naive to other psychological interventions and other drugs).
Janssen	Short guideline	23	18	We note that section 1.9 is named 'Limited response and treatment-resistant depression', we believe this may be confusing, as the recommendations in this section are related to limited response to initial treatment rather than a population	Thank you for your comment. In light of feedback from stakeholders we have amended the title of this section to be 'No or limited response to initial treatment.

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				which is arguably 'treatment resistant'. We realise that there is no firm definition for treatment resistant depression, however, the regulatory definition followed by the Food and Drug Administration (FDA) and Committee for Medicinal Products for Human Use (CHMP) is major depressive disorder resistant to two lines of antidepressants within a single episode. This is also consistent with section 8.1.4 of the Full guideline. The current recommendations in section 1.9 do not relate to this population currently and therefore we believe the title of section 1.9 should be changed to avoid confusion. We suggest 'Limited response to initial treatment' would be a more appropriate title of the section.	
UK University Mindfulness Centres	Summary/Full	General	General	We would like to thank the committee for taking the time to revise the guideline. We have carefully read the draft guideline documents and have a number of comments in relation to the draft recommendation for Mindfulness-based cognitive therapy (MBCT), drawing on our knowledge of the MBCT research trials. We hope that you find our comments helpful.	Thank you for your comment. We have responded separately to each of the issues that you have raised.
UK University Mindfulness Centres	Summary/Full	Summary (Sections	Summary (page 16	MBCT is not currently recommended in the draft guideline as a first line treatment for less severe or more severe depression. We would like to draw the committee's attention to a	Thank you for your comment. Whilst two studies of MBCT were included in the NMA for treatment of a new depressive episode, the committee did not consider that the

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		1.5 and 1.6; pages 16-20) Full (Section 7)	line 15 - page 20 line 18)	meta-analysis of randomised controlled trials which included an analysis focusing specifically on studies restricted to people meeting diagnostic criteria for a current episode of major depression (Strauss et al., 2014). This found that MBCT (and its close variant person-based cognitive therapy [PBCT]) showed significant post-intervention between-group effects in comparison to control conditions on depressive symptom severity with a medium-large effect size (Hedges g=0.73; 95%CI 0.09-1.36). Only one of the included trials was restricted to people with more severe depression, with the other trials including people experiencing both less severe and more severe depression. This finding is in line with theory underpinning MBCT. Rumination, or the tendency to repetitively focus attention on negative thoughts and feelings, and their perceived causes and consequences, is a well-established mechanism of depression (Nolen-Hoeksema et al., 2008). Conversely, mindfulness involves focusing non-judgemental attention on present-moment experiences, which theoretically should interrupt rumination. A recent meta-analysis of mediation studies of randomised controlled trials showed this to be the case – mindfulness-based interventions such as	evidence was strong enough to support recommending this intervention, which was primarily developed for relapse prevention, for first line treatment. The Strauss 2014 systematic review has been checked for relevant studies. Only one study meets our criteria for inclusion and that had already been included.

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				MBCT had a beneficial effect on mental health outcomes by reducing rumination (Gu et al., 2015). On the basis of this evidence we would like the committee to consider recommending MBCT as a first-line treatment for both less severe and more severe depression alongside the other psychological interventions recommended.	
UK University Mindfulness Centres	Summary/Full	Summary (Section 1.8; pages 21-23) Full (Section 11)	Summary (Section 1.8 page 21 line 18 - page 23 line 17)	In comparison to the 2009 guideline, MBCT for relapse prevention is recommended with a number of caveats. MBCT is recommended for people (our emphasis): • who have recovered from *more severe depression* when *treated with medication* (alone or in combination with a psychological therapy), but are assessed as having a higher risk of relapse (summary guideline section 1.8.4). • who have had 3 or more previous episodes of depression and who are assessed as being at higher risk of relapse and *who recovered with medication but who want to stop taking it* (summary guideline section 1.8.9). • *if initial psychological therapy had no explicit*	Thank you for your comment. The decision on the effectiveness of an intervention is not taken on the basis of an analysis of individual trials which meet the criteria for inclusion in a review but from a pooling of the results of several trials. When developing the recommendations for the prevention of relapse the committee took into account a number of factors reported in the evidence. They noted that: • Recent MBCT trials (Williams et al 2014 and Shallcross et al 2015) showed that when compared with active control there was no clinically or statistically significant advantage of MBCT. • The majority of participants in the Kuyken et al meta-analysis were categorised as having severe depression. The following quote is taken from the Kuyken et al

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				relapse prevention component (summary guideline section 1.8.10). The most comprehensive meta-analysis of RCTs of MBCT for relapse prevention to date was published last year in JAMA Psychiatry (Kuyken et al., 2016). This showed significantly reduced between-group risk of depressive relapse within 60 weeks (hazard ratio, 0.69; 95%CI, 0.58-0.82). Moreover, there was a significantly reduced between-group risk of depressive relapse within 60 weeks when comparing MBCT to anti-depressant medication (hazard ratio, 0.77; 95%CI, 0.60-0.98). In relation to the caveats noted above, it is important to highlight that the trials included in the Kuyken et al. (2016) meta-analysis were: • *not* limited to people who had recovered from more severe depression, people with less severe and more severe depression were included (see summary guideline section 1.8.3, page 21), • *not* limited to people who had recovered following treatment with medication or psychological therapy, people were included who had received no previous treatment whatsoever (see summary guideline section 1.8.4, pages 21-22),	paper 'Our analyses suggest that the treatment effect of MBCT on the risk of depressive relapse/recurrence is larger in participants with higher levels of depression symptoms at baseline compared with non-MBCT treatments, suggesting that MBCT may be particularly helpful to those who still have significant depressive symptoms. (See the Davidson (2016) JAMA Psychiatry commentary on the Kuyken et al (2016) meta-analysis). • In the majority of trials of MBCT (including those in Kuyken et al (2016) participants had been in receipt of, or continued to use antidepressants. • Of the trials of MBCT which specified a previous number of episodes as an entry criteria, 7 out of the 9 trials considered as part of the guideline evidence review had 3 or more episodes as their entry criteria. You raise the possibility that the lack of a finding of number of relapses as a mediator support the dropping of this qualifier from the recommendation. However, Kuyken et al note the low heterogeneity of the populations in the included trials may well impact on the analysis of any mediators. They also report in some analyses an association between the number of episodes and relapse. When

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				• *not* limited to people who recovered with medication but wanted to stop taking it (see summary guideline sections 1.8.4 and 1.8.9, pages 21-22). • In addition, the number of previous episodes was *not* a moderator of relapse prevention outcome (see summary section 1.8.9, page 22). In summary, the evidence base for MBCT for relapse prevention categorically does not support the caveats listed in the draft guideline. Further comments are: • The caveat in section 1.8.10 (page 23 lines 5-7) that MBCT should be offered only "if initial psychological therapy had no explicit relapse prevention component" does not appear to be evidence-based. This caveat assumes that explicit relapse prevention components in initial psychological therapy are as effective as MBCT in preventing relapse and it is not clear from the evidence review that this has been demonstrated in randomised controlled trials.	these factors are taken into account the committee considered that it was appropriate to include these qualifiers in the recommendations. In developing recommendation 1.8.5 the committee were aware that a number of psychological interventions, such as CBT and BA, have built into them components that are explicitly focused on relapse prevention. They therefore agreed it was appropriate to include this in the recommendations for MBCT. When developing the recommendation for CBT as a specific relapse prevention intervention the committee took into account not only the evidence of clinical effectiveness but also evidence of cost effectiveness. After considering the cost-effectiveness analyses the committee decided to recommend group CBT over individual CBT. To adopt this approach is entirely consistent with NICE methods. In view of the above the committee decided not to adopt your suggested changes to the recommendations.

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				• We were interested to see that group cognitive behaviour therapy (CBT) is recommended on a par with MBCT for relapse prevention. Although the committee reviewed 7 RCTs of CBT for relapse prevention (see full guideline, section 7), only two of these trials were of group CBT for relapse prevention (Bockting et al., 2005; Wilkinson et al., 2009) – the remaining 5 trials were of individual CBT. Of these two RCTs of group CBT for relapse prevention, one of these is a definitive trial of group CBT showing significant effects on relapse prevention (Bockting et al., 2005). This trial was conducted in a non-UK sample and it is unclear how findings would translate to a UK setting. The other trial (Wilkinson et al., 2009) is a small trial, described as a pilot RCT by the authors (n=45). Moreover, this trial was specifically for older adults (aged 60+). In the Wilkinson et al. (2009) trial effects on relapse prevention were non-significant. In numerical terms, whilst there were lower (but non-significant) relapse rates based on MADRAS in the group CBT arm versus control, there were actually higher (non-significant) relapse rates when using the BDI-II when comparing group CBT to control. There is therefore only one	

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				definitive RCT of group CBT showing effects on relapse prevention, which the other pilot RCT fails to support. Moreover, the definitive RCT was not conducted in the UK. This would seem to fall below the usual NICE standard for inclusion as a recommendation. Based on our review of the evidence above, we would suggest a more evidence-based set of recommendations and we suggest the following re-wording for recommendations in section 1.8: • 1.8.3 For people who have recovered from less severe depression and are assessed as having a higher risk of relapse (our emphasis): o Offer MBCT o Consider *individual* CBT with an explicit focus on relapse prevention, typically 3–4 sessions over 1–2 months o Consider continuing their medication • 1.8.4 For people who have recovered from more severe depression and are assessed as having a higher risk of relapse: o Offer MBCT o Consider Group CBT • Remove section 1.8.9 as it is no longer	

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				necessary with our suggested changes • Remove section 1.8.10 as it is no longer necessary with our suggested changes	
UK University Mindfulness Centres	Summary/Full	Summary (1.10; pages 26-27) Full (Section 9)	Summary (1.10 page 26 line 11 - page 27 line 15)	MBCT is not currently mentioned as a treatment for chronic depression. We would like to draw attention to two pilot trials which show significant effects of MBCT (or its close variant PBCT) on depressive symptom severity in people with chronic depression (Barnhofer et al., 2009; Strauss et al., 2012). We therefore suggest that MBCT could be considered as a treatment for chronic depression in order to increase patient choice.	Thank you for your comment. We do not have any evidence to support recommending MBCT for chronic depression.
UK University Mindfulness Centres	Summary/Full	Summary (1.11 and 1.12) Full (Section 10)	Summary (1.11 and 1.12; page 27 line 16 – page 28 line 15)	MBCT is not mentioned in these sections and we agree that there is insufficient evidence for recommending MBCT in these instances.	Thank you for your comment. Following a further review of the evidence for MBCT in further line treatment we have removed it from the recommendations as the evidence for the effectiveness of other interventions was stronger.

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UK University Mindfulness Centres	Summary/Full	Summary (1.9.9; page 26) Full (Section 8)	Summary (1.9.9 page 26 lines 1-7)	We support the draft recommendation in Section 1.9.9 for MBCT as a second-line intervention for limited response and treatment-resistant depression. This recommendation is in line with the evidence for MBCT in the treatment for a current episode of major depression (see comments above in relation to sections 1.5 and 1.6) and takes account of the recent evidence specifically examining MBCT for treatment-resistant depression (Chiesa et al., 2015; Eisendrath et al., 2016).	Thank you for your comment. Following a further review of the evidence for MBCT in further line treatment we have removed it from the recommendations as the evidence for the effectiveness of other interventions was stronger.
Central Manchester Healthcare NHS FT	Table 2			CBT 2-3 times per week is recommended however currently is only offered once per week and the waiting list is usually quite long. Perhaps a drive for more CBT practitioners may be helpful to ensure depressed adults get the intervention they need in a timely way. Antenatal visits are being conducted but not uniformly due to lack of capacity and staffing in certain areas. This will impact on the quality of services and future outcomes for our families and needs addressing and considering	Thank you for your comment. We recommend 2 sessions of CBT for the first 2-3 weeks. This is what is closest to what is recommended in the treatment manuals, involves no greater resource allocation and in our view is likely to produce better outcomes. We are unclear what your comment about antenatal visits refers to as we do not mention these in the recommendations.
Central Manchester Healthcare NHS FT	Table 2			Cost effectiveness would generate from prevention of depression in the first place. The interventions are very much downstream and reactive. Pro-active prevention is the way forward. The role of the health visitor and	Thank you for your comment. Prevention of depression is outside the scope of this guideline and we are not able to make recommendations on this issue.

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				school nurse is critical in this work. It is widely documented in the literature that Early help/early intervention makes for significant financial returns and equity long term (Allen, Tickell, Munro). Vitamin D supplementation during pregnancy and new birth of baby should be given as this would reduce depression long term and would be significantly cheaper than mental health services in future. The funding was removed for this and could prove to be expensive long term Vitamin d can only be obtained from the sun direct for 20 mins everyday and only 15% from food. This means we may all be deficient and is not an ethnic group problem anymore. All skin colours are at risk of vit d deficiency which can result in depression	
Central Manchester Healthcare NHS FT	Table 2			Vitamin D supplementation as above to support mood and accessible drop in exercise classes and social activities so reduce isolation resulting in depression. A 2 - way process is needed with service uses and health professionals working collaboratively in partnership. Considering the "actual diagnosis" and root cause of the depression so the underlying problems are addressed as opposed to masking the problems with medication which is only mean to be a short term solution anyway. Depression is most often treated	Thank you for your comment. The guideline includes a number of recommendations on assessment which are designed to ensure that a full assessment of need is undertaken and decisions on treatment are not made solely on the basis of a symptom count. Perinatal mental health is outside the scope of this guideline and we are not able to make recommendations on this issue.

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				blindly based on symptoms but can be chemical imbalance or overload of stress. Targeted baby massage for mothers with low mood but the antenatal visit is critical prior to this to identify risks before the low mood arises. Working closely with the psychology team is critical with IY baby incredible years and VIG video interactive guidance bonding and attachment so the foundations are good for later life which begins at conception the 1001 critical days and NBO training which is currently being rolled out across Manchester. Good bonding and attachment with mother na dbaby is crucial for later life mental health. Could we have a campaign and raise awareness re the critical importance of the early stages again perhaps?	
Central Manchester Healthcare NHS FT	Table 2			Having read the equality impact assessment there appears to be no consideration towards hard to reach groups asylum seekers and protected characteristics including LBGT and pregnancy etc? These rae critical to include and consider within the mental health documentation as most likely to suffer with mental health issues	Thank you for your comment. Pregnant women are already covered by existing NICE guidance on Antenatal and perinatal mental health. LGBT groups are already explicitly mentioned in recommendation 1.3.5 as a group where pathways need to be in place to promote their access to mental health services. In light of your comment we have added asylum seekers to this recommendation.
Institute of Food, Brain and Behaviour	Table 2	Q1		The Draft NICE Guidelines 2017 focus is primarily on pharmacological interventions aimed at healthcare professionals, other professionals in direct contact with people	Thank you for your comment. The guideline has appraised the evidence on a range of psychological interventions as well as pharmacological interventions and this is

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				with depression, providers of service for people with depression and their families and carers and adults with depression, their families and carers. The Institute of Food, Brain & Behaviour (IFBB) note that the importance of nutrition in the symptom management (Section 1.47) and relapse prevention (Section 1.8) of depression is entirely omitted. Furthermore, the side-effects during withdrawal (1.4.9) are conservative at best and fail to mention suicidal ideation which is concerning. In Section 1.9, nutrition could play a meaningful role in those who are treatment resistant or have limited response. The IFBB is a leading U.K. authority on the effects of foods on brain function and mood. It is our duty to ensure we are up-to-date on the latest neuroscientific findings in relation to the global fields of nutritional psychiatry and neuroscience. For example, we are aware that the main treatments for Major Depressive Disorder (MDD) are selective serotonin re-uptake inhibitors (SSRIs). However, we also note that several meta-analyses of clinical trials indicate that they have limited efficacy, with effect sizes of around 0.31, making them only slightly more efficacious than placebo (0.3) except in the	reflected in the recommendations that have been made. We have not looked at the evidence on the use of nutrition as an intervention for relapse prevention as it is not currently used in routine clinical practice. Suicidal ideation and withdrawal are considered in separate recommendations in section 1.4. The use of omega-3 fatty acids was investigated in the question on treatment of a new depressive episode. As documented in the 'evidence to recommendations' section in the full guideline, no statistically significant difference in response, remission or discontinuation compared to placebo were found. Therefore the committee did not recommend the use of omega-3 fatty acids. The recommendations in section 1.2 on recognition, assessment and initial management were not part of this update. Therefore the evidence in these areas has not been reviewed and we are not able to make any changes to the recommendations. The question on access to services looked at what were the effective interventions to promote access in people from particular vulnerable groups (older people, BME

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				most severely depressed patients [13]. There are multiple reported side-effects of antidepressant medications including, but not limited to, nausea, fatigue and drowsiness, insomnia, dry mouth, blurred vision, increased appetite and weight gain, sexual dysfunction, constipation, dizziness, agitation, irritability and anxiety. These multiple side-effects result in a high proportion of patients discontinuing treatment. There are also concerns surrounding the safety of SSRIs in both children and adolescents, and noticeably increased risks of violence and/or suicide [14-17]. This poses a serious dilemma for clinicians who must consider these risks versus leaving the depression pharmacologically untreated [18]. It is here that the IFBB strongly recommend a meaningful role for nutritional interventions including supplementation with omega-3 fatty acids. Omega-3 highly unsaturated fatty acids (HUFA) are essential bioactive compounds which can only be obtained via the diet. The key omega-3 HUFAss are docosahexaenoic acid (DHA: 22:6 n-3) and eicosapentaenoic acid (EPA: 20:5 n-3) direct sources of which are present in marine fish and seafood. In relation to plant sources of their precursors, α-Linolenic acid (ALA) is found in green leafy vegetables,	groups and men). Access to dieticians and nutritionists were not part of the review protocol for this question, the evidence in this area has not been appraised and we are not able to make any recommendations on this. Nutritional interventions, other than omega-3 fatty acids, were not prioritised for investigation in the question about treatment for a new depressive episode. The evidence in this area has not been appraised and we are not able to make any recommendations. Making recommendations on mechanism of action and prevention of depression are outside the scope of this guideline.

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				some nut and seed oils (although of these, only flax provides more ALA). But ALA competes for the same enzymes with omega-6s for elongation and desaturation to form the longer chain EPA for the synthesis of signalling molecules and DHA to be incorporated in cell membranes. The starting point for the omega-6 biochemical pathway is linoleic acid (LA, 18:2n-6) which is found in all vegetable oils, nuts, seeds, grains and products containing these - which includes most commercially manufactured processed foods. Modern Western-type diets provide disproportionate amounts of LA compared with ALA [19], which may account for the very limited conversion of ALA to EPA and DHA observed in human studies, due to the competition between the two parent omega-3 and 6s. This competition for synthesis often results in elevated amounts of omega-6 and low omega-3 which is known to upset the biochemistry of the brain, leaving it vulnerable particularly to pro-inflammatory states [20] and defective interneuronal transmission. There is also a well-documented body of research demonstrating the direct relationship between omega-3 insufficiencies and altered neurotransmitter function including significant depletion of dopamine, the neurotransmitter essential for well-being and mood [21-24].	

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				Therefore, the current draft guidelines especially in Section 1.2 would benefit from recognizing the influence of nutrition as a neuromodulator, and recommending the assessment of patients' dietary status. The American Psychiatric Association has already formulated guidelines in relation to the omega-3 status of patients with clinical depression with advice and recommendations for intervention via the diet [25]. The draft guidelines should also include psychosocial education and training about nutrition and the contribution it can make to improving both physical and mental-health and well-being. The potential of referrals to qualified dieticians and nutritionists could be incorporated in Section 1.3 Access to Services. In Section 1.5 First-line treatment for less severe depression, there is also no mention of healthy eating, although there is advice in Section 1.5.6 to follow a physical activity programme. As nutrition works synergistically with exercise and both can alter brain	

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				biochemistry and reduce inflammation it is critical to also mention nutrition. The absence of nutritional guidance is not up-to-date with current science and published data showing a greater efficacy of omega-3 fatty acids in the treatment of patients with clinical depression, than either cognitive behaviour therapy or SSRI's. The guidelines therefore appear to be biased in favour of pharmacological interventions. In 2005, in a keynote lecture to the American Psychiatric Association, Thomas Insel, Director of the National Institutes of Mental Health stated that several meta-analyses had demonstrated that 31% of patients with depression were in remission after 14 weeks of pharmacological treatment but that in most randomized, double-blind clinical trials the placebo response rate also floated around 30%. In other words, treatment with antidepressant medications is known to be practically no better than placebo in most patients. A new meta-analytic review co-authored by researchers at the National Institutes of Health confirms a role for omega-3 in treating clinical depression with an effect size of 0.6 – in other words 60% of patients with depression were in remission after omega-3 treatment compared to placebo	

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				[12]. Given the bi-directional relationship between obesity and depression, it is perverse that nutrition is featured in the guidelines for obesity but woefully lacking in these draft guidelines for depression. The IFBB urges NICE to update these guidelines in relation to the current neuroscientific literature and to incorporate a section on the importance of an intake of balanced nutrients especially in relation to omega-3 fatty acids for which the evidence is strongest. In addition the draft guidelines do not take into account the latest epigenetic research. It is now widely known that nutrition is able to modify the expression of critical genes at the transcriptional level and inhibit the development of pathologic disease processes. In other words, we may carry an adverse gene variant, but whether it is activated or not can depend on stressors in the environment. This has huge implications for the prevention of depression, mood, and other psychiatric disease [10]. However, nutritional status or assessment for insufficiencies does not currently feature in diagnostic evaluations. The Institute of Food, Brain and Behaviour believe this should change. The current draft for the 2017 NICE guidelines do not make reference to published literature and recent meta-analysis	

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				demonstrating (1) low omega-3 index status in blood samples of patients with depression [11] and (2) a meta-analysis published in the British Journal of Psychiatry demonstrating efficacy of omega-3 intervention in patients with MDD [12]. As nutrition and exercise work synergistically these should be recommended as adjunct interventions. Furthermore, MDD and associated physical health conditions (e.g., cardiovascular disease, obesity, Type II diabetes, cancers) are also linked to omega-3 fatty acid deficiencies [5]. In addition, neurodevelopmental disorders such as ADHD, gastrointestinal symptoms and inflammatory disorders are increased in depression and anxiety, and consistent with alterations of gut microbiota and/or gut-brain-immune signalling [6]. These relationships are multi-directional and complex, because psychological stress aggravates both HPA-axis activation and immune function [7, 8]. Robertson et al (2017) recently demonstrated that neurobehavioural changes brought on by manipulating omega-3 intake were associated with altered composition of the gut microbiome, Hypothalamic Pituitary Axis (HPA) stress responses and inflammation [9]. There is a strong positive correlation between diseases of the mind and diseases of the	

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				body; it is not surprising then that MDD frequently co-exists in a bi-directional relationship with obesity, cardiovascular disease and Type 2 diabetes [2]. In a similar fashion, MDD is comorbid with other mental-health conditions including anxiety, sleep disorders, psychotic disorders, dementia, eating disorders, substance use disorders and ADHD [2]. Therefore following a healthy balanced diet is essential in the symptom management of MDD.	

**None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.*

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