Appendix 15: Evidence tables for economic studies

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Pharmacological interventions

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
Benedicte *et al*., 2010 – Eli Lilly Scotland	Comparators: Duloxetine 60 to 120 mg per day SSRIS as a group Venlafaxine XR Mirtazapine	The treatment of patients with MDD who failed on first- line SSRIs was modeled Two patient groups considered (two settings differed in efficacy data, drug dose and resource utilisation): 1. Those with moderate to severe MDD (HAMD-17 score=>19) likely to start new treatment episode in	Cost-utility analysis	Costs: direct medical costs: GP visits for mental health reasons, psychiatrists' visits, hospitalisations and A&E visits and drug costs. Outcomes: QALYs 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) Dropouts: 0.53 (0.48+0.05) (Eli Lilly, HMBU trial, data on file)	Compared with mirtazapine and SSRIs, duloxetine produced 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 £5,000, 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 £20,000,	Perspective: national health service Currency: UK pound sterling Cost year: not mentioned Time horizon: 1 year Discounting: not mentioned, though not relevant Funded by Eli Lilly.

		primary care (duloxetine compared with SSRIs as a group; that is, venlafaxine XR + mirtazapine) Primary care <u>Source of clinical effectiveness data:</u> cycle 1 to 8 weeks duloxetine – all active comparator duloxetine RCTs were pooled, n=2400, from Eli Lilly data on file SSRIs – ad hoc analysis at 8 weeks of pooled patients in 6 comparator RCTs of duloxetine (Thase *et al.*, 2007; Swindle *et al.*, 2004; and data on file) Venlafaxine XR – Two head-to-head		Remission and staying in remission without treatment = 0.86 (Revicki & Wood, 1998)	duloxetine would be the preferred option for treatment of MDD in primary care. The model was sensitive to unilateral changes in key efficacy parameters. Resource use and cost parameters were not sensitive in their 95% CI.	

		trials, n=337 (Perahia *et al.*, 2007) Mirtazapine – meta-analysis (Stahl *et al.*, 1997) Second and subsequent cycles*:* Two venlafaxine XR versus duloxetine trials with 12 weeks first follow-up. SSRI and mirtazapine rates assumed to be weighted average of duloxetine and duloxetine rates <u>Source of resource use estimates:</u> Literature and Scottish physician panel, UK practising GPs <u>Source of unit costs:</u> Drug costs were based on daily defined doses				

		(WHO) and market share data.				
Benedicte *et al*., 2010 – Eli Lilly. Scotland	Comparators: Duloxetine Venlafaxine XR Mirtazapine	Treatment of patients with MDD who failed on first-line SSRIs was modeled: 2. those with => 25 on HAMD-17, likely to be referred to secondary care Setting: secondary care Two settings differed in efficacy data, drug dose and resource utilisation Source of clinical effectiveness data: duloxetine, venlafaxine XR – two head-to-head trials (Perahia *et al*., 2007) Mirtazapine – in the absence of related data-	Cost-utility analysis	Costs: direct medical costs: GP visits for mental health reasons, psychiatrists' visits, hospitalisations and A&E visits and drug costs. Outcomes: QALYs 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) Dropouts: 0.53 (0.48+0.05) [Eli Lilly, HMBU trial, data on file] Remission and staying in remission without treatment = 0.86 (Revicki & 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	Perspective: national health service Currency: UK pound Cost year: not stated Time horizon: 1 year Discounting: not mentioned; however, not relevant Funded by Eli Lilly.

		mean difference bet the less severe and the more severe population in the trial was applied to mirtazapine rates used in primary care setting (not reported) <u>Source of resource use estimates:</u> Scottish Psychiatrists Panel <u>Source of unit costs:</u> Drug costs were based on daily defined doses (WHO) and market share data.			duloxetine to be cost-effective over the whole range of willingness to pay values.	
Borghi & Guest, 2000 UK	<u>Comparators:</u> Mirtazapine Amitriptyline Fluoxetine	Patients in the UK, with moderate and severe depression, and within the age range 18 to 93 years Primary care and hospital <u>Source of clinical</u>	Cost-effectiveness analysis Modelling	<u>Costs:</u> included 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	Mirtazapine was found to be dominant compared with amitriptyline. It both reduced the expected direct NHS costs by £35 per patient and increased the proportion of successfully treated	<u>Perspective:</u> NHS including lost productivity <u>Currency:</u> UK pound sterling <u>Cost year:</u> 1997–1998 <u>Time horizon:</u> 6/7 months <u>Discounting:</u> no discounting

		effectiveness data: meta-analysis of four RCTs Source of resource use estimates: established retrospectively from interviewing a panel of ten GPs and three psychiatrists Source of unit costs: published literature.		who discontinued antidepressant treatment ranged from £50 to £504 over 5 months. The cost of management with mirtazapine was £413 per patient over 7 months, compared with £448 for amitriptyline The cost of management with mirtazapine was £420 per patient over 6 months, compared with £394 for fluoxetine Outcomes: Successfully treated patients (HRSD 17 <= 7 or reduction in HRSD 17>= 50%).	patients from 19.2 to 23.2%. However, this result was sensitive to the cost of managing adverse events. When compared with 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 three factors to which this result was sensitive.	Funded by Organon Ltd Internal validity (26/3/3)
Fernandez *et al*., 2005 Study carried out in six European countries (Denmark, Finland, France,	Intervention: escitalopram 10 to 20mg daily Comparator: venlafaxine XR 75 to 150 mg daily	Outpatients aged 18 to 85 years who fulfilled the DSM-IV criteria for moderate to severe MDD, without suicidal tendencies, MADRS total score >18 at screening, 1 week before and at the start of treatment	Cost-utility analysis	Direct costs: included physician care, care by ancillary health care personnel, laboratory tests, clinical examinations and inpatient care. Health economics experts provided the prices used. These were based on national sources; except for the UK costs were taken from Unit Costs of Health and Social Care published by the University of Kent	The incremental cost-effectiveness analysis was reported via the incremental cost-effectiveness ratio (ICER) confidence surface. Owing to the lack of significant differences in the efficacy of the two drugs, the analysis was	Perspective: those of the health care payer and society Currency: Euros Cost year: European 2003 prices were used to compute the costs Discounting: not relevant because of the short follow-up period. The unit

Germany, Spain and the UK).		Setting: primary care Effectiveness data derived from a single study. Costing was undertaken prospectively on the same patient sample Randomised, double-blind, flexible-dose, multinational clinical trial conducted. Included in trial n=293, lack of data for 42 patients (n=22 escitalopram, n=20 venlafaxine XR). n=251 evaluated (n=126 escitalopram; n=125 venlafaxine XR). 8-week first follow-up. At 8 weeks, n=245 reported valid cost information (four escitalopram and two venlafaxine XR lost relative to the pre-		Total health care costs: €110/patient escitalopram and €161/patient venlafaxine XR Medication costs: €62 escitalopram, €84 venlafaxine XR The inpatient care costs: €46/patient in venlafaxine XR, in escitalopram €0.00. Key cost drivers adjusted, escitalopram had statistically significantly lower health costs than those on venlafaxine XR (coefficient -0.34; p=0.007) The direct costs for the average patient in the sample were 40% higher with venlafaxine XR than with escitalopram (95% CI: 10 to 81) Analysis of effectiveness conducted on the basis of treatment completers only Primary health outcome: QLDS scores. Mean QLDS scores decreased from 18.6 to 12.4 for	not extended to the estimation of acceptability curves. An analysis of the ICER confidence surface demonstrated that health care costs were higher for the venlafaxine XR group than for the ESC group, and showed no between-group difference in the improvement of the EQ-5D score Escitalopram is as effective as venlafaxine in the treatment of MDD and may be associated with lower costs from a societal and health care budget perspective.	costs were adjusted to 2003 values using inflation rates (Consumer Price Index) for each country between 2001 and 2003 Did not conduct sensitivity analysis to explore any areas of uncertainty other than the inclusion of sick leave costs (in order to assess the results from a societal perspective) Funded by Lundbeck A/S.

		study period). Hence, economic evaluation comprised n=122 escitalopram, n=123 venlafaxine XR.		escitalopram ($p<0.01$), and from 18.8 to 12.1 for venlafaxine XR ($p<0.01$) No statistically significant differences were observed between the groups The measure of benefit used was the EQ-5D scores. The mean scores improved from 0.52 to 0.78 for escitalopram ($p<0.01$), and from 0.54 to 0.77 for venlafaxine XR ($p<0.01$). No statistically significant differences were observed between the treatment groups.		
Kendrick *et al*., 2006 UK	Comparators: SSRIs – dosage varied with drug. Daily dose of fluoxetine was 20 mg throughout. For paroxetine,	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	Cost-effectiveness analysis Cost-utility analysis	Costs: It included the costs of drugs, 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 non-psychiatric hospital clinic, contacts with	The incremental cost per depression-free week gained was £32 with SSRIs over TCAs, £59 with SSRIs over lofepramine, and £183 with TCAs over lofepramine. The CEAC showed statistically non significant differences in benefits	Perspective: health service Currency: UK pound sterling Cost year: 2001/2002 Time horizon: 12 months Discounting: not relevant Funded by Health Technology Assessment Programme of the UK

	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 was 50 mg,	UK primary care <u>Source of clinical effectiveness data:</u> RCT, n= 327; n=92 patients were prescribed a different class of antidepressant. <u>Source of resource use estimates:</u> carried out prospectively directly from the clinical records of patients included in the effectiveness study <u>Source of unit costs:</u> derived from several published sources, including cost studies and typical NHS sources		psychiatrist, visits to accident and emergency department, psychiatric inpatient stay, and inpatient stays The expected mean 1-year costs per patient were £762 (+/- £1136) (median £359; 95% CI: 553 to 1059) in the TCA group, £875 (+/- 1566) (median £503; 95% CI: 675 to 1355) in the SSRI group and £867 (+/-1907) (median £384; 95% CI: 634 to 1521) in the lofepramine 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) <u>Outcomes:</u> The primary clinical measure was the number of weeks free from depression, defined as a score < 8 on the	and costs The incremental cost per QALY gained was £5,686 with SSRIs over lofepramine and £2,692 with SSRIs over TCAs, while TCAs were dominant in comparison with lofepramine 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 of cost effectiveness suggested that SSRIs might be the most cost-effective strategy. The study results	NHS Research and Development Directorate.

	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:</u> 70 mg daily, rising in weekly 70-mg steps in divided doses to a maximum of 210 mg.			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 lofepramine 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 lofepramine group.	support the NICE guidelines on depression which recommend SSRIs as first-choice antidepressants in primary care.	
Kendrick *et*	<u>Comparators:</u>	Mild to moderate	Cost-	<u>Costs:</u> Inpatient admissions,	Costs were slightly	<u>Perspective:</u> NHS

al., 2009 UK	SSRI treatment plus supportive care versus supportive care alone	depression in patients with somatic symptoms. At the baseline assessment, they scored between 12 and 19 on the 17-HRSD Primary care <u>Source of clinical effectiveness data:</u> a parallel group, open-label, pragmatic randomised controlled trial <u>Source of resource use estimates:</u> Client Service Receipt Inventory data were augmented with data collected from general practice computerised medical records <u>Source of unit costs:</u> published sources.	effectiveness analysis	Outpatient consultations, all forms of GP contacts, practice, district , community mental health and other nurse contacts, health visitor contacts, counsellor contacts, complementary health care, psychologist, occupational therapist, social worker, housing worker, community support worker, day centre attendance, medication (physical), medication (SSRIs) and other medication (other mental health) <u>Outcomes:</u> unit improvement in HRSD. The SF-36 was also used to calculate quality adjusted life-years (QALYs)	higher in the SSRI plus supportive care arm, but not statistically significantly different. Incremental cost-effectiveness ratios and cost-effectiveness planes suggested that adding an SSRI to supportive care is probably cost-effective, with mean costs of £90 per point improvement on the HRSD and £14,854 per QALY gain. The CEAC for utility suggested that adding an SSRI to supportive care is cost-effective at the value of £20,000 to £30,000 per QALY used by NICE, with a 65 to 75% probability. Informal care costs were relatively high, given that the patients had only mild to moderate	<u>Currency:</u> UK pound sterling <u>Cost year:</u> 2006–07 <u>Time horizon:</u> 26 weeks Discounting, none Funded by NIHR Health Technology Assessment Programme

					depression, but did not differ significantly between arms.	
Romeo *et al*., 2004 Scotland	Comparators: Mirtazapine 30 to 45 mg daily Paroxetine 20 to 30 mg daily	Patients with depression treated in general practice, fulfilling DSM-IV criteria for MDD, with a baseline score of > 18 on 17-HAMD Primary care Source of clinical effectiveness data: clinical effectiveness study, Wade and colleagues (2003), mirtazapine (n=93), paroxetine (n=84) Source of resource use estimates: derived from actual data collected alongside the effectiveness study prospectively	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 (for example, GPs, community psychiatric nurses, physiotherapists and other healthcare 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 £1408 (SD=1777) in the mirtazapine group and £1528 (SD=2,022) in the paroxetine group. The difference was -£120 (95% CI: -750 to +377; p=0.51) Outcomes: primary outcome was	The costs and benefits were not combined in the form of ICERs 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 HAMD 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	Perspective: UK NHS and Society Currency: UK pound sterling Cost year: 2001/2002 Time horizon: 24 weeks Discounting: not relevant Internal Validity: 24/4/7 Funded by Organon Laboratories

		Source of unit costs: derived from the British National Formulary, the NHS Schedule of Reference costs (outpatient attendances), and published literature (contact with health and community professionals, and inpatient services).		change from baseline on the 17-HAMD. Primary measure also expressed as the number of patients classed as HAMD responders (that is, 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 QLDS The change in QLDS score from baseline to the 24-week endpoint was 13 in the mirtazapine group and nine in the paroxetine group, (p=0.021).	suggested that, compared with paroxetine, mirtazapine might be a cost-effective treatment for depression in a primary care setting.	
Wade *et al*., 2005a UK	Comparators: Escitalopram 20 mg daily Citalopram 40 mg daily	Adult patients with severe depression (MADRS total score => 30) Primary and secondary care Source of clinical effectiveness data: a	Cost-effective analysis. This analysis is an adaptation of models described in three other studies	Direct costs: included were drugs (authors noted that there was no price difference between escitalopram 10 mg and citalopram 20 mg [branded and generic]), GP and psychiatrist visits, inpatient psychiatric hospitalisations, discontinuation of treatment, treatment-emergent adverse events and attempted	This analysis suggested that escitalopram was a cost-saving alternative to citalopram for the treatment of severe depression in the UK From both the NHS and societal perspectives, the	Perspective: UK society and NHS Currency: UK pound sterling; reported conversion rate: £1.00 = US$0.62 in January 2003. All unit costs were updated using the British Consumer Price Index

		review of completed studies and estimates based on expert opinion Remission, discontinuation and response rate at week 8 derived from a meta-analysis of 506 patients and extrapolated to 6 months (Llorca *et al*., 2005) Source of resource use estimates: Estimates for the majority of the resources used and costs were derived from published literature (Borghi *et al*., 2000; Netten *et al*., 2001).	(Borghi *et al*., 2000; Hemels *et al*., 2004; Brown *et al*., 1999)	suicide Indirect costs: resulting from absenteeism from work (that is, lost productivity) From the NHS perspective, the expected total cost per patient was £422 (range: £404 to £441) for escitalopram and £454 (range: £436 to £471) for citalopram The expected total cost per successfully treated patient was £786 (range: £702 to £876) for escitalopram and £932 (range: £843 to £1028) for citalopram. Primary outcome measure: patient treated successfully, defined as a patient in remission (that is, MADRS score <=12 at week 24) Secondary outcome measure: first line success (that is, remission [MADRS<=12] without switch of drug treatment)	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 cases, escitalopram was dominant at all ranges of probabilities tested, indicating the robustness of the results.	Cost year: 2003 The number of workdays lost due to severe depression was derived from published literature (Borghi *et al*., 2000; 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 Discounting: not undertaken – costs incurred during less than 2 years Time horizon: 6 months Internal validity: 28/2/5 Funded by H Lundbeck A/S.

				Overall success, 53.7% (50.3 to 57.5) for escitalopram and 48.7% (45.8 to 51.7) for citalopram; and first-line success without switch 41.7% (37.5 to 46.3) for escitalopram and 30.8% (27.5 to 34.6) for citalopram.		
Wade, 2005b UK	Comparators: Escitalopram 10 to 20 mg daily Citalopram generic 20 to 40 mg daily Venlafaxine XR 75 to 150 mg daily	A hypothetical cohort of adult patients (>18 years) with MDD (baseline MADRS scores =>18 to <=40) Primary care Source of clinical-effectiveness data: Meta-analysis of four 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	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 expert opinion Indirect costs: productivity losses were included In the comparison between escitalopram and citalopram, the expected total costs per patient were £465 (95% CI: 436 to 493) for escitalopram and £544 (95% CI: 514 to 573) for citalopram from the NHS perspective. In the comparison between	From the NHS perspective: In the comparison between escitalopram and citalopram, the cost per successfully treated patient was £732 (95% CI: 665 to 807) for escitalopram and £933 (95% CI: 850 to 1,023) for CIT In the comparison between escitalopram and venlafaxine, the cost per successfully treated patient was £546 (95% CI: 481 to 618) for escitalopram and £607	Perspective: NHS and societal Currency: UK pounds sterling Time horizon: 6 months Discounting: not relevant due to the short time frame. 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

		Practice Research Database, published literature and expert advice <u>Source of unit costs:</u> UK cost data.		escitalopram and venlafaxine, the expected total costs per patient were £376 (95% CI: 342 to 410) for escitalopram and £415 (95% CI: 382 to 449) for citalopram from the NHS perspective <u>Outcomes:</u> 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 escitalopram and citalopram, the overall success rate was 63.5% (95% CI: 61.5 to 65.4) with escitalopram and 58.2% (95% CI: 56.3 to 60.3) with citalopram. Escitalopram was also associated with higher first-line success (51.2 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%)	(95% CI: 542 to 677) for citalopram Incremental cost-effectiveness ratios were not calculated because escitalopram always dominated both citalopram and venlafaxine XR, which were more expensive and less effective The sensitivity analysis showed that the base-case results were robust to variations in both costs and probabilities in the comparison between escitalopram and citalopram. However, the results of the comparison between escitalopram and venlafaxine were sensitive to the probability values used	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 Funded by H Lundbeck A/S Internal validity (28/3/4)

				In the comparison between escitalopram and venlafaxine, the overall success rate was 68.9% (95% CI: 66.7 to 70.9) with escitalopram and 68.5% (95% CI: 66.2 to 70.6) with venlafaxine. Escitalopram and venlafaxine were also associated with very similar first-line success, titration, switch and secondary care rates.	in the model, thus the two drugs were considered comparable in primary care Within the setting of primary care in the UK, escitalopram was a cost-effective treatment for MDD in comparison with citalopram and was quite similar to venlafaxine.	
Wade, un-published; Wade, 2008 (published version)	Comparators: Escitalopram 20 mg daily Duloxetine 60 mg daily	Patients with MDD, 18 to 65 years, with MADRS =>26 & CGI-S =>4 and baseline duration of current depressive episode of 12 weeks to 1 year Outpatient Source of clinical effectiveness data: alongside double-blind, multinational randomised study	Cost-effectiveness analysis	Costs: healthcare, medication, physician visits, visits to other healthcare professionals, hospitalisations and sick leave Over 24-weeks, escitalopram was associated with significant cost savings compared with duloxetine (total per patient cost £1127 versus £2,001, respectively [total per-patient monthly cost £188 versus £334, respectively]). In the multivariate analysis, treatment with escitalopram resulted in 49% lower total costs	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	Perspective: societal Currency: UK pound sterling Cost year: 2006 Time horizon: 24 weeks Discounting: none Funded by H Lundbeck A/S.

		Source of resource use estimates: health economic assessment questionnaire alongside trial Source of unit costs: standard UK sources		compared with those taking duloxetine (p=0.002) Outcomes: mean change in SDS score and MADRS scores from baseline to week 24, response (>50% reduction in MADRS score from baseline to last assessment) and remission rates (MADRS <-12 at week 24/last assessment) were included as efficacy measures.	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 escitalopram, given its superior short-term efficacy compared with duloxetine (demonstrated in the underlying clinical trial).	

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Psychosocial and psychological interventions

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
Friedli *et al*., 2000 UK	Comparators: Non directive counselling – (maximum 12 sessions) Usual GP care	People with depression or mixed anxiety/depression Primary care Source of clinical effectiveness data: RCT, Friedli and colleagues (2000), n=136 Source of resource use estimates: RCT, Friedli and colleagues (2000) Source of unit costs: UK National	Cost-minimisation analysis	Costs: number of outpatient consultations, length of inpatient stays, type and amount of medication prescribed The average direct and indirect costs for the counsellor group was £162.09 more per patient after 3 months compared with the GP group. However, over the following 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 No industry funding Internal validity – good (23/3/6).

		Sources				
Guthrie *et al.*, 1999 UK	Comparators: Brief psychodynamic-interpersonal therapy (BPIT) – (eight sessions) Usual care – patients received treatment under the care of their consultant psychiatrist, which normally consisted of regular out-patient consultations of 15 to 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 Secondary care – hospital outpatient department Source of clinical effectiveness data: RCT, N=144 Source of resource use estimates: obtained prospectively from	Cost-effectiveness analysis	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 $1959 (intervention) and $2,465 (usual) Outcomes: SCL-90-R, SF-36, EQ-5D: Benefits were expressed in terms of the EQ-5D questionnaire utility weights and QALMs at baseline, end of trial (T1) and 6 months after trial (T2) Patients in the psychotherapy group achieved 4.87 QALMs (median) compared with 3.48 QALMs in the TAU group from baseline to T2, although this was	6 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-	Perspective: Society Currency: US dollar Cost year: 1996–7 Time horizon: 8 weeks + 6 months Discounting: not relevant Not industry funded Internal validity – moderate (19/7/6).

		the effectiveness study sample. Source of unit costs: UK National estimates		not statistically significant. Median utility weight scores were 0.04 (psychotherapy) and 0.00 (usual) from baseline to T2 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.	psychotic symptoms who are not helped by conventional psychiatric treatment.	
Kaltenhaler, 2002 UK	Comparators: Computerised cognitive behaviour therapy (CCBT) – Beating the Blues (BtB): nine sessions: a 15-minute	People with depression or mixed anxiety/ depression Primary care Source of clinical effectiveness data: sponsor	Cost–effectiveness analysis Cost-utility analysis	Costs: of treatment included. Computer purchase, licence fee, Overheads (space, heat, lighting, and so on). Staff: Practice nurse/assistant psychologist, GP monitoring, IT support and training Controlling for baseline costs, CCBT completers had a mean	Based on a number of assumptions, the data from Bennett and colleagues (2000) suggested that the incremental cost per QALY gained of BtB over TAU lies between £1210and £7,692. If the data	Perspective: NHS (although indirect costs are calculated) Currency: UK pound sterling Cost year: 2000 Time horizon: 6 months No industry funding

	introductory video followed by eight 1-hour therapy sessions. CCBT, plus patients could also receive other forms of TAU from the GP with the exception of face-to-face counselling or other psychological input. TAU – discussions with a GP, referral to a counsellor, practice nurse or mental health professional, and treatment of physical conditions.	submissions. RCT Proudfoot and colleagues (2004) CCBT (n=89) TAU (n=78) <u>Source of resource use estimates and unit costs:</u> data on resource use were collected prospectively alongside the trial and costed using appropriate unit costs.		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. <u>Outcomes:</u> QALYs – a number of strong assumptions have been made and the estimated figures are crude. Estimated utility values from Bennett and colleagues (2000), and Revicki and Wood (1998), were assigned/mapped to BDI scores from the RCT to calculate QALY gains from treatment.	from Revicki and Wood (1998) are used, the corresponding range lies between £3,000 and £6,667 per QALY gained. It should be noted, however, that these estimates are crude and should be treated with caution.	Internal validity (19/9/4)
Kaltenthaler *et al*., 2006	The three products shared	Patients with mild to moderate,	Cost-effectiveness	Provision of CCBT results in the following costs: licence fees,	BtB: The incremental cost	<u>Perspective:</u> NHS

UK	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 – Standard care in primary care. The treatment received in the Proudfoot and colleagues (2004) trial was used as representing TAU in the NHS. TAU patients in	moderate to severe or severe depression. Primary care <u>Source of clinical effectiveness data:</u> BtB (Proudfoot *et al.,* 2004) RCT, n=274 Cope (Marks *et al.,* 2003). Non-comparative trial, n= 39 *Overcoming Depression* – Whitfield (2004). Non-comparative study, n=20 <u>Source of resource use estimates:</u> manufacturer submissions	analysis	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 to £353.00) Expected total cost per patient: - with home access to Cope £171.30 (£122.74 to £268.22) - access at one to five GP practice £195.86 (£137.48 to £312.40) Expected total cost per patient per copy of Overcoming Depression = £72.64 (£42.36 to £133.00) Outcomes: Quality-adjusted life years Utility scores from Richards, 2004. N=62. Mild–moderate: 0.78 +/- 0.20	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	<u>Currency:</u> UK Pound Sterling <u>Cost year</u>: Not reported <u>Time horizon:</u> 18 months <u>Discounting:</u> 3.5 % Internal validity 25/4/6.

	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 (that is, therapist-led CBT [TCBT] using the results of the trial).	<u>Source of unit costs:</u> submissions and published literature.		Moderate–severe: 0.58 +/- 0.31 Severe: 0.38 +/- 0.32 Minimal: 0.88 +/- 0.22 (aged and gender matched normal scores)	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 severity groupings. Authors' 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.	
King *et al.*,	Comparators:	Depression or	Cost-	Costs: direct and non-treatment	Patients in both	Perspective: direct health

2000 Bower *et al.*, 2000 UK	Non-directive counselling (maximum 12 sessions) CBT (max 12 sessions) Usual GP care	Mixed/anxiety Depression Primary care Source of clinical effectiveness data: RCT, King and colleagues (2000) n=464 Source of resource use estimates: RCT, King and colleagues (2000) n=464 Source of unit costs: UK National estimates	effectiveness analysis	costs, costs of loss of production Outcomes: BDI, EuroQol measure of health related quality of life.	psychological therapy groups made significantly greater clinical gains in the first four months; however, all groups had equivalent outcomes at 12 months. There were 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,	service and non-health care loss of productivity Currency: UK pound sterling Cost year: 1997/1998 Time horizon: 4+12 months Discounting: not relevant Not industry funded Internal validity – good (27/0/5)

					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.	
Kuyken *et al.*, 2008 UK	Mindfulness-based cognitive therapy (MBCT) – over 8 weeks Maintenance Antidepressant Medication (m-ADM)	Patients with history of three or more previous episodes of depression Primary care <u>Source of clinical effectiveness data:</u> RCT, n=123; patients followed up at 3-month intervals for 15 months <u>Source of resource</u>	Cost-effectiveness analysis	<u>Costs</u>: All hospital (inpatient, outpatient, emergency department); community health and social services (primary care, social work, complementary therapies); productivity losses resulting from time off work due to illness Total costs per participant (over follow-up): MBCT: $3,370 m-ADM: $2,915 Over 1 year: MBCT: $2,767 m-ADM: $2,340	Societal perspective: ICER of $962 per relapse/recurrence prevented; ICER of $50 per depression-free day NHS & PSS: ICER of $439 per relapse/recurrence prevented; ICER of $23 per depression-free day	<u>Perspective:</u> NHS & PSS <u>Currency:</u> US dollars <u>Cost year:</u> 2005/06 <u>Time horizon:</u> 15 months <u>Discounting:</u> not reported Funded by UK MRC Internal validity: 20/9/6

		use: Study population; Adult Service Use Schedule (AD-SUS) Source of unit costs: national sources		Outcomes: relapse/recurrence prevented; depression-free days Mean total number of relapses/recurrences: MBCT: 1.45 m-ADM: 1.57 Mean total number of depression-free days: not reported		
McCrone *et al.*, 2004 UK	Comparators: Computerised CBT (CCBT) – that is, Beating the Blues (BtB-a 15-minute introductory video followed by eight 50-minute sessions of CBT) with TAU TAU alone –TAU from the GP	18- to 75-year-olds with diagnoses of depression, mixed depression and anxiety, or anxiety disorders – not receiving face-to-face psychological therapy Primary care patients	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,	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	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)

	(included discussions with GP, referral to a counsellor, practice nurse or mental health professional and treatment of physical conditions) with exception of face-to-face counselling or other psychological input.	Source of clinical effectiveness data: Proudfoot and colleagues (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 BNF. The price of the computer program licence was obtained from the manufacturer.		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 to 148). 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	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 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.	

				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 to 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 to 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	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%.	

				(QALYs). 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.,* 1998)	A one-way sensitivity analysis was conducted on the cost 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.	
Miller *et al*., 2003 UK	Comparators: Counselling – six 50-minute weekly sessions. Extra sessions restricted to maximum of two. versus Antidepressant therapy - dothiepin (150 mg nocte), fluoxetine (20 mg OD) and lofepramine (140 to 210 mg taken daily in divided doses).	18- to 70-year-old patients with major depression defined using research diagnostic criteria (RDC) Primary care. Source of clinical effectiveness data: Chilvers and colleagues (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	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	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	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.

		randomised, and 46 (antidepressant group) and 137 (counselling group), respectively, among those not randomised. <u>Source of resource use estimates:</u> 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		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-parametric test, (p=0.005). No significant overall cost-differences between the randomised and patient preference groups were observed. <u>Outcomes:</u> 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; and the time to remission, remission defined as an RDC <4 and a Beck <10 The global outcome was assessed	larger proportion of patients, the antidepressant intervention is the dominant cost-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.	

		inpatient visits were abstracted from case notes. The quantities were derived directly from the effectiveness study Source of unit costs: UK National estimates		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.		
Scott, 2003 UK	Comparators : Cognitive therapy + antidepressants + clinical management Compared with: Antidepressants	25- to 65-year-old psychiatric outpatients with unipolar depression partially remitted despite adequate clinical treatment. Satisfied DSM-III-R criteria for major	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 to 1999 salary scales,	The ICER of cognitive therapy was £4,328 per relapse averted or £12.5 per additional relapse-free day. Based on the cost-effectiveness-acceptability curve	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).

	+ 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 during the 48-week follow-up phase Cognitive therapy = 16 sessions over 20 weeks, with two subsequent booster sessions.	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 <u>Source of clinical effectiveness data:</u> RCT, duration follow-up was 68 weeks n=158 randomised <u>Source of resource use estimates:</u>		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. First, the direct costs were considered excluding the additional costs of cognitive therapy. The second analysis included the cognitive therapy costs The mean direct health care costs (-cognitive therapy) were significantly lower in the cognitive therapy group (£734) than in the control group (£1119). This was due to savings on inpatient admissions (£161, 95% CI: 35 to 356) and day-patient services (£206, 95% CI: 54 to 466)	for cognitive therapy, 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	<u>Discounting:</u> 6% Funded by a grant from the Medical Research Council <u>Quality appraisal:</u> 26/5/4 <u>Limitation/s:</u> 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.

		resource utilisation questionnaires were undertaken prospectively on a sub-group (86%) of the patient sample <u>Source of unit costs:</u> local providers, BNF, PSSRU, salary scales		Cognitive therapy resulted in a mean cost-saving of £385 (95% CI: 1 to 769; p<0.05) When cognitive therapy costs were included, patients receiving cognitive therapy were £779 (95% CI: 387 to 1170; p<0.01) more costly than those receiving standard clinical treatment. However, the incremental cost incurred by these patients (£779) was lower than the overall mean therapy cost of cognitive therapy (£1164) <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% and 18%, respectively, at 20 weeks and 29%	per relapse prevented 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	

				and 47%, respectively, at 68 weeks (adjusted hazard ratio 0.51; 95% confidence interval, CI: 0.32 to 0.93).	therapy and similar approaches appear to have a major role to play in the treatment of residual depression.	
Simon *et al*., 2006 UK	Comparators: Pharmacotherapy – fluoxetine 40 mg daily and outpatient care. Pharmacotherapy with cognitive-behavioural therapy (CBT) – 16 sessions (average 50 minutes each).	Patients experiencing 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 Secondary care Source of clinical effectiveness data: a systematic review of studies was conducted then synthesised using a	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 £1297 for the combination therapy. This represented a total difference of £637 over 15 months. Outcomes: The measure of benefit used-	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	Perspective: UK NHS Currency: UK pound sterling Cost year: 2002/03 Time horizon: Both therapies were conducted for 3 months and had a 12-month follow-up period (that is, 15 months no maintenance therapy) Discounting: not relevant Funded by NICE Quality appraisal: 28/1/6. Although the initial treatment cost of

		meta-analysis <u>Source of resource use estimates:</u> based on the expert opinion of the GDG, literature and a systematic review of the economic evidence (NCCMH, 2005) <u>Source of unit costs:</u> BNF, PSSRU, PPA.		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 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).	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 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	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.

					it was much more uncertain from the currently available evidence(supported by sensitivity analysis) whether its use is cost-effective for moderate depression.	
Simpson *et al.*, 2000 UK	Comparators: Counselling (six sessions) Usual GP care – no restrictions except that GPs could not refer controls to practice counsellors.	People with BDI score of 14+, have experienced depression/anxiety for 6 months or more, aged 18-70 with no history of drug/alcohol misuse Primary care Source of clinical effectiveness data: RCT n=181, Simpson and colleagues (2000) Source of resource	Cost-minimisation analysis	Costs: the analyses focus on the costs of providing specialist and generic health- and social-care services, and other forms of support (GPs, hospital based and 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	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	Perspective: Direct health and social services, and lost productivity Currency: UK pound sterling Cost year: 1997/98 Time horizon: 12 months Discounting: not relevant No industry funding Internal validity – good (22/5/5).

		use estimates: specially adapted version of the Client Service Receipt Inventory, 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		Across the whole study sample, average total costs per person showed little change over time: • £4,906 for the 6 months prior to initial assessment (*n*=179) • £5,061 for the 6 months to first follow-up interview (*n*=161) • £4,995 for the 6 to 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 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	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 significantly higher in the counselling than in the TAU GP group, and this was directly due to the costs of the psychotherapy.	

				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 counselling 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.		
Simpson, 2003 UK	Short-term psychodynamic counselling in primary care – that is, highly trained counsellors employing a Freudian psychodynamic model in six of the 12 sessions Routine 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). Primary care Source of clinical effectiveness data: derived from a single prospective study-RCT conducted in seven GP practices (screening attendees) employing psychodynamic counsellors.	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.	The authors 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	Perspective: Not stated Currency: UK pound sterling Cost year: 1997 to 1998 prices Time horizon: 12 months Discounting: unnecessary because all costs were incurred in one year Funded by a grant from the NHS Executive Health Technology Assessment Programme Internal validity 18/13/4.

		Patients who were seen in the two GP practices employing 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)		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 (£1046 versus £1074) With the exception of short-term increased costs to the GP practices (linked to the use of counselling services), there were no statistically 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.	conclusive results. A sensitivity analysis of the quantities was not conducted.	

		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.		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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