Cost-effectiveness of cognitive-behavioural therapy and drug interventions for major depression

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The health interventions examined in the study were seven strategies for the episodic and maintenance treatment of major depression:

Strategy 1: drug treatment with tricyclic antidepressants (TCAs) for acute major depressive episodes plus a 6-month continuation phase after remission of symptoms;

Strategy 2: drug treatment with selective serotonin re-uptake inhibitors (SSRIs) for acute episodes and 6 months continuation;

Strategy 3: cognitive-behavioural therapy (CBT) treatment of acute major depressive episodes consisting of 12 sessions analysed separately whether provided by a psychologist or a psychiatrist in public or private service and whether provided to individuals or in a group;

Strategy 4: bibliotherapy for acute episodes;

Strategy 5: maintenance treatment with TCAs for 5 years following an acute episode;

Strategy 6: maintenance treatment with SSRIs for 5 years following an acute episode;

Strategy 7: a maintenance variant of CBT with booster sessions over a period of 5 years.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients suffering from major depression.

Setting
The setting was community and secondary care. The economic study was carried out in Australia.

Dates to which data relate
Effectiveness data were derived from studies published between 1983 and 2004. Most resource use data came from a survey published in 1998. Costs were estimated using 1999/2000 prices.
Source of effectiveness data
The effectiveness evidence came from a synthesis of published studies and authors' opinions.

Outcomes assessed in the review
The outcomes estimated from the literature were the size of the eligible population; relative risk (RR) of suicide in prevalent depression and RR of suicide for patients on treatment versus patients not on treatment; effect of antidepressant drugs, CBT, and bibliotherapy; RR of relapse during 6 months continuation of drug treatment, RR of relapse with maintenance treatment, and RR of relapse in 18 months following CBT; disability weight for mild, moderate and severe depression together with disability weight change; adherence with treatments; lag to treatment for current treatment-seeking patterns; and types and proportion of antidepressant drugs received by patients.

Study designs and other criteria for inclusion in the review
Primary studies appear to have been identified selectively rather than through a systematic review of the literature. Some clinical evidence came from the 1997 Survey of Mental Health and Wellbeing (SMHWB). Other data came from meta-analyses of clinical trials and community follow-up studies.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Approximately 19 primary studies were used as the source of clinical data.

Methods of combining primary studies
Primary estimates appear not to have been carried out since each study provided a set of estimates. However, data on treatment effect and RR of relapse were derived from published meta-analyses, in some circumstances updated by the authors with the addition of more recent clinical trials.

Investigation of differences between primary studies
Not stated.

Results of the review
As regards the size of the eligible population, the number of Australians experiencing at least one episode of major depression in the year 2000 was 513,000, of whom 302,200 sought care, but 122,000 did not receive an evidence-based treatment.

RR of suicide in prevalent depression was 20.4 +/- 1.1.

The RR of suicide on treatment versus not on treatment was 1.8 +/- 0.1.

The effect size was 0.55 +/- 0.075 for antidepressant drugs, 0.77 (range: 0.44-1.10) for CBT, and 0.98 (range:
0.62-1.35) for bibliotherapy.

The RR of relapse during 6 months continuation of drug treatment was 0.416 (range: 0.312-0.555).

The RR of relapse with maintenance treatment was 0.437 (range: 0.394-0.485).

The RR of relapse in 18 months following CBT was 0.636 (range: 0.514-0.787).

Disability weights for mild, moderate and severe depression were 0.14, 0.35 and 0.76, respectively.

The disability weight change per standard deviation (SD) change in severity of depression ranged from 0.139 to 0.172.

The ranges for the rate of adherence were 50-69% (SE: 3.3%) with TCAs, 50-73% (SE: 3.7%) with SSRIs, and 50-81% (SE: 4.4%) with CBT.

Lag to treatment for current treatment-seeking patterns was 6 weeks (range: 2 - 4 weeks).

The types of antidepressant drugs and the proportion of patients receiving each antidepressant were as follows:

SSRIs: 77% (SE: 0.9%); TCAs: 15% (SE: 0.7%); monoamine oxidase (MAO) inhibitors: 6% (SE: 0.5%); others: 2% (SE: 0.3%).

**Methods used to derive estimates of effectiveness**

Some assumptions were made due to the lack of reliable published clinical evidence.

**Estimates of effectiveness and key assumptions**

The proportion of patients taking up bibliotherapy was 15%.

The group CBT sessions per day were 2-3. The participants per group CBT were 6-8. The individual CBT sessions per day for psychologist were 5-7. The CBT sessions per half-day public psychiatrist were 2-4.

The reduction in risk of recurrence or relapse was applied to the average time spent in depression.

Suicide rates were similar in patients on CBT as in those on antidepressant drugs.

**Measure of benefits used in the economic analysis**

The summary benefit measure used in the economic analysis was the number of disability-adjusted life-years (DALYs) associated with each treatment. DALYs were calculated using two main components: years lived with disability (YLD) and years of life lost (YLL), which were estimated using the data derived from the literature. Details on the calculation of DALYs, namely on the approaches used to translate the effect size into a health benefit, were reported. Discounted DALYs were estimated at a rate of 3%.

**Direct costs**

The perspective taken in the analysis of costs was that of health-care system, and costs relevant to the government and the patient were included. The following categories of costs were considered: drugs, general practitioner (GP) visits, psychiatrist visits, and psychologist visits. Unit costs were presented separately from quantities of resources used for most items. Resource use was derived from the SMHWB survey. Some assumptions were also made to derive some resource consumption data, and were clearly reported. Costs were mainly estimated from the Pharmaceutical Benefits Scheme, the Medicare Benefit Schedule, and base salaries. A 3% annual discounting rate was applied to costs and it appears relevant in particular for maintenance strategies. Costs were expressed using 1999/2000 prices.
Statistical analysis of costs
Costs were treated deterministically in the base case.

Indirect Costs
Indirect costs were not included in the economic evaluation.

Currency
Australian dollars (AUD).

Sensitivity analysis
A probabilistic sensitivity analysis was carried out using Monte Carlo simulation to derive confidence intervals (CIs) for costs, benefits, and cost-utility ratios. Parameters to populate the probabilistic distributions were mainly derived from the literature although some distributions were set by experts. However, the type of distributions used was not reported.

Estimated benefits used in the economic analysis
DALYs were not reported, but the gains in terms of YLD and YLL associated with each treatment over conventional care were provided.

The YLDs and YLLs (in thousands) associated with each treatment over conventional care were: 6.0 (95% CI: 3.8 - 8.9) and 2.1 (95% CI: 1.5 - 2.9) with SSRIs; 5.9 (95% CI: 3.8 - 8.6) and 2.1 (95% CI: 1.5 - 2.8) with TCAs; 9.0 (95% CI: 5.6 - 14) and 3.0 (95% CI: 2.0 - 4.1) with CBT; 1.1 (95% CI: 0.6 - 1.8) and 0.3 (95% CI: 0.2 - 0.4) with bibliotherapy; 73 (95% CI: 58 - 89) and 22 (95% CI: 16 - 28) with maintenance therapy with SSRIs; 71 (95% CI: 58 - 85) and 21 (95% CI: 16 - 27) with maintenance therapy with TCAs; and 84 (95% CI: 62 - 110) and 23 (95% CI: 16 - 31) with maintenance with CBT.

Cost results
In case of SSRIs, total costs (in millions) were AUD 7 (95% CI: AUD 4 - AUD 11) for the comparator and AUD 120 (95% CI: AUD 99 - AUD 140) for SSRIs.

In case of TCAs, total costs (in millions) were AUD 7 (95% CI: AUD 4 - AUD 11) for the comparator and AUD 51 (95% CI: AUD 44 - AUD 58) for TCAs.

In the case of CBT, total costs (in millions) were AUD 8 (95% CI: AUD 4 - AUD 12) for the comparator, AUD 50 (95% CI: AUD 36 - AUD 71) with individual CBT public psychologist, AUD 120 (95% CI: AUD 87 - AUD 150) with individual CBT private psychologist, AUD 130 (95% CI: AUD 94 - AUD 170) with individual CBT public psychiatrist, AUD 130 (95% CI: AUD 100 - AUD 160) with individual CBT private psychiatrist, and AUD 21 (95% CI: AUD 15 - AUD 31) with group CBT public psychologist.

In the case of bibliotherapy, total costs (in millions) were AUD 1.2 (95% CI: AUD 0.7 - AUD 1.9) for the comparator and AUD 1.4 (95% CI: AUD 1.0 - AUD 1.9) with bibliotherapy.

In the case of maintenance therapy with antidepressants, total costs (in millions) were AUD 220 (95% CI: AUD 180 - AUD 260) for the comparator, AUD 1.900 (95% CI: AUD 1.600 - AUD 2.300) with maintenance therapy with SSRIs, and AUD 640 (95% CI: AUD 530 - AUD 740) with maintenance therapy with TCAs.

In the case of maintenance therapy with CBT, total costs (in millions) were AUD 220 (95% CI: AUD 180 - AUD 260) for the comparator, AUD 190 (95% CI: AUD 130 - AUD 280) with individual CBT public psychologist, AUD 470 (95% CI: AUD 340 - AUD 600) with individual CBT private psychologist, AUD 520 (95% CI: AUD 370 - AUD 700) with individual CBT public psychiatrist, AUD 540 (95% CI: AUD 420 - AUD 660) with individual CBT private...
psychiatrist, and AUD 67 (95% CI: AUD 40 - AUD 110) with group CBT public psychologist.

**Synthesis of costs and benefits**
Incremental cost-utility ratios were calculated in order to combine costs and benefits of the alternative strategies in comparison with usual care.

The incremental cost (in thousands) per DALY avoided relative to the relevant comparator was:

- AUD 14 (95% CI: AUD 11 - AUD 18) with SSRIs; AUD 5.5 (95% CI: AUD 4.2 - AUD 7.2) with TCAs;
- AUD 3.5 (95% CI: AUD 2.3 - AUD 5.4) with individual CBT public psychologist, AUD 8.9 (95% CI: AUD 6.7 - AUD 12) with individual CBT private psychologist, AUD 10 (95% CI: AUD 7.4 - AUD 14) with individual CBT public psychiatrist, AUD 10 (95% CI: AUD 8.1 - AUD 14) with individual CBT private psychiatrist, and AUD 1.1 (95% CI: AUD 0.5 - AUD 2.0) with group CBT public psychologist; AUD 0.1 (95% CI: dominant - AUD 0.4) with bibliotherapy;
- AUD 18 (95% CI: AUD 17 - AUD 20) with maintenance therapy with SSRIs, AUD 4.5 (95% CI: AUD 4.1 - AUD 4.9) with maintenance therapy with TCAs;
- dominant (95% CI: dominant - AUD 0.2) with individual CBT public psychologist, AUD 2.2 (95% CI: AUD 1.7 - AUD 2.8) with individual CBT private psychologist, AUD 2.8 (95% CI: AUD 2.0 - AUD 3.8) with individual CBT public psychiatrist, AUD 3.0 (95% CI: AUD 2.6 - AUD 3.4) with individual CBT private psychiatrist, and dominant with group CBT public psychologist.

The conclusions of the analysis remained the same when some changes in treatment effectiveness were done.

Second filter considerations highlighted some critical points: although good quality data are usually available, there were some concerns regarding the lack of clinical evidence on CBT for non-English speaking patients; most of the interventions are delivered by psychologists; expanding access to CBT is challenging in terms of workforce and funding arrangements; and many clinicians would not prescribe TCAs despite the fact that SSRIs are much more expensive and only marginally more effective.

**Authors' conclusions**
The authors concluded that the most cost-effective interventions were bibliotherapy, group CBT, individual CBT by a psychologist on a public salary, and TCAs for patients with major depression, with cost-utility ratios falling below AUD 10,000 even when taking the upper limit of the uncertainty interval into account. Maintenance treatment with SSRIs was more expensive with incremental costs per DALY ranging from AUD 17,000 to AUD 20,000 per DALY, but was still well below the threshold of AUD 50,000, which is considered the affordable limit.

**CRD COMMENTARY - Selection of comparators**
Each intervention under examination was compared with a relevant intervention that represented the current standard of care. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence was estimated from published studies. It was not stated whether a systematic review of the literature was undertaken to identify primary studies, which might have been identified selectively. Limited information on the other studies used to estimate clinical inputs was provided. However, most data came from clinical trials or meta-analyses of clinical trials. Thus, the validity of primary sources appears to have been high. In addition, the issue of uncertainty around clinical data was addressed using a probabilistic sensitivity analysis.

**Validity of estimate of measure of benefit**
The use of DALYs as the summary benefit measure is appropriate since they capture the impact of the interventions on survival and disability associated with the disease. DALYs are often used for studies evaluating treatments for major depression. The approaches used to calculate DALYs were briefly described although most details had been published in a companion article. Discounted benefits appear to have been estimated, although details on discounting were not presented.

Validity of estimate of costs
The categories of costs included in the analysis were appropriate, given the perspective adopted in the study. Hospitalisation costs were not included because they were likely to be very small. Unit costs and quantities of resources used were extensively provided, and the authors reported all the assumptions regarding resource consumption. This helps replicate the analysis in other settings. The source of costs was reported for all items. The prices to which the analysis referred were reported, which will facilitate reflation exercises in other time periods. No statistical analyses of costs were performed in the base case but probabilistic distributions were assigned in the sensitivity analysis.

Other issues
The authors stated that their findings do not confirm the results of other studies which have shown that SSRIs are more cost-effective than TCAs. The possible reasons for these differences were highlighted. The issue of the generalisability of study results to other settings was addressed, and the authors noted that clinical results are transferable to other countries, while caution is required when generalising the economic findings, due to differences in costs. The authors noted that the exclusion of hospitalisation costs might have underestimated the cost savings associated with the interventions under analysis. However, these costs are likely to be very small and their omission should not have had a strong impact on the final results.

Note:

since this abstract was written the authors have pointed out to us that an important finding, not covered above, was included in the discussion section of the paper, specifically this reports an ICER for the comparison of SSRIs with TCAs of > AUD 250,000 per QALY. The authors state that this "reinforces the argument that, based on cost-effectiveness modelling, TCAs ought to be the drug of choice unless side effects dictate the use of SSRIs as an alternative" and that "this is very much against current practice and 'clinical wisdom'".

The authors have also provided us with a table giving the types of distributions used in the uncertainty analyses, and this can be obtained from CRD. Anyone interested in replicating the model should contact Theo Vos using the e-mail address given in the "Address for correspondence section” below.

Implications of the study
The analysis supports the use of bibliotherapy and CBT for the management of depression. However, the authors note that bibliotherapy could be a treatment option for only a small proportion of people with depression, while CBT, when delivered by psychologists on a 'public' salary, is the next best option, followed by TCAs, CBT by private providers and SSRIs. TCAs should be the drug of choice, unless not well tolerated. The authors note that future studies should provide more robust estimates of benefits associated with treatments for depression.

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