

Economic evidence profiles for review question: What are the relative benefits and harms of further-line psychological, psychosocial, pharmacological and physical interventions (alone or in combination), for adults with depression showing an inadequate response to at least one previous intervention for the current episode?

Table 151: Economic evidence profile for cognitive therapy or cognitive behavioural therapy in addition to antidepressants versus antidepressants alone

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Scott 2003 UK	Minor limitations ²	Partially applicable ³	Intervention: cognitive therapy TAU: antidepressant and clinical management Outcome measure: percentage of relapses avoided	£1,371	18%	£7,621	ICER £8,218 using mean imputation; £8,853 using non-parametric multiple imputation; £12,425 using only the 65% of subjects in the complete case analysis Probability of cognitive therapy being cost-effective 0.60 and 0.80 at WTP of £10,500 and £15,000 per relapse prevented, respectively; probability sensitive to method of missing data imputation
Hollingshurst 2014 UK	Minor limitations ⁴	Directly applicable ⁵	Intervention: cognitive behavioural therapy TAU: GP management and antidepressant or referral as required Outcome measure: QALY	Endpoint: £1,006 Mean over 3-5 years: £311	Endpoint: 0.053 Mean over 3-5 years: 0.052	Endpoint: £17,639 Follow-up: £5,943	Results robust to changes in psychologist unit cost & exclusion of hospitalisation costs Using SF-6D-based QALYs: £35,045/QALY Using completers' data: £21,720/QALY Probability of CBT being cost-effective: Endpoint: 0.74 / 0.91; follow-up: 0.92 / 0.95 at WTP of £20,000/£30,000/QALY, respectively

1. Costs uplifted to 2020 UK pounds using the NHS cost inflation index (Curtis 2020).

2. Time horizon 17 months; analysis conducted alongside RCT (N=158; full data for 65% of participants); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented.

3. UK study; NHS & PSS perspective; outcome measure % of relapses, no QALY used as an outcome

4. Time horizon 12 months plus 3-5 year follow-up; analysis conducted alongside RCT (N=469; NHS and PSS cost and QALY data available for n=368 at 12 months; follow-up data available for n= 248); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented

5. UK study; NHS & PSS perspective; QALYs estimated based on EQ-5D ratings (UK tariff)

Table 152: Economic evidence profile for intensive short-term psychodynamic psychotherapy versus secondary care TAU

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Town 2017/2020 Canada	Potentially serious limitations ²	Partially applicable ³	Outcome measures: QALY and HAMD score	-£301	QALY: 0.03 HAMD: -2.04	dominant	Probability of short-term psychodynamic psychotherapy being cost-effective 0.65 at WTP of £15,000/QALY. ICER £11,369/QALY when high volume service users were removed from analysis

1. Costs converted to UK pounds and uplifted to 2020 prices using Purchasing Power Parity exchange rates and the NHS cost inflation index (Curtis 2020).

2. Time horizon 18 months; analysis conducted alongside RCT (N=60); costs highly skewed; national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented.

3. Canadian study; mental health provider perspective; QALYs estimated based on SF-6D ratings (UK tariff)

Table 153: Economic evidence profile for mirtazapine in addition to SSRIs or SNRIs versus SSRIs or SNRIs alone

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Kessler 2018a/2018 b UK	Minor limitations ²	Directly applicable ³	Outcome measure: QALY	£75	0.009	£430 (-£987 to £1846) [completer analysis] £99 (-£115 to £313) [imputed data analysis]	Difference in costs and QALYs not significant Probability of mirtazapine being cost-effective: 0.69 / 0.71 at WTP of £20,000/ £30,000/QALY, respectively

1. Costs uplifted to 2020 UK pounds using the NHS cost inflation index (Curtis 2020).

2. Time horizon 12 months; analysis conducted alongside RCT (N=480; full data for 75% of participants); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented.

3. UK study; NHS & PSS perspective; QALYs estimated based on EQ-5D-5L ratings (UK tariff)

Table 154: Economic evidence profile for sertraline versus venlafaxine versus bupropion following inadequate response to a SSRI

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Soini 2017 Finland	Potentially serious limitations ²	Partially applicable ³	Outcome measure: QALY Sertraline dominated by	Bupropion vs venlafaxine £15	Bupropion vs venlafaxine 0.0084	Bupropion vs venlafaxine: £2,249/QALY	Probability of cost-effectiveness not possible to estimate, as analysis included

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
			the other two interventions				options not relevant to review question
Singh 2017 US	Potentially serious limitations ⁴	Partially applicable ⁵	Outcome measures: response and remission	Vs bupropion: Sertraline: £198 Venlafaxine: £155	Response, vs bupropion: Sertraline: 1% Venlafaxine: 2% Remission, vs bupropion: Sertraline: 2% Venlafaxine: -1%	Incremental net health benefit (at WTP £23,000 /unit of effectiveness): Response, vs bupropion: Sertraline: -0.0037 Venlafaxine: 0.0062 Remission, vs bupropion: Sertraline: 0.0013 Venlafaxine: -0.0218	At a WTP of £23,000 / unit of effectiveness, venlafaxine had a probability of being the most cost-effective option around 40% (in terms of response); sertraline had a probability of being the most cost-effective option around 45% (in terms of remission)

1. Costs converted to UK pounds and uplifted to 2020 prices using Purchasing Power Parity exchange rates and the NHS cost inflation index (Curtis 2020).
2. Time horizon 12 months; analysis based on decision-analytic modelling; efficacy data from RCT (N=727); national unit costs used; CEACs presented for pairwise comparisons of vortioxetine (which was of no interest) versus each of the other interventions; funded by industry.
3. Finnish study; healthcare payer's perspective; QALYs estimated based on EQ-5D VAS ratings in Finland
4. Time horizon 9 weeks; analysis based on RCT (N=727); national unit costs used; statistical analyses conducted and CEACs presented
5. US study; government payer's perspective; response and remission used as outcome measures

Table 155: Economic evidence profile for various pharmacological interventions following inadequate response to previous antidepressant treatment

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Benedict 2010 UK	Potentially serious limitations ²	Directly applicable ³	Interventions: duloxetine, venlafaxine, mirtazapine Outcome: QALY	Duloxetine vs: Venlafaxine: -£67 Mirtazapine: -£27	Duloxetine versus: Venlafaxine: 0.05 Mirtazapine: 0.08	Duloxetine dominant	Probability of duloxetine being cost-effective at WTP £20,000/QALY: approximately 0.80
Nordström 2010 Sweden	Potentially serious limitations ⁴	Partially applicable ⁵	Interventions: escitalopram, duloxetine, venlafaxine Outcome: QALY	Escitalopram vs: Duloxetine: -£16 Venlafaxine: -£60	Escitalopram versus: Duloxetine: 0.025 Venlafaxine: 0.024	Escitalopram dominant	Probability of escitalopram being cost-effective at WTP £20,000/QALY 0.981 and 0.985 compared with duloxetine and venlafaxine, respectively

1. Costs converted to UK pounds and uplifted to 2020 prices using Purchasing Power Parity exchange rates and the NHS cost inflation index (Curtis 2020).
2. Time horizon 48 weeks; analysis based on decision-analytic modelling; efficacy data derived from meta-analyses of clinical trials with randomisation possibly broken; disutility and costs due to side effects not considered; resource use estimates based on expert opinion; national unit costs used; funded by industry
3. UK study; Scottish NHS perspective; QALYs based on EQ-5D (UK tariff)
4. Time horizon 6 months; analysis based on decision-analytic modelling; efficacy data derived from pooled analysis of trial data, including only participants who had already received antidepressant therapy prior to randomisation; data for duloxetine and venlafaxine pooled together; resource use estimates based on a cohort study conducted in 56 primary care centres in Sweden over 6 months; national unit costs used; CEACs presented for escitalopram versus each of the other drugs considered and not for all 3 options; funded by industry
5. Swedish study; societal perspective but analysis based on healthcare costs presented separately; QALYs based on EQ

Table 156: Economic evidence profile for atypical antipsychotics adjunct to a SSRI versus lithium adjunct to a SSRI

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Edwards 2013 UK	Potentially serious limitations ²	Directly applicable ³	Outcome: QALY	-£1,040	0.028	Lithium as an adjunct to SSRI dominant	Probability of lithium being dominant: 1.00 Results sensitive to efficacy of augmentation strategies and discontinuation rates; robust under different assumptions regarding resource use, as well as under changes in remission and relapse risk at follow-up

1. Costs uplifted to 2020 UK pounds using the NHS cost inflation index (Curtis 2020).
2. Time horizon 12 months; analysis based on decision-analytic modelling; efficacy data taken from a systematic review and indirect comparison using 6 RCTs comparing olanzapine + fluoxetine vs. fluoxetine alone in people with treatment-resistant depression and 1 RCT comparing lithium + fluoxetine vs. fluoxetine alone in people who had failed at least one antidepressant (so not from a population with treatment-resistant depression); a common class effect was assumed for the SSRIs and the AAPs; resource use estimates based on expert opinion; national unit costs used; PSA conducted.
3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)

Table 157: Economic evidence profile for aripiprazole adjunct to antidepressants versus bupropion adjunct to antidepressants versus switching to bupropion

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Yoon 2018 US	Potentially serious limitations ²	Partially applicable ³	Outcomes: Remission QALY	Vs bupropion switch: Aripiprazole adjunct £53 Bupropion adjunct -£22	Remission vs bupropion switch: Aripiprazole adjunct 7% Bupropion adjunct 5% QALY vs bupropion switch: Aripiprazole adjunct 0.0002 Bupropion adjunct -0.001	Remission: Bupropion switch dominated by bupropion adjunct Aripiprazole adjunct vs bupropion adjunct: £3,791/remission QALY: Aripiprazole adjunct vs bupropion switch £348,428/QALY Bupropion switch vs bupropion adjunct: £21,614/QALY	At WTP £15,000/remission, probability of cost-effectiveness: aripiprazole adjunct 76%; bupropion adjunct 23%; bupropion switch: 1%

1. Costs converted to UK pounds and uplifted to 2020 prices using purchasing power parity exchange rates and the NHS cost inflation index (Curtis 2020).

2. Time horizon 12 weeks; analysis conducted alongside RCT (N=1522; complete data for n=1131); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented for the remission outcome. Method of estimating QALYs from EQ-5D unclear (e.g. VAS vs ratings translated into utility values); potential conflict of interest due to relations with pharma industry

3. US study; healthcare perspective; outcome measure % of remission plus QALY based on EQ-5D but unclear whether VAS or ratings translated into utility values was used

Table 158: Economic evidence profile for brexpiprazole versus quetiapine (150 and 300mg/day) versus olanzapine/fluoxetine adjunct to antidepressants versus antidepressant treatment alone

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Sussman 2017 US	Potentially serious limitations ²	Partially applicable ³	Outcomes: Response Remission	Vs AD: BREX £3,194 QUET300 £2,113 QUET150 £1,370 OLZ/FLUO £749	Response vs AD: BREX 0.16 QUET300 0.09 QUET150 0.05 OLZ/FLUO 0.09 Remission vs AD: BREX 0.12 QUET300 0.07 QUET150 0.04 OLZ/FLUO 0.08	QUET150 and QUET300 dominated by OLZ/FLUO using both response and remission as outcomes ICER of BREX vs OLZ/FLUO: £36,619/responder and £53,969/remitter ICER of OLZ/FLUO vs AD: £8,053/responder and £9,986/remitter	Not reported

1. Costs uplifted to 2020 UK pounds using the NHS cost inflation index (Curtis 2020).

2. Time horizon 48 weeks; analysis based on decision-analytic modelling; efficacy data obtained from trials and meta-analyses using indirect comparisons for evidence synthesis; resource use and unit costs taken from published studies, further national unit costs used; no incremental analysis conducted but possible to undertake using reported data; no CEACs; funded by industry

3. US study; payer's perspective; no QALYs used

Table 159: Economic evidence profile for ECT versus TCAs, SSRIs, SNRIs, and lithium augmentation

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
Greenhalgh 2005 UK	Potentially serious limitations ²	Partially applicable ³	Population: adults with depression requiring hospitalisation Strategies: 1. SNRI, SSRI, Li 2. ECT, SSRI, Li; ECT maintenance in ECT 3. ECT, SSRI, Li; Lithium & TCA maintenance in ECT 4. SNRI, ECT, Li; Lithium & TCA maintenance in ECT 5. ECT, SSRI, Li 6. SNRI, SSRI, ECT; Lithium & TCA maintenance in ECT 7. SNRI, ECT, Li; ECT maintenance in ECT	Strategies 2-8 vs 1: £6,397 -£652 -£1,307 -£611 £4,107 £1,926 £5,093	Strategies 2-8 vs 1: -0.032 -0.066 -0.020 0.049 -0.004 0.004	Strategies 1, 2, 3, 6, 7, and 8 dominated ICER of 5 vs. 4: £10,082 /QALY	Results modestly sensitive to use of alternative utility values; results robust to small changes in costs and suicide rates

Study and country	Limitations	Applicability	Other comments	Incremental costs ¹	Incremental effects	ICER ¹	Uncertainty ¹
			8. SNRI, SSRI, ECT; ECT maintenance in ECT Outcome: QALY				

1. Costs uplifted to 2020 UK pounds using the NHS cost inflation index (Curtis 2020).

2. Time horizon 12 months; analysis based on economic modelling, efficacy data from systematic literature review of RCTs and published meta-analyses, and further assumptions; resource use data based on published literature and expert opinion; national unit costs used; sensitivity analysis conducted including PSA (95% CI reported); impact of side effects considered only in terms of discontinuation

3. UK study; NHS perspective; QALYs estimated based on preferences for vignettes using the McSad health state classification system valued by service users with previous depression in Canada using standard gamble techniques