National Institute for Health and Care Excellence

Consultation draft

Depression in adults: treatment and management

Appendix U2.10: Text from CG90 Appendix 17d that has been deleted

NICE Guideline

Appendices

May 2018

Disclaimer

Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Appendix 17d: clinical studies characteristics tables – management of subthreshold depressive symptoms

Contents

Service delivery - studies excluded in the guideline update

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
ADLER2004	Dythymia<50% so in major depression group
BRUCE2007	Assessment of depression
GLICK1986	Not diagnosis of depression (schizophrenia and major affective)
HEDRICK2003	Dythymia<50% so in major depression group
HERMENS2007	Minor depression=17.5% so in major depression group
HUNKELER2006	Dysthymia<50% so in major depression group
LIU2003	Dysthymia <50% so in major depression group
LUDMAN2007	Major depression
MIRANDA2003	Major depression
UNUTZER2001	Dysthymia<50% so in major depression group
UNUTZER2006	Dysthymia<50% so in major depression group
VAN2006	Prevention study
WANG2007	No formal diagnosis of depression and non relevant outcomes used at baseline

References of Excluded Studies

ADLER2004 (Published Data Only)

Adler, D.A., Bungay, K.M., Wilson, I.B., Pei, Y., Supran, S., Peckham, E., Cynn, D.J. & Rogers, W.H. (2004) The impact of a pharmacist intervention on 6-month outcomes in depressed primary care patients. General Hospital Psychiatry, 26, 199-209.

BRUCE2007 (Published Data Only)

Bruce, M.L., Brown, E.L., Rane, P.J., Mlodzianowski, A.E., Meyers, B.S., Leon, A.C., Heo, M., Byers, A.L., Greenberg, R.L., Rinder, S., Katt, W. & Nassisi, P. (2007) A randomized trial of depression assessment intervention in home health care. Journal of the American Geriatrics Society, 55, 1793-1800.

GLICK1986 (Published Data Only)

Glick, I.D., Fleming, L., DeChillo, N., Meyerkopf, N., Jackson, C., Muscara, D. & Good-Ellis, M. (1986) A controlled study of transitional day care for non-chronically-ill patients. American Journal

of Psychiatry, 143, 1551-1556.

HEDRICK2003 (Published Data Only)

Hedrick, S.C., Chaney, E.F., Felker, B., Liu, C.F., Hasenberg, N., Heagerty, P., Buchanan, J., Bagala, R., Greenberg, D., Paden, G., Fihn, S.D. & Katon, W. (2003) Effectiveness of collaborative care depression treatment in veterans' affairs primary care. Journal of General Internal Medicine, 18, 9-16.

HERMENS2007 (Published Data Only)

Hermens, M.L.M., van Hout, H.P.J., Terluin, B., Ader, H.J., Pennix, B.W.J.H., van Marwijk, H.W.J., Bosmans, J.E., van Dyck, R. & de Haan, M. (2007) Clinical effectiveness of usual care with or without antidepressant medication for primary care patients with minor or mild-major depression: a randomised equivalence trial. BMC Medicine, 5, 36.

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HUNKELER2006 (Published Data Only)

Hunkeler, E.M., Katon, W., Tang, L., Williams, J.W., Kroenke, K., Lin, E.H.B., Harpole, L.H., Arean, P., Levine, S., Grypma, L.M., Hargreaves, W.A. & Unutzer, J. (2006) Long term outcomes from the IMPACT randomised trial for depressed elderly patients in primary care. BMJ, 332, 259-263

LIU2003 (Published Data Only)

Liu, C.F., Hedrick, S.C., Chaney, E.F., Heagerty, P., Felker, B., Hasenberg, N., Fihn, S. & Katon, W. (2003) Cost effectiveness of collaborative care for depression in a primary care veteran population. Psychiatric Services, 54 (5), 698-704.

LUDMAN2007 (Published Data Only)

Ludman, E.J., Simon, G.E., Grothaus, L.C., Luce, C., Markley, D.K., Schaefer, J. (2007) A pilot study of telephone care management and structured disease self-management groups for chronic depression. Psychiatric Sevices, 58 (8), 1065-1072.

MIRANDA2003 (Published Data Only)

Miranda, J., Duan, N., Sherbourne, C., Schoenbaum, M., Lagomasino, I., Jackson-Triche, M. & Wells, K.B. (2003 Improving care for minorities: can quality improvement interventions improve care and outcomes for depressed minorities? Results of a randomized, controlled trial. Health Services Research, 38 (2), 613-630.

UNUTZER2001 (Published Data Only)

Unutzer, J., Rubenstein, L., Katon, W.J., Tang, L., Duan, N., Lagomasino, I.T. & Wells, K.B. (2001) Two-year effects of quality improvement programs on medication management for depression. Archives of General Psychiatry, 58, 935-942.

UNUTZER2006 (Published Data Only)

Unutzer, J., Tang, L., Oishi, S., Katon, W., Williams, J.W., Hunkeler, E., Hendrie, H., Lin, E.H.B., Levine, S., Grypma, L., Steffens, D.C., Fields, J. & Langston, C. (2006) Reducing suicidal ideation in depressed older primary care patients. Journal of the American Geriatrics Society, 54, 1550-1556.

VAN2006 (Published Data Only)

van 't Veer-Tazelaar, N., van Marwijkm, H., van Oppen, P., Nijpels, G., van Hout, H., Cuijpers, P., Stalman, W. & Beekman, A. (2006) Prevention of anxiety and depression in the age group of 75 years and over: a randomised controlled trial testing the feasibility and effectiveness of a generic stepped care programme among elderly community residents at high risk of developing anxiety and depression versus usual care. BMC Public Health, 6, 186.

WANG2007 (Published Data Only)

Wang, P.S., Simon, G.E., Avorn, J., Azocar, F., Ludman, E.J., McCulloch, J., Petukhova, M.Z. & Kessler, R.C. (2007) Telephone screening, outreach, and care management for depressed workers and impact on clinical and work productivity outcomes: a randomized controlled trial. JAMA, 298 (12), 1401-1411.

Service delivery - studies excluded in guideline update
Relapse Prevention

Comparisons Included in this Clinical Question - no comparisons

Characteristics of Included Studies - no included studies

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
KATON2001	In main service review bacause it's the only subthreshold service-related study

References of Included Studies - no included studies

References of Excluded Studies

KATON2001 (Published Data Only)

Katon, W., Rutter, C., Ludman, E.J., Von Korff, M., Lin, E., Simon, G., Bush, T., Walker, E. & Unutzer, J. (2001) A randomized trial of relapse prevention of depression in primary care. Archives of General Psychiatry, 58, 241-247.

Psychological and psychosocial interventions - new studies in the guideline update

Comparisons Included in this Clinical Question

Cognitive therapy v Fluoxetine
DUNNER1996

Fluoxetine v Fluoxetine+'Group CBT'
HELLERSTEIN2001A

IPT v Brief supportive psychotherapy v Sertraline v IPT+Sertraline
MARKOWITZ2005

Paroxetine v Problem solving treatment for primary care v Placebo
BARRETT1999

Sertraline v Placebo v Sertraline+CBT v Placebo+CBT
RAVINDRAN1999

Sertraline v Sertraline+IPT v IPT
BROWNE2002

Short-term psychodynamic verbal therapy v short-term psychodynamic art therapy
THYME2007

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
BARRETT1999 Study Type: RCT Blindness: Double blind Duration (days): Mean 77 Setting: Primary Care; USA Notes: RANDOMISATION: Blocked and stratified by site and diagnosis. Computer generated random number allocation	n= 656 Age: Mean 61 Sex: 330 males 326 females Diagnosis: 52% Dysthymia by DSM-IV 48% Minor Depressive Disorder by DSM-IV Exclusions: Major depression; psychosis; schizophrenia or schizoaffective disorder; bipolar disorder; alcohol or substance misuse in past 6 months; antisocial personality disorder; suicidal risk; moderate or severe cognitive impairment; medical illness with prognosis of <6 months to live; in current treatment (unless taking <50mg amitriptyline and willing to discontinue) Notes: Minor depression: symptoms <4weeks No washout period reported Two diagnosis groups reported separately Baseline: Dysthymia: HAMD-17: Prx 14.0 (3.1); PST-PC 13.7 (2.8); Plb 13.5 (2.8) Minor Depression: HAMD-17: Prx 13.6 (2.8); PST-PC 13.7 (3.1); Plb 13.7 (3.1)	**Data Used** Remission: HAMD-17 score <7 Response: 50% reduction in outcome score Number reporting side effects Leaving study due to side effects Leaving study early for any reason HAMD-17 endpoint **Data Not Used** NEO - Five Factor Inventory - not relevant Medical Outcomes Survey - not relevant Hopkins Symptom Checklist - not relevant Duke Severity of Illness Checklist - not relevan Notes: Full data set obtained direct from author Dysthymia and minor depression reported separately SFX data reported for Prx and Plb arms only	**Group 1 N= 217** Paroxetine. Mean dose 20 mg/d - Dysthymia n=111 Minor Depression n=106 **Group 2 N= 218** Problem Solving Therapy - Primary Care. Mean dose 6 sessions - Dysthymia n=115 Minor Depression n=103 **Group 3 N= 221** Placebo - Dythymia n=112 Minor Depression n=109	Funding: John A Hartford Foundation; John D and Catherine T MacArthur Foundation
BROWNE2002 Study Type: RCT Type of Analysis: Completers: completing 6 month MDRS Blindness: Single blind Duration (days): Mean 180 Followup: 18 months after treatment Setting: Primary care; Canada Notes: RANDOMISATION: computerised randomisation schedule	n= 707 Age: Mean 42 Sex: 188 males 398 females Diagnosis: 100% Dysthymic Disorder by DSM-IV Exclusions: Pregnant, lactating, childbearing age and not using contraception, planning pregnancy in next 25 months; history of sertraline use; history of hypersensitivity to other SSRIs; acute suicide risk; participation in other study including investigation products in past month; treatment with depot neuroleptic drugs in past 6 months; on any serotonergic drug; primary or secondary diagnosis of psychotic disorder; clinically significant and unstable medical condition Notes: All demographic and efficacy data reported for 586	**Data Used** MADRS endpoint **Data Not Used** Visual Analogue Scale - not relevant Centre for Epidemiologic Studies Depression Scale - not relevant McMater Familly Assessment Device - not relevant Social Adjustment Scale - not relevant Utilization of services inventory - not relevant MADRS change - not extractable Response: 40% reduction in outcome score - not extractable Leaving study early for any reason - not extractable	**Group 1 N= 196** Sertraline. Mean dose 200mg/d (max) - Continued throughout 18 month follow-up **Group 2 N= 212** Sertraline. Mean dose 200mg/d (max) - Continued throughout 18 month follow-up IPT. Mean dose 10 sessions - Up to 12 1-hour sessions Terminated at 6 months **Group 3 N= 178** IPT. Mean dose 10 sessions - Up to 12 1-hour sessions Terminated at 6 months	Funding: Medical Research Council of Canada; Pharmaceutical Manufacturers Association of Canada; Pharma

	completers only Baseline: MADRS: Stl 24.9 (6.5); Stl+IPT 26.0 (6.3); IPT 24.4 (5.9); All 25.1 (6.2)	Notes: Author emailed 23/05/08 and 28/05/08 for N per group at randomisation, N per group in mean MDRS calculation at 6 months, standard deviations of mean MDRS at 18 months Author responded 13/06/08 with data		
DUNNER1996 Study Type: RCT Type of Analysis: Completers Blindness: No mention Duration (days): Mean 112 Setting: Outpatients; USA Notes: RANDOMISATION: no details	n= 31 Age: Mean 36 Sex: 13 males 11 females Diagnosis: 100% Dysthymic Disorder by DSM-III-R Exclusions: Current treatment with psychotherapy or with fluoxetine within past 2 years; serious concomitant medical conditions; hypersensitivity to fluoxetine; serious risk of suicide; use of an investigational compound in past 30 days; pregnant or lactating women or not using contraception; physical or laboratory abnormalities which would preclude use of fluoxetine; antisocial or borderline personality disorder Notes: n=24 completers reported only Baseline: HAMD-17: Flx 16.5 (4.0); CT 15.4 (3.1) BDI: Flx 20.2 (7.5); CT 18.9 (5.0)	**Data Used** Remission: HAMD-17 score =/<7 and BDI =/< Leaving study due to side effects Leaving study early for any reason BDI endpoint HAMD-17 endpoint **Data Not Used** Tridimensional Personality Questionnaire - not relevant Hamilton Anxiety Rating Scale - not relevant	**Group 1 N= 13** Cognitive Therapy **Group 2 N= 18** Fluoxetine. Mean dose 20mg/d - Fixed dose	Funding: unclear
HELLERSTEIN2001A Study Type: RCT Type of Analysis: 'ITT': Completing 8 week trial only Blindness: No mention Duration (days): Mean 168 Followup: 12 weeks after treatment Setting: Tertiary Care; USA Notes: RANDOMISATION: no details	n= 40 Age: Mean 45 Sex: 20 males 20 females Diagnosis: 100% Primary Dysthymia with early onset by DSM-III-R Exclusions: Organic mental syndromes; major depression; bipolar disorder; severe cyclothymia; psychotic disorder; severe borderline personality disorder; substance or alcohol misuse or dependence in past 6 months; PD, GAD, OCD or PTSD in past 6 months; pregnant or nursing; medical illness assessed as probable cause of dysthymia; undergoing another psychotherapy; serious suicidal risk Notes: Patients are partial responders from 8 week flx trial Baseline: HAMD-17: Flx 19.25 (6.91); Flx/GPT 16.65 (6.75)	**Data Used** Remission: H-17 item1=0 & no longer meets criteria Remission at follow-up Response at follow-up Response: 50% reduction and CGI score 1/2 Leaving study early for any reason **Data Not Used** Satisfaction with Life Scale - not relevant CGI - not relevant Global Assessment of Functioning Scale - not relevant Attributional Style Questionnaire - not relevant Life Orientation Test - not relevant Inventory of Interpersonal Problems - not relevant HAMD-17 endpoint - no data BDI endpoint - no data Cornell Dysthymia Rating Scale - not relevant Notes: Author emailed 30/05/08 to clarify intervention	**Group 1 N= 20** Fluoxetine. Mean dose 38.75(18.93)mg/d **Group 2 N= 20** Fluoxetine. Mean dose 37.36(17.27)mg/d Group CBT. Mean dose 16 sessions - CIGP-CD manual	Funding: Pharma
MARKOWITZ2005				

Study Type: RCT Type of Analysis: ITT: LOCF Blindness: Blind raters Duration (days): Mean 112 Setting: Referral and Advertising; USA Notes: RANDOMISATION: computer-generated random number programme	n= 94 Age: Mean 42 Sex: 35 males 59 females Diagnosis: 100% Dysthymic Disorder by DSM-IV 24% Lifetime criteria for MDD by DSM-IV 10% Social Phobia by DSM-IV 2% Panic Disorder by DSM-IV 1% Anorexia Nervosa by DSM-IV 1% Stimulant Dependence by DSM-IV Exclusions: Major depression in past 6 months; substance misuse or dependence; history of schizophrenia; psychosis; mania or hypomania; organic mental syndrome; cluster A antisocial or borderline personality disorder; mental retardation; significant suicide risk; concurrent psychotherapy or pharmacotherapy; unstable medical condition; hypersensitivity to sertraline; history of non-response to sertraline; at least 12 weeks, IPT; two or more adequate trials of any antidepressant Baseline: HAMD-24: IPT 18.9 (6.0); BSP 19.7 (4.4); Stl 17.8 (3.5); IPT/Stl 19.7 (5.5) BDI: IPT 18.0 (7.2); BSP 17.4 (5.6); Stl 17.5 (6.7); IPT/Stl 18.6 (7.9)	**Data Used** Remission: HAMD-24 score =/<7 and GAF>70 Response: 50% reduction in outcome score Leaving study early for any reason BDI endpoint HAMD-24 endpoint **Data Not Used** Inventory of Interpersonal Problems - not relevant Social Adjustment Scale - not relevant Cornell Dysthymia Rating Scale - not relevant	**Group 1 N= 23** IPT-D. Mean dose 13.2 (4.0) sessions - 50 minute sessions IPT-D: IPT for dysthymic disorder **Group 2 N= 26** Brief Supportive Therapy. Mean dose 9.6 (6.3) sessions - 50 minute sessions **Group 3 N= 24** Sertraline. Mean dose 111.9 (56.3) mg/d **Group 4 N= 21** Sertraline. Mean dose 116.3 (43.9) mg/d IPT-D - 50 minute sessions IPT-D: IPT for dysthymic disorder	Funding: National Institute of Mental Health; Nancy Pritzker Research Network; Weill Cornell Department of Psychiatry; Pharma
RAVINDRAN1999 Study Type: RCT Type of Analysis: Completers Blindness: Double blind Duration (days): Mean 84 Setting: Newspaper adverts; Canada Notes: RANDOMISATION: computer-generated schedule with treatments balanced within blocks of consecutive patients	n= 97 Age: Range 21-54 Sex: 41 males 56 females Diagnosis: 100% Primary Dysthymia by DSM-IV Exclusions: Other axis I disorder or physical illness; clinical diagnosis of personality disorder; symptoms sufficient for, or previous diagnosis of, MDD; multiple adverse drug reactions; hypertension; significant dermatitis; malignant, hematological, endocrine, pulmonary, cardiovascular, renal, hepatic, gastrointestinal or neurologic disease; pregnant or lactating females Notes: DSM-III also used for diagnosis 1 week placebo washout: no responders Baseline: Not extractable	**Data Not Used** Coping Strategies Scale - not relevant Daily Hassles and Uplifts Scales - not relevant Batelle Quality of Life Scale - not relevant Cornell Dysthymia Rating Scale - not relevant CGI - not relevant Hamilton Anxiety Rating Scale - not relevant MADRS endpoint - not extractable HAMD-17 endpoint - not extractable Notes: Author emailed 08/05/08 for HAMD-17 and MADRS endpoint data Author responded 09/05/08: busy until mid June but will try to obtain data	**Group 1 N= 22** Sertraline. Mean dose 177.90 mg/d **Group 2 N= 26** Placebo **Group 3 N= 25** Sertraline. Mean dose 177.90 (28.72) mg/d CBT - weekly 90-minute sessions **Group 4 N= 24** Placebo CBT - weekly 90-minute sessions	Funding: Medical Research Association of Canada; Pharmaceutical Manufacturers Association of Canada; pharmaceutical
THYME2007 Study Type: RCT Study Description: Length of study is unclear; 10 sessions so assume 10 weeks Type of Analysis: Completers Blindness: No mention Duration (days):	n= 43 Age: Mean 34 Sex: all females Diagnosis: 64% Dysthymic Disorder by DSM-IV	**Data Used** BDI follow-up BDI endpoint **Data Not Used** Personality interview - not relevant Symptom Checklist - 90 - not relevant Impact of Event Scale - not relevant	**Group 1 N= 22** Short-term psychodynamic verbal therapy - 10 sessions lasting 45 minutes each; given according to Mann (1973)	Funding: County Council of Vasterbotten; Department of Psychiatry

Setting: Outpatients; Sweden Notes: RANDOMISATION: 'impartial individual' selected marked slips of paper from box	36% Depressive symptoms and difficulties by Exclusions: Psychopharmacological treatment Baseline: BDI: Verbal 22.0 (7.55); Art 22.0 (7.49)	HAMD-21 endpoint - not extractable	**Group 2 N= 21** Short-term psychodynamic art therapy - 10 sessions lasting 60 minutes each; various drawing tasks followed by reflective dialogue between patients and therapist	

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
BARKHAM1999	Replaced dropouts with no post-treatment assessments
BOLTON2003	Major depression >50%
CHOU2004	n<10 p/g
CRAFT2007	'minimal depression'=9.4% only so in major depression group
CUIJPERS2005C	Not RCT
DAI1999	No extractable data
DOYNE1987	Minor depression =22% only so in major depression group
FOSTER2007	No formal diagnosis of depression or minimum baseline score; no extractable data
HANSER1994	Does not separate diagnosis; dropouts replaced; N p/g<10 at end; does not report BDI scores
HARINGSMA2006A	Sample: 39% MDD and remainder no formal diagnosis of depression ('depressive symptoms')
LYNCH1997	No extractable data
MAINA2004	Foreign language
MCNEIL1991	No extractable data (N per group unclear)
MIRANDA1994	Only 33% final sample had minor depression (remainder unclear); no extractable data even from subgroup analysis
MOSSEY1996	No extractable data
NEUGEBAUER2006	N in TAU arm<10
NORTH1990	Review
OXMAN2008	100% minor depression but excludes dysthymia
SANG2007	Foreign language
SEIVEWRIGHT1998	Does not report dysthymia data separately
TYRER1988	No extractable data; n<10 in plb grp
WANG1999	Foreign language
WARING1988	N p/g<10
WILLEMSE2004	Prevention study; no extractable data

References of Included Studies

BARRETT1999 (Published Data Only)

Oxman, T. E., Barrett, J. E., Sengupta, A., Katon, W., Williams, J. W. J., Frank, E., et al. (2001) Status of minor depression or dysthymia in primary care following a randomized controlled treatment. General Hospital Psychiatry, 23, 301-310.

Frank, E., Rucci, P., Katon, W., Barrett, J., Williams, J. W. J., Oxman, T., et al. (2002) Correlates of remission in primary care patients treated for minor depression. General Hospital Psychiatry, 24, 12-19.

Katon, W., Russo, J., Frank, E., Barrett, J., Williams, J. W. J., Oxman, T., et al. (2002) Predictors of nonresponse to treatment in primary care patients with dysthymia. General Hospital Psychiatry, 24, 20-27.

Williams, J. W. J., Barrett, J., Oxman, T., Frank, E., Katon, W., Sullivan, M., et al. (2000) Treatment of dysthymia and minor depression in primary care: A randomized controlled trial in older adults. JAMA, 284, 1519-1526.

Barrett, J. E., Williams, J. W. J., Oxman, T. E., Frank, E., Katon, W., Sullivan, M., et al. (2001) Treatment of dysthymia and minor depression in primary care: a randomized trial in patients aged 18 to 59 years. Journal of Family Practice, 50, 405-412.

*Barret, J.E., Williams, J.W., Oxman, T.E., Katon, W., Frank, E., Hegel, M.T., Sullivan, M. & Schulberg, H.C. (1999) The treatment effectiveness project. A comparison of the effectiveness of paroxetine, problem-solving therapy, and placebo in the treatment of minor depression and dysthymia in primary care patients: background and research plan. General Hospital Psychiatry, 21, 260-273.

BROWNE2002 (Published Data Only)

Browne, G., Steiner, M., Roberts, J., Gafni, A., Byrne, C., Dunn, E., et al. (2002) Sertraline and/or interpersonal psychotherapy for patients with dysthymic disorder in primary care: 6-month comparison with longitudinal 2-year follow-up of effectiveness and costs. Journal of Affective Disorders, 68, 317-330.

DUNNER1996 (Published Data Only)

Dunner, D. L., Schmaling, K. B., Hendrickson, H., Becker, J., Lehman, A., & Bea, C. (1996) Cognitive therapy versus fluoxetine in the treatment of dysthymic disorder. Depression, 4, 34-41.

HELLERSTEIN2001A (Published Data Only)

Hellerstein, D. J., Little, S. A., Samstag, L. W., Batchelder, S., Muran, J. C., Fedak, M., et al. (2001) Adding group psychotherapy to medication treatment in dysthymia: a randomized prospective pilot study. Journal of Psychotherapy Practice & Research, 10, 93-103.

MARKOWITZ2005 (Published Data Only)

Markowitz, J. C., Kocsis, J. H., Bleiberg, K. L., Christos, P. J., & Sacks, M. (2005) A comparative trial of psychotherapy and pharmacotherapy for "pure" dysthymic patients. Journal of Affective Disorders, 89, 167-175.

RAVINDRAN1999 (Published Data Only)

Ravindran, A.V., Anisman, H., Merali, Z., Charbonneau, Y., Telner, J., Bialik, R.J., Wiens, A., Ellis, J. & Griffiths, J. (1999) Treatment of primary dysthymia with group cognitive therapy and pharmacotherapy: clinical symptoms and functional impairments. American Journal of Psychiatry, 156, 1608-1617.

THYME2007 (Published Data Only)

Thyme, K.E., Sundin, E.C., Stahlberg, G., Lindstrom, B., Eklof, H. & Wiberg, B. (2007) The outcome of short-term psychodynamic art therapy compared to short-term psychodynamic verbal therapy for depressed women. Psychoanalytic Psychotherapy, 21 (3), 250-264.

References of Excluded Studies

BARKHAM1999 (Published Data Only)

Barkham, M., Shapiro, D. A., Hardy, G. E., & Rees, A. (1999). Psychotherapy in two-plus-one sessions: outcomes of a randomized controlled trial of cognitive-behavioral and psychodynamic-interpersonal therapy for subsyndromal depression. Journal of Consulting & Clinical Psychology, 67, 201-211.

BOLTON2003 (Published Data Only)

Bolton, P., Bass, J., Neugebauer, R., Verdeli, H., Clougherty, K. F., Wickramaratne, P., et al. (2003) Group interpersonal psychotherapy for depression in rural Uganda: a randomized controlled trial. JAMA, 289, 3117-3124.

CHOU2004 (Published Data Only)

Chou, K. L., Lee, P. W., Yu, E. C., Macfarlane, D., Cheng, Y. H., Chan, S. S., et al. (2004) Effect of Tai Chi on depressive symptoms amongst Chinese older patients with depressive disorders: a randomized clinical trial. International Journal of Geriatric Psychiatry, 19, 1105-1107.

CRAFT2007 (Published Data Only)

Craft, L. L., Freund, K. M., Culpepper, L., & Perna, F. M. (2007) Intervention study of exercise for depressive symptoms in women. Journal of Women's Health, 16, 1499-1509.

CUIJPERS2005C (Published Data Only)

Cuijpers, P., Smit, F., Voordouw, I., & Kramer, J. (2005) Outcome of cognitive behaviour therapy for minor depression in routine practice. Psychology & Psychotherapy: Theory, Research & Practice, 78, 179-188.

DAI1999 (Published Data Only)

Dai, Y., Zhang, S., Yamamoto, J., Ao, M., Belin, T. R., Cheung, F., et al. (1999) Cognitive behavioral therapy of minor depressive symptoms in elderly Chinese Americans: a pilot study. Community Mental Health Journal, 35, 537-542.

DOYNE1987 (Published Data Only)

Doyne, E., Ossip-Klein, D., Bowman, E., Osborn, K., Dougall-Wilson, I., & Neimeyer, R. (1987) Running versus weight lifting in the treatment of depression. Journal of Consulting and Clinical Psychology, 55, 748-754.

FOSTER2007 (Published Data Only)

Foster, R. P. (2007) Treating depression in vulnerable urban women: a feasibility study of clinical outcomes in community service settings. American Journal of Orthopsychiatry, 77, 443-453.

HANSER1994 (Published Data Only)

Hanser, S. B. & Thompson, L. W. (1994) Effects of a music therapy strategy on depressed older adults. Journal of Gerontology, 49, 265-269.

HARINGSMA2006A (Published Data Only)

Haringsma, R., Engels, G. I., Cuijpers, P., & Spinhoven, P. (2006) Effectiveness of the Coping With Depression (CWD) course for older adults provided by the community-based mental health care system in the Netherlands: a randomized controlled field trial. International Psychogeriatrics, 18, 307-325.

LYNCH1997 (Published Data Only)

Lynch, D. J., Tamburrino, M. B., & Nagel, R. (1997) Telephone counseling for patients with minor depression: preliminary findings in a family practice setting. Journal of Family Practice, 44, 293-298.

MAINA2004 (Published Data Only)

Maina, G., Picco, C., Saracco, P., Ziero, S., Ceregato, A., & Bogetto, F. (2004) Combined therapy in minor depressive disorders: Unique therapist or split treatment? [Italian]. Italian Journal of Psychopathology, 10.

MCNEIL1991 (Published Data Only)

McNeil, J.K., LeBlanc, E.M. & Joyner, M. (1991) The effect of exercise on depressive symptoms in the moderately depressed elderly. Psychology and Aging, 6, 487-488.

MIRANDA1994 (Published Data Only)

Miranda, J. & Munoz, R. (1994) Intervention for minor depression in primary care patients. Psychosomatic Medicine, 56, 136-141.

MOSSEY1996 (Published Data Only)

Mossey, J. M., Knott, K. A., Higgins, M., & Talerico, K. (1996) Effectiveness of a psychosocial intervention, interpersonal counseling, for subdysthymic depression in medically ill elderly. Journals of Gerontology Series A-Biological Sciences & Medical Sciences, 51, M172-M178.

NEUGEBAUER2006 (Published Data Only)

Neugebauer, R., Kline, J., Markowitz, J. C., Bleiberg, K. L., Baxi, L., Rosing, M. A., et al. (2006) Pilot randomized controlled trial of interpersonal counseling for subsyndromal depression following miscarriage. Journal of Clinical Psychiatry, 67, 1299-1304.

NORTH1990 (Published Data Only)

North, T.C., McCullagh, P. & Tran, Z.V. (1990) Effect of exercise on depression. Exercise and Sport Sciences Review, 18, 349-415.

OXMAN2008 (Published Data Only)

Oxman, T.E., Hegel, M.T., Hull, J.G. & Dietrich, A.J. (2008) Problem-solving treatment and coping styles in primary care for minor depression. Journal of Consulting and Clinical Psychology, 76, 933-943.

SANG2007 (Published Data Only)

Sang, W. H., Zhang, D. R., Tian, G. Q., Yu, X. Z., Liu, J. C., Yang, L. H., et al. (2007) A comparative study of cognitive-behavior therapy and paroxetine for minor depression. [Chinese]. Chinese Journal of Evidence-Based Medicine, 7.

SEIVEWRIGHT1998 (Published Data Only)

Seivewright, H., Tyrer, P., & Johnson, T. (1998) Prediction of outcome in neurotic disorder: a 5-year prospective study. Psychological Medicine, 28, 1149-1157.

TYRER1988 (Published Data Only)

Tyrer, P., Seivewright, N., Ferguson, B., Murphy, S., & Johnson, A. L. (1993) The Nottingham study of neurotic disorder. Effect of personality status on response to drug treatment, cognitive therapy and self-help over two years. British Journal of Psychiatry, 162, 219-226.

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Pharmacological interventions - new studies in guideline update

Comparisons Included in this Clinical Question

Amisulpride v Amineptine v Placebo
BOYER1999

Amisulpride v Amitriptyline
RAVIZZA1999

Amisulpride v Fluoxetine
AMORE2001
SMERALDI1996

Fluoxetine v Placebo
HELLERSTEIN1993
JUDD2004
VANELLE1997

Fluvoxamine v Maprotiline
DEJONGHE1991

Imipramine v Minaprine
SALZMANN1995

Imipramine v Moclobemide v Placebo
VERSIANI1997

Imipramine v Phenelzine
VALLEJO1987

Imipramine v Ritanserin v Placebo
BAKISH1993

Paroxetine v Maprotiline
SZEGEDI1997

Paroxetine v Placebo
BARRETT1999

Ritanserin v Flupenthixol
GEISLER1992

Sertraline v Imipramine v Placebo
THASE1996A

Sertraline v Placebo
RAVINDRAN1999
RAVINDRAN2000
ROCCA2005

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
AMORE2001 Study Type: RCT Type of Analysis: 'ITT': at least one post baseline evaluation Blindness: Double blind Duration (days): Mean 84 Setting: Outpatients; Italy Notes: RANDOMISATION: not reported	n= 313 Age: Mean 47 Sex: 100 males 213 females Diagnosis: 89% Dysthymic Disorder by DSM-IV 11% Double depression by DSM-IV Exclusions: Suicide risk; history of other psychiatric disorder; mood disorder due to general medical condition; prior treatment with antidepressants; intolerance or inefficacy to either study drug; lack of response to two or more antidepressants; clinically significant concomitant diseases; pregnancy or breastfeeding Notes: No placebo washout reported Baseline: HAMD-17: Ams 17.1 (3.8); Stl 17.6 (3.8) MADRS: Ams 21.6 (5.5); Stl 21.4 (5.3)	**Data Used** Number reporting side effects Leaving study due to side effects Leaving study early for any reason Remission: HAMD-17 score =/<6 MADRS endpoint HAMD-17 endpoint Response: 50% reduction in outcome score **Data Not Used** Social and Occupational Assessment Scale - not relevant CGI - not relevant Hamilton Anxiety Rating Scale - not relevant	**Group 1 N= 157** Amisulpride. Mean dose 100mg/d (max) **Group 2 N= 156** Sertraline. Mean dose 100mg/d (max)	Funding: unclear
BAKISH1993 Study Type: RCT Type of Analysis: 'ITT': treatment for minimum 2 weeks Blindness: Double blind Duration (days): Mean 49 Setting: Outpatients; Canada Notes: RANDOMISATION: no details	n= 50 Age: Mean 38 Sex: 26 males 24 females Diagnosis: 100% Dysthymic Disorder by DSM-III Exclusions: Meeting DSM-III criteria for major depressive disorder; signs or symptoms of psychotic disorders; serious	**Data Used** Leaving study early for any reason Leaving study due to side effects **Data Not Used** Zerssen Befindlichkeits-Skala - Not relevant Hopkins Symptom Checklist - Not relevant CGI - Not relevant HAMD-17 endpoint - no variablility measure	**Group 1 N= 16** Imipramine. Mean dose 200mg/d (max) **Group 2 N= 17** Ritanserin. Mean dose 20mg/d (max) **Group 3 N= 17** Placebo	Funding: unclear

	suicidal risk; women of childbearing potential not using contraceptive; physical illness; substance misuse; present benzodiazepine use; use of any mood-interfering drug or medication that may interact with study drug Notes: Only reports N completing minimum 2 weeks' treatment; original N Not reported 1 week placebo washout: unclear if responders dropped out Baseline: HAMD-17: 15.6 (2.3)	HAMD-17 change - no variablility measure Hamilton Anxiety Rating Scale - Not relevant		
BARRETT1999 Study Type: RCT Blindness: Double blind Duration (days): Mean 77 Setting: Primary Care; USA Notes: RANDOMISATION: Blocked and stratified by site and diagnosis. Computer generated random number allocation	n= 656 Age: Mean 61 Sex: 330 males 326 females Diagnosis: 52% Dysthymia by DSM-IV 48% Minor Depressive Disorder by DSM-IV Exclusions: Major depression; psychosis; schizophrenia or schizoaffective disorder; bipolar disorder; alcohol or substance misuse in past 6 months; antisocial personality disorder; suicidal risk; moderate or severe cognitive impairment; medical illness wiith prognosis of <6 months to live; in current treatment (unless taking <50mg amitriptyline and willing to discontinue) Notes: Minor depression: symptoms <4weeks No washout period reported Two diagnosis groups reported separately Baseline: Dysthymia: HAMD-17: Prx 14.0 (3.1); PST-PC 13.7 (2.8); Plb 13.5 (2.8) Minor Depression: HAMD-17: Prx 13.6 (2.8); PST-PC 13.7 (3.1); Plb 13.7 (3.1)	**Data Used** Remission: HAMD-17 score <7 Response: 50% reduction in outcome score Number reporting side effects Leaving study due to side effects Leaving study early for any reason HAMD-17 endpoint **Data Not Used** NEO - Five Factor Inventory - not relevant Medical Outcomes Survey - not relevant Hopkins Symptom Checklist - not relevant Duke Severity of Illness Checklist - not relevan Notes: Full data set obtained direct from author Dysthymia and minor depression reported separately SFX data reported for Prx and Plb arms only	**Group 1 N= 217** Paroxetine. Mean dose 20 mg/d - Dysthymia n=111 Minor Depression n=106 **Group 2 N= 218** Problem Solving Therapy - Primary Care. Mean dose 6 sessions - Dysthymia n=115 Minor Depression n=103 **Group 3 N= 221** Placebo - Dythymia n=112 Minor Depression n=109	Funding: John A Hartford Foundation; John D and Catherine T MacArthur Foundation
BOYER1999 Study Type: RCT Type of Analysis: 'ITT': at least one post baseline evaluation Blindness: Double blind Duration (days): Mean 84 Setting: Outpatients; France Notes: RANDOMISATION: no details	n= 323 Age: Mean 48 Sex: 81 males 242 females Diagnosis: 100% Primary Dysthymia by DSM-III-R Exclusions: Other DSM-III-R diagnosis; risk of suicide; substance or alcohol misuse; severe somatic disorder; preganancy or lactation; contra-indication to use of either study drug; antidepressant use within past month at daily dose higher than equivalent 50 mg clomipramine; discontinuation of benzodiazepine therapy within past month (regular use) or past week (occasional use); administration of either study drug within past 3 months Notes: n=313 at least one post baseline evaluation No placebo washout reported Baseline: MADRS: 17.9 (0.3 SEM)	**Data Used** Number reporting side effects Leaving study early for any reason Leaving study due to side effects MADRS endpoint MADRS change **Data Not Used** Scale for the Assessment of Negative Symptoms - Not relevant Response: CGI - Not relevant	**Group 1 N= 104** Amisulpride. Mean dose 50mg/d **Group 2 N= 111** Amineptine. Mean dose 200mg/d **Group 3 N= 108** Placebo	Funding: unclear
DEJONGHE1991 Study Type: RCT Type of Analysis: 'ITT': at least 4 weeks' treatment	n= 48 Age: Mean 40 Sex: 19 males 29 females	**Data Used** Leaving study early for any reason Response: 50% reduction in outcome score HAMD-17 endpoint **Data Not Used**	**Group 1 N= 24** Fluvoxamine. Mean dose 300mg/d (max) **Group 2 N= 24** Maprotiline. Mean dose 150mg/d (max)	Funding: unclear

Blindness: Double blind Duration (days): Mean 42 Setting: Outpatients; Netherlands Notes: RANDOMISATION: no details	Diagnosis: 46% Major Depression (without psychotic features) by DSM-III 54% Dysthymic Disorder by DSM-III Exclusions: Other psychiatric diagnosis; suicide risk; behavioural problems; drug or alcohol addiction in past year; exceedingly high or low weight; drug allergy or idiosyncrasy; physical illness interfering with pharmacokinetics, efficacy or assessment; treatment with anticonvulsants, neuroleptics, lithium or ECT in past year; treatment with anaesthetics, opioids or hypnotics in past 3 months; started new somatic or psychiatric treatment in past week; contraindications for antidepressants; needing additional treatment which may interfere with anxiety; pregnancy; unstable social environment; suspected noncompliance; language barrier; participation in drug trial in past 3 months; current psychotherapy Notes: 1 week placebo washout: responders dropped Baseline: HAMD-17: Flv 20.5 (4.7); Mpt 19.6 (4.6)	Psychosomatic Symptom Scale - not relevant CGI - not relevant Zung Depression Selfrating Scale - not relevan		
GEISLER1992 Study Type: RCT Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 42 Setting: Primary Care; Denmark Notes: RANDOMISATION: not reported	n= 67 Age: Mean 48 Sex: 18 males 52 females Diagnosis: 100% Dysthymic Disorder by DSM-III Exclusions: Serious neurologic or somatic conditions; concurrent mental disorder; inadequate contraception; pregnancy or lactation; alcohol, benzodiazepine or other drug misuse within past year; recurrent thoughts of suicide; concomitant treatment with antidepressants, neuroleptics or antiepileptics Notes: 1 week placebo washout: 3 patients dropped out Baseline: HAMD-17: Rts 19.6; Flp 19.8 (no variability data)	**Data Used** Number reporting side effects Leaving study due to side effects Leaving study early for any reason HAMD-17 endpoint **Data Not Used** CGI - not relevant Notes: HAMD-17 endpoint standard deviations calculated from p value 'Corrected' side effects	**Group 1 N= 31** Ritanserin. Mean dose 1.3mg/d **Group 2 N= 36** Flupenthixol. Mean dose 7.4mg/d	Funding: unclear
HELLERSTEIN1993 Study Type: RCT Type of Analysis: 'Completer': 6 weeks at minimum 20mg every 2nd day Blindness: Double blind Duration (days): Mean 56 Setting: Advertisement/physician referral; USA Notes: RANDOMISATION: no details	n= 35 Age: Mean 36 Sex: 16 males 16 females Diagnosis: 100% Primary Dysthymia with early onset by DSM-III-R Exclusions: Current major depressive episode; major depression in partial remission; axis I conditions; history of mania or hypomania; experiencing severe stress; history of suicide attemmpt or self-mutilation; previous trial of fluoxetine or any psychotropic medication within past month Notes: 'Completers': n=32 No placebo washout reported Baseline: HAMD-24: Flx 19.2 (4.33); Plb 18.88 (4.62)	**Data Used** Leaving study early for any reason HAMD-24 endpoint Response: 50% reduction and CGI score 1/2 **Data Not Used** Hopkins Symptom Checklist - Not relevant Cornell Dysthymia Rating Scale - Not relevant	**Group 1 N= 19** Fluoxetine. Mean dose 32.7mg/d **Group 2 N= 16** Placebo	Funding: Pharma
JUDD2004				

Study Type: RCT Type of Analysis: 'ITT': at least one post baseline evaluation Blindness: Double blind Duration (days): Mean 84 Setting: USA Notes: RANDOMISATION: no details	n= 162 Age: Mean 44 Sex: 66 males 96 females Diagnosis: 100% Minor Depression by DIS Exclusions: Major depressive disorder or dysthymic disorder within past 2 years; major depression in partial remission; loss of loved one within past year; serious suicidal risk; substance or alcohol misuse within past year; current diagnosis of axis I disorder; lifetime diagnosis of bipolar disorder (type I), borderline personality disorder, antisocial personality disorder, organic mood disorder, organic psychotic disorder, schizophrenia; use of psychotropic drugs except chloral hydrate within past 7 days; use of MAOI within past 14 days; unstabilised serious medical condition; seizure disorder within past year; severe allergies; non-response or adverse reaction to fluoxetine or participation in fluoxetine study Notes: SCID also used to aid diagnosis 4 week placebo washout: responders dropped Baseline: HAMD-17: ('ITT' n=157) Flx 11.2 (3.7); Plb 10.5 (3.7) BDI: ('ITT' n=147) Flx 13.6 (6.7); 13.9 (6.6)	**Data Used** Leaving study early for any reason Leaving study due to side effects BDI endpoint HAMD-17 endpoint **Data Not Used** CGI - Not relevant Medical Outcomes Survey - Not relevant Global Assessment of Functioning Scale - Not relevant Inventory of Depressive Symptomatology - Not relevant	**Group 1 N= 81** Fluoxetine. Mean dose 20mg/d **Group 2 N= 81** Placebo	Funding: NIMH; academic fund; pharma
RAVINDRAN1999 Study Type: RCT Type of Analysis: Completers Blindness: Double blind Duration (days): Mean 84 Setting: Newspaper adverts; Canada Notes: RANDOMISATION: computer-generated schedule with treatments balanced within blocks of consecutive patients	n= 97 Age: Range 21-54 Sex: 41 males 56 females Diagnosis: 100% Primary Dysthymia by DSM-IV Exclusions: Other axis I disorder or physical illness; clinical diagnosis of personality disorder; symptoms sufficient for, or previous diagnosis of, MDD; multiple adverse drug reactions; hypertension; significant dermatitis; malignant, hematological, endocrine, pulmonary, cardiovascular, renal, hepatic, gastrointestinal or neurologic disease; pregnant or lactating females Notes: DSM-III also used for diagnosis 1 week placebo washout: no responders Baseline: Not extractable	**Data Not Used** Coping Strategies Scale - not relevant Daily Hassles and Uplifts Scales - not relevant Batelle Quality of Life Scale - not relevant Cornell Dysthymia Rating Scale - not relevant CGI - not relevant Hamilton Anxiety Rating Scale - not relevant MADRS endpoint - not extractable HAMD-17 endpoint - not extractable Notes: Author emailed 08/05/08 for HAMD-17 and MADRS endpoint data Author responded 09/05/08: busy until mid June but will try to obtain data	**Group 1 N= 22** Sertraline. Mean dose 177.90 mg/d **Group 2 N= 26** Placebo **Group 3 N= 25** Sertraline. Mean dose 177.90 (28.72) mg/d CBT - weekly 90-minute sessions **Group 4 N= 24** Placebo CBT - weekly 90-minute sessions	Funding: Medical Research Association of Canada; Pharmaceutical Manufacturers Association of Canada; pharmaceutical
RAVINDRAN2000 Study Type: RCT Type of Analysis: 'ITT': at least 1 dose & post baseline evaluation Blindness: Double blind Duration (days): Mean 84 Setting: Outpatients; Canada, France, Spain, Italy, Sweden, UK Notes: RANDOMISATION: no details	n= 310 Age: Mean 45 Sex: 103 males 207 females Diagnosis: 100% Dysthymia =/> 5 years by DSM-III-R Exclusions: Taking psychotropic agents or any medication likely to interact with study drug; concomitant major depressive disorder; dysthymia duration <5 years; pregnancy; clinically significant medical condition; diagnosis of psychotic or paranoid disorder; priniciple diagnosis of anxiety disorder with past 6 months; previous use of sertraline Notes: 1 week placebo washout: responders dropped	**Data Used** Number reporting side effects Leaving study early for any reason Response: 50% reduction in outcome score **Data Not Used** Hamilton Anxiety Rating Scale - not relevant Hospital Anxiety and Depression Scale - not relevant CGI - not relevant SIGH-SAD - not relevant MADRS endpoint - no variablility measure Remission: SIGH-SAD - not relevant	**Group 1 N= 158** Sertraline. Mean dose 127.8mg/d **Group 2 N= 152** Placebo	Funding: pharmaceutical

	Baseline: HAMD-17: Stl 19.2 (6.98); Plb 18.6 (6.62)	Notes: Author emailed 18/04/08 for HAMD-17 endpoint and missing variability data Author responded 18/04/08: will try to obtain data from Pfizer NY		
RAVIZZA1999 Study Type: RCT Type of Analysis: 'ITT': at least one post evaluation & capsule Blindness: Double blind Duration (days): Mean 168 Setting: Outpatients; Italy Notes: RANDOMISATION: unbalanced (2 amisulpride: 1amitriptyline)	n= 253 Age: Mean 47 Sex: 90 males 163 females Diagnosis: 98% Primary Dysthymia by DSM-III-R 2% Single episode of MD in partial remission by DSM-III-R Exclusions: Inefficacy or intolerance to either study drug; suicide risk or attempt in past 2 years; misuse of psychoactive substance; use of antidepressant or psychoactive drug in past 2 weeks; discontinuation of benzodiazepines in past 2 weeks; need for psychoactive agents during trial; severe debilitation; uncontrolled clinically relevant concomitant disease; neoplasms; pheochromocytoma; parkinsonism; pregnant or breastfeeding Notes: 1 week placebo washout: responders dropped Baseline: MADRS: Ams 21.0 (2.8); Amt 21.7 (2.6)	**Data Used** Number reporting side effects Leaving study early for any reason Leaving study due to side effects Response: 50% reduction in outcome score MADRS endpoint **Data Not Used** Sheehan Disability Scale - not relevant CGI - not relevant Hamilton Anxiety Rating Scale - not relevant Widlocher Depressive Retardation Scale-ERD - not relevant	**Group 1 N= 166** Amisulpride. Mean dose 50mg/d **Group 2 N= 87** Amitriptyline. Mean dose 75mg/d (max)	Funding: unclear
ROCCA2005 Study Type: RCT Type of Analysis: ITT Blindness: No mention Duration (days): Mean 365 Setting: Outpatients; Italy Notes: RANDOMISATION: quasi-randomised; alternate allocation	n= 138 Age: Mean 72 Sex: 99 males 39 females Diagnosis: 49% Minor Depressive Disorder by DSM-IV-TR 51% Subsyndromal Depressive Symptomatology by DSM-IV-TR Exclusions: Any other axis I or II psychiatric disorder; impairment or decline of global cognitive functions; score =/>12 on Alzheimer's Disease Assessment Scale; acute or unstable medical or neurological condition that might interfere with safety or results; taken any psychotropic medication in past month Notes: No placebo washout period reported Baseline: HAMD-17: Ctp 12.9; Stl 12.9 (no variability data)	**Data Used** Remission: HAMD-17 score <7 Leaving study due to side effects Leaving study early for any reason **Data Not Used** Verbal Fluency Test - not relevant Wechsler Memory Scale - not relevant Trail Making Test - not relevant Mini-Mental State Examination - not relevant Global Assessment of Functioning Scale - not relevant Geriatric Depression Scale - not relevant HAMD-17 endpoint - no data HAMD-17 change - not extractable Notes: Author emailed 27/05/08 for HAMD-17 endpoint and mean change data (with SDs)	**Group 1 N= 66** Citalopram. Mean dose 20mg/d **Group 2 N= 72** Sertraline. Mean dose 50mg/d	Funding: no external financial or material support
SALZMANN1995 Study Type: RCT Type of Analysis: 'Per protocol': treatment > 14 days	n= 67 Age: Mean 55 Sex: 13 males 54 females	**Data Used** Leaving study due to side effects Number reporting side effects Response: 50% reduction in outcome score	**Group 1 N= 34** Imipramine. Mean dose 100mg/d (max)	Funding: unclear

Blindness: Double blind Duration (days): Mean 42 Setting: Outpatients; Germany Notes: RANDOMISATION: lists	Diagnosis: 100% Dysthymic Disorder by DSM-III Exclusions: Dementia; suicide risk; GAD; depressive symptoms due to other psychiatric illness; obsessional or phobic state; drug or alcohol misuse; severe organic disease; epilepsy or EEG abnormality; prostatic hypertrophy; glaucoma Notes: ITT analysis carried out but not reported 4-7 day placebo washout: responders dropped Baseline: HAMD-17: Imp 27.63 (5.22); Mnp 27.81 (3.94)	HAMD-17 endpoint **Data Not Used** Global Assessment of Therapeutic Success - not relevant Subjective Well-Being Scale - not relevant Figure Symbol Test - not relevant CGI - not relevant HAMD-17 endpoint: items 1-17 without sleep items - not relevant HAMD-17 endpoint: items 1-17 - not relevant	**Group 2 N= 33** Minaprine. Mean dose 200mg/d (max)	
SMERALDI1996 Study Type: RCT Type of Analysis: 'ITT': at least 1 post evaluation & 1 treatment Blindness: Double blind Duration (days): Mean 84 Setting: Outpatients; Italy Notes: RANDOMISATION: no details	n= 281 Age: Mean 49 Sex: 86 males 182 females Diagnosis: 94% Primary Dysthymia by DSM-III-R 6% Single episode of MD in partial remission by DSM-III-R Exclusions: Inefficacy or intolerance to either study drug; suicidal risk or attempt in past 2 years; misuse of or dependence on psychoactive substances; antidepressant or psychoactive drug use in past 2 weeks; discontinuation of benzodiazepine use in past 2 weeks; need of psychoactive agent other than study drug during trial; severe debilitation; clinically relevant concomitant unmanaged disease; cancer; pheochromocytoma; parkinsonian syndrome; pregnancy, breast-feeding, or female not using contraceptive; evidence of poor compliance; participation in clinical trial in past 6 months Notes: Demographic data reported for n=268 only 1 week placebo washout period: responders dropped Baseline: MADRS: Ams 21.2 (2.8); Flx 21.6 (2.9)	**Data Used** Number reporting side effects Leaving study early for any reason Leaving study due to side effects MADRS endpoint Response: 50% reduction in outcome score **Data Not Used** Sheehan Disability Scale - not relevant Widlocher Depressive Retardation Scale-ERD - not relevant CGI - not relevant Hamilton Anxiety Rating Scale - not relevant	**Group 1 N= 142** Amisulpride. Mean dose 50mg/d **Group 2 N= 139** Fluoxetine. Mean dose 20mg/d	Funding: unclear
SZEGEDI1997 Study Type: RCT Type of Analysis: 'ITT': all receiving an active medication Blindness: Double blind Duration (days): Mean 42 Setting: Primary Care & Outpatients; Germany Notes: RANDOMISATION: no details	n= 543 Age: Sex: 152 males 391 females Diagnosis: 45% Minor Depression by Modified RDC criteria 55% Major Depression by Modified RDC criteria Exclusions: Requirement of hospitalisation; psychotic symptoms; suicide risk; severe physical disease; pregnancy or lactation; need of benzodiazepine treatment Notes: Minor depression n=245 Two diagnoses reported separately Baseline: Not extractable	**Data Used** Response: 50% reduction in outcome score **Data Not Used** CGI - not relevant Raskin Depression Rating Scale - not relevant Bech-Rafaelsen Depression Rating Scale - no relevant MADRS change - no variablility measure HAMD-17 change - no variablility measure Notes: Data for minor depression group extracted only	**Group 1 N= 126** Paroxetine **Group 2 N= 119** Maprotiline	Funding: unclear
THASE1996A				

Study Type: RCT Type of Analysis: 'ITT': at least one post baseline evaluation Blindness: Double blind Duration (days): Mean 84 Setting: Outpatients; USA Notes: RANDOMISATION: no details	n= 412 Age: Mean 42 Sex: 143 males 267 females Diagnosis: 100% Primary Dysthymia with early onset =/> 5 years by DSM-III-R Exclusions: Pregnant, nursing or unwilling to use contraception; major medical condition; bipolar disorder; psychosis; panic disorder; concurrent major depressive disorder; generalised anxiety disorder; alcohol or drug dependency within last 6 months; suicidal risk; previous non-response to 2 or more antidepressants; use of psychotropic drugs within last 2 weeks Notes: 1 week placebo washout: responders dropped Baseline: HAMD-17: Stl 12.7 (4.0); Imp 13.4 (3.8); Plb 12.7 (3.9) MADRS:Stl 18.53 (5.8); Imp 18.64 (5.2); Plb 19.0 (5.8)	**Data Used** Leaving study due to side effects Leaving study early for any reason Remission: HAMD-17 score =/<4 Remission: DSM criteria not met & 0 on H-17 item1 MADRS change HAMD-29 change HAMD-17 change **Data Not Used** Hopkins Symptom Checklist - Not relevant Inventory of Depressive Symptomatology - Not relevant Response: CGI - Not relevant	**Group 1 N= 134** Sertraline. Mean dose 139.6mg/d **Group 2 N= 136** Imipramine. Mean dose 198.9mg/d **Group 3 N= 140** Placebo	Funding: part pharmaceutical
VALLEJO1987 Study Type: RCT Type of Analysis: Completers Blindness: Double blind Duration (days): Mean 42 Setting: Outpatients; Spain Notes: RANDOMISATION: no details	n= 73 Age: Mean 42 Sex: 12 males 52 females Diagnosis: 53% Dysthymic Disorder by DSM-III 47% Major Depression Episode with Melancholia by DSM-III Exclusions: Severe physical disease; on-going medical treatment; pregnancy; psychopathic/sociopathic disorder; Briquet's syndrome; alcohol/drug misuse; psychotic illness; bipolar, OCD, somatoform, panic, eating and phobic disorder Notes: Demographic data for completers (n=64) reported only 1 week placebo washout: responders dropped Baseline: HAMD-17 Dysthymic group (n=32): 20.5 (4.0)	**Data Used** Leaving study early for any reason HAMD-17 endpoint **Data Not Used** Eysenck Personality Inventory - not relevant Zung Depression Selfrating Scale - not relevan Notes: HAMD-17 extracted for dysthymic group only	**Group 1 N= 37** Imipramine. Mean dose 250mg/d (max) **Group 2 N= 36** Phenelzine. Mean dose 75mg/d (max)	Funding: unclear
VANELLE1997 Study Type: RCT Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 90 Setting: Mixed; France Notes: RANDOMISATION: no details	n= 140 Age: Mean 43 Sex: 34 males 106 females Diagnosis: 100% Primary Dysthymia by DSM-III-R Exclusions: Depressive disorder other than dysthymia; secondary-type dythymia; uncontrolled somatic disease; requiring psychotherapy; previous fluoxetine treatment received and ineffective; received psychotropic during previous week (except benzodiazepines); requiring other antidepressant, neuroleptic, lithium or other mood regulator Notes: Phase one of three phase design (6 months total) 1 week placebo washout: responders dropped Baseline: HAMD-21: Flx 20.5 (3.1); Plb 20.9 (3.0)	**Data Used** Number reporting side effects Leaving study early for any reason Remission: HAMD-21 score =/< 7 Response: 50% reduction and CGI score 1/2 HAMD-21 change **Data Not Used** Echelle de signes somatiques AMPD-5 - Not relevant Hopkins Somatic Complaints Checklist - Not relevant Paykel Life Event questionnaire - Not relevant Global Assessment of Functioning Scale - Not relevant CGI - Not relevant Hamilton Anxiety Rating Scale - Not relevant	**Group 1 N= 91** Fluoxetine. Mean dose 20mg/d **Group 2 N= 49** Placebo	Funding: unclear

		Notes: Drop-out and side effects data for whole group but response data excludes one centre with anomalous results		
VERSIANI1997 Study Type: RCT Type of Analysis: Completers Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients; International multicentre Notes: RANDOMISATION: no details	n= 315 Age: Mean 41 Sex: 91 males 224 females Diagnosis: 65% Primary Dysthymia by DSM-III-R 35% Double depression by DSM-III-R Exclusions: Previous treatment with either study drug; suicidal; other psychiatric disorder; significant organic disease Notes: 'Completers' (dysthymia n=295): No major protocol violations and treatment > 3 weeks No placebo washout Two diagnosis reported separately Baseline: Dysthmia 'completers': HAMD-17: Imp 19.5 (3.6); Mcl 20.1 (3.8); Plb 19.0 (4.2)	**Data Used** Leaving study early for any reason Leaving study due to side effects HAMD-17 change Remission: DSM criteria not met Response: 50% reduction in outcome score **Data Not Used** Hopkins Symptom Checklist - Not relevant CGI - Not relevant	**Group 1 N= 103** Imipramine. Mean dose 250mg/d (max) **Group 2 N= 108** Moclobemide. Mean dose 750mg/d (max) **Group 3 N= 104** Placebo	Funding: unclear

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
ANON1993	Not RCT
BALLUS2000	Sample not separated by diagnosis so in major depression group
BENKERT1997	MD and minor mixed but % not reported: use for MD
BOGETTO1997	Foreign language
BRASSEUR1980	No clear diagnosis; no clear response criteria; no variability data; unclear dropout rate
BURROWS2002	No formal diagnosis
CASACCHIA1994	Dysthymia <50% so in major depression group
CATTIEZ1990	Diagnosis unclear ('minor' in patient selection but mentions dysthymia and major in results); N used in analysis unclear; randomisation unclear; dropouts unclear; HAMD-17 reported by factor
COSTAESILVA1990	Foreign language
COWEN2005	Commentary
DUNBAR1985	Diagnosis not relevant to guideline
EICH2000A	Foreign language
FAVA1997	No relevant outcomes
FUNKE1986	No formal diagnosis
HELLERSTEIN1994	Open label; N p/g<10
KOCSIS1988	Dysthymia <50% so in major depression group
KOCSIS1989	No outcome data reported except response which cannot be extracted due to unclear size of N
KOK1995	Dysthymia <50% so in major depression group

LAAKMAN1995	Diagnosis (mostly BD)
LECRUBIER1997	Dysthymia <50% so in major depression group
LEON1994	Foreign language; dropouts (during first 2 weeks) replaced
LIU2004E	Foreign language: cannot translate
PAIVA1988	N<10 p/g
PAYKEL1988	Minor depression <50% so in major depression group; N.B. secondary to PAYKEL1988A
PAYKEL1988A	Minor depression <50% so in major depression group; N.B. primary to PAYKEL1988
POGGESI2000	N<10 p/g
RICKELS1974	No relevant outcomes; no formal diagnosis
ROSENBERG2007	Dysthymia <50% so in major depression group
ROSENTHAL1992	Open label; N p/g<10 (in 1 arm)
SCARZELLA1990	Foreign language
SERRANOBLANCO2006	Dysthymic group N<10 p/g: can use for MD
SLETVOLD1989	N<10 p/g
TYRER1988	No extractable data; N<10 in placebo group

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Pharmacological interventions - relapse prevention - new studies in guideline update

Comparisons Included in this Clinical Question

Desipramine v Placebo
MILLER2001A

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
MILLER2001A Study Type: RCT Study Description: 1) Open acute phase: full & partial remitters to phase 2 2) Continuation phase: all (non dropouts) to phase 3 3) Maintenance phase Type of Analysis: 'ITT' Blindness: Double blind Duration (days): Followup: 84 Acute; 112 Continuation; 2years maintenance Notes: RANDOMISATION: no details Info on Screening Process: Kocsis1996: Dysthymia and MD mixed Miller2001A: Dysthymic group only (n=27)	n= 27 Age: Mean 37 Sex: 15 males 12 females Diagnosis: 100% Dysthymia by DSM-III-R Exclusions: Diagnosis of shizophrenia; current substance misuse or dependence; history of mania or hypomania; severe or chronic medical illness; contraindication to desipramine Notes: Kocsis1996 - Dysthymia and MD mixed. Acute and continuation phases: not RCTs and not reported by intervention group; Maintenance phase: not reported by diagnosis so use for MD group Miller2001A - Dysthymics in maintenance phase only (relapse prevention) Baseline: HAMD-17: Dysthymic patients at entry to maintenance phase: Desipramine 3.1 (2.5); Placebo 3.9 (5.2)	**Data Used** Recurrence Notes: Have not extracted data from acute and continuation phases (Kocsis1996) as are not RCTs. Data from dysthymics in maintenance phase only Recurrence: HAMD>12 & GAS <60 on three consecutive ratings	**Group 1 N= 14** Continued to Desipramine. Mean dose 234 (64) mg/d - Total N in group =28 (pure dysthymics reported here) **Group 2 N= 13** Tapered to Placebo - Total N in group =25 (pure dythmics reported here)	Funding: Grant by National Institute of Mental Health, Rockville, MD

Characteristics of Excluded Studies

References of Included Studies

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