Appendix 15. Evidence Tables for Economic Studies

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Kaltenhaler, 2002. UK	Comparators: Computerised Cognitive Behaviour therapy (CCBT) – Beating the Blues (BtB): nine sessions: a 15-minute introductory video followed by eight 1-hour therapy sessions. CCBT plus patients also were allowed to receive other forms of treatment as per usual from the GP with the exception of face-to-face counselling or other psychological input. Treatment as Usual (TAU)- discussions with a GP, referral to a counsellor, practice nurse or mental health professional, and treatment of physical conditions.	People with depression or mixed anxiety/depression Setting: primary care Source of clinical effectiveness data: sponsor submissions. RCT Proudfoot et al. CCBT (n = 89) TAU (n = 78). Source of resource use estimates and unit costs: Data on resource use were collected prospectively alongside the trial and costed using appropriate unit costs.	Cost effectiveness/ utility analysis	Costs: of treatment included. Computer purchase, Licence fee, Overheads (space, heat, lighting, etc.)Staff: Practice nurse/ Assistant psychologist, GP monitoring, IT support &Training. Controlling for baseline costs, CCBT completers had a mean service cost that was £150 greater than that for TAU (the product accounted for most of this difference). This cost difference was not statistically significant. In the first year of implementing Beating the Blues, the costs with an assistant psychologist were £21,691 and with a practice nurse £25,192. Outcomes: QALYs -a number of strong assumptions have been made and the estimated figures are crude Estimated utility values from Bennett et al. and Revicki and Wood et al. were assigned/mapped to BDI scores from the RCT to calculate QALY gains from treatment	Based on a number of assumptions, the data from Bennett et al. 2000 suggested that the incremental cost per QALY gained of BtB over TAU lies between £1210and £7692. If the data from Revicki and Wood are used, the corresponding range lies between £3000 and £6667 per QALY gained. It should be noted, however, that these estimates are crude and should be treated with caution.	Perspective: NHS (although indirect costs are calculated) Currency: pound sterling £ Cost year: 2000 Time horizon: 6 months Discounting: Funded by industry: no Internal validity (19/9/4)

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Leff, 2000. UK	Comparators: Antidepressant therapy-first-line antidepressant -desipramine, second-line-trazodone and fluvoxamine. Couples Therapy	Patients with MDD living with a partner - under 65 and had lived with a heterosexual partner for at least one year. Setting: outpatient care Source of clinical effectiveness data: RCT-Leff et al. 2000, Antidepressant therapy n=25, couples therapy n=29 Source of resource use estimates: collected prospectively using a version of the Client Service Receipt Inventory. Source of unit costs:published national cost estimates that represent real costs from 1996	Cost consequence analysis	Costs included: inpatient, outpatient and day hospital services, day care, GP visits, psychiatric nurse, counsellor and social worker. In addition costs of treatment were calculated based on drug acquisition costs and blood tests in the antidepressant group and the cost of time with the therapist in the couple therapy group. The mean cost difference of the intervention was £58 (range: 45 - 72) more per month for couple therapy during the treatment period versus antidepressant use. The mean cost difference was £20 less (rang: -87 to 20) for hospital services per month and £32 less (range: -91 to 1.4) for community services per month when comparing couple therapy to antidepressant use. During the follow-up period the mean cost difference for hospital services was £26 (range: -88 to 19) less in the couple therapy group and the mean cost difference was £2 (range: -9 to 20) more in the couple therapy group per month. Outcomes: BDI and HSRD scores.No summary measure of benefits was used.	The authors commented that couple therapy was superior to drug treatment when outcomes were assessed with BDI, whereas the HRSD did not discriminate between the two. The authors stated that "for this group, couple therapy is much more acceptable than antidepressant drugs and is at least as efficacious, if not more so, both in the treatment and maintenance phases. It is no more expensive overall". No sensitivity analysis was carried out.	Perspective: health and social services –NHS? Currency: £ Cost year: 1996 Time horizon: 12+12 months Discounting: not relevant Funded by industry: No Internal validity: moderate (16/12/4)

				From the initial assessment to the one-year follow-up, the BDI scores in the couple therapy fell to an average of 6.4 (95% CI: 1.62 - 11.54) lower than the corresponding mean in the medication group. This difference was maintained until the 2-year follow-up. A significant improvement for both groups was recorded with the HRSD scores, and there was no significant advantage for couple therapy over medication. The absolute BDI scores (including mean and standard deviation) were only reported graphically.		

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Simpson, 2000. UK	Comparators: Counselling (6 sessions) Usual GP care- no restrictions except that GPs could not refer controls to practice counselors.	People with Setting: primary care Source of clinical effectiveness data: RCT n=181, Simpson et al, 2000 Source of resource use estimates: specially adapted version of the Client Service Receipt Inventory (CSRI), administered alongside the other assessments. Source of unit costs: Some costs were taken from an annual compendium of nationally applicable unit costs and others were estimated specifically for this research.	Cost minimization analysis	Costs: the analyses focus on the costs of providing specialist and generic health and social care services and other forms of support (GP's, hospital based & community based services, social services, counsellors, medication, alternative therapies, day activities and Police services). The costs associated with informal support or the patients' costs borne as a result of attending treatment have not been estimated because no data were collected for these. Finally, the costs associated with use of employment services (job centres) have not been included; Across the whole study sample, average total costs per person showed little change over time: • £4906 for the 6 months prior to initial assessment (*n* = 179) • £5061 for the 6 months to first follow-up interview (*n* = 161) • £4995 for the 6–12 month period after study entry (*n* = 143). There were no significant differences in the mean total costs, aggregate costs of services, or any of the service-group costs, except for primary care, between the experimental and control groups over time. The cost-burden to GP practices was significantly higher in the experimental than the control group at 6 months.	The primary care costs during the intervention period were significantly higher in the experimental than the control group and this was directly due to the costs of the counselling. This additional cost was not offset by subsequent reduced service use and costs, and did not appear to result in cost-savings at 12 months. No difference was found between the two treatment groups regarding outcomes, and there were no significant differences in the mean total costs, the aggregate costs of services, the costs by service-groups except for primary care. The primary care costs during the intervention period were	Perspective: Direct health and social services and lost productivity Currency: £ Cost year: 1997/98 Time horizon: 12 months Discounting: not relevant Funded by industry: No Internal validity: good(22/5/5)

				Outcomes: BDI, patient satisfaction There was an overall significant improvement in the actual scores over time but no difference between groups or between CBT and psychodynamic counselling approaches at either 6 or 12 months. However, fewer experimental group patients were still cases on the BDI than controls. This difference was statistically significant at 12 months and neared significance at 6 months (using logistic regression with the initial score as a covariate). In addition, most patients were very positive about the counseling and considered it helpful. Visual inspection of the outcomes suggested that more patients with mild or moderate depression at study entry had improved and ceased to be cases, and that more of these patients had become on-cases in the experimental than the control group. However, a multiple regression analysis indicated no significant interactions between group and initial severity of depression. This could be partly due to there being no difference in outcome between the experimental and control group patients who were initially severely depressed and few of these patients ceasing to be cases at follow-up.	significantly higher in the counselling than in the usual GP care group and this was directly due to the costs of the psychotherapy.	

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Guthrie, 1999. UK.	Comparators: Brief Psychodynamic-Interpersonal Therapy (BPIT) (8 sessions) Usual care-patients received treatment under the care of their consultant psychiatrist, which normally consisted of regular out-patient consultations of 15-30 minutes.	Clients with non-psychotic disorders unresponsive to 6 months of routine specialist mental health treatment. Patients had to be between the ages of 18 and 65 years. 75.5 % had depressive illness Setting: Secondary Care - hospital outpatient department. Source of clinical effectiveness data: RCT, n=144 Source of resource use estimates: obtained prospectively from the effectiveness study sample. Source of unit costs:	CEA	Costs: Resources measured included inpatient days, outpatient attendance, accident and emergency visits, day hospital visits, family physician contacts, practice nurse contacts, community psychiatric nurse contacts, prescription medications, and informal care. The total cost (direct plus indirect costs) was $1,959 (intervention) and $2,465 (usual). Outcomes: SCL-90-R, SF-36, EQ-5D: Benefits were expressed in terms of the EuroQol 5D questionnaire utility weights and Quality Adjusted Life Months (QALMs) at baseline, end of trial (T1) and six months after trial (T2). Patients in the psychotherapy group achieved 4.87 QALMs (median) compared with 3.48 QALMs in the treatment as usual group from baseline to T2, although this was not statistically significant. Median utility weight scores were 0.04 (psychotherapy) and 0.00 (usual) from baseline to T2.	Six months after the trial there was significant improvement in quality of life (EQ-5D scores) and cost savings, both in direct treatment costs and when direct non-treatment costs and indirect costs were included, for the depressed patients who received psychotherapy in comparison with controls. From these preliminary findings it is possible to ascertain that BPIT may be cost-effective relative to usual care for patients with enduring non-psychotic symptoms who are not helped by conventional psychiatric treatment.	Perspective: Society Currency: US Dollar $ Cost year: 1996-7 Time horizon: 8 weeks + 6 months Discounting: not relevant Funded by Industry: No Internal Validity: moderate(19/7/6)

				The two groups were not significantly different on the GSI or depression subscale of the SCL-90-R or on any subscale of the SF-36 tool. However, at the 6 month follow-up assessment, patients receiving psychotherapy showed significantly greater improvement on the GSI and the depression subscale of the SCL-90-R, and reported significantly better social functioning on the SF-36 than the control patients.		

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Scott, 2003.[1] United Kingdom	Comparators : *Cognitive therapy (CT)+ antidepressants + clinical management* Compared to *Antidepressants +clinical management alone* for relapse prevention in chronic depression. Clinical management = 30-minute appointments with a psychiatrist every 4 weeks during the treatment phase (20 weeks) and every 8 weeks	25 to 65 yr old psychiatric out-patients with uni-polar depression partially remitted despite adequate clinical treatment. Satisfied DSM-III-R criteria for major depression in an episode within the past 18 months, but not in the past 2 months. At randomisation, the patients were required to have current residual symptoms of at least 8 weeks' duration that reached =>8 17-HRSD and =>9 BDI. Setting: unclear- local clinics or at home Source of clinical effectiveness data: RCT, duration follow-up was 68 weeks n=158 randomised.	Cost-effectiveness analysis.	Costs: Direct: treatment, clinical management, inpatient, day hospital, general practitioner and social worker, psychiatric nurse and therapist, group and marital therapy, and medication. The cognitive therapy costs were calculated using a cost per minute taken from the mid-point of the relevant 1998 - 1999 salary scales, and included the employers' national insurance and superannuation contributions and overhead costs. The additional cost of non-face-to-face activities was estimated using a ratio provided by each therapist. A similar bottom-up approach was used to assess the unit cost of other therapies. Two separate analyses of the total costs were undertaken. 1st, the direct costs were considered excluding the additional costs of CT. 2nd, included the CT costs. The mean direct health care costs (-CT) were significantly lower in the CT group (£734) than in the control group (£1,119). This was due to savings on inpatient admissions (£161, 95% CI:	The ICER of CT was £4,328 per relapse averted or £12.5 per additional relapse-free day. Based on the cost-effectiveness-acceptability curve for CT, if the decision maker would be prepared to pay £6,000, the probability of cognitive therapy being cost-effective would be over 60%, and at £8,500, the probability would be over 80%. The ICER increased to £4,667 using the mean imputation method and to £5,028 using non-parametric multiple imputation. The results were relatively robust to the choice of the method used to impute the missing value. In contrast to the imputation approaches, the ICER increased to £7,056 per relapse prevented	Perspective: UK NHS Currency: UK pound Sterling Cost year: 1998/1999 Time horizon: The duration of the follow-up was 68 weeks (20 weeks for the treatment phase and 48 weeks for the follow-up phase). Discounting: 6% Funded by : grant from Medical Research Council Quality appraisal: 26/5/4 Limitation/s: The uncertainty of the results was partially addressed using sensitivity analyses on the method of handling missing data. However, further sensitivity analyses would only have strengthened the findings.

[1] **Use of cognitive therapy for relapse prevention in chronic depression: cost-effectiveness study**. Scott J, Palmer S, Paykel E, Teasdale J, Hayhurst H. British Journal of Psychiatry, 2003,182: 221-227

	during the 48-week follow-up phase. Cognitive therapy comprised 16 sessions over 20 weeks, with two subsequent booster sessions.	Source of resource use estimates: Resource utilisation questionnaires were undertaken prospectively on a sub-group (86%) of the patient sample. Source of unit costs: local providers, BNF, PSSRU, salary scales		35 - 356) and day-patient services (£206, 95% CI: 54 - 466). CT resulted in a mean cost-saving of £385 (95% CI: 1 - 769; p<0.05). When CT costs were included, patients receiving CT were £779 (95% CI: 387 - 1,170; p<0.01) more costly than those receiving standard clinical treatment. However, the incremental cost incurred by these patients (£779) was lower that the overall mean therapy cost of CT (£1,164). <u>Outcomes:</u> The primary health outcome was reduction in relapse rate and also used to express benefits. The authors did not develop a summary benefit measure. The actuarial cumulative relapse rates for the cognitive therapy and control groups were 10% (ct) and 18% (c) at 20 weeks, and 29% (ct) and 47% (c) at 68 weeks (adjusted hazard ratio 0.51; 95% confidence interval, CI: 0.32 - 0.93).	using only the 65% of patients in the complete case analysis. The results were highly sensitive to the decision to impute the missing value. The author's surmise: In individuals with depressive symptoms that are resistant to standard treatment, adjunctive cognitive therapy is more costly but more effective than intensive clinical treatment alone. Structured psychological therapies such as cognitive therapy, interpersonal therapy and similar approaches appear to have a major role to play in the treatment of residual depression.	

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Miller, 2003.[2] United Kingdom	Comparators: *Counselling* - six 50-minute weekly sessions. Extra sessions restricted to maximum of 2. versus *Antidepressant therapy* - dothiepin (150 mg nocte), fluoxetine (20 mg OD) and lofepramine (140 - 210 mg taken daily in divided doses).	Patients 18 to 70 yrs with major depression defined using research diagnostic criteria (RDC). Setting: primary care. Source of clinical effectiveness data: Chilvers et al. 2001. Prospective RCT, patients were randomly selected from 410 general practices in the Trent health region. 12-month questionnaire completed by 34 in the antidepressant group and 31 in the counselling group among those randomised, and 46 (antidepressant group) and 137 (counselling group), respectively, among those not	Cost-effectiveness analysis.	Costs: The direct costs were for antidepressants, counselling, GP consultations, psychiatric inpatient hospital stays and psychiatric outpatient hospital visits. There was no significant difference between the two randomised treatment groups in the cost of all depression-related health care for the 12 months following entry to the trial. There was a significant cost-difference (counselling plus antidepressants) between the treatment groups when using the non-parametric test, £89.57 in the antidepressant group versus £115.92 in the counselling group, (p=0.031). For patients choosing their treatment modality, there was a significant difference between counselling and antidepressant groups in terms of the overall cost of depression-related health services. These costs were £335.63 (counselling group) and £263.41 (antidepressant group), respectively, when using the non-	Using conventional analysis, the authors found no significant difference between randomised treatment groups in either the outcomes or costs at 12 months. The authors concluded that, according to the study results and following the indications of the net benefits and cost-effectiveness acceptability curves, the counselling intervention is a dominant cost-effective strategy in a small proportion of patients with mild to moderate depression. For a larger proportion of patients, the antidepressant intervention is the dominant cost-	Perspective: UK NHS Currency: UK Pound Sterling Cost year: not stated Time horizon: 12 months follow up Discounting: unnecessary Funded by NHS executive Trent Quality: 20/7/8

[2] **Counseling versus antidepressant therapy for the treatment of mild to moderate depression in primary care: economic analysis.** Miller P, Chilvers C, Dewey M, Fielding K, Gretton V, Palmer B, Weller D, Churchill R, Williams I, Bedi N, Duggan C, Lee A, Harrison G.International Journal of Technology Assessment in Health Care, 2003.19(1):80-90

		randomised. Source of resource use estimates: costing was undertaken prospectively on the same group of patients as the effectiveness study. All GP consultations, drugs prescribed and use of GP-arranged counselling were recorded from the patients' notes. Hospital psychiatric outpatient and inpatient visits were abstracted from case notes. The quantities were derived directly from the effectiveness study Source of unit costs: A published study (Netten et al.), BNF and invoices from counsellors in the trial.		parametric test, (p=0.005). No significant overall cost-differences between the randomised and patient preference groups were observed. Outcomes: The summary benefit measure was the psychiatrist's assessment of the global outcome, which was derived from the effectiveness study. The basis of the primary analysis was treatment completers only. The main outcome measures at 12 months were: the BDI score; the time to remission, remission defined as an RDC <4 and a Beck <10; The global outcome was assessed using the RDC, Beck score and GP notes. The study groups were generally balanced at baseline. However, the patients who preferred counselling were less severely depressed than randomized patients or those who preferred antidepressants. There were no statistically significant differences in any of the outcome measures used in the effectiveness analysis. The analysis also demonstrated that more patients opted for counselling.	effective strategy. For the remaining group of patients, the cost-effectiveness depends on the value placed on an additional patient with a positive outcome by a decision-maker.	

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Friedli, 2000 UK	Comparators: Non directive counselling (max. 12 sessions) Usual GP care	People with depression or mixed anxiety/depression Setting: Primary care Source of clinical effectiveness data: RCT, Friedli et al. 2000, n=136 Source of resource use estimates: Source of unit costs:	Cost-minimisation analysis	Costs: no, of outpatient consultations, length of inpatient stays, type and amount of medication prescribed The average direct &indirect costs for the counsellor group was £162.09 more per patient after 3 month compared to the gp group. However, over the ffg. 6 months the counsellor group was £87 less per patient than the gp group. Outcomes: BDI, Brief Symptom Inventory, Clinical Interview Schedule, modified Social adjustment scale	Referral to counselling was no more clinically effective or expensive than GP care over a nine-month period in terms of costs	Perspective: direct health service and non-health care, lost productivity due to morbidity Currency: £ Cost year: 1995/1996 Time horizon: 9 months Discounting: not relevant Not funded by Industry Internal validity: good (23/3/6)

Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
King, 2000 Bower, 2000 UK	Comparators: Non-directive counselling (max. 12 sessions) CBT (max 12 sessions)	Depression or Mixed/anxiety Depression Setting: primary care Source of clinical effectiveness data: RCT, King et al. 2000 n=464	Cost-effectiveness analysis	Costs: direct and non-treatmetn costs, costs of loss of production Outcomes: BDI, EuroQol measure of health related quality of life.	Patients in both psychological therapy groups made significantly greater clinical gains in the first four months; however, all groups had equivalent outcomes at 12 months. There were	Perspective: direct health service and non-health care loss of productivity Currency: £ Cost year: 1997/1998 Time horizon: 4+12 months Discounting: not relevant Not Funded by industy Internal validity: good (27/0/5)

	Usual GP care	Source of resource use estimates: Source of unit costs:			no significant differences in terms of EuroQol. No differences in direct or lost productivity costs between the three treatments were observed at either four months or 12 months. (Caution: the study was not powered for cost!) The additional costs associated with providing practice-based psychological therapy were offset by savings in visits to primary care, psychotropic medication and other specialist mental health treatments. Overall the results implied the observed equivalence of the three options and this result remained in the sensitivity analysis.	

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Simon, 2006.[3] United Kingdom	Comparators: *Pharmacotherapy* 40 mg fluoxetine /day and outpatient care. *Pharmacotherapy with cognitive-behavioural therapy (CBT)* 16 sessions (average 50 minutes each).	Patients suffering from moderate and severe depression-according to the Hamilton Rating Scale for Depression and the range of cut-off scores proposed by the American Psychiatric Association. Setting: secondary care Source of clinical effectiveness data: a systematic review of studies was conducted then synthesised using a meta-analysis. Source of resource use estimates: based on the expert opinion of the GDG, literature and a systematic review of the economic evidence (NCCMH, 2005).	Cost-utility analysis.	Costs: The direct cost categories of the initial treatment protocols included medication costs, staff costs, dispensing fees, and subsequent health care resource use (hospitalisation, visits to the emergency department, outpatients and general practitioner, community psychiatric nurse and community mental health team visits, and medication costs). The total health care cost per person was £660 for pharmacotherapy and £1,297 for the combination therapy. This represented a total difference of £637 over 15 months. Outcomes: The measure of benefit used-quality-adjusted life-years (QALYs). Results were also reported as the incremental cost per successfully treated patient. Over the 15-month analysis period, the average gain in QALYs from combination therapy was 0.11/ patient with severe depression and 0.04 per patient with moderate depression.	The cost-effectiveness of combination therapy was calculated to be £4,056 per additional successfully treated patient. This resulted in a cost per QALY gained of £5,777 for severe depression and £14,540 for moderate depression. Deterministic and probabilistic SA conducted. When considering the number of successfully treated patients for both moderate and severe depression, an additional benefit of combination therapy over pharmacotherapy alone was observed. However, when the patients' quality of life was also included, the analysis showed that	Perspective: UK NHS Currency: UK pounds sterling £ Cost year: 2002/03 Time horizon: Both therapies were conducted for 3 months and had a 12-month follow-up period i.e. 15 months no maintenance therapy Discounting: not relevant Funded by : NICE Quality appraisal: 28/1/6 Although the initial treatment cost of combination therapy is substantially higher, these costs are partially offset by savings accruing from lower treatment costs in the subsequent year. Targeting combination therapy at severe forms of depression could be a more efficient way of using limited resources.

[3] **Treatment options in moderate and severe depression: decision analysis supporting a clinical guideline.** Simon J, Pilling S, Burbeck R, Goldberg D. British Journal of Psychiatry, 2006,189: 494-501

		Source of unit costs: BNF, PSSRU, PPA.		The QALYs per person with severe depression were 0.52 for the pharmacotherapy treatment and 0.63 for the combination therapy. The QALYs per person with moderate depression were 0.84 for the pharmacotherapy treatment and 0.89 for the combination therapy. The probability of successful treatment was 0.14 for pharmacotherapy, and 0.29 for the combination therapy (a benefit of 0.16 for the combination therapy).	there were greater gains for patients with severe depression versus those with moderate depression. The authors concluded that combination therapy is likely to be a cost-effective first-line secondary care treatment for severe depression, but that it was much more uncertain from the currently available evidence(supported by sensitivity analysis) whether its use is cost-effective for moderate depression.	

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Simpson, 2003. UK	Short-term psychodynamic counselling in primary care – i.e. highly trained counsellors employing a Freudian psychodynamic model in 6 of the 12 sessions. routine general practitioner (GP) treatments for patients with chronic depression	Motivated patients, aged 18 to 70 years, who were depressed => 6 months-scored between 14 and 40 Beck Depression Inventory (BDI). Setting: Primary care Source of clinical effectiveness data: derived from a single prospective study-RCT conducted in seven GP practices (screening attendees) employing psychodynamic counsellors. Patients who were seen in the two GP practices that employed cognitive behaviour counsellors were excluded. The patients were followed up at 6 and 12 months. Up to the 6-month period, the assessors were blind to the treatment received. Outcome data were obtained for 130 (90%) patients at 6 months (n=65 in each group) and for 115 (80%) patients at 12 months (n=60-experimental group, n= 55-control group).	Cost-effectiveness analysis	Costs: The direct costs to health service seem to have been included. The total support costs (including accommodation and living expenses) and total service costs (including specialist mental health services, hospital services, primary care, and community health and social care services) were measured. However, the indirect costs were not included. Lost productivity costs were excluded because there was no difference between the groups at any of the time periods. The primary care subtotal included only the costs of support from GPs, prescribed medication, practice nurses and practice counsellors. The comparison of the costs between the two groups thus focused on the total service costs and primary care costs. There was no statistically significant difference between the experimental and control groups in the mean service costs per person, either at baseline (£349 versus £643), during the 6-month period (£652 versus £537), between 6 and 12 months (£374 versus £515), or during the 12-month follow-up (£1,046 versus £1,074). With the exception of short-term increased costs to the GP practices (linked to the use of counselling services), there were no statistically	The author's conclude that the findings suggested no cost-effectiveness advantage of counselling over routine treatment for general practice attendees with chronic depression. There was very limited evidence of improved outcomes and the cost of primary care treatment increased in the short term. The use of stricter referral criteria to exclude the more severely depressed (BDI +/-24) might have yielded more conclusive results. A sensitivity analysis of the quantities was not conducted.	Perspective: Not stated Currency: UK pound Sterling Cost year: 1997 to 1998 prices Time horizon: 12 months Discounting: unnecessary since all the costs were incurred in one year Internal validity: 18/13/4 Funded by: a grant from the NHS Executive Health Technology Assessment Programme

		Source of resource use estimates: The costing was carried out on the same sample of patients as that used in the effectiveness study. The resource data were derived from the Client Service Receipt Inventory published in 1995 and 2001 Source of unit costs: The unit costs were taken from an annual compendium of costs and from the authors' setting.		significant differences between the treatment options in terms of the primary care costs at each time interval. The primary care costs were £101 versus £119 at baseline, £318 versus £161 during the 6-month period, (p<0.001), £162 versus £196 between 6 and 12 months, and £486 versus £371 during the 12-month period. If the counselling costs were excluded, there were no significant differences between the two groups. Outcomes: The main health outcomes used in the analysis were the BDI score. The author's did not derive a measure of health benefit. Since the authors concluded that the clinical outcomes were comparable (There was very limited evidence that psychodynamic counselling improved outcomes for GP practice patients with chronic depression), the study was effectively a cost-minimisation analysis. There was no difference between patients who withdrew and those who remained in the study. There were no significant differences between the groups on any of the BDI, BSI, IIP and SAS measures, either at the 6- or 12-month follow-up, when using a univariate analysis of covariance		

				and the initial score as covariate. There were no significant differences between the groups in the number of depressed cases on the BDI, BSI and SAS measures at the 6-month follow-up. At the 12-month follow-up, there were fewer cases on the BDI in the experimental group (48%) than in the control group (64%). This difference was statistically significant, (p=0.02). There was no difference between the groups for the BSI and the SAS.		

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Kaltenhaler, 2006. United Kingdom	The three products shared the same basic model structure, a decision tree comparing two arms, CCBT and TAU. *CCBT-* 1. Beating the Blues (BtB) 2. Cope (ST solutions) 3.Overcoming Depression *TAU -* Treatment as Usual-standard care in primary care. the treatment received in the Proudfoot Trial was used	Patients with mild to moderate, moderate to severe or severe depression. Setting: primary care Source of clinical effectiveness data: BtB- Proudfoot, 2004 RCT, n=274. Cope- Marks, 2003. Non-comparative trial, n= 39 Overcoming Depression- Whitfield, 2004. Non-comparative study, n=20. Source of resource use estimates: manufacturer submissions Source of unit costs: submissions and	Cost effective analysis	Provision of CCBT results in the following costs: licence fees, computer hardware, screening patients, clinical support, capital overheads (for clinician, facilities and computers) and the training of staff. Expected Total cost per patient per copy of BtB = £219.30 (152,37-353.00) Expected Total cost per patient: -with home access to Cope £171.30(122.74-268.22) -access at 1-5 GP practice £ 195.86 (137.48-312.40) Expected Total cost per patient per copy of Overcoming Depression = 72.64 (42.36 - 133.00) Outcomes: Quality adjusted Life years Utility scores from Richards, 2004. n=62.	BtB: The incremental cost per QALY compared with TAU was £ 1801. There is an 86.8%, chance of Btb being cost-effective at £30,000 per QALY. Cope: The incremental cost per QALY compared with TAU was £ 7139. There is a 62.6%, chance of Btb being cost-effective at £30,000 per QALY. Overcoming Depression: The incremental cost per QALY compared with TAU was £ 5391. There is a 54.4%, chance of Btb being cost-effective at £30,000 per QALY. The strength of the BtB software being that it has been evaluated in the context of an RCT with a control group. The subgroup analysis found no differences across the	Perspective: NHS Currency: UK Pound Sterling Cost year: Time horizon: 18 months Discounting: 3.5 % Internal validity: 25/4/6

	as representing TAU in the NHS. TAU patients in this trial continued to visit their GP, receive medication and be referred to a specialist, although they were not receiving psychotherapy at the time of entering the trial. *In the model another arm was examined for BtB, i.e. TCBT Therapist-led CBT using the results of the trial.*	published literature.		Mild-moderate: 0.78 +/- 0.20 Moderate-severe:0.58 +/- 0.31 Severe: 0.38 +/- 0.32 Minimal: 0.88 +/- 0.22 (aged and gender matched normal scores)	severity groupings. Author's conclusions: The study findings are subject to substantial uncertainties around the organisational level for purchasing these products and the likely throughput. In addition to concerns with the quality of evidence on response to therapy, longer term outcomes and quality of life. The position of CCBT within a stepped care programme needs to be identified, as well as its relationship to other efforts to increase access to CBT and psychological therapies. Research is needed to compare CCBT with other therapies that reduce therapist time, in particular bibliotherapy and to explore the use of CCBT via the Internet. Independent research is needed, particularly RCTs, that examine areas such as patient preference and therapist involvement within primary care.	

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
McCrone, 2004. UK	Comparators: Computerised CBT (CCBT) i.e. Beating the Blues (BtB-a 15-minute introductory video followed by eight 50-minute sessions of CBT) with TAU TAU alone-Treatment as Usual from the GP (included discussions with GP, referral to a counseller, practice nurse or mental health professional and treatment of physical conditions) with exception of face-to-face	18-75 yr olds with diagnosis of depression, mixed depression and anxiety or anxiety disorders-not receiving face-to-face psychological therapy. Setting: Primary care patients Source of clinical effectiveness data: Proudfoot et al. 2004.TAU n=128. CCBT n=146. Source of resource use estimates: collected prospectively alongside the clinical trial Source of unit costs: from a recognised national source (PSSRU) and the British National Formulary. The price	Cost effectiveness analysis- Cost utility analysis	Costs: Services included: -contacts with mental health care staff (psychiatrists, psychologists, community mental health nurses, counsellors and other therapists), -contacts with primary care staff (GPs, practice nurses, district nurses, and health visitors), -contacts with hospital services (inpatient care for psychiatric and physical health reasons, outpatient care, day surgery, and accident and emergency attendance), -contacts with home helps, -medications (antidepressants, anxiolytics and sedatives), and -contacts with other services (chiropodists, physiotherapists and dieticians). -The cost of buying the licence to use 'Beating the Blues' (plus overheads) was-also considered. At baseline, the direct costs were £236 (+/- 404) in the control group and £203 (+/- 262) in the intervention group. At the end of the study period, these costs were £357 (+/- 575) in the control group and £397 (+/- 589) in the intervention group. The difference of £40 was not statistically significant (95% CI: -28 - 148).	The cost-effectiveness of CCBT over TAU was assessed through cost-effectiveness acceptability curves (CEAC). These showed the probability that the intervention was cost-effective on the basis of theoretical, but unknown values that society was willing to pay for improvements in the benefit measures. In terms of the reduction in BDI score, the CEAC showed that the probability of the intervention being cost-effective over standard care was greater than 80% at a value of £40 per unit reduction in BDI score. If the cost of CCBT was £5 (it was £14.50 in the base-case), then even with a zero value given to a unit	Perspective: NHS(although indirect costs were also calculated) Currency: UK pounds sterling £ Cost year: 1999/2000 Time horizon: 8 months Discounting: not relevant Internal validity: good (23/6/3)

	counselling or other psychological input.	of the computer program licence was obtained from the manufacturer.		Outcomes: The primary outcome measure used in the analysis was the change in the level of depression, as rated using the Beck Depression Inventory (BDI). The secondary outcome measures were the Beck Anxiety Inventory (BAI), the Work and Social Adjustment (WSA) scale, and the number of depression-free days. Depression-free days were based on the BDI scores at four assessment points (immediately post-treatment, and 1, 3 and 6 months following treatment, which corresponded to 8 months post-randomisation). The authors stated that CCBT resulted in improved scores on the BDI, BAI and WSA scales. The mean reduction in BDI score with CCBT over control was 3.5 (95% CI: 0.6 - 6.4). The mean number of depression-free days was 61 (+/- 67.1) in the control group and 89.7 (+/- 74.2) in the intervention group. After controlling for phase of data collection, the difference in depression-free days was 28.4 (95% CI: 10.7 - 45.5). The benefit measures used were a cost per point reduction in the BDI, cost per symptom-free day and quality-adjusted life-years (QALYs).	reduction in BDI score, there was a 45% chance that the intervention was cost-effective. Higher values were required when the cost of the programme increased. In terms of depression-free days, the CEAC suggested that if society placed a value of £5 on a depression-free day, then there would be an 80% chance of the intervention being cost-effective. In terms of QALYs, if society placed a value of £15,000 on a QALY, then there would be a 99% chance of the intervention being cost-effective. At a value of £5,000 per QALY, the probability of the intervention being cost-effective was 85%. A one-way sensitivity analysis was conducted on the cost	

				The utility values used to calculate the QALYs were based on a score of 0.59 for a day with depression, and a score of 1 for a depression-free day. The utility scores were derived from a published study (Lave et al.)	of the CCBT programme, as this was the most uncertain factor. The author's concluded: The use of CCBT for the treatment of patients with depression and anxiety in primary care was cost-effective in comparison with TAU. The BtB programme improved clinical outcomes at negligible extra costs and reduced productivity losses. It was also associated with a high probability of being cost-effective from the perspective of the NHS.	

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Appendix 15. Evidence Tables for Economic Studies

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Borghi & Guest, UK. 2000	Comparators: Mirtazapine Amitriptyline Fluoxetine	Patients in the UK, with moderate and severe depression, and within the age range 18 to 93 years. Setting: Primary care and hospital. Source of clinical effectiveness data: meta-analysis of 4 RCTs Source of resource use estimates: established retrospectively from interviewing a panel of 10 GPs and 3 psychiatrists. Source of unit costs: published literature	Cost-effectiveness analysis, modelling	Costs: included of hospitalisation, GP visits, visits to psychiatrists, antidepressant and concomitant medication, community psychiatric nurse visits, community mental health team visits, and attendance at day wards. The cost of managing a patient who discontinued antidepressant treatment ranged from 50 to 504 over five months. The cost of management with mirtazapine was 413 per patient over seven months, compared with 448 for amitriptyline. The cost of management with mirtazapine was 420 per patient over six months, compared with 394 for fluoxetine. Outcomes: Successfully treated patients (HRSD 17 <= 7 or reduction in HRSD 17>= 50%)	Mirtazapine was found to be dominant compared to amitriptyline. It both reduced the expected direct NHS costs by £35 per patient and increased the proportion of successfully treated patients from 19.2% to 23.2%. However, this result was sensitive to the cost of managing adverse events. When compared to fluoxetine, mirtazapine increased the proportion of successfully treated patients from 15.6% to 19.1% but at an additional cost of £27 per patient. Sensitivity analysis revealed 3 factors to which this result was sensitive.	Perspective: NHS incl. lost productivity Currency: UK pound Sterling Cost year: 1997 - 1998 Time horizon: 6/7 months Discounting: no discounting Funded by: Organon Ltd. Internal validity (26/3/3/)

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Doyle et al. 2001. Casciano et al. 2001. Multinational -UK	Comparators: venlafaxine XR selective serotonin reuptake inhibitors (SSRIs) tricyclic antidepressants (TCAs).	Patients suffering from acute MDD i.e. => 15 HRSD, or >18 on the MADRs. Setting: community - outpatient and inpatient care Source of clinical effectiveness data: meta-analysis (Einarson et al. 1999) Source of resource use estimates & unit costs: from actual data, validated by local economists in each country, and from published studies.	Cost-effectiveness analysis	Costs: included the drugs, physician visits, laboratory tests, and hospitalisation. Expected cost of drugs: UK (outpatient): venlafaxine XR, $1,714; SSRIs, $1,987; and TCAs, $2,104. UK (inpatient): venlafaxine XR, $7,948; SSRIs, $8,288; and TCAs, $8,505. Outcomes: Treatment success (>50% reduction in scores on the HRSD, symptom-free days. The expected cost per successfully treated outpatient was $2,121 in the UK. The expected cost per successfully treated inpatient was $10,672 in the UK.	Venlafaxine dominates the other two options since its expected total health service costs are the lowest, and it is superior in terms of both success rate and symptom free days. Sensitivity analysis confirmed the robustness of these findings.	Perspective: NHS Currency: $ Cost year: 1999 Time horizon: 6 months Discounting: none Funded by : industry Internal validity :good (27/1/3)

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Freeman, 2000. UK	Comparators: Venlafaxine SSRIs TCAs	Patients with MDD Setting: Outpatient primary care Source of clinical effectiveness data: Meta-analysis Source of resource use estimates: literature and expert advice. Source of unit costs: MIMS 1998; Centre for Health Economics, University of York 1998	Cost-effectiveness analysis	Costs: Direct costs included medication, doctor's time and Hospitalization. Costs were not reported. Outcomes: symptom free days (SFDs) SFDs were not reported. It was stated that venlafaxine yielded superior outcomes compared to TCAs and SSRIs.	Treatment with venlafaxine yielded the lowest outpatient cost for a symptom-free day (£10.53), compared with £13.23 for SSRIs and £15.52 for TCAs. Hence, the authors found venlafaxine to be cost-effective in outpatients with MDD and cost saving compared to SSRIs and TCAs. The results of the sensitivity analysis indicated that the findings were robust with respect to assumptions implicit to the model.	Perspective: direct health service Currency: £ Cost year: 1998 Time horizon: 6 months Discounting: not required Funded by : industry – Wyeth Labs Internal validity: good(22/6/4)

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Tome & Isaac, 1998. UK	Comparators: SSRIs + 6-week pindolol SSRI + placebo	Patients with Moderate/severe depression Setting: mental health care Source of clinical effectiveness data: RCT, n=80, Tome et al. 97 Source of resource use estimates: during trial and retrospective examination of notes. Source of unit costs: Jonsson & Bebbington 1993	Cost-effectiveness analysis	Costs: included drugs, psychiatric, psychotherapist, community nurse visits and hospital inpatient visits. Outcomes: Change in BDI score	The year cost of the SSRI and augmentor group is less than that of the SSRI and placebo group. Furthermore, the average change in BDI per £ is 0.1271 for the augmentor group and 0.0753 for the placebo group.	Perspective: direct mental health service Currency: £ Cost year: 1990 Time horizon: 6 months – 1 yr Discounting: not relevant Funded by : yes smith Kline Beecham Internal validity: moderate (15/13/4)

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Wade, 05 United Kingdom	Interventions: Escitalopram (ESC) 10-20 mg daily; citalopram (CIT) generic 20-40 mg daily; venlafaxine-XR (VEN) 75-150 mg daily	A hypothetical cohort of adult patients (>18 years) with MDD(baseline MADRS scores =>18 to <=40. Setting: primary care. Source of clinical effectiveness data: Meta-analysis of 4 studies n=1472 and from head-to-head clinical trials . Authors made some assumptions to derive the clinical estimates. Source of resource use estimates: General Practice research Database, published literature and expert advice. Source of unit costs: UK cost data	Cost-effectiveness analysis.	Direct costs: included drugs, GP visits, psychiatrist visits, hospital and community care {day care, social work, community nurses). Resource use was estimated from published data and experts' opinions. Indirect costs: productivity losses were included In the comparison between ESC and CIT, the expected total costs per patient were £465 (95% CI: 436 - 493) for ESC and £544 (95% CI: 514 - 573) for CIT from the NHS perspective, and £2,307 (95% CI: 2,179 - 2,439) In the comparison between ESC and VEN, the expected total costs per patient were £376 (95% CI: 342 -410) for ESC and £415 (95% CI: 382 - 449) for CIT from the NHS perspective. Outcomes: The summary benefit measure : overall success rate. Other model outputs, such as the rate of first-line success (without switch), rate of titration, switch rate and secondary care rate, were also reported. In the comparison between ESC and CIT, the overall success rate was 63.5% (95% CI: 61.5 - 65.4) with ESC and 58.2% (95% CI: 56.3 - 60.3) with CIT. ESC was also associated with higher first-line success (51.2%	From the NHS perspective: In the comparison between ESC and CIT, the cost per successfully treated patient was £732 (95% CI: 665 - 807) for ESC and £933 (95% CI: 850 - 1,023) for CIT. In the comparison between ESC and VEN, the cost per successfully treated patient was £546 (95% CI: 481 - 618) for ESC and £607 (95% CI: 542 - 677) for CIT. Incremental cost-effectiveness ratios were not calculated because ESC always dominated both CIT and VEN, which were more expensive and less effective. The sensitivity analysis showed that the base-case results were robust to variations in	Perspective: NHS and societal Time horizon: 6 month Currency: UK pounds sterling Discounting was not relevant due to the short timeframe. The price year was 2003. The costs from other years were transformed to 2003 using the UK Consumer Price Index. A simultaneous comparison of the three treatments could not be performed because head-to-head trials had not been published. Thus, two parallel analyses were carried out in the current study. However, the authors noted that an indirect comparison would not have changed the conclusions of the analysis. Internal validity: 28/3/4 Funded by H Lundbeck A/S.

				versus 41.0%), a lower titration rate (27.6% versus 32.6%), a lower switch rate (35.7% versus 47.0%) and a lower secondary care rate (23.0% versus 29.4%). In the comparison between ESC and VEN, the overall success rate was 68.9% (95% CI: 66.7 - 70.9) with ESC and 68.5% (95% CI: 66.2 - 70.6) with VEN. ESC and VEN were also associated with very similar first-line success, titration, switch and secondary care rates.	both costs and probabilities in the comparison between ESC and CIT. However, the results of the comparison between ESC and VEN were sensitive to the probability values used in the model, thus the two drugs were considered comparable in primary care. Within the setting of primary care in the UK, escitalopram (ESC) was a cost-effective treatment for major depressive disorder (MDD) in comparison with CIT and was quite similar to venlafaxine (VEN).	

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Romeo, 2004. Scotland, UK	Comparators: Mirtazapine, a noradrenergic and specific serotonergic antidepressant, 30 to 45 mg/day (mirt) Paroxetine, a selective serotonin reuptake inhibitor, 20 to 30 mg/day (pax)	Patients with depression treated in general practice, fulfilling DSM-IV criteria for a major depressive disorder, with a baseline score of > 18 on 17-HAMD. Setting: primary care Source of clinical effectiveness data: clinical effectiveness study, Wade et al. 2003, n=177 n=93 mirt, n=84 pax. Source of resource use estimates: derived from actual data collected alongside the effectiveness study prospectively. Source of unit costs: derived from the British National Formulary, the National Health Service Schedule of Reference costs (outpatient	Cost-effectiveness analysis.	Costs: The direct costs consisted of health service costs and the costs of social services. The health service costs were those associated with treatment and concomitant medication, contact with specialists (e.g. general practitioners, community psychiatric nurses, physiotherapists and other health care professionals), hospital outpatient services, and acute and long-term inpatient care. The costs of social services were associated with counselling or social worker services, and police custody. The mean, total NHS cost per patient was £1,408 (SD=1,777) in the mirt group and £1,528 (SD=2,022) in the pax group. The difference was -£120 (95% CI: -750 - +377; p=0.51). Outcomes: primary outcome was change from baseline on the 17-HAMD. Primary measure also expressed as the number of patients classed as HAMD responders (i.e. patients with a 50% decrease in the 17-HAMD score from baseline to the assessment point). Secondary outcome also used in the economic study was the improvement in quality of life, as assessed using the Quality of Life in Depression Scale (QLDS).	The costs and benefits were not combined in the form of incremental cost-effectiveness ratios because there were no significant differences in the costs. In addition, there were no significant differences in the benefits between the two groups when the number of HMAD responders was the outcome considered. However, improvement in quality of life was shown to be significantly higher with mirtazapine than with paroxetine, (p=0.021). These results were robust under all scenarios examined in the sensitivity analysis. The results of the study suggested that, compared with paroxetine, mirtazapine might be a cost-effective treatment choice for depression in a primary care setting.	Perspective: UK NHS and Society Currency: UK pound sterling Cost year: 2001/2002 Time horizon: 24 weeks Discounting: not relevant Funded by Organon Laboratories

		attendances), and published literature (contact with health and community professionals, and inpatient services).		The change in QLDS score from baseline to the 24-week end point was 13 in the mirt group and 9 in the pax group, (p=0.021).		

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Wade 2005, UK	Comparators: Escitalopram Dose of 20mg/day. Citalopram Dose of 40mg/day.	Adult patients with severe depression (Montgomery-Asberg Depression Rating Scale [MADRS] total score => 30) Both Primary and Secondary care Effectiveness data was derived from a review of completed studies and estimates based on experts' opinions. Remission, discontinuation, and response rate at week 8 derived from a meta-analysis of 506 patients and extrapolated to 6	Cost-effective analysis. This analysis is an adaptation of models described in three other studies (Borghi et al. 2000, Hemels et al. 2004 and Brown et al. 1999)	COSTS – Direct: included were medications (authors noted that there was no price difference between escitalopram 10 and citalopram 20 mg (branded and generic)), general practitioner, psychiatrist visits, inpatient psychiatric hospitalisations, discontinuation of treatment, treatment-emergent adverse events (AEs) and attempted suicide. Indirect: resulting from absenteeism from work (i.e. lost productivity). From the NHS perspective, the expected total cost per patient was £422 (range: 404 - 441) for escitalopram and £454 (range: 436 - 471) for citalopram. The expected total cost per successfully treated patient was £786 (range: 702 - 876) for escitalopram and £932 (range: 843 -1,028) for citalopram. Primary outcome measure: patient	This analysis suggested that escitalopram was a cost-saving alternative to citalopram for the treatment of severe depression in the UK. From both the UK National Health Service (NHS) and societal perspectives, the relative cost savings per treated patient and per successfully treated patient were 7% and 16%, respectively. Multivariate sensitivity analyses demonstrated that in more than 99% of	Perspective: UK society and National Health Service (NHS) Currency: UK £ reported conversion rate: £1.00 = US$0.62 in January 2003 All unit costs were updated using the British Consumer Price Index. Cost year: 2003 The number of workdays lost due to severe depression was derived from published literature (Borghi et al. 2000 and Netten et al. 2001). The calculation of the societal cost of lost productivity was based on the human capital approach, based on mean market wages for the year 2003.

		months (Llorca et al. 2005). Estimates for the majority of the resources used and costs were derived from published literature (Borghi et al. 2000 and Netten et al. 2001)		treated successfully, defined as a patient in remission (i.e. MADRS score <=12 at week 24). Secondary outcome measure: first line success i.e. remission [MADRS<=12] without switch of drug treatment. Overall success, 53.7% (50.3 - 57.5) for escitalopram and 48.7% (45.8 - 51.7) for citalopram; and first-line success without switch 41.7% (37.5 - 46.3) for escitalopram and 30.8% (27.5 - 34.6) for citalopram.	cases, escitalopram was dominant at all ranges of probabilities tested, indicating the robustness of the results.	Discounting: Not undertaken-costs incurred during less than 2 years. Time horizon: 6-month Quality checklist: 28/2/5 Funded by H Lundbeck A/S.

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Lenox-Smith, 2004. UK	Comparators: SNRIs (venlafaxine), SSRIs; (fluoxetine, paroxetine and fluovoxamine) TCAs; (amitriptyline).	Patients with major depressive disorder Setting: primary care Source of clinical effectiveness data: form a non-systematic review of published literature Source of resource use estimates: not reported	Cost-effectiveness analysis	Costs: costs estimated for drugs, physicians' time, blood tests for monitoring, nursing time, hospital inpatient stay and psychotherapy. The mean expected cost of treating major depressive disorders over a 6-month time horizon was £1,285 for patients initially treated with venlafaxine, £1,348 for patients initially on SSRIs, and £1,385 for patients initiated on TCAs. Venlafaxine contributed to around 9% of the overall costs, SSRIs 8% and TCAs 5%.	One of the most common combinations used in primary care (start with a TCA and switch to an SSRI if this fails) turned out to be the least cost-effective (£33.00). One of the least common combinations (start with venlafaxine and switch to an SSRI or a TCA if this fails) was the most cost-effective option (£20.90 or £21.50, respectively). Looking at a typical primary care organisation	Perspective: UK NHS Currency: £ pound sterling Cost year: 2001 Time horizon: 6 months Discounting: not relevant less that 1 year duration Funded by industry-Wyeth.

		Source of unit costs: different published sources		Outcomes: The measure of benefit was the number of symptom-free days (SFDs). A patient was considered to have SFDs once he or she was in remission. Patients on venlafaxine, SSRIs and TCAs were likely to have 61 (venlafaxine), 52 (SSRIs) and 44 (TCAs) SFDs, respectively. Outcomes assessed were remission, response rate and the dropout rate to adverse events. Remission was defined as a score of 7 or less on the 17-item HAM-D. The response rate was defined as a 50% reduction in the 21-item HAM-D score.	(with 150,000 patients), the overall cost was £1,609,319, with 785 patients attaining remission. If first-line venlafaxine use doubled to 12%, there would have been an extra 2 patients in remission with a saving of $4,094. Looking at the NHS as a whole (with 56 million people), increasing venlafaxine usage from 6 to 12% would have increased the number of remissions by 665 each year with annual savings of $1,528,298. The sensitivity analysis showed that the model was robust. Conclusion: Venlafaxine, may be a costeffective option in comparison with SSRIs and TCAs when used as a first-line drug for depression in primary care in the UK.	

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Peveler et al. HTA 2005 UK	Comparators: TCAs (amitriptyline, dothiepin or imipramine) SSRIs (fluoxetine, sertraline or paroxetine) modified TCA lofepramine	Setting: Primary care Source of clinical effectiveness data: RCT, n=265 Source of resource use estimates: patient records Source of unit costs:	Cost-effectiveness analysis, cost-utility analysis	Costs: Drugs, inpatient stays, visits to GP, GP telephonic contact, home visits, practice nurse visits at surgery, district nurse home visits, contact with community psychiatric nurse, counsellor visits, non-psychiatric clinic,day centre attendance, psychiatric contact and A&E visits. There were no significant differences between arms in mean cost per depression-free week. Outcomes: QALYs. The primary effectiveness outcome was the number of depression-free weeks (HAD-D less than 8, with interpolation of intervening values)	When comparing the different treatment options, no significant differences were found in outcomes or costs within the sample, but when outcomes and costs were analysed together, the resulting cost-effectiveness acceptability curves suggested that SSRIs were likely to be the most cost-effective option, although the probability of this did not rise above 0.6. Choosing lofepramine is likely to lead to a greater proportion of patients switching treatment in the first few weeks.	Perspective: NHS Currency: £ Cost year: ? Time horizon: 1 year Discounting: not relevant Funded by : NHS

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Wade, Unpublished /Wade2008 (published version)	Comparators: Escitalopram 20mg/day vs. Duloxetine 60mg/day	Patients with MDD, 18-65 yrs, with MADRS =>26 & CGI-S =>4 & baseline duration of current depressive episode of 12 weeks to 1 yr. Setting: outpatient Source of clinical effectiveness data: alongside double-blind, multinational randomised study Source of resource use estimates: Health economic assessment questionnaire alongside trial Source of unit costs: Std UK sources	Cost-effectiveness analysis	Costs: healthcare, medication, physician visits, visits to other healthcare professionals, hospitalisations & sick leave Over 24-weeks, escitalopram was associated with significant cost savings compared to duloxetine (total per patient cost £1127 versus £2001, respectively(total per-patient monthly cost £188 vs £334, respectively)). In the multivariate analysis, treatment with escitalopram resulted in 49% lower total costs compared to those on duloxetine (p=0.002) Outcomes: mean change in SDS score and MADRS scores form baseline to week 24, response (>50% reduction in MADRS score from baseline to last assessment) and remission rates (MADRS <-12 @ wk 24/last assessment) were included as efficacy measures.	Escitalopram is associated with significantly lower duration of sick leave and significant savings in the total cost compared with duloxetine; it dominates duloxetine when effectiveness is assessed on the SDS scale. Indirect cost due to sick leave accounted for the most substantial portion of the total cost and should, therefore, be an important consideration when pharmacoeconomic comparisons between treatments are made from the societal perspective. The link between decrease in productivity loss and early (8-week) clinical improvement demonstrated in the additional analyses may explain the reduced sick leave observed with	Perspective: societal Currency: £ Cost year: 2006 Time horizon: 24 weeks Discounting: none Funded by : Industry -Lundbeck

					escitalopram, given its superior short-term efficacy compared to duloxetine (demonstrated in the underlying clinical trial).	

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Kendrick, 2006. UK	Comparators: **SSRIs** dosage varied with drug, daily dose of fluoxetine was 20 mg throughout. For paroxetine, the daily dose was 20 mg, increasing to 30 mg after 3 weeks and to a maximum of 40 mg after 6 weeks. For sertraline, the daily dose was 50 mg, increasing after 3 weeks to 100 mg and after 6 weeks to a maximum of 150 mg. **TCAs** varied with age. For patients aged between 18 and 65 years, the daily dose 50	Adults diagnosed with depression. Patients accepting antidepressant treatment were also eligible, including those with comorbid physical or mental illness and those aged over 65 years. Setting: UK primary care Source of clinical effectiveness data:RCT, n= 327, n=92 patients were prescribed a different class of antidepressant. Source of resource use estimates: carried out prospectively directly from the clinical records of patients included in the effectiveness study Source of unit costs: derived from several published sources,	Cost-effectiveness analysis and cost-utility analysis.	Costs: It included the costs of medications, visits to GPs at surgery, contacts with GP by telephone, home visits by GPs, contacts with practice nurse at surgery, home visits by district nurse, contacts with community psychiatric nurses, visits to counsellor, attendance at day centre, attendance at nonpsychiatric hospital clinic, contacts with psychiatrist, visits to accident and emergency department, psychiatric inpatient stay, and inpatient stays. The expected mean 1-year costs per patient were £762 (+/- 1,136) (median £359; 95% CI: 553 to 1,059) in the TCA group, £875 (+/-1,566) (median £503; 95% CI: 675 to 1,355) in the SSRI group and £867 (+/-1,907) (median £384; 95% CI: 634 to 1,521) in the LOF group. Costs in all prescriptions and in antidepressant prescriptions only were significantly different between the groups (with higher figures in the SSRI group), but differences in the total costs did not reach statistical significance, (p=0.09). Outcomes: The primary clinical measure was the number of weeks	The incremental cost per depression-free week gained was £32 with SSRI over TCA, £59 with SSRI over LOF, and £183 with TCA over LOF. The cost effectiveness acceptability curve showed statistically non significant differences in benefits and costs. The incremental cost per QALY gained was £5,686 with SSRI over LOF and £2,692 with SSRI over TCA, while TCA was dominant in comparison with LOF. Authors' conclusions: analysis showed a lack of statistically significant differences in costs and benefits among the three treatments considered for patients with depression in primary care. Rough estimates	Perspective: Health service Currency: £ UK Cost year: 2001/2002 Time horizon: 12 months Discounting: not relevant Funded by: Health Technology Assessment Programme of the UK National Health Service Research and Development Directorate.

	mg, rising in 25-mg weekly steps to a maximum of 150 mg. For patients older than 65 years, the daily dose was 25 mg, rising in 25-mg weekly steps to a maximum of 120 mg. **<u>lofepramine (LOF)</u>** - The daily dose was 70 mg, rising in weekly 70-mg increments in divided doses to a maximum of 210 mg.	including cost studies and typical NHS sources.		free from depression, defined as a score < 8 on the Hospital Anxiety and Depression Scale - Depression sub-scale (HADS-D). Quality of life also measured with EuroQol EQ-5D questionnaire. The number of disease-free weeks was obtained directly from the effectiveness analysis. The QALYs were estimated by applying a tariff of health state values, based on a representative UK sample, to the utility scores from the EQ-5D. The numbers of depression-free weeks over 12 months (based on repeated measures analysis of variance) were 35.5 for the TCA group, 36.6 for the SSRI group and 34.8 for the LOF group. The differences were not statistically significant. The average numbers of QALYs, adjusted for baseline EQ-5D, were 0.55 (95% CI: 0.48 to 0.61) for the TCA group, 0.59 (95% CI: 0.52 to 0.64) for the SSRI group and 0.55 (95% CI: 0.49 to 0.61) for the LOF group.	of cost-effectiveness suggested that SSRIs might be the most cost-effective strategy. The study results support the NICE guidelines on depression which recommend SSRIs as first-choice antidepressants in primary care.	

Study, year and country	**Intervention details**	**Study population Setting Study design – data source**	**Study Type**	**Costs: description and values Outcomes: description and values**	**Results: Cost-effectiveness**	**Comments Internal validity (Yes/No/NA) Industry support**
Benedict – Eli Lilly.	<u>Comparators:</u> *Duloxetine*	The treatment of patients with MDD who failed on 1st line SSRIs	Cost-utility analysis	<u>Costs:</u> direct medical costs: GP visits for mental health reasons, psychiatrists' visits, hospitalisations and A&E visits	Compared to mirtazapine and SSRIs duloxetine produced	Perspective: national health service

Scotland	(dulx) *(60 –120 mg)* SSRIS as a group Venlafaxine XR (ven) Mirtazapine (mirt)	was modeled: 2 patient groups considered (2 settings differed in efficacy data, drug dose and resource utilization.): 1. those with moderate to severe MDD (HAMD-17 score=>19) likely to start new treatment episode in primary care (dulx compared to SSRIs as a group i.e. ven+mirt) Setting: primary care. Source of clinical effectiveness data: cycle 1 – 8 weeks Dulx - all active comparator dulx RCTs were pooled, n=2400, from Eli Lilly data on file. SSRI's - ad-hoc analysis at 8 wks of pooled patients in 6 comparator RCTs of dulx(Thase et al. 07, Swindle et al. 04 and data on file)		and drug costs. <u>Outcomes:</u> Quality adjusted life years Average baseline utility score of all patients: 0.48. Remitters: 0.79 (0.48+0.31) Responders: 0.68 (0.48+0.20) Non-responders: 0.55 (0.48+0.07) Drop-outs:0.53 (0.48+0.05) [Eli Lilly, HMBU trial, data on file] Remission and staying in remission without treatment = 0.86 (Revicki and Wood 1998)	additional benefits at higher costs leading to ICERs of approx. 2,400 and 6,300/ QALY. If the willingness to pay per QALY gained is below £5000, SSRIs are the preferred treatment choice. Above that value duloxetine is the preferred option in the base case. At NICE willingness to pay threshold of £20k, duloxetine would be the preferred option for treatment of MDD in primary care. The model was sensitive to uni-lateral changes in key efficacy parameters. Resource use and cost parameters were not sensitive in their 95% CI.	Currency: UK pound Cost year: not mentioned Time horizon: 1 yr Discounting: not mentioned, though not relevant Funded by : Eli Lilly

		Ven - 2 head-to-head trials, n=337 (Perahia et al. 07) Mirt – meta-analysis Stahl et al. 97 2nd and subsequent cycles : 2 ven vs. dulx trials with 12 wks ff-up. SSRI and mirt rates assumed to be weighted average of ven and dulx rates Source of resource use estimates: Literature and Scottish physician panel, UK practising GPs Source of unit costs: Drug costs were based on daily defined doses (WHO) and market share data.				

Appendix 15. Evidence Tables for Economic Studies

Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
Benedict – Eli Lilly. Scotland	Comparators: Duloxetine (dul) Venlafaxine XR (ven) Mirtazapine (mirt)	Treatment of patients with MDD who failed on 1st line SSRIs was modeled: 2. those with => 25 on HAMD-17, likely to be referred to secondary care Setting: secondary care. 2 settings differed in efficacy data, drug dose and resource utilization. Source of clinical effectiveness data: Dulx, Ven – 2 head-to-head trials (Perahia et al. 07) Mirt – in the absence of related data-mean difference bet the less severe and the more severe population in the trial was applied to mirt rates used in primary care	Cost-Utility Analysis	Costs: direct medical costs: GP visits for mental health reasons, psychiatrists' visits, hospitalisations and A&E visits and drug costs. Outcomes: Quality adjusted life years Average baseline utility score of all patients: 0.48. Remitters: 0.79 (0.48+0.31) Responders: 0.68 (0.48+0.20) Non-responders: 0.55 (0.48+0.07) Drop-outs:0.53 (0.48+0.05) [Eli Lilly, HMBU trial, data on file] Remission and staying in remission without treatment = 0.86 (Revicki and Wood 1998)	The QALY benefit with duloxetine is slightly greater compared to venlafaxine than in the primary care scenario. It is still achieved at lower costs, making duloxetine the dominant treatment choice. The same relationship holds for mirtazapine. In the secondary care setting the model was less sensitive to changes given the greater advantage in efficacy data point estimates. However, the model was sensitive to drug relapse rates. The CEAC from the probabilistic analysis shows a higher likelihood for duloxetine to be cost-effective over the whole range of willingness to pay values.	Perspective: national health service Currency: UK pound Cost year: not stated Time horizon: 1 yr Discounting: not mentioned, however not relevant. Funded by Eli Lilly

		setting(not reported) Source of resource use estimates: Scottish Psychiatrists Panel Source of unit costs: Drug costs were based on daily defined doses (WHO) and market share data.				

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Greenhalgh 2005- HTA UK	Comparators : ECT Other inpatient treatments for severe depression – TCAs, SSRIs, SNRIs, + Lithium Augmentation Maintenance /continuation therapy modelled : TCA, Lithium, ECT and no therapy. Psychotherapy for non-responders	Adult patients suffering form MDD Setting: inpatient care Source of clinical effectiveness data: A mathematical model was constructed using data from the clinical effectiveness evidence review and other relevant studies to derive clinical outcomes Source of resource use estimates: Published literature, expert panel Source of unit costs:BNF, 2001; Unit costs of health and social care	Cost-utility analysis using decision tree model incorporating monte carlo simulation techniques	Costs: Pharmacological therapies, ect treatments, laboratory tests, GP, psychiatrists and psychiatric nurse visits Outcomes:HSRD, QALYs	The modelling did not demonstrate that any of the scenarios had a clear economic benefit over the other available options. Specifically with ECT it does not indicate whether it should be a 1st, 2nd or 3rd line treatment. This is mainly due to that there is a lot of uncertainty around the values of the main parameters, efficacy, and failure to complete treatment and quality of life measures. This may be due in part to the lack of RCTs concerned with ECT in the severely depressed. However, it could also be the nature of depressive illness. The clinical evidence suggested that ECT is an effective treatment for depression for some people, whereas for others it could even have a detrimental effect.	Perspective: NHS Currency: £ Cost year: Time horizon: 12 months Discounting: not relevant Funded by

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Study, year and country	Intervention details	Study population Setting Study design – data source	Study Type	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments Internal validity (Yes/No/NA) Industry support
NICE, 2003	Comparators: ECT Antidepressant therapy	Adults with severe depressive illness Setting: inpatient mental health care Source of clinical effectiveness data: NICE literature review Source of resource use estimates: Source of unit costs:	Cost-utility analysis	Costs: Outcomes: QALY The results of the depressive illness model showed that, for eight different scenarios, total costs range from £10,592 to £15,354, and total quality-adjusted life years (QALYs) range from 0.424 to 0.539.	Given the small differences in total costs and QALYs between the strategies, ECT and pharmacotherapy are likely to be equally cost-effective.	Perspective: NHS Currency: £ Cost year:? Time horizon: 1 year Discounting: not relevant Funded by :

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Kendrick, 2006 UK	Comparators: usual general practitioner (GP) care generic community mental health nurse (CMHN) care problem-solving treatment (PST) provided by specially trained CMHNs	Patients between 18-65 years who had a new episode of anxiety, depression or reaction to life difficulties. had symptoms of between 4 weeks and 6 months in duration, and a score of =>3 GHQ-12. Setting: community care – primary care Source of clinical effectiveness data: RCT, n=247 Source of resource use estimates: carried out prospectively on a sub-group of patients from the sample used in the effectiveness study. Source of unit costs: derived from official published sources	Cost-utility analysis	Costs: nurse training and supervision, drugs, GP visits at surgery, GP home visits, GP telephone consultation, practice nurse visit at surgery, visit to social worker, home social worker, psychiatrist visit at the hospital clinic, psychiatrist visit at home, psychologist visit, outpatient visit, accident and emergency visit, hospital admission, further hospital contacts and out-of-pocket patient costs. The total costs were reported per patient. The mean total direct health service cost to the NHS was 283 (SD=300) in the GP group, 569 (SD=350) in the generic CMHN group and 608 (SD=501) in the PST-CMHN group. Outcomes: Primary heath outcome was psychiatric symptoms on the self-completed CIS-R (computerised version PROQSY 3). Quality-adjusted life-years (QALYs). The EuroQol EQ-5D instrument and public tariffs were used to estimate utility levels. QALYs were estimated as the area under the curve from the EQ-5D utilities, assuming a linear	An incremental cost-effectiveness analysis was performed by demonstrating incremental costs and incremental QALYs comparing PST-CMHN care with GP care, and generic CMHN care with GP care. In both cases, care provided by nurses was dominated by GP care. The sensitivity analysis on resource use data demonstrated the robustness of the base-case estimates.	Perspective: NHS and societal perspective Currency: £ Cost year: 2003 Time horizon: 26 weeks Discounting: not relevant Funded by : NHS R&D Internal validity: 31/1/3

				relationship between the values. No statistically significant differences between the three groups were observed in EQ-5D utility levels at 8 and 26 weeks.		

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