**Economic evidence tables for review question: For adults with a new episode of more severe depression or more severe depression, what are the relative benefits and harms of psychological, psychosocial, pharmacological and physical interventions alone or in combination?**

**Table 43. Economic evidence table for self-help with support: computerised cognitive behavioural therapy (CBT) with support added to treatment as usual versus treatment as usual alone**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Gilbody 2015/ Littlewood 2015<br>UK<br>Cost-utility analysis | Interventions:<br>Computerised, commercially produced CBT (Beating the Blues) with therapist support in addition to treatment as usual (cCBT1)<br>Computerised, free to use cCBT (MoodGYM) with therapist support in addition to treatment as usual (cCBT2)<br>Treatment as usual, comprising GP care with no constraints on the range of treatments that | Adults with symptoms of depression (PHQ-9 score ≥10)<br>Pragmatic multicentre RCT (Gilbody2015 / Littlewood 2015, N=691)<br>Source of efficacy and resource use data: RCT (EQ-5D data available for n=416 at 24 months; NHS cost data available for n=580)<br>Source of unit costs: national sources | Costs: intervention (licence fee, cost of support), GP or nurse visits (including telephone call appointments), out-of-hours GP services, inpatient stays, outpatient visits, other community services (including counsellors, psychologists, psychiatrists, CMHT and IAPT services), depression-related medication (antidepressants, antipsychotics, mood stabilisers, sleeping tablets, anxiety medication)<br>Mean total cost per person (SE):<br>cCBT1: £1,186 (£80); cCBT2: £1,098 (£135); TAU: £1,121 (£62)<br>Adjusted mean differences (95% CI)<br>cCBT1 vs TAU: £104 (-£67 to £275)<br>cCBT2 vs TAU: -£106 (-£262 to £50)<br>Primary outcome measure: QALYs estimated based on EQ-5D (UK tariff)<br>Number of QALYs per person (SE): | cCBT1 dominated by TAU<br>TAU vs cCBT2 £6,933/QALY<br>Probability of each intervention being cost effective at WTP £20,000/QALY:<br>cCBT1: 0.038<br>cCBT2: 0.417<br>TAU: 0.545<br>Using SF-6D QALYs:<br>cCBT1 dominated by TAU<br>cCBT2 dominant<br>Probability of each intervention being cost-effective at WTP £20,000/QALY:<br>cCBT1: 0.007<br>cCBT2: 0.756<br>TAU: 0.237<br>Results robust to inclusion of depression-related costs only | Perspective: NHS & PSS<br>Currency: GBP£<br>Cost year: 2012<br>Time horizon: 2 years<br>Discounting: 3.5% annually<br>Applicability: directly applicable<br>Quality: minor limitations |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| | could be accessed (TAU) | | cCBT1: 1.333 (0.034)<br>cCBT2: 1.356 (0.033)<br>TAU: 1.389 (0.033)<br>Adjusted mean differences (95% CI)<br>cCBT1 vs TAU: -0.044 (-0.117 to 0.030)<br>cCBT2 vs TAU: -0.015 (-0.092 to 0.061) | and to consideration of completers' data only (instead of imputed data analysis)<br>Little evidence of an interaction effect between preference and treatment allocation on outcomes | |

**Table 44. Economic evidence table for counselling versus antidepressants**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Miller 2003<br>UK<br>Cost effectiveness analysis | Interventions:<br>Generic psychological therapy comprising 6 weekly 50-minute sessions (counselling)<br>Routinely prescribed antidepressant drugs, comprising dothiepin (150 mg) taken at night, fluoxetine (20 mg) taken once daily or lofepramine (140–210 mg) taken daily in divided doses, or a different drug if it was judged necessary by GP (AD) | Adults aged 18-70 years who met diagnostic criteria for major depression (assessed by their GP).<br>Exclusion criteria: psychosis, suicidal tendencies, postnatal depression, recent bereavement, drug or alcohol misuse<br>RCT (Bedi2000 /Chilvers 2001, N=103); people refusing randomisation but agreeing to participate in the patient preference trial were given the treatment of their choice (N=220)<br>Source of efficacy data: RCT (at 12 months n=81) and preference trial (at 12 months n=163) | Costs: intervention (counselling, medication), depression-related GP visits, psychiatric inpatient & outpatient care<br>Mean cost (SD) per person:<br>RCT<br>Counselling: £302 (£38)<br>AD: £344 (£62); p=0.777<br>Preference trial:<br>Counselling: £336 (£25)<br>AD: £263 (£34) p =0.005<br>Primary outcome measure: global outcome, assessed by a psychiatrist blind to treatment allocation, using the research diagnostic criteria (RDC), BDI score and GP notes. The outcome was good if the person responded to treatment within 8 weeks and then remained well | RCT: ICER of AD vs. counselling £263/ extra person with a good global outcome<br>Probability of counselling being cost-effective: 0.25 and 0.10 at a WTP of £500 and £2,000 per extra person with a good global outcome, respectively<br>Sensitivity analysis: assuming missing data were good: probability of counselling being cost-effective increases for any WTP; assuming missing data were poor: probability of counselling being cost- | Perspective: NHS (only depression-related costs considered)<br>Currency: UK£<br>Cost year:1995<br>Time horizon: 12 months<br>Discounting: NA<br>Applicability: partially applicable<br>Quality: potentially serious limitations |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| | | Source of resource use data: RCT (at 12 months n=103) and preference trial (at 12 months n=215)<br>Source of unit costs: national sources and local costs for counsellors | % of people with good global outcome:<br>RCT<br>Counselling: 25%, AD: 41%, p=0.196<br>Preference trial:<br>Counselling: 36%, AD: 28%, p=0.191 | effective slightly increases for WTP<£1,500 and decreases for WTP >£1,500.<br>Preference trial: ICER of counselling vs. AD £912/ extra person with a good global outcome | |

**Table 45. Economic evidence tables for SSRIs: sertraline versus placebo**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Hollingworth 2020<br>UK<br>Cost-utility analysis | Interventions:<br>Sertraline<br>Placebo | Adults aged 18-74 years presenting to primary care with depression or low mood during the past 2 years who had not received antidepressant or anti-anxiety medication in the previous 8 weeks.<br>Pragmatic RCT (N=655) (Lewis 2019)<br>Source of efficacy & resource use data: RCT, analysis based on data imputation. n=505 with utility (EQ-5D) data available; cost data available for n=381 | Costs: sertraline, primary care consultations and phone calls (GP, nurse), medication, inpatient and outpatient care, accident and emergency, community care, home visits, other community care<br>Mean imputed total cost /person (SD):<br>Sertraline: £154 (£19)<br>Placebo: £177 (£26)<br>Difference: −£22 (−£87 to £42)<br>Sub-group with mild depression:<br>Difference: −£19 (−£154 to £116)<br>Sub-group with moderate depression:<br>Difference: £4 (−£145 to £152)<br>Sub-group with severe depression:<br>Difference: −£41 (−£109 to £27)<br><br>Outcome measure: QALY estimated based on EQ-5D (UK tariff) | Imputed incremental net monetary benefit (95% CI) at WTP £20,000 /QALY: whole sample: £122 (£18 to £226)<br>Sub-group with mild depression: £102 (−£114 to £317)<br><br>Sub-group with moderate depression: £135 (−£69 to £339)<br><br>Sub-group with severe depression: £131 (−£18 to £281)<br><br>Probability of sertraline being cost-effective at WTP | Perspective: NHS & personal social services<br>Currency: GBP£<br>Cost year: 2018<br>Time horizon: 12 weeks<br>Discounting: NA<br>Applicability: directly applicable<br>Quality: minor limitations |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| | | Source of unit costs: national sources | Mean imputed QALYs / person (SD):<br>Sertraline: 0.182 (0.002)<br>Placebo: 0.177 (0.002)<br>Difference: 0.005 (−0.003 to 0.012)<br>Sub-group with mild depression:<br>Difference: 0.004 (−0.004 to 0.012)<br>Sub-group with moderate depression:<br>Difference: 0.007 (0 to 0.014)<br>Sub-group with severe depression:<br>Difference: 0.005 (−0.002 to 0.011) | £20,000 /QALY: >95% in whole sample; >70% in each sub-group | |

**Table 46. Economic evidence tables for SSRIs: escitalopram versus citalopram**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Wade 2005b<br>UK<br>Cost effectiveness analysis | Interventions:<br>Escitalopram<br>Citalopram | Adults with major severe depression with baseline MADRS score ≥ 30<br>Decision-analytic modelling<br>Source of efficacy data: published meta-analysis of RCTs<br>Source of resource use data: published literature and expert opinion<br>Source of unit costs: national sources | Costs: study medication, GP and psychiatrist visits, inpatient psychiatric hospitalizations, treatment discontinuation, treatment-emergent AEs, attempted suicide. Sick leave<br>Mean (range) total NHS cost per person:<br>Escitalopram: £422 (£404-£441)<br>Citalopram £454 (£436-£471)<br>Outcome measures: % of remission, defined as MADRS score ≤ 12, and % remission without switch<br>% of remission: mean (range)<br>Escitalopram: 53.7% (50.3%-57.5%)<br>Citalopram: 48.7% (45.8%-51.7%)<br>% of remission without switch: mean (range)<br>Escitalopram: 41.7% (37.5 %-46.3%)<br>Citalopram: 30.8% (27.5%-34.6%) | Escitalopram dominates citalopram<br>Results robust to changes in drug-specific probabilities and cost data<br>PSA: Escitalopram was dominant in >99.8% of iterations | Perspective: NHS (and societal)<br>Currency: GBP£<br>Cost year: 2003<br>Time horizon: 26 weeks<br>Discounting: NA<br>Applicability: directly applicable<br>Quality: potentially serious limitations |

**Table 47. Economic evidence tables for SSRIs versus SNRIs: escitalopram versus citalopram versus venlafaxine**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Wade 2005a<br><br>UK<br><br>Cost effectiveness analysis | Interventions:<br>Escitalopram<br><br>Citalopram<br><br>Venlafaxine | Adults with major depression with baseline MADRS score between 18-40<br><br>Decision-analytic modelling<br><br>Source of efficacy data: meta-analysis of head-to-head RCTs between escitalopram and citalopram; and between escitalopram and venlafaxine<br><br>Source of resource use data: General Practice Research Database, published literature and expert opinion<br><br>Source of unit costs: national sources | Costs: study medication, staff time (GP, psychiatrist, hospitalisation, community services, attempted suicide; sick leave<br><br>Mean (range) total NHS cost per person:<br>Escitalopram: £465 (£436-£493)<br>Citalopram: £544 (£514-£573)<br><br>Escitalopram: £376 (£342-£410)<br>Venlafaxine: £415 (£382-£449)<br><br>Outcome measure: % of remission, defined as MADRS score ≤ 12<br><br>% of remission: mean (range)<br>Escitalopram: 63.5% (61.5%-65.4%)<br>Citalopram: 58.2% (56.3%-60.3%)<br><br>Escitalopram: 68.9% (66.7%-70.9%)<br>Venlafaxine: 68.5% (66.2%-70.6%) | Escitalopram dominates both citalopram and venlafaxine | Perspective: NHS (and societal)<br>Currency: UK£<br>Cost year: 2003<br>Time horizon: 26 weeks<br>Discounting: NA<br>Applicability: directly applicable<br>Quality: potentially serious limitations |

**Table 48. Economic evidence tables for SSRIs versus SNRIs: escitalopram versus duloxetine**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Wade 2008<br>UK | Interventions:<br>Escitalopram<br>Duloxetine | Outpatients aged 18–65 years with moderate-to-severe | Costs: medication, staff time (GP, psychiatrist, cardiologist, ear-nose-throat specialist, gastroenterologist, dermatologist, psychologist, nurse, social worker, physiotherapist, | Escitalopram dominant across all outcomes | Perspective: NHS & sick leave |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Cost-effectiveness analysis | | depression (baseline Montgomery-Aberg Depression Rating Scale [MADRS] total score ≥26 and a Clinical Global Impression Severity [CGI-S] score ≥4) and duration of current depressive episode of 12 weeks to 1 year<br>International multi-centre RCT (N=295) (Wade 2007)<br>Source of efficacy & resource use data: RCT, analysis based on data imputation; completers for economic analysis n=223<br>Source of unit costs: national sources | occupational therapist, alternative therapy), hospitalisation (psychiatry, emergency, general practice, surgery), sick leave<br><br>Mean difference in healthcare costs (SD):<br>-£145 (-£387 to -£42)<br><br>Outcome measures: Sheehan Disability Scale score (SDS), MADRS score, response response (MADRS score decrease ≥50%) and remission (MADRS score ≤12)<br><br>Mean difference in effects:<br>MADRS change in total score 1.7 (-0.1 to 3.4)<br>SDS change in total score 2.4 (0.4 to 4.1)<br>Response probability 5.0% (-2.8% to 12.7%)<br>Remission probability 3.3% (-5.7% to 11.8%) | | Currency: GBP£<br>Cost year: 2006<br>Time horizon: 24 weeks<br>Discounting: NA<br>Applicability: directly applicable<br>Quality: potentially serious limitations |

**Table 49. Economic evidence tables for SSRIs versus mirtazapine: paroxetine versus mirtazapine**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Romeo 2004<br><br>UK<br><br>Cost effectiveness analysis | Interventions:<br>Mirtazapine 30–45 mg/day | Adults with major depression and baseline $HAMD_{17}$ score >18 treated in primary care<br><br>RCT (N=197) (Wade2003) | Costs: medication, hospital inpatient stays and outpatient attendances, day care; contacts with GPs, community psychiatric nurses, social workers, opticians, physiotherapists and other specialists<br>Mean total NHS cost per person:<br>Mirtazapine: £1408 (SD (£1777) | Mirtazapine dominates paroxetine<br><br>Results robust to changes in costs | Perspective: NHS and social care (and societal)<br>Currency: UK£<br>Cost year: 2002 |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| | Paroxetine 20–30 mg/day | Source of efficacy & resource use data: RCT (data available for economic analysis n=177)<br><br>Source of unit costs: national sources | Paroxetine: £1528 (SD £2022)<br>Mean difference -£120 (95%CI -£750 to £377, p=0.51)<br>Outcome measure: % of response defined as at least 50% decrease in $HAMD_{17}$; changes in Quality of Life in Depression Scale (QLDS) from baseline to endpoint<br>% of response:<br>Mirtazapine: 63%<br>Paroxetine: 56% (p=0.31)<br>Change in QLDS<br>Mirtazapine: 13<br>Paroxetine: 9 (p=0.021, favouring mirtazapine) | Probability of mirtazapine being cost-effective 80% and 89%, at WTP zero and £1000 for a point improvement in $HAMD_{17}$ | Time horizon: 24 weeks<br>Discounting: NA<br>Applicability: partially applicable<br>Quality: potentially serious limitations |

**Table 50. Economic evidence tables for SSRIs versus SNRIs versus mirtazapine: SSRIs versus duloxetine versus venlafaxine versus mirtazapine**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Benedict 2010<br><br>UK<br><br>Cost-utility analysis | Interventions:<br><br>Duloxetine<br><br>SSRIs<br><br>Venlafaxine<br><br>Mirtazapine | Adults with moderate to severe major depression defined by a $HAMD_{17}$ score ≥19, having a new treatment episode in primary care<br><br>Decision-analytic modelling<br><br>Source of efficacy data: meta-analyses of clinical trials -randomisation likely broken | Costs: medication, A&E Visits, GPs, psychiatrists, hospitalisation<br><br>Mean total cost per person:<br>Duloxetine £543<br>SSRIs £486<br>Venlafaxine £585<br>Mirtazapine £516<br><br>Outcome measure: QALY estimated based on EQ-5D ratings (UK tariff)<br><br>Number of QALYs per person: | Duloxetine dominant over venlafaxine.<br>SSRIs dominant over mirtazapine<br>ICER of duloxetine versus SSRIs: £6,304/QALY<br><br>Probability of duloxetine being cost-effective at WTP £20,000/QALY: approximately 70%<br><br>Results sensitive to changes in efficacy (response / relapse) and utility values | Perspective: Scottish NHS<br>Currency: UK£<br>Cost year: likely 2003<br>Time horizon: 48 weeks<br>Discounting: NA<br>Applicability: directly applicable<br>Quality: potentially |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| | | Source of resource use data: expert opinion<br>Source of unit costs: national sources | Duloxetine 0.665<br>SSRIs 0.656<br>Venlafaxine 0.663<br>Mirtazapine 0.654 | | serious limitations |

**Table 51. Economic evidence tables for SSRIs versus SNRIs versus TCAs: fluoxetine versus venlafaxine versus amitriptyline**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Lenox-Smith 2009<br><br>UK<br><br>Cost-utility analysis | Interventions:<br><br>Venlafaxine<br><br>Fluoxetine<br><br>Amitriptyline | Adult outpatients with major depression<br><br>Decision-analytic modelling<br><br>Source of efficacy data: pooled data from meta-analysis; a single RCT for amitriptyline vs. venlafaxine<br><br>Source of resource use data: Delphi panel<br><br>Source of unit costs: national sources | Costs: medication, lab testing, clinical examinations, community psychiatric nursing, inpatient and outpatient services, staff time (GP, psychiatrist, psychologist), psychotherapy<br><br>Mean total cost per person:<br>Venlafaxine £1530<br>Fluoxetine £1539<br>Amitriptyline £1558<br><br>Outcome measure: QALY estimated based on the presumed utilities of a depression-free day and a severely depressed day<br><br>Mean QALYs per person<br>Venlafaxine 0.098<br>Fluoxetine 0.090<br>Amitriptyline 0.085 | Venlafaxine dominates fluoxetine and amitriptyline<br><br>Results robust to changes in costs.<br><br>Results sensitive to the value of the utility gain associated with a depression-free day | Perspective: NHS<br>Currency: UK£<br>Cost year: 2006<br>Time horizon: 24 weeks<br>Discounting: NA<br>Applicability: partially applicable<br>Quality: potentially serious limitations |

**Table 52. Economic evidence table for combined CBT & antidepressant (fluoxetine) versus antidepressant alone**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Simon 2006<br>UK<br>Cost effectiveness and cost-utility analysis | Interventions:<br>Combination therapy comprising 16 sessions of CBT lasting 50min each and antidepressant therapy (fluoxetine) (Combo)<br>Antidepressant therapy alone, comprising fluoxetine 40mg daily for 3 months and standard outpatient care (AD) | Adults with moderate depression and adults with severe depression<br>Decision-analytic modelling (decision tree)<br>Source of efficacy data: systematic literature review & meta-analysis of RCTs<br>Source of resource use data: published literature and expert opinion<br>Source of unit costs: national sources | Costs: intervention (clinical psychologist's time for CBT, antidepressant medication, dispensing fee, outpatient care with consultant psychiatrist or specialist registrar), subsequent depression treatment over 12months<br>Mean total cost per person:<br>Combo £1,297; AD £660; difference £637<br>Outcome measures:<br>Probability of successful treatment (remission and no relapse over 12 months) with remission defined as HRSD-17 ≤ 6 or HRSD-24 ≤ 8<br>QALYs estimated based on vignettes valued by service users using SG<br>Outcome results:<br>Probability of successful treatment:<br>Combo 0.29; AD 0.14; difference 0.16<br>QALYs per person with severe depression: Combo 0.63; AD: 0.52; difference 0.11<br>QALYs per person with moderate depression Combo 0.89; AD 0.84; difference 0.04 | ICER of Combo vs AD:<br>£4,056 per additional successfully treated person (95% CI £1,400 to £18,300)<br>Moderate depression:<br>£14,540/QALY (95%CI £4,800 to £79,400/QALY)<br>Probability of Combo being cost-effective at WTP £30,000/QALY 0.88<br>Severe depression:<br>£5,777/QALY (95% CI £1,900 to £33,800/QALY)<br>Probability of Combo being cost-effective at WTP £30,000/QALY 0.97<br>Results sensitive to changes in relative efficacy (in terms of remission, relapse) | Perspective: NHS<br>Currency: GBP£<br>Cost year: 2003<br>Time horizon: 15 months<br>Discounting: NA<br>Applicability: partially applicable<br>Quality: minor limitations |

**Table 53. Economic evidence table for combined CBT & antidepressant (citalopram) versus CBT alone versus antidepressant alone**

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Koeser 2015<br>UK | Interventions:<br>Antidepressant therapy alone, | Adults with moderate or severe major depression | Costs: intervention (clinical psychologist's time for CBT, antidepressant medication, | Combo dominated by CBT | Perspective: NHS<br>Currency: GBP£ |

| Study country and type | Intervention and comparator | Study population, design and data sources | Costs and outcomes (descriptions and values) | Results | Comments |
|---|---|---|---|---|---|
| Cost-utility analysis | comprising citalopram 20mg daily for 15 months and standard outpatient care (AD)<br>Cognitive Behavioural Therapy (CBT) comprising 16 acute + 2 booster sessions for responders, each lasting 50 min<br>Combination therapy comprising CBT and AD treatment (Combo) | Decision-analytic modelling (decision tree)<br>Source of efficacy data: systematic screening of database containing RCTs that compare psychological treatments (single or combined) for adults with depression with a control intervention; NMA<br>Source of resource use data: published literature that reported expert opinion and analysis of RCT data<br>Source of unit costs: national sources | dispensing fee, outpatient care with consultant psychiatrist or specialist registrar), service use associated with remission, response, no response<br>Mean total cost per person:<br>AD: £3,645; CBT: £4,418<br>Combo: £5,060<br>Outcome measures:<br>QALYs estimated based on EQ-5D (UK tariff)<br>Mean total QALYs per person:<br>AD: 1.236; CBT: 1.274<br>Combo: 1.274 | ICER of CBT vs AD: £20,039/QALY<br>Probability of being best at WTP £25,000/QALY:<br>CBT: 0.43<br>AD: 0.37<br>Combo: 0.20<br>Results sensitive to changes in inclusion criteria for RCTs for acute and follow-up treatment and to use of SF-6D values | Cost year: 2012<br>Time horizon: 27 months<br>Discounting: 3.5% annually<br>Applicability: directly applicable<br>Quality: minor limitations |