Depression in adults: treatment and management

Appendices O-R

NICE Guideline
Appendices
18 July 2017

Draft for Consultation

Developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists
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Figure 1: Flow diagram of economic study selection for review on interventions and services for adults with depression
## Appendix P: Economic evidence – health economic checklists

### P.1 Service delivery models for people with depression

#### P.1.1 Simple collaborative care


<table>
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<th>Economic Question: service delivery models</th>
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<td>Section 1: Applicability (relevance to specific review question and the NICE reference case)</td>
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<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Older adults with major depression</td>
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<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
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<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS</td>
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<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
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<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 18 months</td>
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<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>QALYs based on SF-6D (UK tariff)</td>
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<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
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<td>1.9 Overall judgement: Directly applicable</td>
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Other comments: None

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<td>NA</td>
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<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=485; at 18 months n=344; cost data available for n=447</td>
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<td>2.5 Are the estimates of relative intervention effects from the</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
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<td></td>
<td></td>
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<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>No</td>
<td>Intervention and primary care costs exclusively considered</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Statistical analyses conducted; CEACs presented</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Potentially serious limitations</td>
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Other comments:

| --- |

**Economic Question:** service delivery models

**Section 1: Applicability (relevance to specific review question and the NICE reference case)**

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<td>1.1 Is the study population appropriate for the review question?</td>
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<td>Adults with depression</td>
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<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
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<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
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<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
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<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
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</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9 Overall judgement: Directly applicable</td>
<td></td>
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Other comments: None
### Economic evidence – health economic checklists


| 2.1 | Does the model structure adequately reflect the nature of the topic under evaluation? | NA |
| 2.2 | Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Partly 12 months |
| 2.3 | Are all important and relevant outcomes included? | Yes |
| 2.4 | Are the estimates of baseline outcomes from the best available source? | Partly RCT, N=581 |
| 2.5 | Are the estimates of relative intervention effects from the best available source? | Partly RCT |
| 2.6 | Are all important and relevant costs included? | Yes |
| 2.7 | Are the estimates of resource use from the best available source? | Partly RCT |
| 2.8 | Are the unit costs of resources from the best available source? | Yes National sources |
| 2.9 | Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
| 2.10 | Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes Statistical analyses conducted; CEACs presented |
| 2.11 | Is there any potential conflict of interest? | No |
| 2.12 | Overall assessment: Minor limitations |

**Other comments:**

### Economic Question: service delivery models

**Section 1: Applicability (relevance to specific review question and the NICE reference case)**

| 1.1 | Is the study population appropriate for the review question? | Yes | Older adults who screened positive for subthreshold depression |
| 1.2 | Are the interventions appropriate for the review question? | Yes |
| 1.3 | Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
| 1.4 | Are the perspectives clearly stated and are they appropriate for the review question? | Yes | NHS/PSS |
| 1.5 | Are all direct effects on individuals included, and are all other effects included where they are material? | Yes |
| 1.6 | Are all future costs and outcomes discounted appropriately? | NA | Time horizon 12 months |
| 1.7 | Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and | Yes |
### Section 2: Study limitations (level of methodological quality)

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<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=705; complete data used in base-case economic analysis n=448</td>
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<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
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<td>2.6 Are all important and relevant costs included?</td>
<td>No</td>
<td>Intervention and primary care costs exclusively considered</td>
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<td>2.7 Are the estimates of resource use from the best available source?</td>
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<td>2.8 Are the unit costs of resources from the best available source?</td>
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<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
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<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Statistical analyses conducted; CEACs presented</td>
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<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
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<td>2.12 Overall assessment: Potentially serious limitations</td>
<td></td>
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<tr>
<td>Other comments: Attrition was markedly greater in the collaborative care arm</td>
<td></td>
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- outcomes used in line with analytical perspectives taken (item 1.4 above).
- Are costs and outcomes from other sectors fully and appropriately measured and valued? NA


#### Economic Question: service delivery models

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<th>Question</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
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<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with a history of</td>
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<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
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<tr>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
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<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
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<tr>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
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<td>Are all future costs and outcomes discounted appropriately?</td>
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<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
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<tr>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
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1.9 Overall judgement: Partially applicable

Other comments: None

### Section 2: Study limitations (level of methodological quality)

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<th>Question</th>
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<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
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<tr>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
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<td>Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>HROQL not considered</td>
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<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT,N=386; n=315 completed all follow-up assessments and n=377 remained enrolled throughout</td>
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<th>Methodology</th>
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<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
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<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly RCT</td>
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<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Unclear</td>
<td>Probably local data</td>
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<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
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<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
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**Overall assessment:** Potentially serious limitations

**Other comments:** Analyses of clinical data included only those completing all blinded follow-up assessments; cost analyses included only those remaining enrolled throughout the follow-up period. Participation in follow-up interviews was significantly greater in the intervention group than in usual care, introducing a possibility of bias.

### P.1.21 Complex collaborative care


**Economic Question:** settings for the delivery of care for people with depression

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<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
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<td>1.1 Is the study population appropriate for the review question?</td>
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</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
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<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
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<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
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<td>2.3 Are all important and relevant outcomes included?</td>
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<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
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<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
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<tr>
<td>2.6 Are all important and relevant costs included?</td>
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<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
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<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
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<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
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<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
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<td>2.11 Is there any potential conflict of interest?</td>
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<td>Other comments:</td>
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<td>Sick-listed workers with major depression</td>
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<td>1.2 Are the interventions appropriate for the review question?</td>
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<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
<td>Dutch study</td>
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<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Healthcare system</td>
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<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
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<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
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<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>QALYs based on EQ-5D ratings (Dutch tariff)</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
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<tr>
<td>1.9 Overall judgement: Partially applicable</td>
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Other comments:

### Section 2: Study Limitations (Level of Methodological Quality)

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<th>Question</th>
<th>Yes/Partly/No/Unclear/NA</th>
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<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
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<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=124</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td>Non-psychiatric inpatient costs not considered</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Bootstrapping conducted</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Minor limitations</td>
<td></td>
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Other comments:

Economic Question: Service delivery models

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<thead>
<tr>
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<th>Yes/Partly/No/Unclear/NA</th>
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<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with major depression treated in primary care</td>
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<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
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</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
<td>Dutch study</td>
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<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Healthcare system (and societal)</td>
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<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>QALYs based on EQ-5D ratings (Dutch tariff)</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9 Overall judgement: Partially applicable</td>
<td></td>
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Other comments:

Section 2: Study limitations (level of methodological quality)

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<th>Comments</th>
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<td>NA</td>
<td>RCT</td>
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<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
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<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=150; 93 identified by screening and 47 by GP referral; economic analysis based only on n=93 identified by screening</td>
</tr>
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<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT (n=93)</td>
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<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td>Non-psychiatric inpatient costs not considered</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT (n=93)</td>
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<table>
<thead>
<tr>
<th>2.8</th>
<th>Are the unit costs of resources from the best available source?</th>
<th>Yes</th>
<th>National sources</th>
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<tbody>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Bootstrapping conducted</td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
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<td>2.12</td>
<td>Overall assessment: Potentially serious limitations</td>
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**Other comments:**

## P.1.31 Medication management


**Economic Question: service delivery models**

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<th>Yes/ Partly/ No/Unclear/ NA</th>
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<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
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<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
<tr>
<td>1.9</td>
<td>Overall judgement: Partially applicable</td>
<td></td>
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**Other comments:** None

#### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Yes/Partly/No/Unclear/NA</th>
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<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Unclear</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
</tr>
<tr>
<td>2.12 Overall assessment: Potentially serious limitations</td>
<td></td>
</tr>
</tbody>
</table>

Other comments: base-case analysis was complete case analysis regardless of assigned treatment. In addition, a per protocol analysis was included. Participants were included in the per protocol analysis if the prescription for antidepressant medication was written out by their GP and they completed all of the follow-up assessments. Participants in the intervention group were excluded from the per protocol analysis if they indicated that they had not watched the intervention videotape or did not receive the 3 coaching contacts. In sensitivity analysis, the mean value per treatment group was imputed for missing values in participants who did not complete all follow-up assessments. Imputation was limited to participants who had completed the baseline assessment (n=135).


#### Economic Question: service delivery models

<table>
<thead>
<tr>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
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</table>

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<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
<td>Spanish study</td>
</tr>
<tr>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Societal &amp; healthcare</td>
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<tr>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 6 months</td>
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<tr>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>QALYs based on EQ-5D ratings (Spanish tariff)</td>
</tr>
<tr>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
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</table>

1.9 Overall judgement: Partially applicable

Other comments: None

#### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
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<tr>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>6 months</td>
</tr>
<tr>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
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<tr>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=179; N=179; 71% completed at 6 months; n=151 received intervention as allocated</td>
</tr>
<tr>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
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</tr>
<tr>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
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<tr>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>Regional sources</td>
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<tr>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Bootstrapping conducted; CEACs presented</td>
</tr>
<tr>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

2.12 Overall assessment: Potentially serious limitations

Other comments: base-case analysis was based on intention to treat, with multiple imputation of...
### P.1.4 Step 1.41 Stepped care


Missing data. In addition, a per protocol analysis was conducted in which participants who did not receive the intervention were excluded. Also, a complete case analysis was conducted, without the 52 participants who were lost to follow-up at 6 months. Results contradictory, depending on measure of outcome used.

<table>
<thead>
<tr>
<th>Economic Question: service delivery models</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section 1: Applicability (relevance to specific review question and the NICE reference case)</td>
</tr>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
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<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
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<td>1.9 Overall judgement: Directly applicable</td>
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Other comments: None

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<th>Comments</th>
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<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>Cohort study</td>
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</table>

2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? Partly 8 months

2.3 Are all important and relevant outcomes included? Yes

2.4 Are the estimates of baseline outcomes from the best available source? Partly Prospective cohort study with matched sites, N=403

2.5 Are the estimates of relative intervention effects from the best available source? Partly Prospective cohort study

2.6 Are all important and relevant costs included? Partly Medication costs not considered

2.7 Are the estimates of resource use from the best available source? Partly Prospective cohort study

2.8 Are the unit costs of resources from the best available source? Yes IAPT financial data and national sources

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? Yes

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? Yes Statistical analyses conducted; CEACs presented

2.11 Is there any potential conflict of interest? No

2.12 Overall assessment: Potentially serious limitations

Other comments: low response rate at recruitment (403/3391, 11.9%); IAPT service assessed over the first 2 years of establishment, therefore costs associated with learning effects were likely


Economic Question: service delivery models

Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Question</th>
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<tbody>
<tr>
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<td>Yes</td>
<td>Adults with a ICD10 depressive syndrome receiving inpatient care</td>
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<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>Stepped care</td>
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<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
<td>German study</td>
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<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>3rd party payer</td>
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<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
<td>HRQoL not reported</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted</td>
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<td>Time horizon up to remission or</td>
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<table>
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<tbody>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
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</table>

1.9 Overall judgement: Partially applicable

Other comments: None

### Section 2: Study limitations (level of methodological quality)

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<table>
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<tr>
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<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
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<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Partly</td>
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<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
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<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
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<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>Unclear</td>
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2.12 Overall assessment: Potentially serious limitations

Other comments:

### P.1.5 Integrated care pathways


Economic Question: service delivery models

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<table>
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<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
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### Economic evidence – health economic checklists


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<td>1.2 Are the interventions appropriate for the review question?</td>
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<td></td>
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<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly US study</td>
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</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Healthcare &amp; service users’ time &amp; mileage</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 18 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>QALYs based on SF-12/SF-6D (UK tariff)</td>
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<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9 Overall judgement: Partially applicable</td>
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**Other comments:**

### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
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<th>Question</th>
<th>Answer</th>
<th>Details</th>
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<td>RCT</td>
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<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
<td>18 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=364; 87% completed at 6 months, 79% at 12 months and 78% at 18 months</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>Regional sources in base-case analyse; national sources in secondary analysis</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain</td>
<td>Yes</td>
<td>Bootstrapping</td>
</tr>
</tbody>
</table>

Update 2017

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Is there any potential conflict of interest? No
Overall assessment: Minor limitations


Economic Question: service delivery models

Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>1.1 Is the study population appropriate for the review question?</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults above 65 years of age with depression (major or minor)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.2 Are the interventions appropriate for the review question?</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>US study</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</th>
<th>Partly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare &amp; service users’ and carers’ time &amp; mileage</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time horizon 6 months</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time horizon 6 months</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.6 Are all future costs and outcomes discounted appropriately?</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>See notes</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</th>
<th>Partly</th>
</tr>
</thead>
<tbody>
<tr>
<td>See notes on</td>
<td></td>
</tr>
</tbody>
</table>

| 1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? | NA |

Overall judgement: Partially applicable

Other comments: Primary outcome measures were the Center for Epidemiologic Studies Depression Scale (CES-D) score; number of depression-free days (DFD) derived from the 20-item CES-D (score=0 indicated depression-free day, ≥ 16 full symptoms and intermediate severity scores were assigned a value between depression-free and fully symptomatic by linear interpolation); QALYs estimated based on depression-free days (QALY-DFD), using utility weights of health=1, depression=0.59; QALYs estimated based on SF-36 (QALY-SF), using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG

Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCT</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</th>
<th>Partly</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.3 Are all important and relevant outcomes included?</th>
<th>Partly</th>
</tr>
</thead>
<tbody>
<tr>
<td>See notes on</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>Applicability</th>
<th>Source Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=840; within VA n=365, outside VA n=475; individuals with major depression within VA n=214, outside VA n=302.</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>national sources</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td>Bootstrapping conducted; CEACs presented</td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

**Overall assessment**: Potentially serious limitations

Other comments: separate analyses undertaken for participants within and outside the Veteran Affairs (VA) system; sub-analyses for people with major depression performed. Contradictory results across sub-analyses

### P.2.1 Interventions for first-line treatment of adults with a new episode of less severe depression

#### P.2.1.3 Psychological interventions


AND


**Economic Question**: psychological interventions as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
AND  

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>depression</td>
</tr>
<tr>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS</td>
</tr>
<tr>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 26 weeks</td>
</tr>
<tr>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Overall judgement: Directly applicable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other comments: None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Section 2: Study limitations (level of methodological quality)</td>
<td>Yes/ Partly/ No/Unclear/ NA</td>
<td>Comments</td>
</tr>
<tr>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>26 weeks</td>
</tr>
<tr>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT (N=247; analysis based on n=184)</td>
</tr>
<tr>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Bootstrapping conducted; cost effectiveness planes presented</td>
</tr>
<tr>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>
AND

2.12 Overall assessment: minor limitations
Other comments:


Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with depression (BDI 14-40) lasting at least 6 months, with or without comorbid anxiety</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>Psychodynamic counselling</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Health and social services</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
<td>HRQoL not measured</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>time horizon 12 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
<td>BDI and other secondary outcomes</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9 Overall judgement: Partially applicable</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other comments: None

<table>
<thead>
<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>1 year</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>HRQoL not measured</td>
</tr>
</tbody>
</table>

| 2.4 | Are the estimates of baseline outcomes from the best available source? | Partly | RCT, N=145; completers n=115 |
| 2.5 | Are the estimates of relative intervention effects from the best available source? | Partly | RCT |
| 2.6 | Are all important and relevant costs included? | Yes |
| 2.7 | Are the estimates of resource use from the best available source? | Partly | RCT, completers n=115 |
| 2.8 | Are the unit costs of resources from the best available source? | Yes | National sources where available; local costs for intervention |
| 2.9 | Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
| 2.10 | Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Partly | Statistical tests undertaken; bootstrapping conducted |

| 2.11 | Is there any potential conflict of interest? | No |
| 2.12 | Overall assessment: Potentially serious limitations |

Other comments:


Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

| Section 1: Applicability (relevance to specific review question and the NICE reference case) | Yes/ Partly/ No/Unclear/ NA | Comments |
| 1.1 | Is the study population appropriate for the review question? | Yes | Adults with depression in a primary care setting |
| 1.2 | Are the interventions appropriate for the review question? | Yes | cCBT |
| 1.3 | Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
| 1.4 | Are the perspectives clearly stated and are they appropriate for the review question? | Yes | NHS |
| 1.5 | Are all direct effects on individuals included, and are all other effects included where they are material? | Yes |
| 1.6 | Are all future costs and outcomes discounted appropriately? | Yes | 3.5% annually |
| 1.7 | Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | Yes |
| 1.8 | Are costs and outcomes from other sectors fully and | NA |

appropriately measured and valued?

1.9 Overall judgement: Directly applicable

Other comments: None

Section 2: Study limitations (level of methodological quality) | Yes/ Partly/ No/Unclear/ NA | Comments
--- | --- | ---
2.1 Does the model structure adequately reflect the nature of the topic under evaluation? | Yes | 
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Yes | 18 months 
2.3 Are all important and relevant outcomes included? | Yes | QALYs estimated 
2.4 Are the estimates of baseline outcomes from the best available source? | Partly | analysis of individual-level RCT data 
2.5 Are the estimates of relative intervention effects from the best available source? | Partly | analysis of individual-level RCT data and published RCT data; and further assumptions 
2.6 Are all important and relevant costs included? | Yes | Crude cost estimates 
2.7 Are the estimates of resource use from the best available source? | Partly | Based on manufacturer submissions, published data and further assumptions 
2.8 Are the unit costs of resources from the best available source? | Yes | National sources, intervention costs from manufacturers 
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes | 
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes | PSA, CEACs presented 
2.11 Is there any potential conflict of interest? | No | 
2.12 Overall assessment: Potentially serious limitations

Other comments:


Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

Section 1: Applicability (relevance to specific review question and the NICE reference case) | Yes/ Partly/ No/Unclear/ NA | Comments

| 1.1 | Is the study population appropriate for the review question? | Partly | Adults with depression, mixed depression and anxiety or anxiety |
| 1.2 | Are the interventions appropriate for the review question? | Yes | cCBT |
| 1.3 | Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
| 1.4 | Are the perspectives clearly stated and are they appropriate for the review question? | Yes | NHS (& societal) |
| 1.5 | Are all direct effects on individuals included, and are all other effects included where they are material? | Partly | HRQoL changes based on assumptions |
| 1.6 | Are all future costs and outcomes discounted appropriately? | NA | time horizon 8 months |
| 1.7 | Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | Partly | BDI main outcome; QALY estimated based on assumptions around BDI measurements |
| 1.8 | Are costs and outcomes from other sectors fully and appropriately measured and valued? | NA | |
| 1.9 | Overall judgement: Partially applicable | |

Other comments: None

### Section 2: Study limitations (level of methodological quality)

| 2.1 | Does the model structure adequately reflect the nature of the topic under evaluation? | NA | RCT |
| 2.2 | Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Partly | 8 months |
| 2.3 | Are all important and relevant outcomes included? | Partly | HRQoL changes based on assumptions |
| 2.4 | Are the estimates of baseline outcomes from the best available source? | Partly | RCT, N=274 |
| 2.5 | Are the estimates of relative intervention effects from the best available source? | Partly | RCT |
| 2.6 | Are all important and relevant costs included? | Yes | |
| 2.7 | Are the estimates of resource use from the best available source? | Partly | RCT |
| 2.8 | Are the unit costs of resources from the best available source? | Yes | National sources, intervention cost from manufacturer |
| 2.9 | Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes | |

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Partly</td>
<td>Statistical tests undertaken; bootstrapping conducted</td>
</tr>
<tr>
<td>Is there any potential conflict of interest?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Overall assessment: Potentially serious limitations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other comments:


Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the study population appropriate for the review question?</td>
<td>Partly</td>
<td>Adults with symptoms of depression</td>
</tr>
<tr>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>cCBT with support</td>
</tr>
<tr>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS &amp; PSS</td>
</tr>
<tr>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
<td>3.5% annually</td>
</tr>
<tr>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Overall judgement: Directly applicable</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other comments: None

#### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
<td>2 years</td>
</tr>
<tr>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=691; EQ-5D data available for n=416 at 24</td>
</tr>
</tbody>
</table>

2.5 Are the estimates of relative intervention effects from the best available source? Partly RCT

2.6 Are all important and relevant costs included? Yes

2.7 Are the estimates of resource use from the best available source? Partly RCT

2.8 Are the unit costs of resources from the best available source? Yes National sources

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? Yes

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? Yes Statistical tests undertaken; regression analysis to control for covariates conducted; Cholesky decomposition to account for covariance in costs and QALYs and PSA undertaken

2.11 Is there any potential conflict of interest? No

2.12 Overall assessment: Minor limitations


Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

Section 1: Applicability (relevance to specific review question and the NICE reference case)

1.1 Is the study population appropriate for the review question? Partly Adults with depressive symptoms in workplace

1.2 Are the interventions appropriate for the review question? Yes cCBT with support

1.3 Is the system in which the study was conducted sufficiently similar to the current UK context? Yes UK study

1.4 Are the perspectives clearly stated and are they appropriate for the review question? Yes NHS (& societal)

1.5 Are all direct effects on individuals included, and are all Yes

| other effects included where they are material? | NA | time horizon 12 weeks for outcomes; 6 weeks for costs |
| 1.6 Are all future costs and outcomes discounted appropriately? | | |
| 1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | Yes | |
| 1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? | NA | |
| 1.9 Overall judgement: Directly applicable | | |

**Section 2: Study limitations (level of methodological quality)**

<table>
<thead>
<tr>
<th></th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>No</td>
<td>12 weeks for outcomes; 6 weeks for costs</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=637; completion 56% at 6 weeks &amp; 36% at 12 weeks</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>No</td>
<td>Intervention cost appears to have been omitted</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Partly</td>
<td>Statistical tests undertaken; bootstrapping conducted but no uncertainty results reported</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Very serious limitations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other comments: inadequate reporting of results; no incremental analysis conducted (although it is possible to conduct from reported data) and no uncertainty results presented; intervention cost appears to have been omitted

**Economic Question:** psychological interventions as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th></th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Partly</td>
<td>Adults with moderate-severe depression</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>cCBT with and without support</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS &amp; PSS</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9 Overall judgement: Directly applicable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other comments: None</td>
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#### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th></th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
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<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=369; complete cost data across the trial period available for n=209</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

| 2.10 | Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes | Statistical tests undertaken; regression analysis to control for covariates conducted; Cholesky decomposition to account for covariance in costs and QALYs and PSA undertaken |

| 2.11 | Is there any potential conflict of interest? | No |

| 2.12 | Overall assessment: Minor limitations |

Other comments: |


**Economic Question:** psychological interventions as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
<tr>
<td>1.9</td>
<td>Overall judgement: Directly applicable</td>
<td></td>
</tr>
</tbody>
</table>

Other comments: None

Section 2: Study limitations (level of methodological quality) | Yes/ Partly/ No/Unclear/ NA | Comments
--- | --- | ---
2.1 Does the model structure adequately reflect the nature of the topic under evaluation? | NA | RCT
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Yes | 18 months
2.3 Are all important and relevant outcomes included? | Yes |
2.4 Are the estimates of baseline outcomes from the best available source? | Partly | RCT, N=440; QALYs available for n=309
2.5 Are the estimates of relative intervention effects from the best available source? | Partly | RCT
2.6 Are all important and relevant costs included? | Yes |
2.7 Are the estimates of resource use from the best available source? | Partly | RCT, costs available for n=327
2.8 Are the unit costs of resources from the best available source? | Yes | National sources
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes | Statistical tests including bootstrapping undertaken; CEACs presented
2.11 Is there any potential conflict of interest? | No |
2.12 Overall assessment: Minor limitations |

Other comments:

P.2.2.1 Pharmacological interventions


Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression

Section 1: Applicability (relevance to specific review question and the NICE reference case) | Yes/ Partly/ No/Unclear/ NA | Comments
--- | --- | ---
1.1 Is the study population appropriate for the review question? | Yes | Adults with depressive symptoms and a baseline HDRS-17 score 12-19
1.2 Are the interventions appropriate for the review question? | Yes |

| 1.3 | Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
| 1.4 | Are the perspectives clearly stated and are they appropriate for the review question? | Yes | Health and social services |
| 1.5 | Are all direct effects on individuals included, and are all other effects included where they are material? | Yes |
| 1.6 | Are all future costs and outcomes discounted appropriately? | NA | Time horizon 12 & 26 weeks |
| 1.7 | Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | Partly | Derived from SF-36; SF-6D UK algorithm used |
| 1.8 | Are costs and outcomes from other sectors fully and appropriately measured and valued? | NA |

1.9 Overall judgement: Directly applicable
Other comments: None

**Section 2: Study limitations (level of methodological quality)**

| 2.1 | Does the model structure adequately reflect the nature of the topic under evaluation? | NA | RCT |
| 2.2 | Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Partly | 26 weeks |
| 2.3 | Are all important and relevant outcomes included? | Yes |
| 2.4 | Are the estimates of baseline outcomes from the best available source? | Partly | RCT |
| 2.5 | Are the estimates of relative intervention effects from the best available source? | Partly | RCT, N=220; 12-week completers n=196; 6-month follow-up n=160 |
| 2.6 | Are all important and relevant costs included? | Yes |
| 2.7 | Are the estimates of resource use from the best available source? | Partly | RCT |
| 2.8 | Are the unit costs of resources from the best available source? | Yes | National sources |
| 2.9 | Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
| 2.10 | Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes | Bootstrapping conducted, CEACs presented |
| 2.11 | Is there any potential conflict of interest? | No |

2.12 Overall assessment: Minor limitations
Other comments:

Economic Question: pharmaceutical interventions as first-line treatment for adults with a new episode of depression

<table>
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<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
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<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with a new episode of depression presenting in primary care</td>
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<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
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<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
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<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Healthcare</td>
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<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
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<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
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<td>1.9 Overall judgement: Directly applicable</td>
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Other comments: None

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<th>Comments</th>
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<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Non-parametric bootstrapping</td>
</tr>
</tbody>
</table>
### Economic evidence – health economic checklists


<table>
<thead>
<tr>
<th></th>
<th>2.11 Is there any potential conflict of interest?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>

#### 2.12 Overall assessment: Minor limitations

Other comments:

### P.2.31 Physical interventions


**Economic Question:** physical therapy as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
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<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
<tr>
<td>1.9</td>
<td>Overall judgement: Directly applicable</td>
<td></td>
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</table>

Other comments: None

#### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th></th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
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</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
</tr>
<tr>
<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer/Details</th>
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</thead>
<tbody>
<tr>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly RCT</td>
</tr>
<tr>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes National sources; acupuncture cost based on published data</td>
</tr>
<tr>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes One-way SA; multiple imputation and regression analysis of costs and QALYs to account for baseline factors; PSA undertaken and CEACs presented</td>
</tr>
<tr>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
</tr>
<tr>
<td>Overall assessment: Potentially serious limitations</td>
<td>Other comments: results sensitive to changes in intervention costs and use of complete case analysis</td>
</tr>
</tbody>
</table>

---


**Economic Question:** physical therapy as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with a recent first or new episode of mild /moderate depression</td>
</tr>
<tr>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>Exercise</td>
</tr>
<tr>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS &amp; PSS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q</th>
<th>Question</th>
<th>Answer</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td>QALYs estimated using EQ-5D ratings (UK tariff)</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9</td>
<td>Overall judgement: Directly applicable</td>
<td></td>
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**Section 2: Study limitations (level of methodological quality)**

<table>
<thead>
<tr>
<th>Q</th>
<th>Question</th>
<th>Type</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>2.1</td>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT (N=361; at 12 months EQ-5D data n=195; complete resource use data n=156)</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
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<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
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<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>One-way SA; CEACs using bootstrapping</td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12</td>
<td>Overall assessment: Potentially serious limitations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Other comments:** results robust to multiple imputation used in sensitivity analysis; high attrition rates (>50%)

---

**P.2.41 Psychological, pharmacological, physical and combined interventions**

**Study: Guideline economic analysis**

**Economic Question:** psychological, pharmacological and combined interventions for treatment of new episodes
### Study: Guideline economic analysis

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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<td>Yes</td>
<td>Adults with a new episode of less severe depression</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
<td>Discount rate 3.5%</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>1.9 Overall judgement:</td>
<td>Directly applicable</td>
<td></td>
</tr>
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<td>Other comments:</td>
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### Section 2: Study limitations (level of methodological quality)

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<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>Study: Guideline economic analysis</td>
<td>supplemented by recent resource use data and costs</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes PSA conducted; CEACs presented</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
</tr>
<tr>
<td>2.12 Overall assessment: <strong>Minor limitations</strong></td>
<td></td>
</tr>
<tr>
<td>Other comments:</td>
<td></td>
</tr>
</tbody>
</table>

### P.3.1 Interventions for first-line treatment of adults with a new episode of more severe depression

#### P.3.1.3 Psychological interventions


**Economic Question:** psychological interventions as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes Adults with depression</td>
</tr>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes UK study</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes NHS</td>
</tr>
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<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA Time horizon 12 weeks</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
<tr>
<td>1.9</td>
<td>Overall judgement: Directly applicable</td>
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#### Section 2: Study limitations (level of methodological quality)

<table>
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<th>Item</th>
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### Economic evidence – health economic checklists


<table>
<thead>
<tr>
<th>Question</th>
<th>NA</th>
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<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td>Partly</td>
</tr>
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<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>No</td>
<td>12 weeks</td>
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<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td>Partly</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>No</td>
<td>RCT (N=459; economic analysis based on n=375 or 380, depending on outcome used)</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Yes</td>
<td>National sources &amp; published studies</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Yes</td>
<td>Partly</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources &amp; published studies</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Bootstrapping conducted, CEACs presented</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.12 Overall assessment: potentially serious limitations</td>
<td>Partly</td>
<td>Overall assessment: potentially serious limitations</td>
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#### Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Older adults aged ≥ 65 years with depression (BDI ≥14)</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>CBT</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>Health and social services</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
<td>HRQoL not measured</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Item</th>
<th>Question</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 10 months</td>
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<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
<td>BDI</td>
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<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
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</table>

1.9 Overall judgement: Partially applicable

Other comments: None

### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Item</th>
<th>Question</th>
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<th>Comments</th>
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<tbody>
<tr>
<td>2.1</td>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>10 months</td>
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<tr>
<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>HRQoL not measured</td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=204; analysis on n=167</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>No</td>
<td>Only primary and community healthcare services considered</td>
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<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT, analysis on n=198</td>
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<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Statistical tests including bootstrapping undertaken; CEACs presented</td>
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<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
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2.12 Overall assessment: Potentially serious limitations

Other comments:


**Economic Question:** psychological interventions as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
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<tr>
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<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Partly</td>
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<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
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<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
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1.9 Overall judgement: Directly applicable

Other comments: None

#### Section 2: Study limitations (level of methodological quality)

<table>
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<tbody>
<tr>
<td>2.1</td>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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</tr>
<tr>
<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
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Update 2017

2.11 Is there any potential conflict of interest? No
2.12 Overall assessment: Potentially serious limitations
Other comments:


**Economic Question:** psychological interventions as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with depression</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>Behavioural activation</td>
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<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
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<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS</td>
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<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 3 months</td>
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<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
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<td></td>
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1.9 Overall judgement: **Directly applicable**
Other comments: None

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<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
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<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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<td>3 months</td>
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<td>2.3 Are all important and relevant outcomes included?</td>
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<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT (N=47, completers n=38)</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
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<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
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<td>RCT</td>
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<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
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</table>

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? Yes

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? Yes Bootstrapping conducted, CEAC presented

2.11 Is there any potential conflict of interest? No

2.12 Overall assessment: potentially serious limitations

Other comments:


Economic Question: psychological interventions as first-line treatment for adults with a new episode of depression

Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
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<th>Yes/ Partly/ No/Unclear/ NA</th>
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<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
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<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
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1.9 Overall judgement: Partially applicable

Other comments: None

Section 2: Study limitations (level of methodological quality)

<table>
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<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
</tr>
</tbody>
</table>

2.4 Are the estimates of baseline outcomes from the best available source?  
Partly  
RCT (N=103; at 12 months n=81) & preference trial (N=220; at 12 months n=163)

2.5 Are the estimates of relative intervention effects from the best available source?  
Partly  
RCT & preference trial

2.6 Are all important and relevant costs included?  
Partly  
Only depression-related costs measured

2.7 Are the estimates of resource use from the best available source?  
Partly  
RCT (n=103) & preference trial (n=215)

2.8 Are the unit costs of resources from the best available source?  
Yes  
National sources & local costs for counsellors

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?  
Yes

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?  
Yes  
Statistical tests including bootstrapping undertaken; CEACs presented

2.11 Is there any potential conflict of interest?  
No

2.12 Overall assessment: Potentially serious limitations

Other comments:

P.3.21 Pharmacological interventions


Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression

Section 1: Applicability (relevance to specific review question and the NICE reference case)  
Yes/ Partly/ No/Unclear/ NA  
Comments

1.1 Is the study population appropriate for the review question?  
Yes  
Adults with a new episode of moderate to severe depression treated in primary care

1.2 Are the interventions appropriate for the review question?  
Yes

1.3 Is the system in which the study was conducted  
Yes  
UK study
<table>
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<tbody>
<tr>
<td><strong>1.4</strong> Are the perspectives clearly stated and are they appropriate for the review question?</td>
</tr>
<tr>
<td><strong>1.5</strong> Are all direct effects on individuals included, and are all other effects included where they are material?</td>
</tr>
<tr>
<td><strong>1.6</strong> Are all future costs and outcomes discounted appropriately?</td>
</tr>
<tr>
<td><strong>1.7</strong> Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
</tr>
<tr>
<td><strong>1.8</strong> Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
</tr>
<tr>
<td><strong>1.9</strong> Overall judgement: Directly applicable</td>
</tr>
<tr>
<td><strong>Other comments:</strong> None</td>
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**Section 2: Study limitations (level of methodological quality)**

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>2.1</strong> Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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<td></td>
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<tr>
<td><strong>2.2</strong> Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>48 weeks</td>
</tr>
<tr>
<td><strong>2.3</strong> Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>Disutility from side effects not considered</td>
</tr>
<tr>
<td><strong>2.4</strong> Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>Meta-analyses of clinical trials</td>
</tr>
<tr>
<td><strong>2.5</strong> Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>Meta-analyses of clinical trials - randomisation possibly broken</td>
</tr>
<tr>
<td><strong>2.6</strong> Are all important and relevant costs included?</td>
<td>Partly</td>
<td>Cost of side effects not considered</td>
</tr>
<tr>
<td><strong>2.7</strong> Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Expert opinion</td>
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<td><strong>2.8</strong> Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
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<td><strong>2.9</strong> Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td><strong>2.10</strong> Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td></td>
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<td><strong>2.11</strong> Is there any potential conflict of interest?</td>
<td>Yes</td>
<td>Funded by industry</td>
</tr>
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<td><strong>2.12</strong> Overall assessment: Potentially serious limitations</td>
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<td></td>
</tr>
<tr>
<td><strong>Other comments:</strong></td>
<td></td>
<td></td>
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</table>


**Economic Question:** pharmacological interventions as first-line treatment for adults with a new episode of depression

### Section 1: Applicability (relevance to specific review question and the NICE reference case)

| 1.1 Is the study population appropriate for the review question? | Yes | Adult outpatients with major depression |
| 1.2 Are the interventions appropriate for the review question? | Yes | (venlafaxine included but not considered for guideline) |
| 1.3 Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
| 1.4 Are the perspectives clearly stated and are they appropriate for the review question? | Yes | NHS |
| 1.5 Are all direct effects on individuals included, and are all other effects included where they are material? | Partly | Side effects not considered |
| 1.6 Are all future costs and outcomes discounted appropriately? | NA | Time horizon 24 weeks |
| 1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | Partly | Utility values estimated based on the presumed utilities of a depression-free day and a severely depressed day |
| 1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? | NA |

1.9 Overall judgement: Partially applicable

Other comments: None

### Section 2: Study limitations (level of methodological quality)

| 2.1 Does the model structure adequately reflect the nature of the topic under evaluation? | Yes |
| 2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Partly | 24 weeks |
| 2.3 Are all important and relevant outcomes included? | Partly | Side effects not considered |
| 2.4 Are the estimates of baseline outcomes from the best available source? | Partly | Meta-analysis of RCTs |
| 2.5 Are the estimates of relative intervention effects from the best available source? | Partly | Meta-analysis of RCTs; method of synthesis unclear, but randomisation appears to have

<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Partly</td>
<td>Costs of side effects not considered</td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Delphi panel</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>Yes</td>
<td>Funded by industry</td>
</tr>
</tbody>
</table>

#### 2.12 Overall assessment: Very serious limitations

Other comments:


**Economic Question:** pharmacological interventions as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with major depression (baseline MADRS score 18-40)</td>
</tr>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>(venlafaxine was included but not part of RQ)</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS and societal</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
<td>Side effects / HRQoL not considered</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 26 weeks</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No</td>
<td>Outcome was measured as % of remission (MADRS score ≤ 12)</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

1.9 Overall judgement: Partially applicable

Other comments: None

### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly, 26 weeks</td>
<td></td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly, HRQoL not measured</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly, Meta-analysis of RCTs</td>
<td></td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly, Meta-analysis of RCTs</td>
<td></td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Partly, Cost of side effects not considered</td>
<td></td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly, GP database and expert opinion</td>
<td></td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes, National sources</td>
<td></td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Partly, SA results not based on incremental analysis</td>
<td></td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>Yes, Funded by industry</td>
<td></td>
</tr>
</tbody>
</table>

2.12 Overall assessment: Potentially serious limitations

Other comments:

---


### Economic Question: pharmacological interventions as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes, Adults with major severe depression (baseline MADRS score ≥ 30)</td>
<td></td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted</td>
<td>Yes, UK study</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes - NHS and societal</td>
</tr>
<tr>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly - Side effects / HRQoL not considered</td>
</tr>
<tr>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA - Time horizon 26 weeks</td>
</tr>
<tr>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>No - Outcome was measured as % of remission (MADRS score ≤ 12)</td>
</tr>
<tr>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Section 2: Study limitations (level of methodological quality)**

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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</thead>
<tbody>
<tr>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly - 26 weeks</td>
</tr>
<tr>
<td>Are all important and relevant outcomes included?</td>
<td>Partly - HRQoL not considered</td>
</tr>
<tr>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly - Meta-analysis of RCTs</td>
</tr>
<tr>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly - Meta-analysis of RCTs</td>
</tr>
<tr>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly - Published literature and expert opinion</td>
</tr>
<tr>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes - National sources</td>
</tr>
<tr>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
</tr>
<tr>
<td>Is there any potential conflict of interest?</td>
<td>Yes - Funded by industry</td>
</tr>
</tbody>
</table>

**Overall judgement: Partially applicable**

Other comments: None

**P.3.31 Combined pharmacological and psychological interventions**

2

**Economic Question:** combination therapy as first-line treatment for adults with a new episode of depression

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with moderate / severe depression</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 15 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>Utilities used to estimate QALYs were derived from service users that valued vignettes using SG</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

1.9 Overall judgement: Partially applicable

Other comments: None

<table>
<thead>
<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td>Decision tree</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>15 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>Side effects not considered</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Yes</td>
<td>Systematic review &amp; meta-analysis</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Yes</td>
<td>Systematic review &amp; meta-analysis</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Partly</td>
<td>Costs of side effects not considered</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Published literature and expert opinion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.8</th>
<th>Are the unit costs of resources from the best available source?</th>
<th>Yes</th>
<th>National sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>One-way SA; PSA &amp; CEACs</td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

**2.12 Overall assessment: Minor limitations**

Other comments: costs and disutility associated with side effects not considered but since drugs were used in both arms of the model, the impact of this omission is considered to be negligible and depends on the difference of treatment discontinuation between the two arms.


**Economic Question:** combination therapy as first-line treatment for adults with a new episode of depression

#### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>1.1</th>
<th>Is the study population appropriate for the review question?</th>
<th>Yes</th>
<th>Adults with moderate or severe depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
<td>3.5% annually; time horizon 27 months</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td>EQ-5D (UK tariff)</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

**1.9 Overall judgement: Directly applicable**

**Other comments:** None

#### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>2.1</th>
<th>Does the model structure adequately reflect the nature of the topic under evaluation?</th>
<th>Yes</th>
<th>Decision tree</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
<td>27 months</td>
</tr>
</tbody>
</table>

2.3 Are all important and relevant outcomes included? Partly Side effects not considered

2.4 Are the estimates of baseline outcomes from the best available source? Partly NMA of RCTs identified in a database

2.5 Are the estimates of relative intervention effects from the best available source? Yes NMA of RCTs identified in a systematic database

2.6 Are all important and relevant costs included? Partly Costs of side effects not considered

2.7 Are the estimates of resource use from the best available source? Partly published literature based on expert opinion and RCT data

2.8 Are the unit costs of resources from the best available source? Yes National sources

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? Yes

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? Yes One-way SA; PSA & CEACs

2.11 Is there any potential conflict of interest? No

2.12 Overall assessment: Minor limitations

Other comments:

P.3.41 Physical interventions


Economic Question: physical therapy as first-line treatment for adults with a new episode of depression

Section 1: Applicability (relevance to specific review question and the NICE reference case) Yes/ Partly/ No/Unclear/ NA Comments

1.1 Is the study population appropriate for the review question? Yes Adults with major depression who require hospitalisation

1.2 Are the interventions appropriate for the review question? Yes ECT & medication

1.3 Is the system in which the study was conducted sufficiently similar to the current UK context? Yes UK study

1.4 Are the perspectives clearly stated and are they appropriate for the review question? Yes NHS

1.5 Are all direct effects on individuals included, and are all other effects included where they are material? Partly Impact of side effects

<table>
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<tr>
<th>Question</th>
<th>Rating</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
<tr>
<td>Are QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
<td>QALYs estimated based on preferences for vignettes using the McSad system valued by Canadian service users with previous depression using SG</td>
</tr>
<tr>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Overall judgement: Partially applicable</td>
<td></td>
<td></td>
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<tr>
<td><strong>Section 2: Study limitations (level of methodological quality)</strong></td>
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</tr>
<tr>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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<tr>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>Systematic review and further assumptions</td>
</tr>
<tr>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>Systematic review and further assumptions</td>
</tr>
<tr>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Published literature and expert opinion</td>
</tr>
<tr>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>PSA; 95% CI reported</td>
</tr>
<tr>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Overall assessment: Potentially serious limitations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other comments: None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Psychological, pharmacological and combined interventions

**Study: Guideline economic analysis**

**Economic Question:** psychological, pharmacological and combined interventions for treatment of new episodes

### Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
<tr>
<td>1.9 Overall judgement: Directly applicable</td>
<td></td>
</tr>
</tbody>
</table>

Other comments: None

### Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Study: Guideline economic analysis

| 2.8 | Are the unit costs of resources from the best available source? | Yes | National sources |
| 2.9 | Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
| 2.10 | Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes | PSA conducted; CEACs presented |
| 2.11 | Is there any potential conflict of interest? | No |
| 2.12 | Overall assessment: Minor limitations |

Other comments:

P.4.1 Interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

P.4.1.4 Psychological interventions


Economic Question: psychological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

Section 1: Applicability (relevance to specific review question and the NICE reference case) | Yes/ Partly/ No/Unclear/ NA | Comments |
---|---|---|
1.1 | Is the study population appropriate for the review question? | Yes | Adults with partially remitted major depression despite adequate clinical treatment |
1.2 | Are the interventions appropriate for the review question? | Yes |
1.3 | Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
1.4 | Are the perspectives clearly stated and are they appropriate for the review question? | Yes | NHS/PSS |
1.5 | Are all direct effects on individuals included, and are all other effects included where they are material? | Partly | HRQoL not measured |
1.6 | Are all future costs and outcomes discounted appropriately? | Partly | Annual rate of 6%; time horizon 17 months |
1.7 | Is QALY used as an outcome, and was it derived using | No | % of relapses |

NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).

1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? NA

1.9 Overall judgement: Partially applicable

Other comments: None

<table>
<thead>
<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>17 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>HRQoL not considered</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>RCT, N=158</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>RCT</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>RCT, full data on 65% of participants</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Partly</td>
<td>National sources; inpatient cost data from local sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>Statistical analyses conducted; CEAC presented</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Minor limitations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other comments:


**Economic Question:** psychological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review</td>
<td>Yes</td>
<td>Adults aged 18-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td>75 years with major depression, who had adhered to antidepressant medication for at least 6 weeks in primary care, but who continued to have significant depressive symptoms</td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS for cost-utility analysis; health &amp; social care provider for cost consequence analysis, with service user expenses and productivity losses assessed in additional analyses</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
<td>3.5% annually on costs and outcomes</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td>Other outcomes (e.g. response, remission) considered as well</td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

**Section 2: Study limitations (level of methodological quality)**

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>NA</td>
<td>RCT</td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
<td>3-5 years’ follow up</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>
### Economic evidence – health economic checklists


| 2.4 | Are the estimates of baseline outcomes from the best available source? | Partly | RCT, N=467 |
| 2.5 | Are the estimates of relative intervention effects from the best available source? | Partly | RCT |
| 2.6 | Are all important and relevant costs included? | Yes |
| 2.7 | Are the estimates of resource use from the best available source? | Partly | RCT |
| 2.8 | Are the unit costs of resources from the best available source? | Yes | National sources |
| 2.9 | Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
| 2.10 | Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Yes | Statistical analyses conducted; CEAC presented |

#### P.4.2.1 Pharmacological interventions


**Economic Question:** pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/Partly/No/Unclear/NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and</td>
<td>Partly</td>
</tr>
</tbody>
</table>

outcomes used in line with analytical perspectives taken (item 1.4 above).

1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? NA

1.9 Overall judgement: Partially applicable

Other comments: None

Section 2: Study limitations (level of methodological quality)

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>26 weeks</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>Large study of series of RCTs</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>No</td>
<td>Data for each arm obtained from 2 different studies, thus breaking rules of randomisation</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Partly</td>
<td>Cost of side effects not considered</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>PSA conducted but no CEAC presented</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Very serious limitations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other comments:</td>
<td>only incremental QALYs presented</td>
<td></td>
</tr>
</tbody>
</table>


Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

Section 1: Applicability (relevance to specific review question and the NICE reference case)

<table>
<thead>
<tr>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Economic evidence – health economic checklists</td>
<td></td>
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</tbody>
</table>

<p>| | | |</p>
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<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Partly</td>
</tr>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Partly</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Section 2: Study limitations (level of methodological quality)**

<table>
<thead>
<tr>
<th></th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
</tr>
</tbody>
</table>

| 2.6 Are all important and relevant costs included? | Yes | participants who had already received antidepressant therapy |
| 2.7 Are the estimates of resource use from the best available source? | Partly | Naturalistic study |
| 2.8 Are the unit costs of resources from the best available source? | Yes | National sources |
| 2.9 Is an appropriate incremental analysis presented or can it be calculated from the data? | Yes |
| 2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis? | Partly | CEACs presented for escitalopram versus each of the other drugs considered |
| 2.11 Is there any potential conflict of interest? | Yes | Funded by industry |

2.12 Overall assessment: Potentially serious limitations

Other comments:


Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

Section 1: Applicability (relevance to specific review question and the NICE reference case) | Yes/ Partly/ No/Unclear/ NA | Comments

| 1.1 Is the study population appropriate for the review question? | Yes | Adults with severe major depression who failed previous treatment with SSRIs |
| 1.2 Are the interventions appropriate for the review question? | Yes |
| 1.3 Is the system in which the study was conducted sufficiently similar to the current UK context? | Yes | UK study |
| 1.4 Are the perspectives clearly stated and are they appropriate for the review question? | Yes | Scottish NHS |
| 1.5 Are all direct effects on individuals included, and are all other effects included where they are material? | Yes |
| 1.6 Are all future costs and outcomes discounted appropriately? | NA | Time horizon 48 weeks |
| 1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | Yes |

<table>
<thead>
<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>48 weeks</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>Disutility from side effects not considered</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>Meta-analyses of clinical trials</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>Meta-analyses of clinical trials - randomisation possibly broken</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Partly</td>
<td>Cost of side effects not considered</td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>Yes</td>
<td>Funded by industry</td>
</tr>
</tbody>
</table>

2.12 Overall assessment: Potentially serious limitations
Other comments:


#### Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with major depression who have failed to achieve remission with SSRIs</td>
</tr>
</tbody>
</table>

| 1.2 | Are the interventions appropriate for the review question? | Yes |
| 1.3 | Is the system in which the study was conducted sufficiently similar to the current UK context? | Partly | US study |
| 1.4 | Are the perspectives clearly stated and are they appropriate for the review question? | Yes | 3rd party payer |
| 1.5 | Are all direct effects on individuals included, and are all other effects included where they are material? | Partly | Side effects and HRQoL not considered |
| 1.6 | Are all future costs and outcomes discounted appropriately? | NA | Time horizon 6 months |
| 1.7 | Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above). | No | Outcome measure was probability of remission |
| 1.8 | Are costs and outcomes from other sectors fully and appropriately measured and valued? | NA |

1.9 Overall judgement: Partially applicable

Other comments: None

### Section 2: Study limitations (level of methodological quality)

| 2.1 | Does the model structure adequately reflect the nature of the topic under evaluation? | Yes |
| 2.2 | Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | Partly | 6 months |
| 2.3 | Are all important and relevant outcomes included? | Partly | Side effects and HRQoL not considered |
| 2.4 | Are the estimates of baseline outcomes from the best available source? | Partly | Baseline data from published trials |
| 2.5 | Are the estimates of relative intervention effects from the best available source? | No | review of published trial data and further assumptions – synthesis by naïve addition of data (leading to breaking of randomisation) |
| 2.6 | Are all important and relevant costs included? | Yes |
| 2.7 | Are the estimates of resource use from the best available source? | Partly | Analysis of 1,814 persons enrolled in 10 antidepressant studies |
| 2.8 | Are the unit costs of resources from the best available source? | Unclear | Medication costs from national sources; other unit costs taken from other studies, unclear |

Update 2017

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Partly</td>
<td>Results of sensitivity analysis reported using primarily each intervention’s CER and not ICERs.</td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Very serious limitations</td>
<td>Other comments:</td>
<td></td>
</tr>
</tbody>
</table>

### Other comments:


### Economic Question: pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with treatment-resistant unipolar depression (TRD) defined as failure to respond to at least 2 previous antidepressants in the current episode of depression</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
</tr>
<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
<td>Side effects not considered</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 12 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

1.9 Overall judgement: Directly applicable

Other comments: Evidence on lithium derived from people who had failed at least one antidepressant

<table>
<thead>
<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
<td>12 months</td>
</tr>
<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>Side effects not considered</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
<td>Pooled trial data identified in a systematic review</td>
</tr>
<tr>
<td>2.5 Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
<td>Indirect comparison using a common baseline comparator; data on lithium not from TRD population</td>
</tr>
<tr>
<td>2.6 Are all important and relevant costs included?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.7 Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
<td>Clinical expert opinion; weighted medication costs were used, based on expert opinion</td>
</tr>
<tr>
<td>2.8 Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.11 Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12 Overall assessment: Potentially serious limitations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Other comments:


**Economic Question:** pharmacological interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review</td>
<td>Yes</td>
<td>Adults with</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>question?</th>
<th>major depression who responded inadequately to previous antidepressant therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>Are the interventions appropriate for the review question?</td>
</tr>
<tr>
<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
</tr>
<tr>
<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
</tr>
<tr>
<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
</tr>
<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
</tr>
<tr>
<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
</tr>
<tr>
<td>1.9</td>
<td>Overall judgement: Partially applicable</td>
</tr>
</tbody>
</table>

Section 2: Study limitations (level of methodological quality) Yes/ Partly/ No/Unclear/ NA Comments

| 2.1  | Does the model structure adequately reflect the nature of the topic under evaluation? | Yes |
| 2.2  | Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? | No 6 weeks |
| 2.3  | Are all important and relevant outcomes included? | Partly Side effects and HRQoL not considered |
| 2.4  | Are the estimates of baseline outcomes from the best available source? | Partly Pooled published trial data |
| 2.5  | Are the estimates of relative intervention effects from the best available source? | Partly Meta-analysis of published phase 3 clinical trials and indirect comparison using placebo as baseline comparator |
| 2.6  | Are all important and relevant costs included? | Yes |
| 2.7  | Are the estimates of resource use from the best available source? | Partly Administrative databases and assumptions |
| 2.8  | Are the unit costs of resources from the best available source? | Yes National |
P.5.1 Interventions aimed at preventing relapse in people whose depression has responded to treatment

P.5.1.3 Psychological interventions


Economic Question: psychological interventions for relapse prevention

<table>
<thead>
<tr>
<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with three or more previous major depressive episodes, on a therapeutic dose of maintenance antidepressants and currently in full or partial remission</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
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<tr>
<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS; societal perspective</td>
</tr>
<tr>
<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Partly</td>
<td>HRQoL not measured</td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>NA</td>
<td>Time horizon 15 months</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken</td>
<td>No</td>
<td>% of relapses prevented; number of</td>
</tr>
</tbody>
</table>

(item 1.4 above).

1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued? NA

1.9 Overall judgement: Partially applicable

Other comments: None

**Section 2: Study limitations (level of methodological quality)**

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<thead>
<tr>
<th></th>
<th>Yes/ Partly/ No/Unclear/ NA</th>
<th>Comments</th>
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<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Partly</td>
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<tr>
<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
</tr>
<tr>
<td>2.12</td>
<td>Overall assessment: Minor limitations</td>
<td></td>
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<tr>
<td>Other comments:</td>
<td></td>
<td></td>
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**Economic Question: psychological interventions for relapse prevention**

<table>
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<th>Comments</th>
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<tr>
<td>1.1</td>
<td>Is the study population appropriate for the review question?</td>
<td>Yes</td>
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<table>
<thead>
<tr>
<th></th>
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<th>maintenance antidepressant</th>
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<td>Are the interventions appropriate for the review question?</td>
<td>Yes</td>
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<td>1.3</td>
<td>Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
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<td>1.4</td>
<td>Are the perspectives clearly stated and are they appropriate for the review question?</td>
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<td>1.5</td>
<td>Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
</tr>
<tr>
<td>1.6</td>
<td>Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
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<tr>
<td>1.7</td>
<td>Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Partly</td>
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<td>1.8</td>
<td>Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
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<tr>
<td>1.9</td>
<td>Overall judgement: Directly applicable</td>
<td>Yes/Partly/No/Unclear/NA</td>
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**Section 2: Study limitations (level of methodological quality)**

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<td>2.1</td>
<td>Does the model structure adequately reflect the nature of the topic under evaluation?</td>
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<td>2.2</td>
<td>Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
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</tr>
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<td>2.3</td>
<td>Are all important and relevant outcomes included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.4</td>
<td>Are the estimates of baseline outcomes from the best available source?</td>
<td>Partly</td>
</tr>
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<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Partly</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
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</table>
### Psychological, pharmacological and combined interventions

#### Study: Guideline economic analysis

**Economic Question:** psychological, pharmacological and combined interventions for relapse prevention

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<th>Section 1: Applicability (relevance to specific review question and the NICE reference case)</th>
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<th>Comments</th>
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<tr>
<td>1.1 Is the study population appropriate for the review question?</td>
<td>Yes</td>
<td>Adults with depression that is in remission, at medium or high risk of relapse</td>
</tr>
<tr>
<td>1.2 Are the interventions appropriate for the review question?</td>
<td>Yes</td>
<td></td>
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<tr>
<td>1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?</td>
<td>Yes</td>
<td>UK study</td>
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<td>1.4 Are the perspectives clearly stated and are they appropriate for the review question?</td>
<td>Yes</td>
<td>NHS/PSS</td>
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<td>1.5 Are all direct effects on individuals included, and are all other effects included where they are material?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>1.6 Are all future costs and outcomes discounted appropriately?</td>
<td>Yes</td>
<td>Discount rate 3.5%</td>
</tr>
<tr>
<td>1.7 Is QALY used as an outcome, and was it derived using NICE’s preferred methods? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).</td>
<td>Yes</td>
<td></td>
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<tr>
<td>1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?</td>
<td>NA</td>
<td></td>
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<tr>
<td>1.9 Overall judgement: Directly applicable</td>
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Other comments: None

<table>
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<tr>
<th>Section 2: Study limitations (level of methodological quality)</th>
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<th>Comments</th>
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<tbody>
<tr>
<td>2.1 Does the model structure adequately reflect the nature of the topic under evaluation?</td>
<td>Yes</td>
<td></td>
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<tr>
<td>2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?</td>
<td>Yes</td>
<td>10 years</td>
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<tr>
<td>2.3 Are all important and relevant outcomes included?</td>
<td>Partly</td>
<td>Disutility due to serious (but rare) side effects not considered</td>
</tr>
<tr>
<td>2.4 Are the estimates of baseline outcomes from the best available source?</td>
<td>Yes</td>
<td>Review of naturalistic</td>
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</table>
## Study: Guideline economic analysis

<p>| | | | |</p>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>2.5</td>
<td>Are the estimates of relative intervention effects from the best available source?</td>
<td>Yes</td>
<td>Systematic review &amp; pairwise meta-analysis or NMA, as appropriate</td>
</tr>
<tr>
<td>2.6</td>
<td>Are all important and relevant costs included?</td>
<td>Partly</td>
<td>Cost of managing serious (but rare) side effects not considered</td>
</tr>
<tr>
<td>2.7</td>
<td>Are the estimates of resource use from the best available source?</td>
<td>Yes</td>
<td>Study based on large UK primary care database, supplemented by recent resource use data and costs</td>
</tr>
<tr>
<td>2.8</td>
<td>Are the unit costs of resources from the best available source?</td>
<td>Yes</td>
<td>National sources</td>
</tr>
<tr>
<td>2.9</td>
<td>Is an appropriate incremental analysis presented or can it be calculated from the data?</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?</td>
<td>Yes</td>
<td>PSA conducted; CEACs presented</td>
</tr>
<tr>
<td>2.11</td>
<td>Is there any potential conflict of interest?</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>2.12</td>
<td>Overall assessment: Minor limitations</td>
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<td></td>
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<tr>
<td>Other comments:</td>
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<td></td>
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</table>
Appendix Q: Economic evidence – evidence tables

Q.1 Service delivery models for people with depression

Q.1.1 Simple collaborative care – references to included studies


AND


## Study evidence tables

<table>
<thead>
<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Study population</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosanquet et al., 2017</td>
<td>UK</td>
<td>Cost-utility analysis</td>
<td>Adults aged ≥ 65 years with major depressive disorder. Exclusion criteria: alcohol dependency; psychotic symptoms; recent suicidal risk/self-harm; significant cognitive impairment</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Pragmatic, multi-centre open RCT (N=485)</td>
<td>ICER of SCC vs TAU: £26,010/QALY</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Source of efficacy and resource use data: RCT (Bosanquet2017); (N=485; at 18 months n=344; cost data available for n=447)</td>
<td>Probability of SCC being cost-effective: 0.39 and 0.55 at WTP £20,000 and £30,000/QALY, respectively.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Source of unit costs: national sources</td>
<td>Sensitivity analysis: Including only participants who engaged with 5 or more sessions in the analysis. ICER £9,876/QALY</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Perspective: NHS/PSS (intervention and primary care exclusively considered)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Currency: GBP£</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cost year: 2012/13</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time horizon: 18 months</td>
<td></td>
</tr>
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<td></td>
<td></td>
<td>Discounting: NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Applicability: directly applicable</td>
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<td></td>
<td></td>
<td>Quality: potentially serious limitations</td>
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1. Study population details.
2. Cost-utility analysis.
3. Intervention details.
4. Study design details.
5. Costs and outcomes details.
7. Comments.
<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green et al., 2014 UK Cost-utility analysis</td>
<td>Interventions: Simple collaborative care in addition to usual primary care (SCC), comprising care managers making 6-12 contacts with service users over 14 weeks; contacts involved education about depression, medication management, behavioural activation and relapse prevention instructions. Care managers provided GPs with advice on medication and regular updates on service user progress including medication adherence. Treatment as usual (TAU), defined as GP care that includes antidepressant treatment and referral for other treatments, including Improving Access to Psychological Therapies (IAPT) services</td>
<td>Adults with depression Multi-centre cluster RCT (N=581) Source of efficacy data: RCT (Richards2013); (data available for n=466) Source of resource use data: RCT (data available for n=447) Source of unit costs: national sources</td>
<td>Costs: intervention (care manager’s time and supervision by specialists), staff time (GP, mental health nurse, practice nurse, counsellor, mental health worker, social worker, home care worker, occupational therapist, psychiatrist, psychologist, psychiatric nurse/care coordinator), walk-in-centre, voluntary group, inpatient psychiatric and general stay, A&amp;E, day hospital, other outpatient contact, day care centre, drop-in club; informal care and service user expenses in sensitivity analysis Mean NHS/PSS cost per person (SD): SCC: £1,887 (£3,714); TAU: £1,571 (£2,442) Unadjusted difference: £316 Adjusted difference: £271 (95%CI: -£203 to £886) Primary outcome measure: QALY based on EQ-5D ratings (UK tariff); SF-6D (UK tariff) used in sensitivity analysis Mean number of QALYs per person (SD): SCC: 0.605 (0.261); TAU: 0.554 (0.286) Unadjusted difference: 0.051 Adjusted difference: 0.019 (95%CI: -0.019 to 0.06)</td>
<td>ICER of SCC vs TAU: £14,248/QALY Probability of SCC being cost-effective: 0.58 and 0.65 at WTP £20,000 and £30,000/QALY, respectively. Results robust to multiple imputation of missing data, use of SF-6D utility values, use of alternative SCC costs; SCC dominant using a broader perspective; excluding one participant with an extremely high level of self-reported resource use, ICER became £3,334/QALY and probability of cost effectiveness 0.76 and 0.79 at WTP £20,000 and £30,000/QALY, respectively</td>
<td>Perspective: NHS/PSS; broader perspective (informal care costs and service user expenses) considered in sensitivity analysis Currency: GBP£ Cost year: 2011 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: minor limitations</td>
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## Study Evidence Tables

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study type</th>
<th>Intervention details</th>
<th>Study population</th>
<th>Study design</th>
<th>Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simon et al., 2002</td>
<td>US</td>
<td>Cost effectiveness analysis</td>
<td>Interventions: Simple collaborative care comprising an educational book and videotape on effective management of depression; 2 visits to a depression prevention specialist including shared decision making on maintenance antidepressant treatment; plus 3 scheduled telephone contacts and 4 personalised mailings for monitoring depressive symptoms and treatment adherence (SCC) Treatment as usual (TAU), including primary care and referral to specialty mental health care</td>
<td>Adults with a history of either recurrent major depression (i.e. at least 3 depressive episodes in the previous 5 years) or dysthymia (depressive symptoms present continuously for the past 2 years) that had recovered from a depressive episode following antidepressant treatment in primary care</td>
<td>RCT (Katon2001)</td>
<td>Source of efficacy and resource use data: RCT; N=386, n=315 (82%) completed all follow-up assessments; n=377 (98%) remained enrolled throughout the follow-up period</td>
<td>Source of unit costs: local data</td>
<td>Costs: medication, staff time, any inpatient and outpatient services for mental health or general medical care Mean total cost per person: SCC: $2,691 (95% CI $2,320 to $3,062) TAU: $2,619 (95% CI $2,139 to $3,099) Incremental $13 (95% CI -$584 to $511), after adjustment for gender, age, baseline Hopkins Symptoms Checklist (HSCL) depression score and chronic disease score</td>
<td>ICER of SCC vs. TAU $1 per depression-free day (95% CI - $134 to $344)</td>
</tr>
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</table>
### Complex collaborative care – references to included studies

<table>
<thead>
<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Study population</th>
<th>Study design</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morriss et al., 2016 UK</td>
<td>Cost-utility analysis</td>
<td>Interventions: Complex collaborative care, comprising secondary outpatient specialist depression services offering tailored integrated pharmacological and psychological (CBT, MBCT and compassion focused therapy, as appropriate) treatment within a collaborative care approach for 12-15 months (CCC) Usual secondary mental health care (TAU)</td>
<td>Adults with persistent unipolar moderate or severe depression, with HDRS total≥16, GAF&lt;60, that have received treatment for depression for at least 6 months and are currently receiving secondary mental healthcare Multi-site single-blind RCT (N=187) Source of efficacy and resource use data: RCT</td>
<td>Costs: primary care (GP surgery and home attendances), practice / district / community psychiatric nurse, psychotherapist, inpatient and outpatient (psychiatric or other care, A&amp;E attendances, medication Mean total cost per person (95% CI): CCC: £9,315 (£7,547 to £11,084) TAU: £5,869 (£4,501 to £7,238) Incremental total cost (bias-corrected bootstrapped): £3,446 (£1,915 to £5,180) Primary outcome measure: QALYs based on EQ-5D-3L ratings (UK tariff) Mean QALYs per person (95% CI): CCC: 0.753 (0.659 to 0.847) TAU: 0.646 (0.538 to 0.754) Incremental QALYs (bias-corrected bootstrapped): 0.079 (0.007 to 0.149)</td>
<td>ICER of CCC vs. TAU £43,603/QALY Controlling for baseline differences and cluster effects: probability of CCC being cost-effective exceeds 0.50 at WTP of £42,000/QALY</td>
<td>Perspective: NHS and personal social services Currency: GBP£ Cost year: 2014 Time horizon: 18 months Discounting: NA Applicability: directly applicable Quality: minor limitations</td>
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</table>
### Study Country Study type

<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Study type</th>
<th>Study population</th>
<th>Study design</th>
<th>Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goorden et al., 2014 The Netherlands Cost-utility analysis</td>
<td>Interventions: Complex collaborative care (CCC) provided by a trained occupational physician – care manager who was guided by a web-based stepped care protocol and received close supervision by a consultant psychiatrist, in addition to treatment as usual. Service users were offered manual guided self-help, 6–12 sessions of problem solving treatment (PST), a workplace intervention and, if considered necessary, antidepressant medication. If symptoms were persistent after 18 weeks of</td>
<td>Sick-listed workers with major depression RCT (N=126)</td>
<td>Costs: intervention (occupational physician – care manager’s time, training and supervision), staff time (GP, mental health care professional, public and private psychologist/psychiatrist, operational physician, other specialist, paramedic, social worker, alternative medicine practitioner), self-help group, day care, psychiatric inpatient care, medication; productivity losses reported separately</td>
<td>Mean total healthcare cost per person: CCC €3,874 (95 %CI €2,778 to €5,718) TAU €4,583 (95 %CI €3,108 to €6,794) Primary outcome measure: QALYs based on EQ-5D ratings (Dutch tariff) Mean total number of QALYs per person: ICER of TAU vs CCC €14,589/QALY Following bootstrapping and inspection of the cost effectiveness plane: 75% of replications were in the south-west quadrant (CCC less costly and less effective), 21% into the north-west quadrant (CCC dominated), 3% in the south-east quadrant (CCC dominant), and 1% in the north-east quadrant (CCC more costly and</td>
<td>Perspective: healthcare system; productivity losses reported separately Currency: Euro (€) Cost year: 2009 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: minor limitations</td>
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<td>Study Country Study type</td>
<td>Intervention details</td>
<td>Study population Study design Data sources</td>
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<tr>
<td>Goorden et al., 2015 The Netherlands Cost-utility analysis</td>
<td>Interventions: Complex collaborative care (CCC) provided by a depression care manager, usually a qualified nurse, who collaborated with a GP and a liaison psychiatrist in order to provide and guide more structured and adherent depression treatment in primary care. Treatment consisted of problem solving, manual guided self-help (both provided by the care</td>
<td>People aged ≥17 years with major depression according to the MINI. Exclusion criteria: being suicidal, psychotic symptoms, dementia, drug or alcohol dependence, already under specialty mental health treatment RCT (N=150; 93</td>
<td>Costs: GP, psychiatric / mental health care practice nurse, psychiatric inpatient care, specialist outpatient care, private psychologist / psychiatrist, occupational physician, other specialist, paramedic, social worker, counselling centre for drugs, alcohol, etc, alternative medicine, self-help group, day care, psychotropic medication Mean total healthcare cost per person: CCC €4,011 (95% CI €2,679 to €5,513) TAU €2,838 (95% CI €2,463 to €3,244) Difference: €1,173 (95% CI, -€216 to €2726)</td>
<td>ICER of TAU vs CCC €53,717/QALY Probability of CCC being cost-effective: 0.20 and 0.70 at WTP €20,000 and €80,000/QALY, respectively.</td>
<td>Perspective: healthcare system; productivity losses reported separately Currency: Euro (€) Cost year: 2013 Time horizon: 12 months Discounting: NA Applicability: partially</td>
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<td>treatment, the service users were referred to secondary mental health care. Treatment as usual (TAU), comprising sickness guidance by the company’s occupational physician. Both interventions were provided at an occupational healthcare setting. Service users were free to engage in any other treatment as well.</td>
<td>Study population Study design Data sources</td>
<td>Costs and outcomes: description and values</td>
<td>Results: Cost-effectiveness</td>
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<td>CCC 0.11 (95% CI 0.07 to 0.14) TAU 0.16 (95%CI 0.11 to 0.19) Difference: -0.05 (95%CI -0.11 to 0.00)</td>
<td>more effective). Results not sensitive to day care and psychiatric inpatient care costs.</td>
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<td>manager), and, if necessary, antidepressants (prescribed by the GP). Care managers and GPs received training in CCC. Treatment as usual (TAU) in primary care, comprising prescription of antidepressants or referral to psychotherapy</td>
<td>identified by screening and 47 by GP referral) Source of efficacy and resource use data: RCT (Huijbregts 2013, n=93 identified by screening) Source of unit costs: national sources</td>
<td>Primary outcome measure: QALYs based on EQ-5D ratings (Dutch tariff) Mean total number of QALYs gained per person: CCC 0.07 (95% CI 0.05 to 0.09) TAU 0.05 (95% CI 0.03 to 0.06) Difference: 0.02 (95% CI −0.004 to 0.04)</td>
<td>applicable Quality: potentially serious limitations</td>
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### Medication management – references to included studies

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<tr>
<td>Bosmans et al., 2007 The Netherlands Cost effectiveness analysis</td>
<td>Interventions: Medication management (MM), comprising coaching and education by a pharmacist to improve adherence to antidepressant therapy. This consisted of 3 contacts with the pharmacist (mean duration 13-20 minutes) during which pharmacists gave service users information about the use of antidepressants, plus a take-home video reviewing important facts on depression and antidepressant treatment Treatment as usual (TAU) comprising standard oral and written information that is routinely issued in the</td>
<td>Adults with depression treated in primary care, with a new prescription for a non-tricyclic antidepressant, who had not received antidepressant treatment in the past 6 months RCT (N=151) Source of efficacy and resource use data: RCT (Brook2005, N=151; analysis based on n=88 completers of both 3- and 6-month follow-ups) Source of unit costs: national</td>
<td>Costs: intervention (25-minute take home video, drug coaching contacts at the pharmacy), healthcare and non-healthcare staff time (GP, psychologist, social worker, psychiatrist), other specialist outpatient appointment (homeopath, physiotherapist, community mental healthcare, haptonomist, magnetic therapist, acupuncture therapist, spiritualist, foot reflex therapist, company doctor), abdominal x-ray, medication, absenteeism from paid labour Mean societal cost per person: MM: €3,275; TAU: €2,961 Mean difference €315 (95%CI –€1,922 to €2,416). Mean direct cost per person: MM: €724; TAU: €712 Mean difference €12 (95%CI not reported). Primary outcome measures: adherence to antidepressant treatment measured using an electronic pill container; depressive symptoms measured using the Hopkins Symptom Checklist (HSCL) Mean adherence per arm:</td>
<td>From a societal perspective: ICER of MM vs. TAU €14,900 per extra person with improvement in adherence €2,550 per point improvement in SCL Probability of MM being cost-effective around 0.65 at WTP of €50,000 per extra person with improvement in adherence. Results robust to per protocol analysis, the price of producing the video-tape, the</td>
<td>Perspective: societal Currency: Euro (€) Cost year: 2002 Time horizon: 6 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations</td>
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<tr>
<td>Rubio-Valera et al., 2013 Spain Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Medication management (MM), comprising an educational intervention provided by the pharmacist, focusing on improving service users’ knowledge of antidepressant medication, making them aware of the importance of compliance to the medication, reassuring them about possible side-effects, and stressing the importance of carrying out GPs’ advice. In service users with a sceptical attitude towards antidepressants, the intervention aimed to reduce stigma. Pharmacists were trained</td>
<td>Adults aged 18-75 years initiating treatment with antidepressants because of depression RCT (N=179) Source of efficacy and resource use data: RCT (Rubio-Valera2012, N=179; 71% completed at 6 months; n=151 received intervention as allocated) Source of unit costs: regional sources</td>
<td>Costs: intervention (pharmacist time, pharmacist training), publicly funded healthcare services (GP, nurse, psychologist, psychiatrist, other medical specialists, social worker, hospital emergency visits, hospital stay, diagnostic tests, medication), privately funded healthcare services (psychiatrist, psychologist, medical specialist, GP), absenteeism from paid labour. Mean societal cost per person: MM: €1,091; TAU: €767 Mean difference €324 (95%CI –€97 to €745). Mean direct cost per person: MM: €444; TAU: €425 Mean difference €49 (95%CI not reported). Primary outcome measures: adherence to antidepressant treatment measured using electronic pharmacy records; remission of depressive symptoms defined as a reduction</td>
<td>Under a healthcare perspective: ICER of MM vs. TAU €962 per extra adherent service user €3,592/QALY TAU dominant in terms of remission Probability of MM being cost-effective 0.71 and 0.76 for WTP €6,000 /adherent service user and €30,000 /QALY, respectively. Using remission, maximum probability of MM being cost-effective 0.46. Results robust to per</td>
<td>Perspective: societal and healthcare Currency: Euro (€) Cost year: 2009 Time horizon: 6 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations</td>
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<td>for the intervention. Treatment as usual from GP and pharmacist (TAU), comprising filling the prescriptions, addressing service users’ questions about medication and giving basic advice about how to take the antidepressant.</td>
<td>in the Patient Health Questionnaire 9-item (PHQ-9) of at least 50%; QALYs based on EQ-5D ratings (Spanish tariff) Incremental probability of adherence per person: 0.04 (95%CI -0.2 to 0.1) Incremental probability of remission per person: -0.01 (95%CI -0.2 to 0.1) Incremental QALYs per person: 0.01 (95%CI -0.02 to 0.03)</td>
<td>protocol or complete case analysis, use of DSM-IV criteria for depression, intervention costs or method for estimating indirect costs.</td>
<td>protocol or complete case analysis, use of DSM-IV criteria for depression, intervention costs or method for estimating indirect costs.</td>
<td>protocol or complete case analysis, use of DSM-IV criteria for depression, intervention costs or method for estimating indirect costs.</td>
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Q.1.4.1 Stepped care – references to included studies

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<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Intervention details</th>
<th>Study population</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
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<tr>
<td>Mukuria et al., 2013 UK</td>
<td>Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Stepped care approach: Improving Access to Psychological Therapies (IAPT) service comprising: Step 1 watchful waiting; Step 2 guided self-help including bibliotherapy with support, computerised CBT with support and CBT-based telephone support for problem-solving; Step 3 CBT ± medication. IAPT was provided in addition to treatment as usual Treatment as usual alone (TAU), comprising GP care, primary care counselling and referral to mental health professionals in secondary care. IAPT was evaluated in Doncaster demonstration site. Comparator sites were selected to match IAPT site regarding size &amp; type of population served based on deprivation, ethnicity and age; People 16-64 years old with a new or recurrent episode of depression or anxiety, who were likely to benefit from psychological therapies. More than 95% of people in IAPT had a primary diagnosis of depression by their GP. Prospective cohort study with matched sites (N=403) Source of efficacy and resource use data: cohort study (N=403; available 8-month cost and QALY data for n=297) Source of unit costs: Costs: intervention (staff time, training, equipment, facilities and overheads), other mental healthcare (psychiatrist, psychologist, community psychiatric nurse, psychotherapist/ counsellor, other mental health professionals and voluntary sector services), primary and secondary care, social care; medication costs not considered Mean total cost per person (SD): IAPT: £1,190 (£2,193); TAU: £934 (£1,666) Unadjusted difference: £256 (95% CI: £266 to £779) Adjusted difference: £236 (95%CI: £214 to £689)</td>
<td>Source of efficacy and resource use data: cohort study (N=403; available 8-month cost and QALY data for n=297) Source of unit costs: Costs: intervention (staff time, training, equipment, facilities and overheads), other mental healthcare (psychiatrist, psychologist, community psychiatric nurse, psychotherapist/ counsellor, other mental health professionals and voluntary sector services), primary and secondary care, social care; medication costs not considered Mean total cost per person (SD): IAPT: £1,190 (£2,193); TAU: £934 (£1,666) Unadjusted difference: £256 (95% CI: £266 to £779) Adjusted difference: £236 (95% CI: £214 to £689)</td>
<td>ICER of IAPT vs. TAU £9,440 per participant with RCS improvement £29,500/QALY using SF-6D £16,857/QALY using predicted EQ-5D scores Probability of IAPT being cost-effective using SF-6D QALYs: &lt;0.40 at WTP £30,000/QALY; using EQ-5D QALYs: 0.38 and 0.53 at WTP £20,000 and £30,000 / QALY, respectively. Using national unit costs instead of IAPT financial data resulted in an ICER of £3,800 per participant achieving RCS improvement and</td>
<td>Perspective: NHS and social services; productivity losses estimated separately Currency: GBP£ Cost year: 2008/09 Time horizon: 8 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations</td>
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## Economic evidence – evidence tables

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<th>Study Country Study type</th>
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|                          | geographical location; local implementation of 'pathways to work'; ethnic diversity; recent changes in organisational structure. Also, comparator sites were selected based on how well they performed according to average Quality and Outcomes Framework points, a voluntary annual reward and incentive programme for all GPs in England that assesses areas of clinical care, organisation, patient experience & other services. | IAPT data and national sources | function were used in sensitivity analysis  
Proportion of people with a PHQ-9 RCS significant improvement (95% CI):  
IAPT: 0.221 (0.164 to 0.278)  
TAU: 0.205 (0.116 to 0.293)  
Unadjusted difference: 0.016 (-0.089 to 0.122)  
Adjusted difference: 0.025 (-0.078 to 0.127)  
Mean number of SF-6D QALYs per person (95% CI):  
IAPT: 0.026 (0.018 to 0.033)  
TAU: 0.018 (0.007 to 0.029)  
Unadjusted difference 0.007 (-0.006 to 0.021)  
Adjusted difference 0.008 (-0.005 to 0.021)  
Mean number of EQ-5D QALYs per person (95% CI):  
IAPT: 0.038 (0.027 to 0.049)  
TAU: 0.025 (0.009 to 0.040)  
Unadjusted difference: 0.013 (-0.007 to 0.033)  
Adjusted difference: 0.014 (-0.005 to 0.032) | £11,875/QALY using SF-6D |          |

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<th>Study Country Study type</th>
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<td>Ricken et al., 2011 Germany Cost effectiveness analysis</td>
<td>Interventions: Stepped care comprising a standardised stepwise drug treatment regimen (SC) Treatment as usual (TAU)</td>
<td>Adults with a depressive syndrome according to ICD-10, with an indication for antidepressant therapy, receiving care in an inpatient setting. Exclusion criteria: organic mental disorders, alcohol or substance dependence, substance-related affective disorders, ongoing prophylactic medication with a mood stabilizer that could not be discontinued, a new antidepressant started within the last 21 days, postpartum depression, pregnancy or breast-feeding, severe general medical illness prohibiting standard antidepressant medication, involuntary court ordered hospitalisation, and/or rejection of psychopharmacology treatment. RCT (N=148) Source of efficacy and resource use data: RCT (Bauer2009, N=148; completers n=103) Source of unit costs: national sources</td>
<td>Costs: medication, hospitalisation Mean hospitalisation cost per person (SD): SC: €10,830 (€8,632); TAU: €15,202 (€12,483), p=0.026 Mean medication cost per person (SD): SC: €155 (€183); TAU: €184 (€216), p=0.188 Primary outcome measures: remission, defined as a Bech–Rafaelsen-Melancholia-Scale (BRMS) score &lt;7 Probability of remission: SC: 0.541; TAU: 0.392 Hazard ratio 2.02, p=0.07</td>
<td>SC dominant</td>
<td>Perspective: 3rd party payer Currency: Euro (€) Cost year: likely 2004 Time horizon: time from enrolment to study endpoint, i.e. dropout or remission Discounting: NA Applicability: partially applicable Quality: potentially serious limitations</td>
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### Integrated care pathways – references to included studies


### Study Country
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<th>Intervention details</th>
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<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
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<td>Pyne et al., 2015 US</td>
<td><strong>Interventions:</strong> On-site, practice-based integrated care, comprising treatment provided by local primary care providers, coordinated by on-site nurse depression care managers; the latter contacted service users either face-to-face or by telephone. Service users could be referred to specialists at off-site locations. Off-site, telemedicine-based integrated care, which used off-site specialists to support local primary care providers. Five types of providers were involved: on-site primary care providers, off-site depression care managers who contacted service users via telephone, a psychologist, a psychiatrist and a clinical pharmacist. At any time service users had access to CBT delivered via interactive video.</td>
<td><strong>Study design</strong></td>
<td><strong>Costs:</strong> intervention (training of depression care managers, education material, interactive video equipment, staff time, telephone line), outpatient visits, inpatient care, emergency room care, medication, service users' time and mileage. Adjusted incremental total cost per person: Off-site vs. on-site $1,146 (95%CI $396 to $1,897); p=0.003. Primary outcome measures: number of depression-free days derived from the 20-item HSCL (score ≤ 0.5 indicated depression-free day, ≥ 1.7 full symptoms and intermediate severity scores were assigned a value between depression-free and fully symptomatic by linear interpolation); QALYs based on SF-12/SF-6D algorithm (UK tariff). Adjusted incremental number of depression-free days per person off-site vs. on-site: 110 (95%CI 80 to 140); p&lt;0.001 Adjusted incremental QALYs per person off-site vs. on-site: 0.04 (95%CI 0.02 to 0.07); p=0.003.</td>
<td>ICER of off-site vs. on-site $36,033/QALY using regional costs $28,126/QALY using national costs ICER using depression-free days as the measure of outcome reported only after exclusion of inpatient costs: $10.75 / depression-free day Probability of off-site being cost-effective 0.86 at WTP $50,000/QALY Results sensitive to telephone line charges</td>
<td><strong>Perspective:</strong> healthcare &amp; service users' time and mileage <strong>Currency:</strong> US$ <strong>Cost year:</strong> 2009 <strong>Time horizon:</strong> 18 months <strong>Discounting:</strong> NA <strong>Applicability:</strong> partially applicable <strong>Quality:</strong> minor limitations</td>
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<td>Study Country</td>
<td>Study type</td>
<td>Interventions</td>
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<td>Wiley-Exley <em>et al.</em>, 2009 US</td>
<td>Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Integrated care (IC) comprising collaboration between primary and specialty mental health care; a behavioural health professional was co-located in the primary care setting and the primary care provider continued involvement in the mental health care of the service user. Primary care with a specialty referral system (SRS) for referral to a behavioural health provider outside the primary care setting, who had primary responsibility for the mental health needs of the service user. Both service delivery models were assessed within and outside the Veteran Affairs (VA) system.</td>
<td>Adults above 65 years of age with depression (major or minor)</td>
<td>Multi-site pragmatic RCT (N=840)</td>
<td>Costs: outpatient visits, inpatient care, nursing home, rehabilitation, emergency room, medication, service users’ and caregivers’ time and travel costs. Adjusted incremental total cost per person: All: VA: -$651, p=ns; Non-VA: $46, p=ns Major depression: VA: $877, p=ns; Non-VA: -$380, p=ns</td>
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Source of efficacy and resource use data: RCT (Krahn2006, N=840); within VA n=365, outside VA n=475; individuals with major depression within VA n=214, outside VA n=302) Source of unit costs: national sources

Primary outcome measures: Center for Epidemiologic Studies Depression Scale (CES-D) score; number of depression-free days (DFD) derived from the 20-item CES-D (score =0 indicated depression-free day, ≥ 16 full symptoms and intermediate severity scores were assigned a value between depression-free and fully symptomatic by linear interpolation); QALYs estimated based on depression-free days (QALY-DFD), using utility weights of health=1, depression=0.59); QALYs estimated based on SF-36 (QALY-SF), using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG

Adjusted incremental CES-D score per person: $322/CES-D point change $94/DFD $45,965/QALY-DFD $58,815/QALY-SF

Probability of IC being cost-effective <0.50 for WTP of $40,000/QALY-SF and above Major depression non-VA sample:
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<td>All: VA: -1.3, p=ns; Non-VA: 2.9, p&lt;0.01 Major depression: VA: -2.8, p&lt;0.05; Non-VA: 3.45, p&lt;0.05 Adjusted incremental DFDs per person: All: VA: 3.89, p=ns; Non-VA: -5.73, p=ns Major depression: VA: 9.29, p=ns; Non-VA: -5.20, p&lt;0.05 Adjusted incremental QALY-DFD per person: All: VA: 0.005, p=ns; Non-VA: -0.016, p&lt;0.05 Major depression: VA: 0.019, p=ns; Non-VA: -0.011, p&lt;0.05 Adjusted incremental QALY-SF per person: All: VA: 0.007, p=ns; Non-VA: 0.0004, p=ns Major depression: VA: 0.015, p=ns; Non-VA: -0.005, p=ns</td>
<td>SRS is dominant in terms of CES-D ICER of SRS vs. IC: $73/DFD $34,167/QALY-DFD $79,590/QALY-SF Probability of IC being cost-effective &gt;0.50 for WTP $50,000/QALY-SF and above</td>
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Q.2.1 Interventions for first-line treatment of adults with a new episode of less severe depression

Q.2.1.2 Psychological interventions – references to included studies

3 Problem solving

7 AND


11 Psychodynamic counselling

14 Computerised CBT

19 Computerised CBT with support
Depression in adults: treatment and management
Economic evidence – evidence tables

1 Computerised CBT with support vs computerised CBT

7 Behavioural activation versus cognitive behavioural therapy (CBT)
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<tr>
<td>Kendrick et al., 2005 &amp; 2006a UK Cost-utility analysis</td>
<td>Interventions: Problem-solving treatment provided by nurses Generic community mental health (MH) nurse care Usual GP care</td>
<td>Adults with a new episode of anxiety, depression or reaction to life difficulties with duration of symptoms 4 weeks to 6 months; and a General Health Questionnaire 12-item version (GHQ–12) ≥3. 75% of participants had depression. Exclusion criteria: current psychological treatment or contact with psychiatric services; severe mental disorder or substance misuse; dementia; active suicidal ideas Pragmatic RCT (N=247) (Kendrick2006) Source of efficacy &amp; resource use data: RCT, analysis based on n=184 with clinical data available; cost data available for n=159 Source of unit costs: national sources</td>
<td>Costs: intervention, training &amp; supervision, medication, staff time (GP, practice nurse, counsellor, social worker, psychiatrist, psychologist), outpatient visit, A&amp;E, inpatient care, other hospital contacts For societal perspective: out of pocket expenses and productivity losses Mean total NHS cost per person (SD): Problem solving: £608 (£501) MH nurse care: £569 (£350) GP care: £283 (£300) Adjusted differences vs GP care (95% CI): Problem solving: £325 (£204 to £484) MH nurse care: £286 (£174 to £411) Outcome measure: QALY based on EQ-5D ratings (UK tariff) Mean QALYs gained per person (SD): Problem solving: 0.39 (0.09) MH nurse care: 0.40 (0.07) GP care: 0.40 (0.07) Adjusted differences in QALY vs GP care (95% CI): Problem solving: -0.02 (-0.05 to 0.012) MH nurse care: 0 (-0.03 to 0.03)</td>
<td>Under NHS perspective: usual GP care dominant Perspective: NHS (and societal) Currency: GBP£ Cost year: 2003 Time horizon: 26 weeks Discounting: NA Applicability: directly applicable Quality: minor limitations</td>
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<tr>
<td>Study Country Study type</td>
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<td>Simpson et al., 2003 UK</td>
<td>Interventions: Psychodynamic counselling (6-12 sessions each lasting 50 min) provided by highly trained, BAC accredited counsellors, who received regular supervision in addition to GP treatment as usual.</td>
<td>Adults aged 18-70 with depression (BDI 14-40) lasting at least 6 months, with or without comorbid anxiety. Exclusion criteria: symptoms of anxiety only; depression lasting &gt;5 years; people ‘difficult’ or ‘hard to treat’; history of drug or alcohol related problems, suicide attempts or psychosis; had seen a counsellor in the last 6 months.</td>
<td>Costs: GPs, practice nurses &amp; counsellors, medication, specialist mental health, hospital, community health and social care services. Mean total cost per person (sd): Psychodynamic counselling £1046 (£1728), TAU £1074 (£1509); mean difference -£28, adjusted 95%CI £597 to £588.</td>
<td>No significant differences in costs or outcomes between interventions.</td>
<td>Perspective: health and social services. Currency: GBP£. Cost year: 1998. Time horizon: 12 months. Discounting: NA. Applicability: partially applicable. Quality: potentially serious limitations.</td>
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<td>Kaltenthaler et al., 2006 UK Cost-utility analysis</td>
<td>Interventions: Computerised CBT – 3 packages examined: Beating the Blues (cCBT1) Cope (cCBT2) Overcoming Depression (cCBT3) Treatment as usual, defined as GP visits, medication and possible referral to a specialist (TAU)</td>
<td>Adults with depression treated in a primary care setting Decision-analytic modelling Source of efficacy data: analysis of RCT individual-level data for cCBT1 and cCBT2; published RCT data for cCBT3; and further assumptions Source of resource use data: manufacturer submissions, published data and other assumptions Source of unit costs: national sources</td>
<td>Costs: intervention (licence fees, computer hardware, screening of patients for suitability, clinical support, capital overheads, training), healthcare costs according to severity of depression (including medication, primary, inpatient and outpatient care) Mean total cost per person: cCBT1: £584 cCBT2: £630 cCBT3: £501 TAU: £437 Outcome measure: QALY estimated based on EQ-5D (UK tariff) Mean QALYs per person cCBT1: 1.10 cCBT2: 1.05 cCBT3: 1.03 TAU: 1.02</td>
<td>ICER vs TAU: cCBT1: £1,801/QALY cCBT2: £7,139/QALY cCBT3: £5,391/QALY Probability of each intervention being cost-effective vs TAU at WTP £30,000/QALY: cCBT1: 0.87 cCBT2: 0.63 cCBT3: 0.54</td>
<td>Perspective: NHS Currency: GBP£ Cost year: likely 2003 Time horizon: 18 months Discounting: 3.5% annually Applicability: directly applicable Quality: potentially serious limitations</td>
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<td>Study Country</td>
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<td>McCrone et al., 2004 UK</td>
<td>Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Computerised CBT (Beating the Blues), consisting of a 15min introductory video followed by 8 50min sessions of CBT (cCBT) Treatment as usual (TAU), consisting of a variety of interventions, including discussions with the GP, referral to a counsellor, practice nurse or mental health professional, and treatment of physical conditions.</td>
<td>Adults aged 18-75 years with a diagnosis of depression, mixed depression and anxiety or anxiety disorders, who were not currently receiving face-to-face psychological therapy RCT (Proudfoot2004a, N=274) Source of efficacy and resource use data: RCT (cost data available for n=261)</td>
<td>Costs: intervention (programme, computers and overheads), inpatient care (physical and psychiatric), outpatient care, day surgery, A&amp;E, staff time (GP, practice nurse, district nurse, CPN, nurse practitioner, counsellor, clinical psychologist, psychiatrist, health visitor, social worker, physiotherapist, other therapist), psychotropic medication, other services Productivity losses considered in societal perspective Mean total NHS cost per person (SD): cCBT: £397 (£589); TAU: £357 (£575) Mean difference: £40 (90% CI £28 to £148) Outcome measures: BDI score; number of depression-free days (DFDs) defined based on BDI scores; QALY assuming that a DFD scores 1 and a day with depression scores 0.59 Outcome results: BDI difference: -3.5 (95% CI 0.6–6.4) Number of DFDs (SD): cCBT: 89.7 (74.2); TAU 61.0 (67.1) Difference: 28.4 (95% CI 10.7-45.5). Difference in QALYs: 0.032</td>
<td>ICER of cCBT vs TAU: £11/point improvement on BDI £1/DFD £1,250/QALY Probability of cCBT being cost-effective: 0.14 and 0.81 at WTP zero and £40 per point improvement in BDI, respectively 0.15 and 0.80 at WTP zero and £5 per additional DFD, respectively 0.85 and 0.99 at WTP £5,000 and £15,000 per QALY, respectively</td>
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<td>Littlewood et al., 2015 UK Cost-utility analysis</td>
<td>Interventions: Computerised, commercially produced CBT (Beating the Blues) with therapist support in addition to treatment as usual (cCBT1) Computerised, free to use cCBT (MoodGYM) with therapist support in addition to treatment as usual (cCBT2) Treatment as usual, comprising GP care with no constraints on the range of treatments that could be accessed (TAU)</td>
<td>Adults with symptoms of depression (PHQ-9 score ≥10) Pragmatic multicentre RCT (Gilbody2015, N=691) 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) Source of unit costs: national sources</td>
<td>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) Mean total cost per person (SE): cCBT1: £1,186 (£80) cCBT2: £1,098 (£135) TAU: £1,121 (£62) Adjusted mean differences (95% CI) cCBT1 vs TAU: £104 (-£67 to £275) cCBT2 vs TAU: £106 (-£262 to £50) Primary outcome measure: QALYs estimated based on EQ-5D (UK tariff) Number of QALYs per person (SE): cCBT1: 1.333 (0.034) cCBT2: 1.356 (0.033) TAU: 1.389 (0.033) Adjusted mean differences (95% CI) cCBT1 vs TAU: -0.044 (-0.117 to 0.030) cCBT2 vs TAU: -0.015 (-0.092 to 0.061)</td>
<td>cCBT1 dominated by TAU TAU vs cCBT2 £6,933/QALY Probability of each intervention being cost effective at WTP £20,000/QALY: cCBT1: 0.038 cCBT2: 0.417 TAU: 0.545 Using SF-6D QALYs: cCBT1 dominated by TAU cCBT2 dominant Probability of each intervention being cost-effective at WTP £20,000/QALY: cCBT1: 0.007 cCBT2: 0.756 TAU: 0.237 Results robust to inclusion of depression-related costs only and to consideration of completers’ data only (instead of imputed data analysis) Little evidence of an interaction effect between preference and treatment allocation on outcomes</td>
<td>Perspective: NHS &amp; PSS Currency: GBP£ Cost year: 2012 Time horizon: 2 years Discounting: 3.5% annually Applicability: directly applicable Quality: minor limitations</td>
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<td>Phillips et al., 2014 UK Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Computerised CBT (MoodGYM) comprising 5 1hr modules, usually taken weekly, plus support in the form of telephone interviews (cCBT) ‘Attention’ control (five websites with general information about mental health)</td>
<td>Adults with depressive symptoms, as measured by PHQ-9 responses, identified via occupational health settings Pragmatic RCT (Phillips2014, N=637) Source of efficacy and resource use data: RCT (for clinical analysis: completion 56% at 6 weeks; 36% at 12 weeks; for cost analysis: completion rates not reported) Source of unit costs: national sources</td>
<td>Costs: hospital (inpatient and outpatient care), community services, staff time (GP, psychiatrist, district nurse, counsellor, occupational health providers, other providers, medication) Intervention cost appears to have been omitted from analysis Productivity losses considered in societal perspective Mean total NHS cost per person (SD): cCBT: £29 (£110); Control: £38 (£125) Outcome measures: Work and Social Adjustment Scale (WSAS); QALYs estimated based on EQ-5D (UK tariff) Outcome results: WSAS difference: -0.470 (95% CI -1.837 to 0.897) QALY: cCBT: 0.082; control: 0.083 at 6 weeks cCBT: 0.167; control: 0.170 at 12 weeks</td>
<td>ICER of control vs cCBT: £3,667/QALY</td>
<td>Perspective: NHS (and societal) Currency: GBP£ Cost year: likely 2010 Time horizon: 12 weeks for outcomes; 6 weeks for costs Discounting: NA Applicability: directly applicable Quality: very serious limitations</td>
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<td>Brabyn et al., 2016 UK Cost-utility analysis</td>
<td>Interventions: Telephone-facilitated computerised CBT (cCBT1) Minimally</td>
<td>Adults with depression, as defined by a PHQ9 score of ≥ 10 and &lt; 3 for item 9 (measuring suicidal thoughts), not currently in receipt of cCBT or specialist psychological therapy;</td>
<td>Costs: intervention (telephone support), community care (GP visits and home visits, nurse, counsellor, psychiatric nurse, other primary care, all day based services), hospital services (inpatient mental health care, inpatient non-mental health care, outpatient</td>
<td>cCBT1 dominant over cCBT2 Probability of cCBT1 being cost effective at WTP £20,000 and £30,000/QALY: 0.55</td>
<td>Perspective: NHS &amp; PSS Currency: GBP£ Cost year: 2013 Time horizon: 12 months</td>
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<td>Supported computerised CBT (cCBT2)</td>
<td>In both arms a freely available cCBT program was used (MoodGYM)</td>
<td>Antidepressant medication or comorbid physical illness or non-psychotic functional disorders not excluded. Exclusion criteria: actively suicidal, bereaved or given birth within the last year, diagnosis of psychotic depression, primary diagnosis of alcohol or drug abuse</td>
<td>Psychiatric visit, clinical psychologist, non-mental health outpatient visits, medication</td>
<td>Results robust to inclusion of mental health-related costs only</td>
<td>Discounting: NA Applicability: directly applicable Quality: minor limitations</td>
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<tr>
<td>Richards et al., 2016 UK Cost-utility analysis</td>
<td>Interventions: Behavioural activation (20 sessions over 16 weeks, plus 4 booster sessions if participants wanted them)</td>
<td>Adults meeting DSM-IV criteria for major depressive disorder from primary care and psychological therapy services Exclusion criteria: people receiving psychological therapy; alcohol or drug dependence; acutely suicidal or attempted suicide in past 2</td>
<td>Costs: intervention, community health and social care, hospital, medication</td>
<td>BA dominant Probability of BA being cost-effective: 0.8 at a WTP of £20,000-£30,000/QALY Results robust</td>
<td>Perspective: NHS &amp; PSS Currency: GBP£ Cost year: 2014 Time horizon: 18 months Discounting:</td>
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## Economic evidence – evidence tables

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<td>months; cognitive impairment; bipolar disorder or psychosis or psychotic symptoms</td>
<td>Mean QALY per person (SD): BA: 0.985 (0.422) CBT: 0.935 (0.433) Difference: 0.050 (-0.046 to 0.145)</td>
<td>to imputation of missing data</td>
<td>3.5% annually Applicability: directly applicable Quality: minor limitations</td>
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<td>delivered by Band 5 therapists (BA) Cognitive behavioural therapy (20 sessions over 16 weeks, plus 4 booster sessions if participants wanted them) delivered by Band 7 therapists (CBT)</td>
<td>Non-inferiority RCT (Richards2016, N=440) Source of efficacy and resource use data: RCT (costs available for n=327; outcomes available for n=309) Source of unit costs: national sources</td>
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### Pharmacological interventions – references to included studies

2. **SSRIs (fluvoxamine, sertraline, paroxetine, citalopram or escitalopram) plus GP supportive care vs. GP supportive care alone**


3. **TCAs (amitriptyline, dothiepin or imipramine) versus SSRIs (fluoxetine, sertraline or paroxetine) versus lofepramine**


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<tr>
<td>Kendrick et al., 2009 UK Cost effectiveness and cost-utility analysis</td>
<td>Interventions: SSRIs (fluoxetine, fluvoxamine, sertraline, paroxetine, citalopram or escitalopram) plus GP supportive care GP supportive care alone, comprising</td>
<td>Adults with depressive symptoms for ≥ 8 weeks, who had received no antidepressant treatment within the previous 12 months, were not in receipt of counselling or psychological therapies at baseline, had a baseline HAMD17 score 12-19 and at least one</td>
<td>Costs: medication, primary care (face-to-face GP consultations, GP telephone contacts, practice nurse contacts), secondary care (inpatient, outpatient, day patient, accident and emergency), community health services (health visitors, district nurses, counselling or psychological therapists), social care services (social workers, housing workers) Mean (SD) total cost per person: At 12 weeks: SSRI &amp; GP: £341 (£454); GP alone: £388 (£932) Difference adjusted for baseline:</td>
<td>12 weeks SSRI &amp; GP dominates GP alone At zero WTP per unit of reduction on HAMD17, probability of SSRI &amp; GP being cost-effective was 54.9% At a WTP of £20,000–£30,000/QALY, probability of SSRI &amp; GP dominates GP alone</td>
<td>Perspective: health and social care Currency: UK£ Cost year: 2007 Time horizon: 12 and 26 weeks Discounting: NA Applicability: directly applicable</td>
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### Economic evidence – evidence tables

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<tr>
<td>UK</td>
<td>RCT (Kendrick 2009, N=220)</td>
<td>Consultations at 2, 4, 8 and 12 weeks after the baseline assessment</td>
<td>Symptom on the Bradford Somatic Inventory (BSI). Exclusion criteria: significant substance misuse and an Alcohol Use Disorders Identification Test (AUDIT) score ≥ 12</td>
<td>RCT (Kendrick 2009, N=220)</td>
<td>Source of efficacy &amp; resource use data: RCT (N=220; 12-week completers n=196; 6-month follow-up n=160)</td>
<td>-£28 (95% CI -£656 to £117) At 26 weeks: SSRI &amp; GP: £759 (£1730); GP alone: £629 (£1092) Difference adjusted for baseline: £153 (95% CI -£500 to £304) Outcome measures: HAMD17 score; QALY based on SF-36 ratings (UK tariff) Mean (SD) HAMD17 score per person: At 12 weeks SSRI &amp; GP: 8.73 (5.20); GP alone: 11.22 (5.78) At 26 weeks SSRI &amp; GP: 7.92 (5.67); GP alone: 9.73 (5.57) Mean QALYs gained per person: From baseline to 12 weeks SSRI &amp; GP 0.159; GP alone 0.152 Difference adjusting for baseline 0.005 From baseline to 26 weeks SSRI &amp; GP 0.331; GP alone 0.318 Difference adjusted for baseline 0.010</td>
<td>GP being cost-effective was 80-85%. 26 weeks ICER of SSRI &amp; GP vs. GP alone £90/unit of improvement on HAMD17 or £14,854/QALY SSRI &amp; GP has a greater than 0.50 probability of being cost-effective when the WTP exceeds £80 per unit reduction on HAMD17 At a WTP at £20,000–£30,000/QALY, probability of SSRI &amp; GP being cost-effective was 0.65-0.75</td>
<td>Quality: minor limitations</td>
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<th>Study Country</th>
<th>Study type</th>
<th>Interventions: TCAs (amitriptyline, dothiepin or imipramine)</th>
<th>Study population</th>
<th>Study design</th>
<th>Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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<tr>
<td>UK</td>
<td>RCT (Peveler et al., 2005 and Kendrick et al., 2006b)</td>
<td>TCAs (amitriptyline, dothiepin or imipramine)</td>
<td>Adults with a new episode of depression willing to receive antidepressant treatment in primary care, including those with comorbid physical or mental illness.</td>
<td>RCT (Peveler et al., 2005 and Kendrick et al., 2006b)</td>
<td>Source of unit costs: national sources</td>
<td>Costs: GP time (surgery contact, by telephone, home visit), other staff time (practice nurse, district nurse, CPN, counselor, psychiatrist), day centre, non-psychiatric hospital clinic, A&amp;E, psychiatric and non-ICERs SSRI vs. TCAs £59/DFW TCAs vs. LOF £183/DFW (TCAs)</td>
<td>Perspective: NHS Currency: UK£ Cost year: 2002 Time horizon: 12 months</td>
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### Economic evidence

#### Update 2017

**Study Country Study type**

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<tr>
<td><strong>Cost effectiveness and cost-utility analysis</strong></td>
<td>psychiatric in-patient stay</td>
<td>extendedly dominated</td>
<td>Discounting: NA; Applicability: directly applicable</td>
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<td><strong>Study type</strong></td>
<td><strong>Intervention details</strong></td>
<td><strong>Outcome measures</strong></td>
<td><strong>Quality:</strong> minor limitations</td>
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<tr>
<td>SSRIs (fluoxetine, sertraline or paroxetine)</td>
<td>Exclusion criteria: already taking antidepressants, pregnant, breast-feeding, terminal illness</td>
<td>SSRI vs. LOF £32/DFW</td>
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<td>Lofepramine (LOF)</td>
<td>Open-label RCT, with partial preference design (following randomisation, treatment could be prescribed from a different class to the one allocated at random, if participants or their doctor preferred an alternative). (Peveler 2005; N=327; entered preference group n=92; followed-up at 12 months n=171)</td>
<td>LOF vs. TCAs £23,250/QALY (LOF extendedly dominated)</td>
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<td>Treatment lasted 6 months after remission or for at least 12 months if participant had experienced ≥ 2 depressive episodes within the past 5 years.</td>
<td>Source of efficacy data: RCT (n=264 for depression-free weeks, n=262 for QALYs)</td>
<td>SSRI vs. LOF £5,686/QALY</td>
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<td>Source of resource use data: RCT (n=324; sub-analysis included for those who provided efficacy data, and used in estimation of ICERS/CEACs)</td>
<td>LOF vs. TCAs £23,250/QALY (LOF extendedly dominated)</td>
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<td>Number of depression-free weeks per person (95%CI):</td>
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<td>TCAs 25.3 (21.3 to 29.0)</td>
<td>SSRI vs. TCAs £2,692/QALY</td>
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<td>SSRIs 28.3 (24.3 to 32.2)</td>
<td>Probability of SSRIs being cost-effective approximately 0.6 at WTP of £20,000/QALY</td>
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<td>LOF 24.6 (20.6 to 28.9)</td>
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<td>Mean total cost per person (95%CI):</td>
<td>p=0.327</td>
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<td>TCAs £762 (£553 to £1059)</td>
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<td>SSRIs £875 (£675 to £1355)</td>
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<td>LOF £867 (£634 to £1521)</td>
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<td>p=0.09</td>
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<td>Outcome measures: number of depression-free weeks (DFW, defined as a Hospital Anxiety and Depression Scale - Depression subscale (HADS-D) &lt;8) and QALYs based on EQ-5D ratings (UK tariff)</td>
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<td>Mean QALYs per person, adjusted for baseline (95%CI):</td>
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<td>TCAs 0.548 (0.481 to 0.606)</td>
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<td>SSRIs 0.586 (0.523 to 0.641)</td>
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<td>LOF 0.552 (0.493 to 0.612)</td>
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<td>(p=0.09)</td>
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<td>SSRI vs. LOF £5,686/QALY</td>
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<td>LOF vs. TCAs £23,250/QALY (LOF extendedly dominated)</td>
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<td>SSRI vs. TCAs £2,692/QALY</td>
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<td>Probability of SSRIs being cost-effective approximately 0.6 at WTP of £20,000/QALY</td>
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</table>
### Q.2.3.1 Physical interventions – references to included studies

2. **Acupuncture versus counselling versus usual care**


6. **Exercise versus usual care**


<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spackman et al., 2014 UK Cost-utility analysis</td>
<td>Interventions: Acupuncture 12 weekly sessions Counselling 12 weekly sessions Treatment as usual (TAU)</td>
<td>Adults with depression (BDI-II score ≥20), who were in contact with primary care services for this reason within the past 5 years, and were continuing to experience moderate to severe depression Open parallel-arm RCT (MacPherson 2013, N=755) Source of efficacy and resource use data: RCT (at 12 months EQ-5D data n=572; complete resource use data n=150; multiple imputation used) Source of unit costs: national sources</td>
<td>Costs: intervention, GP, practice nurse, other health professional, NHS hospital outpatient clinic, hospital ward, hospital mental health unit, other hospital unit, accident and emergency, community mental health nurse, psychologist or psychiatrist, NHS counsellor Mean total cost per person: Acupuncture £1,227; counselling £1,450; TAU £958 Primary outcome measure: QALYs estimated using EQ-5D ratings (UK tariff) QALYs per person: Acupuncture 0.663; counselling 0.666; TAU 0.604 using imputed data and seemingly unrelated regression controlling for the baseline HRQoL</td>
<td>ICER of counselling vs. acupuncture: £71,757/QALY acupuncture vs. TAU £4,560/QALY counselling vs. TAU (when acupuncture is not suitable) £7,935/QALY Probability of cost effectiveness at £20,000/QALY: acupuncture 0.62; counselling 0.36; TAU 0.02 Results sensitive to small changes in intervention costs; results robust to inclusion of depression-related resource use only. In complete case analysis acupuncture dominated counselling.</td>
<td>Perspective: NHS Currency: GBPE Cost year: 2012 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations</td>
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<tr>
<td>Study Country Study type</td>
<td>Study population</td>
<td>Study design Data sources</td>
<td>Costs and outcomes: description and values</td>
<td>Results: Cost-effectiveness</td>
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<tr>
<td>Chalder et al., 2012 UK Cost-utility analysis</td>
<td>Adults 18-69 years of age, with a recent first or new episode of mild/moderate depression (BDI score ≥14), who were not taking antidepressants at the time of assessment or had had prescribed antidepressants within 4 weeks of assessment but had had an antidepressant-free period of 4 weeks prior to that</td>
<td>Pragmatic, multicentre RCT (N=361, excluded from clinical analysis due to high attrition rates) Source of efficacy and resource use data: RCT (at 12 months EQ-5D data n=195; complete resource use data n=156; multiple imputation used in sensitivity analysis) Source of unit costs: national sources</td>
<td>Costs: intervention (physical activity facilitator’s time), primary care professionals’ time (GP, practice nurse, phlebotomist, health visitor, district nurse, midwife, nurse practitioner, mental health worker, counsellor, community psychiatric nurse, physiotherapist), paramedic, A&amp;E, outpatient care, walk-in centre, NHS Direct out-of-hours care, medication, productivity losses Mean total service cost per person: Physical activity £ 646; TAU £350 Difference: £296 (95%CI £202 to £390) Primary outcome measure: QALYs estimated using EQ-5D ratings (UK tariff) QALYs per person: Physical activity: 0.809; TAU 0.795 Difference 0.014 (95%CI -0.033 to 0.061)</td>
<td>Under NHS &amp; PSS perspective: Using completers’ data: ICER of physical activity vs. TAU: £20,834/QALY Probability of physical activity being cost-effective at £20,000 and £30,000/QALY: 0.49 and 0.57, respectively Using imputed data: ICER of physical activity vs. TAU £19,394/QALY Probability of physical activity being cost-effective at £20,000 and £30,000/QALY: 0.50 and 0.60, respectively</td>
<td>Perspective: NHS &amp; PSS (and societal) Currency: GBP£ Cost year: 2009 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations</td>
</tr>
</tbody>
</table>
Q.3.1 Interventions for first-line treatment of adults with a new episode of more severe depression

Q.3.13 Psychological interventions – references to included studies

<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Interventions details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horrell et al., 2014</td>
<td>Psychoeducational one-day self-confidence workshop Wait list</td>
<td>Adults with depression, as indicated by a BDI≥14 No exclusion criteria in relation to antidepressants or concurrent</td>
<td>Costs: intervention (venue, advertising, workshop materials, volunteer time, staff time including training, preparation, administration, delivering the intervention and volunteer time), medication, primary care, outpatient and inpatient care, specialist mental health and community-based services such as social work and alternative</td>
<td>Psychoeducation dominant in terms of BDI-II change scores and DFDs; Less costly and less effective in terms of QALYs; ICER of WL</td>
<td>Perspective: NHS (and societal) Currency: GBP£ Cost year: 2011 Time horizon: 12 weeks</td>
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<tr>
<td>Study</td>
<td>Country</td>
<td>Study type</td>
<td>Intervention details</td>
<td>Study population</td>
<td>Study design</td>
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<td></td>
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<td>utility</td>
<td>psychological therapy</td>
<td>Multicentre open RCT (N=459; completers n=382) (Horrell 2014) Source of efficacy &amp; resource use data: RCT; cost effectiveness analysis based on n=380; cost-utility analysis based on n=375 Source of unit costs: national sources and other published studies</td>
<td>Psychological therapy</td>
</tr>
</tbody>
</table>
| Holman et al., 2011 | UK | Cost | Interventions: Cognitive behavioural therapy (12) | Older adults aged ≥ 65 years with depression (BDI ≥14) and, if on an antidepressant, a stable dose of medication for at least 8 weeks | Costs: intervention (CBT) and community health service costs (contacts with GP’s, practice and district nurses, health visitors, psychiatrists, clinical | ICER of CBT vs. TAU £120 /additional point reduction | Perspective: health and social services (only primary and
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<tr>
<th>Study Country Study type</th>
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</thead>
<tbody>
<tr>
<td>depression effectiveness analysis</td>
<td>sessions) in addition to treatment as usual (CBT) Treatment as usual (TAU)</td>
<td>prior to randomization Single-blind RCT (Serfaty2009, N=204) Source of efficacy and resource use data: RCT (at 10 months n=198 for costs, n=167 for outcomes) Source of unit costs: national sources</td>
<td>psychologists, occupational therapists, physiotherapists, community psychiatric nurses and general counsellors; medication not considered but likely similar between groups; secondary care not considered Mean cost difference per person: £427 (95% CI: £56 to £787, p &lt; 0.001) Primary outcome measure: BDI-II Mean BDI-II difference per person: 3.6 (95%CI: 0.7 to 6.5, p = 0.018) in BDI-II Probability of CBT being cost-effective: 0.90 at a WTP of £270 /point reduction in BDI-II</td>
<td>community healthcare services considered) Currency: GBP£ Cost year: 2008 Time horizon: 10 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations</td>
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<tr>
<td>Hollinghurst et al., 2010 UK Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Computerised CBT delivered online using real-time therapist interaction through written messaging comprising up to 10 55min sessions (CBT)</td>
<td>Adults aged 18-75 years who were identified in primary care as having a new episode of depression, defined by a BDI score ≥14 and an ICD–10 diagnosis of depression using the Revisited Clinical Interview Schedule (CIS–R) RCT (Kessler2009,</td>
<td>Costs: intervention, staff time (GP, practice nurse, counsellor, health visitor, occupational health therapist, psychiatrist, phlebotomist, physiotherapist), walk-in centre, NHS Direct, A&amp;E, inpatient and outpatient care, medication Personal expenses (private sector healthcare, over-the-counter drugs, social and domestic help, travel costs and out-of-pocket loss of earnings) and productivity losses considered in societal perspective</td>
<td>Complete data: ICER of CBT vs WL: £3,528/extra person recovering £17,173/QALY Probability of CBT being cost-effective: 0.56 and 0.71 at WTP £20,000 &amp; £30,000/QALY, respectively Imputed missing data:</td>
<td>Perspective: NHS (and societal) Currency: GBP£ Cost year: 2007 Time horizon: 8 months Discounting: NA Applicability:</td>
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### Study Country Study type
<table>
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<tr>
<th>Study Country Study type</th>
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</thead>
<tbody>
<tr>
<td>Waiting list (WL)</td>
<td>N=297</td>
<td>Source of efficacy and resource use data: RCT (BDI data available for n=210; QALYs available for n=165; NHS cost data available for n=137)</td>
<td>Mean total NHS cost per person (SD): CBT: £764 (£380); WL: £295 (£359)</td>
<td>ICER of CBT vs WL: £10,083/QALY</td>
<td>directly applicable</td>
</tr>
<tr>
<td>Ekers et al., 2011 UK Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Behavioural activation (BA), delivered over 12 hourly sessions by 2 mental health nurses on post qualification pay bands with no previous formal therapy training; therapists</td>
<td>Adults with depression (confirmed by the revised Clinical Interview Schedule - CIS-R), on stable or no antidepressant medication for 6 weeks, attending general practice or primary care mental health services</td>
<td>Costs: intervention: therapist time, supervision &amp; training costs spread over 3 years; 2 scenarios employed, based on 2 estimates of workload according to Improving Access to Psychological Therapy (IAPT) service specifications: 65 treatments/year in a depression-specific role (scenario A) or 33 treatments/year treating depression and anxiety (scenario B); primary (general &amp; mental health) care, secondary (general &amp; mental health) care, community and social services, medication</td>
<td>Scenario A ICER of BA vs. TAU • £9.45 per BDI-II point reduction • £5,006/QALY At a WTP of £20,000/QALY, probability of BA being cost-effective was 0.98</td>
<td>directly applicable</td>
</tr>
<tr>
<td></td>
<td>Pragmatic RCT (N=47; completers n=38) (Ekers2011)</td>
<td>Cost differences adjusted for baseline:</td>
<td></td>
<td>Scenario B ICER of BA vs. TAU • £11.04 per BDI-II point reduction</td>
<td>Quality: potentially serious limitations</td>
</tr>
</tbody>
</table>

**Notes:**
- Update 2017
- Study population: Study design: Data sources: Costs and outcomes: description and values: Results: Cost-effectiveness: Comments
## Economic evidence – evidence tables

### Miller et al., 2003

<table>
<thead>
<tr>
<th>Study Country Study type</th>
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</tr>
</thead>
<tbody>
<tr>
<td>UK Cost effectiveness analysis</td>
<td>Interventions: Generic psychological therapy comprising 6 weekly 50-minute sessions (counselling) Routinely prescribed antidepressant drugs, comprising dothiepin (150 mg)</td>
<td>Adults aged 18-70 years who met diagnostic criteria for major depression (assessed by their GP). Exclusion criteria: psychosis, suicidal tendencies, postnatal depression, recent bereavement, drug or alcohol misuse RCT (Bedi2000, N=103); people refusing randomisation but agreeing to participate in the</td>
<td>Costs: intervention (counselling, medication), depression-related GP visits, psychiatric inpatient &amp; outpatient care Mean cost (SD) per person: RCT Counselling: £302 (£38) AD: £344 (£62); p=0.777 Preference trial: Counselling: £336 (£25) AD: £263 (£34) p =0.005</td>
<td>RCT: ICER of AD vs. counselling £263/ extra person with a good global outcome 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 Sensitivity analysis:</td>
<td>Perspective: NHS (only depression-related costs considered) Currency: UK£ Cost year: 1995 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: potentially</td>
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</table>

### Update 2017

<table>
<thead>
<tr>
<th>Study Country Study type</th>
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</tr>
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<tbody>
<tr>
<td>UK Cost effectiveness analysis</td>
<td>received 5-day training and 1 hour clinical supervision fortnightly Treatment as usual (TAU) comprising GP care or primary care by mental health workers</td>
<td>Source of efficacy &amp; resource use data: RCT, based on participants’ primary care records and self-completed questionnaires Source of unit costs: national sources</td>
<td>Scenario A: £149 (95%CI -£56 to £355) Scenario B: £175 (95%CI -£31 to £380) Imputed, bias-corrected costs – scenario A: BA: £583 (95%CI £442 to £771) TAU: £413 (95%CI £279 to £560) Imputed, bias-corrected costs – scenario B: BA: £609 (95%CI £473 to £797) TAU: £413 (95%CI £284 to £587)</td>
<td>£5,756/QALY At a WTP of £20,000/QALY, probability of BA being cost-effective was 0.97</td>
<td></td>
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<tr>
<td>UK Cost effectiveness analysis</td>
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<td>Mean change in BDI-II: -15.78 (95% CI -24.55 to -7.02) Mean bias-adjusted QALYs gained: BA: 0.05 (95%CI 0.04 to 0.07) TAU: 0.02 (95%CI 0.00 to 0.03)</td>
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<tr>
<td>Study Country Study type</td>
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<td>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)</td>
<td>patient preference trial were given the treatment of their choice (N=220) Source of efficacy data: RCT (at 12 months n=81) and preference trial (at 12 months n=163) Source of resource use data: RCT (at 12 months n=103) and preference trial (at 12 months n=215) Source of unit costs: national sources and local costs for counsellors</td>
<td>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 % of people with good global outcome: RCT Counselling: 25%, AD: 41%, p=0.196 Preference trial: Counselling: 36%, AD: 28%, p=0.191</td>
<td>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-effective slightly increases for WTP&lt;£1,500 and decreases for WTP &gt;£1,500. Preference trial: ICER of counselling vs. AD £912/ extra person with a good global outcome</td>
<td>serious limitations</td>
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</tbody>
</table>
**Q.3.21 Pharmacological interventions – references to included studies**

**SSRIs versus mirtazapine [versus duloxetine and venlafaxine XR that were not part of the guideline decision problem]**


**Fluoxetine versus amitriptyline [versus venlafaxine XR that was not part of the guideline decision problem]**


**AND**


**Escitalopram versus citalopram [versus venlafaxine XR that was not part of the guideline decision problem]**


<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Benedict et al., 2010 UK Cost-utility analysis</td>
<td>Interventions: SSRIs Mirtazapine (Duloxetine and venlafaxine also included but not considered here as they were not part of review question)</td>
<td>Adults with moderate to severe major depression defined by a HAMD17 score ≥19, having a new treatment episode in primary care Decision-analytic modelling Source of efficacy data: meta-analyses of clinical trials - randomisation likely broken Source of resource use data: expert opinion Source of unit costs: national sources</td>
<td>Costs: medication, A&amp;E Visits, GPs, psychiatrists, hospitalisation Mean total cost per person: SSRIs £486 Mirtazapine £516 Outcome measure: QALY estimated based on EQ-5D ratings (UK tariff) Number of QALYs per person: SSRIs 0.656 Mirtazapine 0.654</td>
<td>SSRIs dominated mirtazapine PSA favouring duloxetine which is not part of the guideline decision problem Results sensitive to changes in efficacy (response / relapse) and utility values</td>
<td>Perspective: Scottish NHS Currency: UK£ Cost year: likely 2003 Time horizon: 48 weeks Discounting: NA Applicability: directly applicable Quality: potentially serious limitations</td>
</tr>
</tbody>
</table>
### Economic Evidence

#### Lenox-Smith et al., 2009

**UK**  
**Cost-utility analysis**

**Intervention details**  
Interventions: Fluoxetine; Amitriptyline (Venlafaxine also included but not considered here as it was not part of review question)

**Study population**  
Adult outpatients with major depression  
Decision-analytic modelling  
Source of efficacy data: pooled data from meta-analysis for fluoxetine versus amitriptyline; a single RCT for amitriptyline vs. venlafaxine; method of synthesis unclear, but most likely randomisation was broken  
Source of resource use data: Delphi panel  
Source of unit costs: national sources

**Data sources**  
Source of efficacy data: pooled data from meta-analysis for fluoxetine versus amitriptyline; a single RCT for amitriptyline vs. venlafaxine; method of synthesis unclear, but most likely randomisation was broken.

**Costs and outcomes: description and values**

- Costs: medication, lab testing, clinical examinations, community psychiatric nursing, inpatient and outpatient services, staff time (GP, psychiatrist, psychologist), psychotherapy
- Mean total cost per person: Fluoxetine £1539; Amitriptyline £1558
- Outcome measure: QALY estimated based on the presumed utilities of a depression-free day and a severely depressed day
- Mean QALY gains per person: Fluoxetine 0.090; Amitriptyline 0.085

**Results: Cost-effectiveness**

- Fluoxetine dominates amitriptyline
- Results robust to changes in costs.
- Results sensitive to the value of the utility gain associated with a depression-free day

**Comments**

- Perspective: NHS
- Currency: GBP£
- Cost year: 2006
- Time horizon: 24 weeks
- Discounting: NA
- Applicability: partially applicable
- Quality: very serious limitations

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#### Wade et al., 2005a

**UK**  
**Cost effectiveness analysis**

**Intervention details**  
Interventions: Escitalopram; Citalopram (Venlafaxine XR included but not part of decision problem)

**Study population**  
Adults with major depression with baseline MADRS score between 18-40  
Decision-analytic modelling  
Source of efficacy data: meta-analysis of head-to-head RCTs

**Costs and outcomes: description and values**

- Costs: study medication, staff time (GP, psychiatrist, hospitalisation, community services, attempted suicide; sick leave
- Mean (range) total NHS cost per person: Escitalopram: £465 (£436-£493); Citalopram: £544 (£514-£573)
- Outcome measure: % of remission

**Results: Cost-effectiveness**

- Escitalopram dominates citalopram
- Results robust under different scenarios (changes in rates of remission, relapse, discontinuation, unit costs)

**Comments**

- Perspective: NHS (and societal)
- Currency: GBP£
- Cost year: 2003
- Time horizon: 26 weeks
- Discounting: NA
- Applicability: very serious limitations
<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wade et al., 2005b (severe depression) UK Cost effectiveness analysis</td>
<td>Interventions: Escitalopram Citalopram</td>
<td>Adults with major severe depression with baseline MADRS score $\geq$ 30 Decision-analytic modelling Source of efficacy data: published meta-analysis of RCTs Source of resource use data: published literature and expert opinion Source of unit costs: national sources</td>
<td>Costs: study medication, GP and psychiatrist visits, inpatient psychiatric hospitalizations, treatment discontinuation, treatment-emergent AEs, attempted suicide. Sick leave Mean (range) total NHS cost per person: Escitalopram: £422 (£404-£441) Citalopram £454 (£436-£471) Outcome measures: % of remission, defined as MADRS score $\leq$ 12, and % remission without switch % of remission: mean (range) Escitalopram: 53.7% (50.3%-57.5%) Citalopram: 48.7% (45.8%-51.7%) % of remission without switch: mean</td>
<td>Escitalopram dominates citalopram Results robust to changes in drug-specific probabilities and cost data PSA: Escitalopram was dominant in &gt;99.8% of iterations</td>
<td>Perspective: NHS (and societal) Currency: GBP£ Cost year: 2003 Time horizon: 26 weeks Discounting: NA Applicability: partially applicable Quality: potentially serious limitations</td>
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<tr>
<td>Study Country Study type</td>
<td>Intervention details</td>
<td>Study population Study design Data sources</td>
<td>Costs and outcomes: description and values (range)</td>
<td>Results: Cost-effectiveness</td>
<td>Comments</td>
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<td>Escitalopram: 41.7% (37.5%-46.3%)</td>
<td>Citalopram: 30.8% (27.5%-34.6%)</td>
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### Q.3.3.3 Combined pharmacological and psychological interventions – references to included studies

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

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<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Koeser et al., 2015 UK Cost-utility analysis</td>
<td>Interventions: Antidepressant therapy alone, comprising citalopram 20mg daily for 15 months and standard outpatient care (AD) Cognitive Behavioural Therapy (CBT) comprising 16 acute + 2 booster sessions for responders, each lasting 50 min Combination therapy comprising CBT and AD treatment (Combo)</td>
<td>Adults with moderate or severe major depression Decision-analytic modelling (decision tree) 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 Source of resource use data: published literature that reported expert opinion and analysis of RCT data Source of unit costs: national sources</td>
<td>Costs: intervention (clinical psychologist’s time for CBT, antidepressant medication, dispensing fee, outpatient care with consultant psychiatrist or specialist registrar), service use associated with remission, response, no response Mean total cost per person: AD: £3,645 CBT: £4,418 Combo: £5,060 Outcome measures: QALYs estimated based on EQ-5D (UK tariff) Mean total QALYs per person: AD: 1.236 CBT: 1.274 Combo: 1.274</td>
<td>Combo dominated by CBT ICER of CBT vs AD: £20,039/QALY Probability of being best at WTP £25,000/QALY: CBT: 0.43 AD: 0.37 Combo: 0.20 Results sensitive to changes in inclusion criteria for RCTs for acute and follow-up treatment and to use of SF-6D values</td>
<td>Perspective: NHS Currency: GBPE Cost year: 2012 Time horizon: 27 months Discounting: 3.5% annually Applicability: directly applicable Quality: minor limitations</td>
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</table>
Q.3.43 Physical interventions – references to included studies

ECT versus SSRIs, SNRIs, or SSRIs & lithium


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<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population</th>
<th>Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greenhalgh et al., 2005 UK Cost-utility analysis</td>
<td>Interventions: Electroconvulsive therapy (ECT), TCAs, SSRIs, SNRIs and lithium augmentation (Li) combined in 8 strategies of 3 lines of therapy plus maintenance therapy of SSRI unless otherwise specified: 1. SNRI, SSRI, Li 2. ECT, SSRI, Li; ECT maintenance in ECT 3. ECT, SSRI, Li; Lithium &amp; TCA maintenance in ECT 4. SNRI, ECT, Li; Lithium &amp; TCA maintenance in ECT 5. ECT, SSRI, Li 6. SNRI, SSRI, ECT; Lithium &amp; TCA maintenance in ECT 7. SNRI, ECT, Li; ECT maintenance in ECT</td>
<td>Adults with major depressive disorder who require hospitalisation Decision-analytic modelling (decision tree) Source of efficacy data: systematic literature review of RCTs and published meta-analyses, and further assumptions Source of resource use data: published literature and expert opinion Source of unit costs: national sources</td>
<td>Costs: intervention (ECT, medication, hospitalisation), continued care for non-responders (nursing home placement with psychiatric provision), maintenance treatment (laboratory testing, contacts with GP, psychiatrist and psychiatric nurse) Mean total cost per person (95% CI): Strategy 1. £11,400 (£9,349 to £13,718) Strategy 2. £15,354 (£13,445 to £17,361) Strategy 3. £10,997 (£9,080 to £13,045) Strategy 4. £10,592 (£8,874 to £12,435) Strategy 5. £11,022 (£9,016 to £13,069) Strategy 6. £13,939 (£11,161 to £17,049) Strategy 7. £12,591 (£10,678 to £14,497) Strategy 8. £14,548 (£11,680 to £17,717) Primary outcome measure: QALYs estimated based on preferences for vignettes using the McSad health state classification system valued by service users with previous depression in Canada using SG</td>
<td>Strategies 1, 2, 3, 6, 7, and 8 dominated ICER of Strategy 5 vs. strategy 4: £6,232/QALY Results modestly sensitive to use of alternative utility values; results robust to small changes in costs and suicide rates</td>
<td>Perspective: NHS Currency: GBP£ Cost year: 2001 Time horizon: 12 months Discounting: NA Applicability: partially applicable Quality: potentially serious limitations</td>
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### Study Country Study type

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<tr>
<th>Study population</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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<tr>
<td>8. SNRI, SSRI, ECT; ECT maintenance in ECT</td>
<td>Mean total QALYs per person (95% CI):</td>
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<td>Strategy 1. 0.490 (0.453 to 0.526)</td>
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<td>Strategy 2. 0.458 (0.422 to 0.493)</td>
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<td>Strategy 3. 0.424 (0.389 to 0.459)</td>
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<td>Strategy 4. 0.470 (0.431 to 0.508)</td>
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<td>Strategy 5. 0.539 (0.498 to 0.579)</td>
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<td>Strategy 6. 0.489 (0.452 to 0.524)</td>
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<td>Strategy 7. 0.486 (0.449 to 0.522)</td>
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<td>Strategy 8. 0.494 (0.459 to 0.529)</td>
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### Q.4 Interventions for the treatment of adults with a depressive episode who responded inadequately or were intolerant to previous treatment

#### Q.4.14 Psychological interventions – references to included studies

5 Cognitive behavioural therapy (CBT) as an adjunct to pharmacotherapy


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AND

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<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population</th>
<th>Study design</th>
<th>Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Scott et al., 2003 UK Cost effectiveness analysis</td>
<td>Interventions: Cognitive therapy (16 sessions in 20 weeks plus 2 booster sessions) in addition to antidepressants (minimum dose equivalent to ≥ 125mg of amitryptiline) and clinical management (30-min appointments with a psychiatrist every 4 weeks during 20 weeks and every 8 weeks during the 48-week follow-up) (CT &amp; AD) Antidepressants and clinical management alone (AD)</td>
<td>Outpatients 21-65 years that met DSM-III-R criteria for major depression, who were in an episode within the past 18 months but not in the past 2 months. At randomisation they had residual symptoms over at least 8 weeks with HAMD ≥ 8 and BDI ≥ 9. Exclusion criteria: past history of bipolar disorder; current history of significant Axis I or II comorbidity; currently receiving formal psychotherapy; having previously received CT for &gt; 5 sessions. RCT</td>
<td>Costs: CT, medication, clinical management, inpatient care, day hospital, GP, social worker, community psychiatric nurse, therapist/counsellor, group therapy, marital therapy. Mean cost per person: CT &amp; AD: £1898 AD: £1119 Cost difference: £779 (95% CI £387 to £1170) Primary outcome measure: percentage of relapses Cumulative relapse rates: CT &amp; AD: 29% AD: 47% Adjusted HR 0.51 (95% CI 0.32-0.93)</td>
<td>ICER of CT &amp; AD vs AD: £4328 per relapse prevented £4667 using mean imputation £5028 using non-parametric multiple imputation £7056 using only the 65% of subjects in the complete case analysis Probability of CT &amp; AD being cost-effective 0.60 and 0.80 at WTP of £6000 and £8500 per relapse prevented, respectively Probability sensitive to method of missing data imputation</td>
<td>Perspective: NHS/PSS Currency: GBP£ Cost year: 1999 Time horizon: 17 months Discounting: 6% Applicability: partially applicable Quality: minor limitations</td>
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### Study evidence tables

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<thead>
<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Intervention details</th>
<th>Study population</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hollinghurst et al., 2014; Wiles et al., 2016</td>
<td>UK</td>
<td>Cost consequence and cost-utility analysis</td>
<td>Interventions: Cognitive behavioural therapy comprising 12-18 sessions lasting about an hour each, taking place at a GP surgery or a similar location, in addition to treatment as usual (CBT) Treatment as usual alone, comprising GP care, including antidepressant treatment as judged appropriate by the person’s GP or a referral as required (TAU)</td>
<td>Costs: medication, primary and community mental and general health care, specialist (secondary) mental health care, personal out-of-pocket expenditure such as travel costs, use of private therapies and over-the-counter medications; productivity losses</td>
<td>AT 12 MONTHS ICER of CBT vs. TAU £14,911/QALY</td>
<td>Perspective: NHS/PSS for cost-utility analysis; health and social care provider for cost consequence analysis, with service user expenses and productivity losses assessed in additional analyses</td>
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<td>Adults aged 18-75 years with major depression, who had adhered to antidepressant medication for at least 6 weeks in primary care, but who continued to have significant depressive symptoms; people had a BDI-II score of at least 14 or more and an ICD-10 diagnosis of depression using the Revised Clinical Interview Schedule (CIS-R)</td>
<td>RCT (Wiles2013, N=469)</td>
<td>Mean total cost per person (SD): NHS/PSS cost: CBT £1614 (£1100); TAU £763 (£997); difference: £850 (95%CI £683 to £1017)</td>
<td>Probability of CBT being cost-effective 0.74 and 0.91 at WTP of £20,000/QALY and £30,000/QALY, respectively</td>
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<td>Source of efficacy data and resource use data: RCT (NHS and PSS cost and QALY data available for n=368 at 12 months; follow-up data available for n= 248)</td>
<td>Source of unit costs: national sources</td>
<td>Personal expenditure: CBT £80 (£12), TAU £127 (£35); difference -£47 (95%CI -£120 to £25)</td>
<td>Results robust to changes in psychologist unit costs and exclusion of hospitalisation costs.</td>
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<td>Out-of-pocket expenses: CBT £694 (£4,824), TAU £517 (£2,464); difference £176 (95%CI -£662 to £1014)</td>
<td>Results sensitive to use of SF-6D instead of EQ-5D, with ICER rising at £29,626/QALY</td>
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<td>Lost productivity: CBT £1,067 (£3,887), TAU £1,102 (£3,529); difference -£36 (95%CI -£797 to £726)</td>
<td>Analysis of completers’ data (instead of imputation of missing data): ICER £18,361/QALY AT 3-5 YEARS</td>
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<td>AT 3-5 YEARS</td>
<td>Probability of CBT being cost-effective at a WTP of £30,000/QALY, £20,000/QALY and £10,000/QALY respectively</td>
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<td>Mean annual NHS/PSS cost (SD): CBT £885 (£938); TAU £604 (£904); difference: £281 (95%CI £32 to £531)</td>
<td>Results: Cost-remission: CBT 39.6%, TAU 18.2%; OR 2.74 (95%CI 2.03 to 4.10) at 12 months; follow-up data available for n=368 at 5 YEARS</td>
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<td>Outcome measures: response (reduction of at least 50% in BDI-II score); BDI-II score; remission (BDI-II &lt;10; SF-12 mental and physical subscales; EQ-5D; QALYs estimated using EQ-5D &amp; SF-6D ratings (latter in sensitivity analysis) (UK tariff)</td>
<td>Probability of CBT being effective 0.74 and 0.91 at WTP of £20,000/QALY and £30,000/QALY, respectively</td>
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<td>AT 12 MONTHS</td>
<td>Analysis of completers’ data (instead of imputation of missing data): ICER £18,361/QALY AT 3-5 YEARS</td>
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<td>Response: CBT 55.3%, TAU %31.3; OR 2.89 (95%CI 2.03 to 4.10)</td>
<td>Probability of CBT being cost-effective at a WTP of £30,000/QALY, £20,000/QALY and £10,000/QALY respectively</td>
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<td>BDI-II score (mean, SD): CBT 17.0 (14.0), TAU 21.7 (12.9); difference -5.1 (-7.1 to -3.1)</td>
<td>Probability of CBT being cost-effective at a WTP of £30,000/QALY, £20,000/QALY and £10,000/QALY respectively</td>
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<td>Remission: CBT 39.6%, TAU 18.2%; OR 2.74 (95%CI 2.03 to 4.10)</td>
<td>Probability of CBT being cost-effective at a WTP of £30,000/QALY, £20,000/QALY and £10,000/QALY respectively</td>
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</table>

**Data sources**

- **Study design**: RCT (NHS and PSS data available for n=469)
- **Source of efficacy data and resource use data**: RCT (NHS and PSS cost and QALY data available for n=368 at 12 months; follow-up data available for n= 248)
- **Study population**: Adults aged 18-75 years with major depression, who had adhered to antidepressant medication for at least 6 weeks in primary care, but who continued to have significant depressive symptoms; people had a BDI-II score of at least 14 or more and an ICD-10 diagnosis of depression using the Revised Clinical Interview Schedule (CIS-R)
- **Intervention details**: Cognitive behavioural therapy comprising 12-18 sessions lasting about an hour each, taking place at a GP surgery or a similar location, in addition to treatment as usual (CBT) Treatment as usual alone, comprising GP care, including antidepressant treatment as judged appropriate by the person’s GP or a referral as required (TAU)
- **Perspective**: NHS/PSS for cost-utility analysis; health and social care provider for cost consequence analysis, with service user expenses and productivity losses assessed in additional analyses

**Discounting**

- 3.5% annually

**Quality**: minor limitations

**Time horizon**: 12 months

**Follow-up analysis**: 3-5 years (median 45.5 months, interquartile range 42.5 to 51.1)
### Economic evidence – evidence tables

<table>
<thead>
<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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<tr>
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<td>(95% CI 1.82 to 4.13) SF-12 mental sub-scale (mean, SD): CBT 39.1 (14.6), TAU 35.4 (12.8); difference 4.8 (2.7 to 6.9) SF-12 physical sub-scale (mean, SD): CBT 44.6 (13.2), TAU 41.1 (13.5); difference -0.7 (95% CI -2.1 to 0.8) QALYs: CBT 0.62 (0.22), TAU 0.56 (0.25); difference 0.053 (95% CI 0.019 to 0.087) AT 3-5 YEARS Response: CBT 43%, TAU 27%; OR 2.09 (95% CI 1.19 to 3.67) BDI-II score (mean, SD): CBT 19.2 (13.8), TAU 23.4 (13.2); difference -3.6 (-6.6 to -0.6) Remission: CBT 28%, TAU 18%; OR 1.77 (95% CI 0.93 to 3.39) SF-12 mental sub-scale (mean, SD): CBT 38.7 (12.1), TAU 34.6 (11.8); difference 3.5 (0.7 to 6.3) SF-12 physical sub-scale (mean, SD): CBT 42.2 (13.8), TAU 39.2 (13.5); difference 0.9 (95% CI -0.2 to 3.8) Mean annual QALYs: CBT 0.60 (0.17), TAU 0.54 (0.20); difference 0.052 (95% CI 0.003 to 0.102)</td>
<td>£20,000/QALY and £30,000/QALY: 0.92 and 0.95, respectively</td>
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</table>
Q.4.21 Pharmacological interventions – references to included studies

Continuation of current treatment (citalopram) versus switching to another antidepressant (venlafaxine, sertraline) or augmentation with bupropion


Escitalopram versus duloxetine and venlafaxine


Duloxetine versus venlafaxine XR and mirtazapine


Various antidepressants (generic SSRIs including citalopram, fluoxetine and paroxetine, escitalopram, paroxetine controlled release, sertraline, and venlafaxine extended release)


Augmentation with lithium or atypical antipsychotics (including combination of olanzapine / fluoxetine)


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<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Intervention details</th>
<th>Study design</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Olgiati et al., 2013</td>
<td>US</td>
<td>Cost-utility analysis</td>
<td>Interventions: Different strategies for non-remitters: A. Continuation of current treatment (citalopram) for 13 weeks B. Choice to: a. switch to sertraline or venlafaxine for 13 weeks or b. augment with bupropion for 13 weeks Remitters (HAMD17&lt;7) continued treatment with citalopram for another 13 weeks</td>
<td>Study population Adult outpatients with chronic depression, with a HAMD17 ≥ 14, who were treated with citalopram for 13 weeks and received 2nd line treatment following no remission; exclusion criteria: indications for hospital treatment such as psychotic symptoms, suicidal risk or inpatient detoxification for alcohol / substance dependence; obsessive compulsive disorder, eating disorder Decision-analytic modelling Source of efficacy data: data for A taken from RCT (Wade2006); data for B taken from a study comprising series of RCTs (Rush2006/STAR*D), thus breaking randomisation rules Source of resource use data: expert opinion Source of unit costs: national sources</td>
<td>Costs: medication, primary care, outpatient visits, community mental health services Mean total cost per person: Strategy A: $724 Strategy B: $800 Strategy Ba: $809 Strategy Bb: $849 Outcome measure: QALY estimated based on service Canadian/US users’ preferences for vignettes Incremental number of QALYs per person: Strategy B versus strategy A: 0.007 Strategy Ba versus strategy A: 0.006 Strategy Bb versus strategy A: 0.008</td>
<td>ICER of strategy B versus strategy A: Deterministic analysis: $11,481/QALY Probabilistic analysis: $10,665/QALY (95%CI: $6,498 to $14,832) ICER of strategy Ba versus strategy A: $14,738/QALY ICER of strategy Bb versus strategy A: $15,458/QALY Results robust to changes in utility scores and the probability of remission after 3 months of citalopram (strategy A)</td>
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</table>
### Economic evidence

**Study**

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<tr>
<th>Study Country</th>
<th>Study type</th>
<th>Intervention details</th>
<th>Study population</th>
<th>Study design</th>
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</thead>
<tbody>
<tr>
<td>Nordström et al., 2010</td>
<td>Sweden</td>
<td>Cost effectiveness and cost-utility analysis</td>
<td>Interventions: Escitalopram, Duloxetine, Venlafaxine extended release (XR)</td>
<td>Adults with major depression who initiated treatment with one of the assessed interventions in primary care, who had had a history of treatment with another antidepressant within the previous 6 months</td>
<td>Decision-analytic modelling</td>
<td>Escitalopram dominant over duloxetine and venlafaxine</td>
<td>Perspective: societal; healthcare costs reported separately</td>
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<td>Data sources:</td>
<td>Costs: medication, staff time (GP, psychiatrist, other doctors e.g. neurologist, cardiologist, psychotherapist, counsellor, psychologist, nurse), hospitalisation, treatment of side effects, indirect costs (sick leave)</td>
<td>Cost effectiveness at WTP £20,000/QALY (€22,080/QALY) 0.981 and 0.985 compared with duloxetine and venlafaxine, respectively</td>
<td>Currency: Euros(€)</td>
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<td>Mean total healthcare cost per person: Escitalopram €973, Duloxetine €990, Venlafaxine €1,014</td>
<td>Results robust to changes in remission rates, relapse rates, number of GP visits, or incidence of nausea</td>
<td>Cost year: 2009</td>
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<td>Outcome measures: probability of remission (defined as a MADRS total score ≤ 12) achieved after 8 weeks of treatment and sustained until the end of 6 months; QALY estimated based on EQ-5D ratings (UK tariff)</td>
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<td>Time horizon: 6 months</td>
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<td>Probability of remission: Escitalopram: 50.1%, Duloxetine: 33.6%, Venlafaxine: 33.6%</td>
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<td>Discounting: NA</td>
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<td>Mean QALYs per person: Escitalopram 0.322, Duloxetine 0.297, Venlafaxine 0.298</td>
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<td>Applicability: partially applicable</td>
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<td>Quality: potentially serious limitations</td>
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</table>
### Study Country
#### Study type
- Benedict et al., 2010
- UK
- Cost-utility analysis

#### Study population
- Adults with severe major depression defined by a HAMD17 score ≥25, who failed previous SSRI treatment and were referred to mental health specialists in secondary care
- Decision-analytic modelling

#### Study design
- Source of efficacy data: meta-analyses of clinical trials - randomisation possibly broken
- Source of resource use data: expert opinion
- Source of unit costs: national sources

#### Data sources
- Costs: medication, A&E Visits, GPs, psychiatrists, hospitalisation

#### Costs and outcomes:
- Mean total cost per person:
  - Duloxetine £1,622
  - Venlafaxine XR £1,667
  - Mirtazapine £1,640

#### Results: Cost-effectiveness
- Duloxetine dominates venlafaxine XR and mirtazapine
- Probability of duloxetine being cost-effective at WTP £20,000/QALY: approximately 0.80
- Results robust to sensitivity analysis

#### Comments
- Perspective: Scottish NHS
- Currency: GBP£
- Cost year: likely 2003
- Time horizon: 48 weeks
- Discounting: NA
- Applicability: potentially serious limitations

---

### Study Country
#### Study type
- Malone, 2007
- US
- Cost-effectiveness analysis

#### Study population
- Adults with major depression who failed to achieve remission with SSRIs
- Decision-analytic modelling

#### Study design
- Source of efficacy data: review of published trial data and further assumptions – synthesis by naïve addition of data (leading to breaking of randomisation)

#### Data sources
- Costs: medication, physician visits, laboratory tests, inpatient mental health care

#### Costs and outcomes:
- Mean total healthcare cost per person:
  - Generic SSRIs $3,095
  - Escitalopram $3,127
  - Paroxetine CR $3,206
  - Sertraline $3,178
  - Venlafaxine $3,172

#### Results: Cost-effectiveness
- Paroxetine CR and sertraline dominated by other options
- ICER of venlafaxine XR vs. generic SSRIs $2,073 per person achieving remission

#### Comments
- Perspective: 3rd party payer
- Currency: US$
- Cost year: not reported, likely 2005
- Time horizon: 6 months
- Discounting: NA
- Applicability: partially applicable
<table>
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<tr>
<th>Study Country Study type</th>
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<tbody>
<tr>
<td>Sertraline Venlafaxine extended release [XR]</td>
<td>analysis of 1,814 persons enrolled in 10 antidepressant studies Source of unit costs: medication costs from national sources; other unit costs taken from other studies, unclear whether these were national or local</td>
<td>Outcome measure: probability of remission (defined as a HDRS score ≤ 7 or a MADRS total score ≤ 10) Probability of remission: Generic SSRIs 18.5% (weighted average) Escitalopram 19.4% Paroxetine CR 17.7% Sertraline 19.5% Venlafaxine XR 22.2%</td>
<td>dominated] Results of sensitivity analysis reported using primarily each intervention’s CER and not ICERs.</td>
<td>Quality: very serious limitations</td>
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<tr>
<td>Edwards et al., 2013 UK Cost-utility analysis</td>
<td>Interventions: An atypical antipsychotic drug (AAP) as an adjunct to an SSRI Lithium as an adjunct to an SSRI</td>
<td>Adults with treatment-resistant depression (TRD) defined as failure to respond to at least 2 previous antidepressants in the current episode of depression Decision-analytic modelling Source of efficacy data: systematic review and indirect comparison using 6 RCTs comparing olanzapine + fluoxetine vs. fluoxetine alone in people with TRD and 1 RCT comparing lithium + fluoxetine vs. fluoxetine alone in people who had failed at least one antidepressant; a common class effect was assumed for the SSRIs and the AAPS. Data on lithium taken from population that had failed to respond to 1 previous SSRI (so not a TRD population)</td>
<td>Costs: medication (weighted costs according to expert opinion; it was estimated that AAP comprises 30% aripiprazole, 30% olanzapine, 20% quetiapine, and 20% risperidone; and an SSRI comprises 20% citalopram, 20% escitalopram, 30% fluoxetine, and 30% sertraline), healthcare professional time (GP, CMHT, CRHTT), hospitalisation and monitoring (laboratory testing) Mean total cost per person: AAP £5,644; Lithium £4,739 Outcome measure: QALYs estimated using EQ-5D</td>
<td>Augmentation with lithium dominates augmentation with AAP Probability of lithium being dominant 1 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</td>
<td>Perspective: NHS/PSS Currency: GBP£ Cost year: 2011 Time horizon: 12 months Discounting: NA Applicability: directly applicable Quality: potentially serious limitations Other comments: a fixed baseline MADRS score was assumed; change in MADRS scores at endpoint</td>
</tr>
<tr>
<td>Study Country</td>
<td>Study type</td>
<td>Intervention details</td>
<td>Study population</td>
<td>Study design</td>
<td>Data sources</td>
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</table>

**Study**

**Taneja et al., 2012**

**Country**

**US**

**Study type**

Cost effectiveness analysis

**Intervention details**

Interventions: Aripiprazole 2-20 mg/day and antidepressant therapy (ARI) Quetiapine 150 mg/day or 300 mg/day and antidepressant therapy (QUE) Fixed-dose combination of olanzapine 6, 12, or 18 mg/day with fluoxetine 50 mg/day (OLZ/FLUO) Antidepressant therapy alone (AD)

**Study population**

Adults with major depression who responded inadequately to previous antidepressant therapy

**Study design**

Decision-analytic modelling

**Data sources**

Source of efficacy data: meta-analysis of published phase III clinical trials and indirect comparison using placebo as baseline comparator

Source of resource use data: administrative databases and assumptions

Source of unit costs: national sources

**Costs and outcomes: description and values**

Costs: medication, outpatient care for depression, treatment of adverse events

Mean total healthcare cost per person:

ARI $847

QUE 150 mg/day $541

QUE 300 mg/day $672

OLZ/FLUO $791

AD $192

Outcome measure: probability of response (defined as at least 50% reduction in MADRS total score)

Probability of response:

ARI 49%

QUE 150 mg/day 34%

QUE 300 mg/day 38%

OLZ/FLUO 45%

AD 30%

**Results: Cost-effectiveness**

QUE 150 & 300 mg/day and OLZ/FLUO extendedly dominated ICER of ARI vs. AD $3,447 per person responding Results sensitive to changes in relative effectiveness

**Comments**

Q.5 Interventions aimed at preventing relapse in people whose depression has responded to treatment

Q.5.1 Psychological interventions – references to included studies


<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Interventions</th>
<th>Study population</th>
<th>Study design</th>
<th>Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuyken et al., 2008 UK Cost effectiveness analysis</td>
<td>Interventions: Mindfulness-based cognitive therapy with support to taper or discontinue antidepressant treatment, comprising 8 x 2 hour group sessions over consecutive weeks, with 4 follow-up sessions in the following year (MBCT-TS) Maintenance antidepressant treatment plus medication adherence</td>
<td>Adults with ≥ 3 previous major depressive episodes, on a therapeutic dose of maintenance antidepressants over the last 6 months, and currently either in full or partial remission from the most recent episode. Exclusion criteria: organic brain damage, comorbid diagnoses of current substance dependence, current/past psychosis, bipolar disorder, persistent antisocial behaviour, persistent self-injury requiring clinical management/therapy, unable to engage with MBCT for physical, practical, or other reasons, formal concurrent psychotherapy Pragmatic single-blind parallel 2-group RCT</td>
<td>Source of efficacy data: RCT (Kuyken2008); (N=123,</td>
<td>Costs: MBCT-TS, medication, hospital (inpatient, outpatient, emergency department) and community health and social services (e.g., primary care, social work, complementary therapies), plus productivity losses. Mean NHS/PSS cost per person: MCBT-TS: $2076, AD: $1577 Mean societal cost per person (SD): MCBT-TS: $3373 ($4002), AD: $2915 ($4838); difference $457 (95%CI -$1130 to $2043, p=0.87) Primary outcome measure: time to and % of relapse/recurrence Secondary outcomes: severity/duration of relapses/recurrences, severity of residual depressive symptoms, number of comorbid psychiatric diagnoses, quality of life using the WHO Quality of Life instrument (WHOQOL-BREF). Percentage of people relapsing:</td>
<td>ICER of MCBT-TS vs AD: $439/additional relapse or recurrence prevented and $23/depression-free day (NHS/PSS perspective) $962 /additional relapse or recurrence prevented and $50 /depression-free day (societal perspective) Probability of MBCT-TS being cost-effective at zero willingness to pay for preventing an additional relapse/recurrence: 0.42;</td>
<td>Perspective: NHS/PSS (and societal) Currency: international $ Cost year: 2006 Time horizon: 15 months Discounting: NA Applicability: partially applicable Quality: minor limitations</td>
<td></td>
</tr>
</tbody>
</table>
### Economic evidence – evidence tables

<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td>monitoring (AD)</td>
<td>Source of resource use data: RCT (N=123, completers=115) Source of unit costs: national sources</td>
<td>MBCT-TS: 47%; ADs: 60% Hazard ratio 0.63 (95%CI 0.39 to 1.04, p=0.07) Difference in secondary outcomes: MBCT-TS more effective than AD in reducing residual depressive symptoms and psychiatric comorbidity and in improving quality of life in the physical and psychological domains.</td>
<td>probability of MBCT-TS exceeds 0.50 at willingness to pay ≥ $1,000 per relapse/recurrence averted (societal perspective)</td>
<td></td>
</tr>
<tr>
<td><strong>2</strong></td>
<td>Kuyken et al., 2015 UK Cost-effectiveness and cost-utility analysis</td>
<td>Adults with ≥ 3 previous major depressive episodes, in full or partial remission from their most recent episode, and on a therapeutic dose of maintenance antidepressants Exclusion criteria: current major depressive episode, comorbid diagnoses of current substance misuse, organic brain damage, current or past psychosis including bipolar disorder, persistent antisocial behaviour, persistent self-injury needing clinical</td>
<td>Costs: MBCT-TS, medication, inpatient &amp; outpatient care, A&amp;E, ambulance, staff time (GP, practice nurse, district nurse, health visitor, community psychiatric nurse, midwife, community psychiatrist, clinical psychologist, occupational therapist, physiotherapist, counselling, art/drama/music therapist, chiropodist, dietician, social worker, support worker), advice service, day centre Plus out-of-pocket expenses and productivity losses Mean health and social care cost per person (SD): MCBT-TS: £2485 (£4077), AD: £2360 (£4206); difference £124 (95%CI -£750 to £973, p=0.80). Mean societal cost per person (SD): MCBT-TS: £3204 (£4012), AD: £2755 (£4465); difference £449 (95%CI -£842 to £1286, p=0.68)</td>
<td>Primary outcome measure: time to and % of relapse/recurrence Secondary outcomes: depression-free days</td>
<td>Using primary outcome: ICER of MCBT-TS vs AD: £4,955 (NHS/PSS perspective) or £10,604 (societal perspective) per additional relapse or recurrence averted Using QALYs, MBCT-TS is dominated by AD Using any of the outcomes, the probability of</td>
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<tr>
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<td>Using primary outcome: ICER of MCBT-TS vs AD: £4,955 (NHS/PSS perspective) or £10,604 (societal perspective) per additional relapse or recurrence averted Using QALYs, MBCT-TS is dominated by AD Using any of the outcomes, the probability of</td>
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## Depression in adults: treatment and management

### Economic evidence – evidence tables

<table>
<thead>
<tr>
<th>Study Country Study type</th>
<th>Intervention details</th>
<th>Study population Study design Data sources</th>
<th>Costs and outcomes: description and values</th>
<th>Results: Cost-effectiveness</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(MBCT-TS) Maintenance antidepressant treatment plus GP support in maintaining a therapeutic level of medication over 2 years (AD)</td>
<td>management or therapy, formal concurrent psychotherapy. Pragmatic single-blind parallel 2-group RCT Source of efficacy data: RCT (Kuyken2015); (N=424, completers=366) Source of resource use data: RCT (N=424, completers=248) Source of unit costs: national sources</td>
<td>recorded by the depression module of the Structured Clinical Interview for DSM–IV (SCID), residual depressive symptoms assessed by the GRID-HAMD and the BDI, psychiatric and medical comorbidity using the relevant SCID modules and the Medical Symptom Checklist (MSCL), respectively, quality of life using the WHO Quality of Life instrument (WHOQOL-BREF) and the EQ-5D-3L (used to estimate QALYs) Percentage of people relapsing: MBCT-TS: 44%; ADs: 47% Hazard ratio 0.89 (95%CI 0.67 to 1.18, p=0.43) Difference in secondary outcomes: no statistically significant differences QALYs: MBCT-TS: 1.49; ADs: 1.53</td>
<td>MBCT-TS being cost-effective did not exceed 0.49 (NHS/PSS perspective) or 0.52 (societal perspective)</td>
<td></td>
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</table>
### Appendix R: Health economic profiles

#### R.1 Service delivery models for adults with depression

#### R.1.1 Collaborative care

**Table 1: Clinical / economic question: simple collaborative care in addition to TAU versus TAU for adults with depression**

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty £/effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosanquet et al., 2017 UK</td>
<td>Potentially serious limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>£490</td>
<td>0.019</td>
<td>£26,535</td>
<td>Probability of intervention being cost-effective: 0.39 and 0.55 at WTP £20,404 and £30,606/QALY, respectively. Including only participants who engaged with 5 or more sessions in the analysis, ICER fell at £10,075/QALY</td>
</tr>
<tr>
<td>Green et al., 2014 UK</td>
<td>Minor limitations⁴</td>
<td>Directly applicable⁵</td>
<td>Outcome: QALY</td>
<td>£287</td>
<td>0.019</td>
<td>£15,092</td>
<td>Probability of intervention being cost-effective: 0.58 and 0.65 at WTP £21,185 and £31,778/QALY, respectively. Results robust to multiple imputation of missing data, use of SF-6D utility values, use of alternative intervention costs</td>
</tr>
<tr>
<td>Lewis et al., 2017 UK</td>
<td>Potentially serious limitations⁶</td>
<td>Directly applicable⁷</td>
<td>Outcome: QALY</td>
<td>£429</td>
<td>0.044</td>
<td>£9,827</td>
<td>Probability of intervention being cost-effective: 0.92 and 0.97 at WTP £20,404 and £30,606/QALY, respectively. Accounting for the true observed intervention contact rate (rather than the expected that was used in the base-case analysis), ICER fell at £3,395/QALY</td>
</tr>
</tbody>
</table>

**Notes:**

1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis conducted alongside RCT (N=485; at 18 months n=344; cost data available for n=447); national unit costs used; statistical analyses conducted; CEACs presented; consideration of intervention and primary care costs only
3. UK study; NHS & PSS perspective; QALY estimates based on SF-6D (UK tariff)
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simon et al., 2002 US</td>
<td>Potentially serious limitations²</td>
<td>Partially applicable³</td>
<td>Outcome: number of depression-free days (days with a Hopkins Symptoms Checklist (HSCL) depression score ≤ 0.5; days with a HSCL score above 0.5 but &lt; 2 considered 50% depression free)</td>
<td>£13.91</td>
<td>13.9</td>
<td>£1.1</td>
<td>ICER 95% CI: -£143 to £368</td>
</tr>
</tbody>
</table>

### Notes:

1. Costs converted and uplifted to 2015 UK pounds using purchasing power parity (PPP) exchange rates and the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=386, n=377 used for cost analysis and n=315 used for clinical analysis); local prices used; statistical analyses conducted, including bootstrapping; analyses of clinical data included only those completing all blinded follow-up assessments; cost analyses included only those remaining enrolled throughout the follow-up period; participation in follow-up interviews was significantly greater in the intervention group than in usual care, introducing a possibility of bias.
3. US study; 3rd party payer perspective; no QALYs estimated
### Table 3: Clinical / economic question: complex collaborative care versus secondary mental health care for adults with depression

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morriss et al., 2016 UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>£3,477</td>
<td>0.079</td>
<td>£43,993</td>
<td>Controlling for baseline differences and cluster effects: probability of complex collaborative care being cost-effective exceeds 50% at WTP of £42,376/QALY</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK HCHS index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis conducted alongside RCT (N=187; 84% completed at 6 months, 72% at 12 months and 59% at 18 months); national unit costs used; statistical analyses conducted; CEACs presented.
3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)

### Table 4: Clinical / economic question: complex collaborative care in addition to TAU versus TAU for adults with depression

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goorden et al., 2014 The Netherlands</td>
<td>Minor limitations²</td>
<td>Partially applicable³</td>
<td>Occupational setting Outcome: QALY</td>
<td>-£644</td>
<td>-0.05</td>
<td>£13,233</td>
<td>Following bootstrapping and inspection of the cost effectiveness plane: in 75% of replications collaborative care less costly and less effective; in 21% collaborative care dominated; in 3% collaborative care dominant; in 1% collaborative care more costly and more effective</td>
</tr>
<tr>
<td>Goorden et al., 2015 The Netherlands</td>
<td>Potentially serious limitations⁴</td>
<td>Partially applicable³</td>
<td>Primary care setting Outcome: QALY</td>
<td>£1089</td>
<td>0.02</td>
<td>£49,894</td>
<td>Probability of CCC being cost-effective: 0.20 and 0.70 at WTP £18,576 and £74,304/QALY, respectively.</td>
</tr>
</tbody>
</table>

Notes:
2. Time horizon 12 months; analysis conducted alongside RCT (N=126); national unit costs used.
3. Dutch study; healthcare system perspective; QALY based on EQ-5D ratings but Dutch tariff
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosmans et al., 2007 The Netherlands</td>
<td>Potentially serious limitations</td>
<td>Partially applicable</td>
<td>Outcomes: Adherence Difference in HSCL score</td>
<td>£324</td>
<td>0.021 -0.15</td>
<td>£15,314/extra adherence £2,621/point improvement in HSCL</td>
<td>Probability of intervention being cost-effective around 0.65 at WTP of £51,391 per extra person with improvement in adherence</td>
</tr>
<tr>
<td>Rubio-Valera et al., 2013 Spain</td>
<td>Potentially serious limitations</td>
<td>Partially applicable</td>
<td>Outcomes: Adherence Remission QALY</td>
<td>£44</td>
<td>0.04 -0.01</td>
<td>£863/extra adherence Dominated using remission as an outcome £3,224/QALY</td>
<td>Probability of intervention being cost-effective 0.71 and 0.76 for WTP £5,385/adherent service user and £26,927/QALY, respectively. Using remission, maximum probability of intervention being cost-effective was 0.46</td>
</tr>
</tbody>
</table>

### Medication management

Table 5: Clinical / economic question: medication management in addition to TAU versus TAU for adults with depression

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosmans et al., 2007 The Netherlands</td>
<td>Potentially serious limitations</td>
<td>Partially applicable</td>
<td>Outcomes: Adherence Difference in HSCL score</td>
<td>£324</td>
<td>0.021 -0.15</td>
<td>£15,314/extra adherence £2,621/point improvement in HSCL</td>
<td>Probability of intervention being cost-effective around 0.65 at WTP of £51,391 per extra person with improvement in adherence</td>
</tr>
<tr>
<td>Rubio-Valera et al., 2013 Spain</td>
<td>Potentially serious limitations</td>
<td>Partially applicable</td>
<td>Outcomes: Adherence Remission QALY</td>
<td>£44</td>
<td>0.04 -0.01</td>
<td>£863/extra adherence Dominated using remission as an outcome £3,224/QALY</td>
<td>Probability of intervention being cost-effective 0.71 and 0.76 for WTP £5,385/adherent service user and £26,927/QALY, respectively. Using remission, maximum probability of intervention being cost-effective was 0.46</td>
</tr>
</tbody>
</table>

### Notes:

2. Time horizon 6 months; no consideration of HRQoL outcomes; analysis conducted alongside RCT (N=151; economic analysis based on n=88 completers of both 3- and 6-month follow-up); national unit costs used; CEACs presented.
3. Dutch study; societal perspective; no QALY outcome
4. Time horizon 6 months; analysis conducted alongside RCT (N=179; 71% completed at 6 months; n=151 received intervention as allocated); regional unit costs used; CEACs presented; contradictory results depending on the outcome measure used
5. Spanish study; healthcare perspective; QALYs based on EQ-5D ratings, Spanish tariff
### R.1.3.1 Stepped care

#### Table 6: Clinical / economic question: stepped care in addition to TAU versus TAU for adults with depression

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mukuria et al., 2013 UK</td>
<td>Potentially serious limitations²</td>
<td>Directly applicable³</td>
<td>Outcomes: proportion with reliable and clinically significant improvement on PHQ-9 QALY - SF-6D (UK tariff) QALY - predicted EQ-5D (UK tariff), estimated from SF-6D using empirical mapping</td>
<td>£259</td>
<td>0.025</td>
<td>£10,363/improved participant</td>
<td>Probability of IAPT being cost-effective using SF-6D QALYs: &lt;0.40 at WTP £32,933/QALY; using EQ-5D QALYs: 0.38 and 0.53 at WTP £21,955 and £32,933/QALY, respectively. Using national unit costs instead of IAPT financial data: £4,171/improved participant; £13,036/QALY using SF-6D</td>
</tr>
<tr>
<td>Ricken et al., 2011 Germany</td>
<td>Potentially serious limitations⁴</td>
<td>Directly applicable⁵</td>
<td>Outcome: probability of remission, defined as a Bech–Rafaelsen-Melancholia-Scale (BRMS) score &lt;7</td>
<td>-£4,170</td>
<td>0.15</td>
<td>Dominant</td>
<td>Difference in costs p&lt;0.05; difference in effect p=0.07</td>
</tr>
</tbody>
</table>

Notes:
2. Time horizon 8 months; prospective cohort study with matched sites (N=403); low response rate at recruitment (403/3,391, 11.9%); IAPT service was assessed over the first 2 years of establishment, therefore costs associated with learning effects were likely; IAPT financial data used – results sensitive to the use of national unit costs; CEACs presented.
3. UK; NHS and social service perspective; QALY based on SG-6D (UK tariff); QALYs based on predicted EQ-5D ratings (UK tariff), estimated from SF-6D using an empirical mapping function, used in sensitivity analysis.
4. Time horizon from enrolment to study endpoint, i.e. drop-out or remission; consideration of hospitalisation and medication costs only; analysis conducted alongside RCT (N=148; completers n=103); national unit costs used.
5. German study; 3rd party payer perspective; no QALYs used, but intervention dominant so judgements on cost effectiveness were straightforward.
### R.1.4 Integrated care pathways

#### Table 7: Clinical / economic question: off-site versus on-site integrated care (primary care liaison) for adults with depression

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyne et al., 2015 US</td>
<td>Minor limitations&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Partially applicable&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Outcome: QALY Study included number of free days as an outcome measure, however, this analysis did not include inpatient costs, hence ICER not reported here</td>
<td>£823</td>
<td>0.04</td>
<td>£25,875/QALY (regional costs) £20,197/QALY (national costs)</td>
<td>Probability of off-site being cost-effective 0.86 at a cost effectiveness threshold of £35,905/QALY</td>
</tr>
</tbody>
</table>

**Notes:**
2. Time horizon 18 months; analysis conducted alongside RCT (N=364); unit costs from regional sources; national sources used in sensitivity analysis; bootstrapping conducted, CEACs presented
3. US study; health care provider perspective including service users’ time and mileage; QALYs based on SF-12/SF-6D algorithm (UK tariff)

#### Table 8: Clinical / economic question: integrated care versus primary care with referral system to specialist care for adults with depression

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiley-Exley et al., 2009 US</td>
<td>Potentially serious limitations&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Partially applicable&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Separate analyses for: Full (major and minor depression) VA sample Full non-VA sample Major depression VA sample Major depression non-VA sample Outcomes used: CES-D score; number of depression-free days derived from CES-D; QALYs estimated based</td>
<td>-£580 £41 £781 -£339</td>
<td>0.007 0.0004 0.015 -0.005</td>
<td>Dominant £84,566/QALY £52,395/QALY £70,902/QALY (less effective, less costly)</td>
<td>Probability of IC being cost-effective: &gt;0.70 for any WTP/QALY &lt;0.40 for any WTP/QALY &lt;0.50 for WTP of £35,600/QALY and above &gt;0.50 for WTP £44,500/QALY and above</td>
</tr>
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</table>
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kendrick et al., 2005 &amp; 2006</td>
<td>Minor limitation</td>
<td>Directly applicable</td>
<td>Outcome: QALY</td>
<td>£446</td>
<td>-0.02</td>
<td>Problem solving dominated by TAU</td>
<td>Significant difference in costs; non-significant difference in effects; majority of bootstrapped iterations showed</td>
</tr>
</tbody>
</table>

Notes:
2. Time horizon 6 months; analysis conducted alongside multi-site pragmatic RCT (N=840 with major or minor depression, assessed within and outside the Veteran Affairs (VA) system; within VA n=365, outside VA n=475; individuals with major depression within VA n=214, outside VA n=302); national unit costs; bootstrapping conducted, CEACs presented
3. US study; health care provider perspective including service users’ time and mileage; QALYs based on SF-36, using preferences for matched vignettes created following cluster analysis of SF-12 mental and physical component scores, elicited by US service users with depression using SG.

R.2.1 First-line treatment of adults with a new episode of less severe depression

R.2.1.2 Psychological interventions

3 Table 9: Clinical / economic question: problem solving versus treatment as usual
### Table 10: Clinical / economic question: psychodynamic counselling versus treatment as usual

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
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</thead>
<tbody>
<tr>
<td>Simpson et al. 2003 UK</td>
<td>Potentially serious limitation</td>
<td>Partially applicable</td>
<td>Primary outcome: change on the BDI; various other scales used as secondary outcomes</td>
<td>-£47</td>
<td>Non-reported</td>
<td>Similar costs and outcomes between interventions</td>
<td>Non-significant difference in costs and outcomes</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 26 weeks; analysis conducted alongside RCT (N=247; analysis based on n=184 with clinical data available; cost data available for n=159); national unit costs used; statistical analyses conducted; cost effectiveness planes presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)

### Table 11: Clinical / economic question: computerised CBT (with minimal support) versus treatment as usual

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaltenthaler</td>
<td>Potentially serious limitation</td>
<td>Partially applicable</td>
<td>Outcome: QALY</td>
<td>From £88</td>
<td>From 0.01</td>
<td>From £2,470 to</td>
<td>Probability of cCBT being cost-effective</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=145; cost and outcome data at 12 months available for n=115); local prices used for intervention, national unit costs used for other cost elements; statistical analyses (including bootstrapping) conducted; costs and outcomes not combined/summarised in a cost effectiveness measure; no uncertainty around cost effectiveness suggested.
3. UK study; NHS and social services perspective; QALY was not used as an outcome
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>et al., 2006 UK</td>
<td>serious limitation²</td>
<td>applicable³</td>
<td>3 commercially produced computerised CBT packages assessed to £265 (depending on package)</td>
<td>to 0.08 (depending on package)</td>
<td>£9,791 (depending on package)</td>
<td>at WTP £41,146/QALY: 0.54-0.87 (depending on package)</td>
<td></td>
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<tr>
<td>McCrone et al., 2003 UK</td>
<td>Potentially serious limitation⁴</td>
<td>Partially applicable⁵</td>
<td>Outcomes: BDI score number of depression-free days (DFDs) QALY</td>
<td>£62</td>
<td>-3.5 28.4 0.032</td>
<td>£17 / BDI unit change £2 / DFD £1,944 / QALY</td>
<td>Probability of cCBT being cost-effective: 0.14 and 0.81 at WTP zero and £62 per point improvement in BDI, respectively 0.15 and 0.80 at WTP zero and £8 per additional DFD, respectively 0.85 and 0.99 at WTP £7,775 and £23,324 per QALY, respectively</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis based on decision-analytic economic modelling; efficacy data based on analysis of individual-level RCT data, published RCT data and further assumptions; resource use data based on manufacturer submissions, published data and other assumptions; manufacturer prices used for intervention, national unit costs used for other cost elements; sensitivity analyses, including PSA conducted; CEACs presented
3. UK study; NHS perspective; QALY estimated based on EQ-5D ratings (UK tariff)
4. Time horizon 8 months; analysis conducted alongside RCT (N=274, cost data available for n=261); manufacturer prices used for intervention, national unit costs used for other cost elements; statistical analyses (including bootstrapping) conducted; QALY estimates based on assumption around BDI measurements.
5. UK study; NHS perspective; DFDs and QALY estimated based on assumptions around BDI measurements and around the utility of DFDs, respectively

### Table 12: Clinical / economic question: computerised CBT with support versus treatment as usual

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
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</thead>
<tbody>
<tr>
<td>Littlewood et al., 2015 UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY 2 computerised CBT programmes assessed (one commercially produced, the other</td>
<td>£108 -£110 (depending on package)</td>
<td>-0.044 -0.015 (depending on package)</td>
<td>cCBT package 1 dominated cCBT package 2 less costly, less effective £7,193</td>
<td>Probability of each intervention being cost effective at WTP £20,000/QALY: cCBT package 1 0.038; cCBT package 2 0.417; TAU: 0.545 Using SF-6D QALYs:</td>
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### Economic evidence profile

<table>
<thead>
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<th>Study and country</th>
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<th>Applicability</th>
<th>Other comments</th>
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<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
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<tbody>
<tr>
<td></td>
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<td></td>
<td>freely available)</td>
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</table>

**Notes:**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 2 years; analysis conducted alongside RCT (N=691; at 24 months EQ-5D data available for n=416 and NHS cost data available for n=580); national unit costs used; statistical analyses including regression analysis to control for covariates conducted; Cholesky decomposition conducted to account for covariance in costs and QALYs; CEACs presented; deterministic sensitivity analysis conducted.
3. UK study; NHS & PSS perspective; QALY estimated based on EQ-5D ratings (UK tariff).

### Table 13: Clinical / economic question: computerised CBT with support versus computerised CBT (with minimal support)

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brabyn et al., 2016 UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY A freely available computerised CBT programme was used in both arms</td>
<td>-£3</td>
<td>0.003</td>
<td>Computerised CBT with support dominant</td>
<td>Probability of computerised CBT with support being cost effective 0.55 at WTP both £20,000 and £30,000/QALY Results robust to inclusion of mental health-related costs only</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=369; complete cost data across the trial period available for n=209); national unit costs used.
### Economic evidence profile

Statistical analyses including regression analysis to control for covariates conducted; Cholesky decomposition conducted to account for covariance in costs and QALYs; CEACs presented; deterministic sensitivity analysis conducted.

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

### Table 14: Clinical / economic question: behavioural activation versus CBT

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Richards et al., 2016 UK</td>
<td>Minor limitations&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Directly applicable&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Outcome: QALY</td>
<td>-£346</td>
<td>0.050</td>
<td>Behavioural activation dominant</td>
<td>Probability of behavioural activation being cost-effective 0.8 at a WTP both £20,000 and £30,000/QALY Results robust to imputation of missing data</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 18 months; analysis conducted alongside RCT (N=440; costs available for n=327; QALYs available for n=309); national unit costs used; statistical analyses including bootstrapping conducted; CEACs presented; deterministic sensitivity analysis conducted.
3. UK study; NHS & PSS perspective; QALY estimated based on EQ-5D ratings (UK tariff)

### R.2.22 Pharmacological interventions

### Table 15: Clinical / economic question: SSRIs added to supportive care versus supportive care alone

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kendrick et al., 2009 UK</td>
<td>Minor limitations&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Directly applicable&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Outcomes: HAMD17 and QALY</td>
<td>12 weeks: -£33 26 weeks £180</td>
<td>12 weeks: -2.49 0.005 26 weeks: -1.81 0.010</td>
<td>12 weeks: SSRI &amp; supportive care dominant 26 weeks: £106/HAMD17 reduction in score £17,429/QALY</td>
</tr>
</tbody>
</table>
Table 16: Clinical / economic question: TCAs versus SSRIs versus lofepramine

Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peveler et al., 2005; Kendrick et al., 2006b</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcomes: number of DFWs, defined as a HADS-D score &lt;8; QALY</td>
<td>Versus lofepramine: TCAs: -£149; SSRIs: £11</td>
<td>Versus lofepramine: DFWs: TCAs: 0.7; SSRIs: 3.7; QALYs: TCAs: -0.004; SSRIs: 0.034</td>
<td>SSRIs vs lofepramine £45/DFW (TCAs extendedly dominated); SSRIs vs TCAs £3,821/QALY (lofepramine extendedly dominated)</td>
<td>Probability of SSRIs being cost-effective 0.6 at WTP £20,000/QALY</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside an open label RCT (N=327; entered preference group n=92; followed-up at 12 months n=171); national unit costs used; statistical analyses (including bootstrapping) conducted; CEACs presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D ratings (UK tariff)

Table 17: Clinical / economic question: acupuncture versus counselling versus treatment as usual

R.2.32 Physical interventions

3
## Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spackman et al., 2014 UK</td>
<td>Potentially serious limitations</td>
<td>Directly applicable</td>
<td>Outcome: QALY</td>
<td>Versus counselling: -£231 Versus TAU: £279</td>
<td></td>
<td></td>
<td></td>
<td>Probability of cost effectiveness at WTP £20,000/QALY: acupuncture 0.62, counselling 0.36, TAU 0.02 Results sensitive to small changes in intervention costs; results robust to inclusion of depression-related resource use only. In complete case analysis acupuncture dominated counselling.</td>
</tr>
<tr>
<td>Chalder et al., 2012 UK</td>
<td>Potentially serious limitations</td>
<td>Directly applicable</td>
<td>Outcome: QALY</td>
<td>£325</td>
<td>0.014</td>
<td>£22,871</td>
<td></td>
<td>Probability of cost effectiveness at £20,000 and £30,000/QALY: 0.49 and 0.57, respectively Using imputed data: ICER £21,290/QALY Probability of cost effectiveness at £20,000 and £30,000/QALY: 0.50 and 0.60, respectively</td>
</tr>
</tbody>
</table>

### Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=755; at 12 months EQ-5D data available for n=572; complete resource use data for n=150; multiple imputation used); acupuncture cost based on published data, for all other costs national unit costs used; statistical analyses conducted, including multiple imputation and regression analysis of costs and QALYs to account for baseline factors; PSA undertaken and CEACs presented; one way sensitivity analysis undertaken
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)
### Economic evidence profile

<table>
<thead>
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<th>Study and country</th>
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<th>Applicabilit y</th>
<th>Other comments</th>
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<th>NMB (£) per person¹</th>
<th>Uncertainty¹</th>
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</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations²</td>
<td>Directly applicable ³</td>
<td>Outcome: QALY</td>
<td>Versus pill placebo:</td>
<td>Cital -50,274</td>
<td>Cital 29.4</td>
<td>Mirtaz 31,816</td>
</tr>
<tr>
<td>Citalopram 31,522</td>
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### R.2.41 Psychological, pharmacological, physical and combined interventions

#### Table 19: Clinical / economic question: various interventions

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation s</th>
<th>Applicability</th>
<th>Other comments</th>
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<tr>
<td>Guideline economic analysis UK</td>
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<td>Outcome: QALY</td>
<td>Versus pill placebo:</td>
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<td>Cital 29.4</td>
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Results of individual psych interventions sensitive to utility values, cost of relapse and unit cost of therapist.
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost / 1000 people (£) (^1)</th>
<th>Incremental effect / 1000 people</th>
<th>NMB (£) per person (^1)</th>
<th>Uncertainty (^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horrell et al., 2014 UK</td>
<td>Potentially serious limitations (^2)</td>
<td>Directly applicable (^3)</td>
<td>Outcomes: BDI-II scores, number of depression-free days (DFDs), QALY</td>
<td>-£7</td>
<td>5.96</td>
<td>Not reported (not possible to estimate as reported costs and outcomes were not adjusted for baseline differences)</td>
<td>Probability of psychoeducation being cost-effective: 0.30, 0.80 and 0.99 at WTP zero, £32 and £74 per BDI-II point improvement, respectively; 0.90 at WTP £15/DFD gained; 0.50 at WTP £20,656/QALY, max probability 0.56, irrespective of WTP per QALY gained</td>
</tr>
</tbody>
</table>

### Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 3 months; analysis conducted alongside RCT (N=459, completers n=382); national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)

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**R.3.1 First-line treatment of adults with a new episode of more severe depression**

**R.3.1.2 Psychological interventions**

3. **Table 20: Clinical / economic question: psychoeducational workshop versus wait list**

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) (^1)</th>
<th>Incremental effect</th>
<th>ICER (£/effect) (^1)</th>
<th>Uncertainty (^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horrell et al., 2014 UK</td>
<td>Potentially serious limitations (^2)</td>
<td>Directly applicable (^3)</td>
<td>Outcomes: BDI-II scores, number of depression-free days (DFDs), QALY</td>
<td>-£7</td>
<td>5.96</td>
<td>Not reported (not possible to estimate as reported costs and outcomes were not adjusted for baseline differences)</td>
<td>Probability of psychoeducation being cost-effective: 0.30, 0.80 and 0.99 at WTP zero, £32 and £74 per BDI-II point improvement, respectively; 0.90 at WTP £15/DFD gained; 0.50 at WTP £20,656/QALY, max probability 0.56, irrespective of WTP per QALY gained</td>
</tr>
</tbody>
</table>

### Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 3 months; analysis conducted alongside RCT (N=459, completers n=382); national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)
### Table 21: Clinical / economic question: individual CBT versus treatment as usual

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
</table>
| Holman et al., 2011 UK | Potentially serious limitations<sup>2</sup> | Partially applicable<sup>3</sup> | CBT delivered online using real-time therapist interaction through written messaging Outcome: change in BDI-II score | £487 | 3.6 | £137 | Probability of CBT being cost-effective 0.90 at WTP £308 per point reduction in BDI-II.

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 10 months; analysis conducted alongside RCT (N=204, at endpoint available cost data for n=198, available outcome data for n=167); only primary and community service costs considered; secondary care costs omitted; national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; health and social services perspective; QALY not used as an outcome

### Table 22: Clinical / economic question: individual CBT delivered online versus wait list

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
</table>
| Hollinghurst et al., 2010 UK | Potentially serious limitations<sup>2</sup> | Directly applicable<sup>3</sup> | Outcomes: % of recovery (BDI <10), QALY | £550 | 16.5% 0.034 | £20,150 | Probability of computerised CBT being cost-effective: 0.56 and 0.71 at WTP £20,000 and £30,000/QALY, respectively. After imputation of missing data: ICER £11,831/QALY Probability of computerised CBT being cost-effective: 0.94 and 0.98 at WTP £20,000 and £30,000/QALY, respectively.

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 8 months; analysis conducted alongside RCT (N=297; BDI data available for n=210; QALYs available for n=165; NHS cost data available for n=137); national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS perspective; QALY estimates based on EQ-5D (UK tariff)
## Table 23: Clinical / economic question: behavioural activation versus treatment as usual

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ekers et al., 2011 UK</td>
<td>Potentially serious limitations²</td>
<td>Directly applicable³</td>
<td>Outcomes: change in BDI-II score; QALY Intervention delivered by nurses with no previous training 2 scenarios: therapists delivering 65 treatments/year in a depression-specific role (A) or 33 treatments/year treating depression and anxiety (B)</td>
<td>A: £164</td>
<td>B: £192</td>
<td>BDI -15.78 QALY 0.03</td>
<td>A: £10/BDI-II point reduction £5,495/QALY B: £12/BDI-II point reduction £6,319/QALY</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 3 months; analysis conducted alongside RCT (N=47, completers n=38); primary, secondary and community care costs considered; national unit costs used; statistical analyses conducted including bootstrapping, CEACs presented.
3. UK study; NHS and personal social services perspective; QALY estimates based on EQ-5D (UK tariff)

## Table 24: Clinical / economic question: counselling versus antidepressants (AD)

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller et al., 2003 UK</td>
<td>Potentially serious limitations²</td>
<td>Partially applicable³</td>
<td>Outcome: % of people with good ‘global outcome’, reflecting response to treatment within 8 weeks and remaining well RCT: £77 Preference trial: £134 Preference trial: 8%</td>
<td>RCT: AD vs counselling £483 Preference trial: counselling vs AD £1,675</td>
<td>RCT: probability of counselling being cost-effective 0.25 and 0.10 at WTP £918 and £3,674 /extra person with good global outcome, respectively Assuming missing data reflected good outcomes, probability of counselling being cost-effective increased at any WTP Assuming missing data represented poor outcomes, probability of counselling being cost-effective slightly increased for WTP &lt; £2,755 /good global outcome and decreased for WTP &gt; £2,755 /good global outcome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes:
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation s</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benedict et al., 2010 UK</td>
<td>Potentially serious limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>-£41</td>
<td>0.002</td>
<td>SSRIs dominant</td>
<td>Probabilistic analysis favoured duloxetine, which was not part of decision problem for this review question. Results sensitive to efficacy and utility data.</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
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).

### R.3.2.1 Pharmacological interventions

2 **Table 25: Clinical / economic question: SSRIs versus mirtazapine**

### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation s</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benedict et al., 2010 UK</td>
<td>Potentially serious limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>-£41</td>
<td>0.002</td>
<td>SSRIs dominant</td>
<td>Probabilistic analysis favoured duloxetine, which was not part of decision problem for this review question. Results sensitive to efficacy and utility data.</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
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).

3 **Table 26: Clinical / economic question: escitalopram versus citalopram**

### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation s</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wade et al., 2005a</td>
<td>Potentially serious</td>
<td>Directly applicable³</td>
<td>Population: adults with moderate-to-severe</td>
<td>-£108</td>
<td>5.3%</td>
<td>Escitalopram dominant</td>
<td>Results robust under different scenarios (changes in rates of remission, relapse,</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 12 months; analysis conducted alongside RCT (N=103, at 12 months efficacy data for n=81 and resource data for n=103) and preference trial (N=220; at 12 months efficacy data for n=163 and resource use data n=215); only depression-related costs considered; national unit costs used except for counsellors, where local costs were used; statistical analyses conducted including bootstrapping, CEACs presented.  
3. UK study; NHS perspective; QALY not used as an outcome.
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>limitations</td>
<td>applicable</td>
<td>depression Outcome: % of remission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wade et al., 2005b UK</td>
<td>Potentially serious limitations</td>
<td>directly applicable</td>
<td>Population: adults with severe depression Outcome: % of remission</td>
<td>-£44</td>
<td>5%</td>
<td>Escitalopram dominant</td>
<td>Results robust to changes in drug-specific probabilities and cost data PSA: Escitalopram dominant in &gt;99.8% of iterations</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 26 weeks; analysis based on economic modelling, efficacy data from pooled RCTs; resource use data based on a general practice database, expert opinion and published studies; national unit costs used; statistical analyses conducted including PSA, funded by industry, side effects not considered in estimation of costs
3. UK study; NHS perspective; QALY not used as an outcome but intervention dominant (so no further judgements on cost effectiveness required)
4. Time horizon 26 weeks; analysis based on economic modelling, efficacy data from pooled RCTs; resource use data based on a general practice database, expert opinion and published studies; national unit costs used; statistical analyses conducted including PSA, funded by industry.

#### R.3.3.1 Combined pharmacological and psychological interventions

2 Table 27: Clinical / economic question: combination therapy (CBT and fluoxetine) versus antidepressant therapy (fluoxetine)

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
</table>
| Simon et al., 2006 UK | Minor limitations | partially applicable | Population: adults with moderate or severe depression Outcomes: % of successful treatment (remission and no relapse over 12 months, remission defined as HAMD17 ≤ 6 or HAMD24 ≤ 8); QALY | £874 | % successful treatment: 16% QALYs - moderate depression 0.04 - severe depression 0.11 | £5,563 /extra successfully treated person £19,942/QALY for moderate depression £7,923/QALY for severe depression | 95% CIs: £1,920 to £25,099 /extra successfully treated person £6,583 to £108,901/QALY for moderate depression £2,606 to 446,358/QALY for severe depression Results sensitive to changes in relative efficacy (remission and relapse). Probability of Combo being cost-
**Table 28: Clinical / economic question: combination therapy (CBT and citalopram) versus CBT versus antidepressant therapy (citalopram)**

<table>
<thead>
<tr>
<th>Economic evidence profile</th>
<th>Study and country</th>
<th>Limitation(s)</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koeser et al., 2015 UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Population: adults with moderate or severe depression</td>
<td>Outcome: QALY</td>
<td>Vs citalopram: CBT £802 Combo £1,468</td>
<td>Vs citalopram: CBT 0.038 Combo 0.038</td>
<td>Combo dominated by CBT CBT vs citalopram: £20,791</td>
<td>Probability of CBT, citalopram, Combo being cost-effective at WTP £26,000/QALY: 0.43, 0.37 and 0.20, respectively Results sensitive to changes in inclusion criteria for RCTs for acute and follow-up treatment Using SF-6D values: ICER of CBT vs citalopram £33,805/QALY</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Time horizon 27 months; analysis based on economic modelling, efficacy data from systematic review and network meta-analysis; resource use data based on published estimates of expert opinion and analysis of RCT data; PSA conducted, CEACs presented; side effects not considered in estimation of costs or QALYs
3. UK study; NHS perspective; QALYs generated based on EQ-5D ratings (UK tariff)
## Physical interventions

### Table 29: Clinical / economic question: ECT as part of different sequencing strategies

<table>
<thead>
<tr>
<th>Economic evidence profile</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study and country</strong></td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Greenhalgh et al., 2005 UK</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
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
## Psychological, pharmacological, physical and combined interventions

### Table 30: Clinical / economic question: various interventions

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost / 1000 people (£)</th>
<th>Incremental effect / 1000 people</th>
<th>NMB (£) per person</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>Versus pill placebo: Sertraline 13,593 Mirtazapine 34,754 BA 707,004 CBT indiv 991,804 CBT group -99,791 PDPT 991,943 Counselling 1,023,704 cCBT 69,476 Exercise -44,045 CBT ind + sertr 1,052,806</td>
<td>Versus pill placebo: Sertraline 57.4 Mirtazapine 49.0 BA 108.4 CBT individual 53.4 CBT group 93.8 PDPT 98.0 Counselling 93.2 cCBT -1.6 Exercise 52.8 CBT ind + sertr 157.3</td>
<td>CBT ind + sert 27,658 CBT group 27,541 BA 27,025 Sertraline 26,698 Exercise 26,664 PDPT 26,533 Mirtaz 26,510 Counselling 26,405 CBT indiv 25,642 Pill placebo 25,564 cCBT 25,464</td>
<td>Probability of cost effectiveness at WTP £20,000/QALY: CBT individual + sertraline 0.31; CBT group 0.24; BA 0.13; sertraline 0.05; Exercise 0.13; PDPT 0.03; mirtaz 0.06; counselling 0.05; CBT individual 0.00; pill placebo 0.00; cCBT 0.00</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2016 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
2. Decision-analytic hybrid model, time horizon 12 weeks + 2 years; relative effects based on guideline systematic review and NMA; baseline effects derived from review of naturalistic studies; resource use based on published data supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs and CEAF presented
3. UK study; NHS & PSS perspective; QALY estimates based on EQ-5D (UK tariff)
R.4.1 Interventions for adults with depression who responded inadequately or were intolerant to previous treatment

R.4.1.3 Psychological interventions

Table 31: Clinical / economic question: cognitive therapy or cognitive behavioural therapy in addition to TAU versus TAU alone

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scott et al., 2003 UK</td>
<td>Minor limitation</td>
<td>Partially applicable</td>
<td>Intervention: cognitive therapy TAU: antidepressant therapy plus medical management Outcome measure: percentage of relapses avoided</td>
<td>£1,265</td>
<td>18%</td>
<td>£7,030</td>
<td>ICER £7,581 using mean imputation; £8,167 using non-parametric multiple imputation; £11,462 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 £9,746 and £13,807 per relapse prevented, respectively; probability sensitive to method of missing data imputation</td>
</tr>
<tr>
<td>Hollinghurst et al., 2014; Wiles et al., 2016 UK</td>
<td>Minor limitation</td>
<td>Directly applicable</td>
<td>Intervention: cognitive behavioural therapy TAU: GP care, including antidepressant treatment or referral as required Outcome measure: QALY</td>
<td>Endpoint: £928 Mean over 3-5 years: £287</td>
<td>Endpoint: 0.053 Mean over 3-5 years: 0.052</td>
<td>Endpoint: £16,271 Follow-up: £5,482</td>
<td>Results robust to changes in psychologist unit cost &amp; exclusion of hospitalisation costs Using SF-6D-based QALYs: £32,328/QALY Using completers’ data: £20,036/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</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
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
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benedict et al., 2010 UK</td>
<td>Potentially serious limitations²</td>
<td>Directly applicable³</td>
<td>Interventions: duloxetine, venlafaxine, mirtazapine Outcome: QALY</td>
<td>Duloxetine versus: Venlafaxine: -£62 Mirtazapine: -£25</td>
<td>Duloxetine versus: Venlafaxine: 0.05 Mirtazapine: 0.08</td>
<td>Duloxetine dominant</td>
<td>Probability of duloxetine being cost-effective at WTP £20,000/QALY: approximately 0.80</td>
</tr>
<tr>
<td>Nordström et al., 2010 Sweden</td>
<td>Potentially serious limitations⁴</td>
<td>Partially applicable⁵</td>
<td>Interventions: escitalopram, duloxetine, venlafaxine Outcome: QALY</td>
<td>Escitalopram versus: Duloxetine: -£15 Venlafaxine: -£55</td>
<td>Escitalopram versus: Duloxetine: 0.025 Venlafaxine: 0.024</td>
<td>Escitalopram dominant</td>
<td>Probability of escitalopram being cost-effective at WTP £20,000/QALY: 0.981 and 0.985 compared with duloxetine and venlafaxine, respectively</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs converted and uplifted to 2015 UK pounds using purchasing power parity (PPP) exchange rates and the UK HCHS index (Curtis & Burns, 2015).
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-5D (UK tariff).
### Table 33: Clinical / economic question: lithium versus antipsychotics as adjuncts to SSRI treatment

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)(^1)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards et al., 2103 UK</td>
<td>Potentially serious limitations(^2)</td>
<td>Directly applicable(^3)</td>
<td>Outcome: QALY</td>
<td>-£959</td>
<td>0.028</td>
<td>Lithium as an adjunct to SSRI dominant</td>
<td>Probability of lithium being dominant 1 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</td>
</tr>
</tbody>
</table>

Notes:
1. Costs uplifted to 2015 UK pounds using the UK hospital & community health services (HCHS) index (Curtis & Burns, 2015).
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)

### R.5 Interventions for relapse prevention

#### R.5.1 Psychological interventions

### Table 34: Clinical / economic question: mindfulness-based cognitive therapy versus maintenance antidepressant treatment

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)(^1)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)(^1)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuyken et al., 2008 UK</td>
<td>Minor limitations(^2)</td>
<td>Partially applicable(^3)</td>
<td>Outcome: % of people avoiding relapse</td>
<td>£380</td>
<td>13%</td>
<td>£335/relapse prevented (adjusted)</td>
<td>Not statistically significant differences in costs or outcomes</td>
</tr>
<tr>
<td>Kuyken et al., 2008 UK</td>
<td>Minor limitations(^4)</td>
<td>Directly applicable(^5)</td>
<td>Outcomes: % of people avoiding relapse and QALYs</td>
<td>£129</td>
<td>3%</td>
<td>£5,141/relapse prevented (adjusted)</td>
<td>Not statistically significant differences in costs or outcomes Probability of MBCT being</td>
</tr>
</tbody>
</table>
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)$^1$</th>
<th>Incremental effect</th>
<th>ICER (£/effect)$^1$</th>
<th>Uncertainty$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations$^2$</td>
<td>Directly applicable$^3$</td>
<td>Outcome: QALY</td>
<td>£111</td>
<td>0.0004</td>
<td>£293,305</td>
<td>Probability of SSRIs being cost-effective at WTP £20,000/QALY: 0.30</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SSRIs improves as number of previous episodes increases and severity of future relapses increases</td>
</tr>
</tbody>
</table>

Notes:
1. Costs reported in 2016 UK pounds.
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations(^2)</td>
<td>Directly applicable(^3)</td>
<td>Outcome: QALY</td>
<td>£159</td>
<td>-0.008</td>
<td>Dominated</td>
<td>Probability of SNRIs being cost-effective at WTP £20,000/QALY: 0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Notes:
1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff
### Table 37: Clinical / economic question: maintenance TCAs versus clinical management (TCAs tapering) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>£176</td>
<td>-0.010</td>
<td>Dominated</td>
<td>Probability of TCAs being cost-effective at WTP £20,000/QALY: 0.09</td>
</tr>
</tbody>
</table>

Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SNRIs improves as number of previous episodes increases and severity of future relapses increases.

#### Notes:
1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented.
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff.

### Table 38: Clinical / economic question: maintenance mirtazapine versus clinical management (mirtazapine tapering) in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)¹</th>
<th>Incremental effect</th>
<th>ICER (£/effect)¹</th>
<th>Uncertainty¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations²</td>
<td>Directly applicable³</td>
<td>Outcome: QALY</td>
<td>£151</td>
<td>-0.011</td>
<td>Dominated</td>
<td>Probability of mirtazapine being cost-effective at WTP £20,000/QALY: 0.95</td>
</tr>
</tbody>
</table>

Conclusions robust to use of alternative utility values for less severe depression, changes in cost of relapse. Cost effectiveness of SNRIs improves as number of previous episodes increases and severity of future relapses increases.
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£)(^1)</th>
<th>Incremental effect</th>
<th>ICER (£/effect)(^1)</th>
<th>Uncertainty(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations(^2)</td>
<td>Directly applicable(^3)</td>
<td>Outcome: QALY Interventions in [] considered in SA only</td>
<td>MBCT &amp; AD £188 MBCT &amp; AD taper £65 AD £51 [group CT &amp; AD £164]</td>
<td>MBCT &amp; AD: 0.058 MBCT &amp; AD taper: 0.064 AD: 0.038 [Group CT &amp; AD: 0.052]</td>
<td>MBCT &amp; AD taper £129,554 MBCT &amp; AD £129,309 [group CT &amp; AD £129,220] AD £129,050 AD taper £128,344</td>
<td>Probability of being cost-effective: AD base-case analysis: MBCT &amp; AD taper 0.83; MBCT &amp; AD 0.16; AD 0.01; AD taper 0.00 AD sensitivity analysis: MBCT &amp; AD taper 0.76; MBCT &amp; AD 0.09; Group CT &amp; AD low cost 0.15; AD 0.00; AD taper 0.00 Results robust to an increase</td>
</tr>
</tbody>
</table>

**Notes:**
1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff

### Psychological, pharmacological and combined interventions

**Table 39:** Clinical / economic question: MBCT combined with maintenance antidepressant treatment versus MBCT combined with clinical management (antidepressant tapering) versus maintenance antidepressant treatment versus clinical management (antidepressant tapering) versus group CT combined with maintenance antidepressant treatment in people at high risk of relapse who remitted following acute pharmacological treatment and who experienced more severe depression if they relapsed

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) vs clinical management (AD taper)(^1)</th>
<th>Incremental effect vs clinical management (AD taper)</th>
<th>NMB (£)(^1)</th>
<th>Uncertainty(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis UK</td>
<td>Minor limitations(^2)</td>
<td>Directly applicable(^3)</td>
<td>Outcome: QALY Interventions in [] considered in SA only</td>
<td>MBCT &amp; AD £188 MBCT &amp; AD taper £65 AD £51 [group CT &amp; AD £164]</td>
<td>MBCT &amp; AD: 0.058 MBCT &amp; AD taper: 0.064 AD: 0.038 [Group CT &amp; AD: 0.052]</td>
<td>MBCT &amp; AD taper £129,554 MBCT &amp; AD £129,309 [group CT &amp; AD £129,220] AD £129,050 AD taper £128,344</td>
<td>Probability of being cost-effective: AD base-case analysis: MBCT &amp; AD taper 0.83; MBCT &amp; AD 0.16; AD 0.01; AD taper 0.00 AD sensitivity analysis: MBCT &amp; AD taper 0.76; MBCT &amp; AD 0.09; Group CT &amp; AD low cost 0.15; AD 0.00; AD taper 0.00 Results robust to an increase</td>
</tr>
</tbody>
</table>
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation s</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) vs clinical management (AD taper)(^1)</th>
<th>Incremental effect vs clinical management (AD taper)</th>
<th>NMB (£)(^1)</th>
<th>Uncertainty(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis</td>
<td>Minor limitations(^2)</td>
<td>Directly applicable(^3)</td>
<td>Outcome: QALY</td>
<td>CT £674 Fluoxetine £225 No treat -£9</td>
<td>CT: 0.014 Fluoxetine: -0.016 No treat: -0.014</td>
<td>Pill placebo £131,837 No treat £131,584 CT £131,405</td>
<td>Probability of being cost-effective: pill placebo 0.58; no treat 0.37; CT 0.04; fluoxetine 0.01</td>
</tr>
</tbody>
</table>

Notes:
1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff

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### Table 40: Clinical / economic question:

CT versus fluoxetine versus clinical management (pill placebo) versus no treatment (wait list)

in people at medium risk of relapse who remitted following acute pharmacological treatment and who experienced less severe depression if they relapsed

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation s</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) vs clinical management (pill placebo)(^1)</th>
<th>Incremental effect vs clinical management (pill placebo)</th>
<th>NMB (£)(^1)</th>
<th>Uncertainty(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis</td>
<td>Minor limitations(^2)</td>
<td>Directly applicable(^3)</td>
<td>Outcome: QALY</td>
<td>CT £674 Fluoxetine £225 No treat -£9</td>
<td>CT: 0.014 Fluoxetine: -0.016 No treat: -0.014</td>
<td>Pill placebo £131,837 No treat £131,584 CT £131,405</td>
<td>Probability of being cost-effective: pill placebo 0.58; no treat 0.37; CT 0.04; fluoxetine 0.01</td>
</tr>
</tbody>
</table>
## Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) vs clinical management (pill placebo)</th>
<th>Incremental effect vs clinical management (pill placebo)</th>
<th>NMB (£)$</th>
<th>Uncertainty$</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td></td>
<td></td>
<td></td>
<td>Fluo £131,275</td>
<td>Results robust to an increase in number of previous episodes, assuming zero cost of clinical management, and a 50% increase in cost of relapse. CT becomes most cost effective option if number of sessions is reduced to 4; 2nd most cost-effective option if number of sessions is reduced to 4 but preventive effect lasts only 1 year or future relapse episodes are more severe; least cost-effective if less severe depression has a higher utility value or cost of relapse is reduced by 50% or preventive effect of CT lasts only one year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**

1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff
### Table 41: Clinical / economic question: CT versus fluoxetine versus clinical management (pill placebo) versus no treatment (wait list) versus MBCT versus group CT in people at high risk of relapse who remitted following acute pharmacological treatment and who experienced more severe depression if they relapsed

#### Economic evidence profile

| Study and country | Limitations | Applicability | Other comments | Incremental cost (£) vs clinical management (pill placebo)
|-------------------|-------------|---------------|----------------|--------------------------------------------------|
| Guideline economic analysis UK | Minor limitations<sup>2</sup> | Directly applicable<sup>3</sup> | Outcome: QALY Interventions in [] considered in SA only | CT: £674  
Fluoxetine: £225  
No treat: £8  
[MBCT £101]  
Group CT: £94 |
| | | | | CT: 0.032  
Fluoxetine: -0.013  
No treat: -0.032  
[MBCT 0.012]  
Group CT: 0.001 |
| | | | | [MBCT £128,523]  
Pill placebo £128,389  
CT £128,357  
[group CT £128,315]  
Fluo £127,897  
No treat £127,759 |

Uncertainty<sup>1</sup>

<p>| |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Probability of being cost-effective:</td>
</tr>
<tr>
<td>Base-case analysis:</td>
</tr>
<tr>
<td>Pill placebo 0.39; CT 0.28; fluoxetine 0.06; no treat 0.27;</td>
</tr>
<tr>
<td>Sensitivity analysis:</td>
</tr>
<tr>
<td>CT 0.14; fluoxetine 0.04; no treat 0.00; MBCT 0.35; group CT 0.25; pill placebo 0.22</td>
</tr>
</tbody>
</table>

Results robust to the assumption of zero clinical management cost and to 50% change in the cost of relapse; results moderately sensitive to utility values.

CT is most cost-effective if number of previous episodes increases to 5 or number of sessions is reduced to 4, even if preventive effect lasts only 1 year; least cost-effective if future relapses are less severe.

#### Notes:

1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented.
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitations</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) vs clinical management (pill placebo)</th>
<th>Incremental effect vs clinical management (pill placebo)</th>
<th>NMB (£)</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline economic analysis\nUK</td>
<td>Minor limitations\n2</td>
<td>Directly applicable\n3</td>
<td>Outcome: QALY</td>
<td>Combo £826\nAD £23\nPsych &amp; AD taper £765</td>
<td>Combo: 0.059\nAD: 0.048\nPsych &amp; AD taper: 0.036</td>
<td>AD £129,281\nCombo £128,694\nPsych &amp; AD taper £128,344\nAD taper £128,308</td>
<td>Probability of being cost-effective: AD 0.95; Combo 0.04; AD taper 0.00; Psych &amp; AD taper 0.00</td>
</tr>
</tbody>
</table>

3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff

Table 42: Clinical / economic question: combined psychological (CBT) and pharmacological (fluoxetine) maintenance treatment versus pharmacological treatment alone versus psychological treatment combined with clinical management (antidepressant tapering) versus clinical management (antidepressant tapering) at high risk of relapse who remitted following acute pharmacological treatment and who experienced more severe depression if they relapsed

Notes:
### Economic evidence profile

<table>
<thead>
<tr>
<th>Study and country</th>
<th>Limitation</th>
<th>Applicability</th>
<th>Other comments</th>
<th>Incremental cost (£) vs clinical management (pill placebo)</th>
<th>Incremental effect vs clinical management (pill placebo)</th>
<th>NMB (£)</th>
<th>Uncertainty</th>
</tr>
</thead>
</table>

1. Costs reported in 2016 UK pounds.
2. Decision-analytic Markov model, time horizon 10 years; relative effects based on guideline systematic review and meta-analysis; baseline effects derived from review of naturalistic studies; disutility and costs due to common side effects considered – disutility and costs due to serious (but less common) side effects not considered; resource use based on published data from a large naturalistic study (N=88,935) supplemented by most up-to-date resource use and unit cost data; national unit prices used; PSA conducted; CEACs presented
3. UK study; NHS & PSS perspective; QALYs based on EQ-5D measurements and the UK population tariff