Cost-effectiveness of cognitive behavioural therapy and selective serotonin reuptake inhibitors for major depression in children and adolescents

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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 use of cognitive-behavioural therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) for the treatment of major depressive disorder (MDD) in children and adolescents.

The model evaluated seven strategies. Four strategies involved CBT offered to all children who would not be offered CBT under current practice, using four different providers. Two strategies involved SSRIs. In one, an SSRI was offered as first-line treatment to all children who were not offered evidence-based medicine (EBM; the use of CBT and/or SSRIs) in current practice. In the other, an SSRI was offered as second-line treatment. The seventh strategy, the comparator, included a mixture of no treatment, treatment with EBM and treatment with non-EBM.

In the model, CBT consisted of 12 one-hour sessions, plus two parent or family sessions over 14 weeks. The four different provider scenarios modelled were private psychologist, public psychologist, private psychiatrist and public psychiatrist. For SSRIs, the treatment modelled consisted of 9 months' treatment. The daily dose was 20 mg fluoxetine, citalopram or paroxetine, 50 or 100 mg sertraline, or 100 mg fluvoxamine.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a cohort of 48,552 children and adolescents aged between 6 and 17 years, in the Australian population, who presented with a new episode of MDD in the year 2000.

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

Dates to which data relate
The effectiveness and resource use data were obtained from studies published between 1990 and 2004. The cost data referred to the years 1999 to 2001.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies.

Modelling
A decision tree analysis, based on evidence from trials and systematic reviews, was undertaken to calculate the expected costs and benefits of the seven strategies. The health benefits were modelled for the duration of the episode of MDD, estimated to be 20.8 weeks in those not seeking treatment and 34.8 weeks among those who did receive treatment. For those who received SSRIs as a second-line treatment, the average duration of an episode of MDD was 41.4 weeks for those not adhering to CBT, and 74.0 weeks for those not remitting by the end of treatment with CBT. The costs were modelled for the duration of the intervention.

**Outcomes assessed in the review**
The main clinical effectiveness parameters in the model were the effect sizes of CBT and SSRIs. Disease prevalence, current practice and adherence to treatment were also included.

**Study designs and other criteria for inclusion in the review**
To inform the effect sizes of CBT and SSRIs, the studies had to be randomised controlled trials. The trial participants had to be aged under 18 years and have diagnosed depression (MDD or dysthymia).

**Sources searched to identify primary studies**
Trials of CBT and SSRIs were identified from published meta-analyses, the Cochrane Controlled Trials Register and MEDLINE, and from the reference lists in included trials, review articles, books and clinical practice guidelines. Authors of published trials were also contacted for additional trials.

**Criteria used to ensure the validity of primary studies**
Not reported.

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

**Number of primary studies included**
Ten primary studies provided the effectiveness evidence.

**Methods of combining primary studies**
The results of the individual primary studies were combined by meta-analysis, to derive the effect sizes of CBT and SSRI. The effect size (standardised mean difference) was calculated using Hedge's g and the random-effects model of DerSimonian and Laird. The authors first calculated an effect size for each study by averaging across the relevant outcomes. All continuous outcome measures related to depression and health-related quality of life were included. The authors noted, however, that some measures considered relevant could not be included because the data were not presented in a way that could be incorporated into the calculation of the effect size.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The weighted mean effect size was 0.41 (95% confidence interval, CI: 0.15 - 0.67) for CBT and 0.29 (95% CI: 0.11 - 0.46) for SSRIs.

The authors reported that some unexplained heterogeneity was present in the effect size for CBT (Q=12.04, d.f.=7, p=0.099) but not for SSRIs (Q=0.9, d.f.=3, p=0.8).
Measure of benefits used in the economic analysis

The measure of benefit used was the disability-adjusted life-years (DALYs). The disability weights were defined for three health states (mild, moderate and severe MDD). These were derived from a Dutch weighting system (Stouthard et al., see Other Publications of Related Interest). To translate the effect size into a change in DALY, the authors used both the "conversion factor method" and the "survey severity method".

Direct costs

Discounting was not undertaken, which was appropriate given the short timeframe of the study. The quantity/cost boundary adopted was that of the health service and patients and/or relatives. The costs and the quantities were reported separately. The direct costs measured included the cost of supplying SSRIs, the cost of general practitioner, paediatrician and psychiatrist visits, and the costs of sessions with psychologists and a public psychiatrist. Non-adherence costs were also included. The costs were derived from the Medicare Benefits Schedule and Pharmaceutical Benefits Scheme from the Australian Department of Health and Ageing, the Australian Psychological Society, the Victorian Hospitals Industrial Association, and the Austin and Repatriation Medical Centre. Resource use was estimated from the published literature, supplemented by expert advice. The authors clearly noted the assumptions made within the costing procedure. The unit cost data came from the years 1999 to 2001. The authors did not report any adjustment to a specific price year.

Statistical analysis of costs

The costs were treated deterministically as point estimates.

Indirect Costs

The indirect costs were not included in the study.

Currency

Australian dollars (Aus$).

Sensitivity analysis

A sensitivity analysis was conducted around the effectiveness data, costs, and incremental cost-effectiveness ratios (ICERs). This was primarily because of uncertainty in the analytical methods and because of the lack of evidence for some parameters (e.g. lag to treatment). A probabilistic sensitivity analysis was undertaken using Monte Carlo simulations. The probability distributions were reported in the paper.

Estimated benefits used in the economic analysis

CBT has greater effectiveness in children and adolescents than SSRIs, and therefore yielded a greater, total years lived with disability saved.

The DALYs saved with CBT compared with current practice for each of the four provider scenarios was 360 (range: 120 - 920).

The DALYs saved with SSRIs as first-line treatment compared with current practice was 230 (range: 88 - 510), and as second-line treatment compared with no further treatment 130 (range: 47 - 230).

Cost results

CBT was more expensive when provided by a private psychiatrist and least expensive when provided by a public psychologist.
The total intervention cost (millions) of CBT was Aus$5.8 (range: 3.3 - 9.4) when provided by a public psychologist, Aus$13 (range: 6.9 - 21) with a private psychologist, Aus$14 (range: 7.6 - 24) with a public psychiatrist, and Aus$15 (range: 8.3 - 23) with a private psychiatrist.

The total costs (millions) of SSRIs were Aus$7.8 (range: 4.6 - 12) when provided as first-line treatment and Aus$3.1 (range: 1.6 - 5.5) when provided as second-line treatment.

The incremental costs (millions) of CBT were Aus$3.4 (range: 1.7 - 6.3) when provided by a public psychologist, Aus$10 (range: 5.5 - 17) with a private psychologist, Aus$12 (range: 6.1 - 20) with a public psychiatrist, and Aus$12 (range: 6.7 - 20) with a private psychiatrist.

The incremental cost (millions) of SSRIs as first-line treatment was Aus$5.4 (range: 13 - 53).

**Synthesis of costs and benefits**

Cost-effectiveness ratios were derived to calculate the cost per DALY saved compared with current practice. CBT provided by public psychologists was the most cost-effective intervention for MDD in children and adolescents at Aus$9,000 per DALY saved (95% CI: 3,900 - 24,000). The cost-effectiveness of the other three providers ranged from Aus$28,000 to Aus$34,000 per DALY saved.

The cost-effectiveness of SSRIs as both first- and second-line treatment was Aus$23,000 per DALY saved.

The major contributors to uncertainty around the ICERs for CBT were the effect size, the variation factor around the cost to the patient of private psychiatrist visits, and the cost to the government of public psychologist and public psychiatrist visits.

For SSRIs, the effect size was the major contributor to uncertainty around the ICERs. Other parameters contributing to uncertainty in the effectiveness data and total costs were the proportion of children and adolescents currently receiving non-EBM, adherence with treatment, and the prevalence of MDD.

**Authors' conclusions**

Cognitive-behavioural therapy (CBT) provided by a public psychologist was the most effective and cost-effective option for the first-line treatment of depression in children and adolescents.

**CRD COMMENTARY - Selection of comparators**

The comparator was chosen to reflect current practice in the authors' setting. The reader should consider whether this comparator reflects current practice in their setting.

**Validity of estimate of measure of effectiveness**

Although the authors did not state that a systematic review of the literature was undertaken, the search methods and inclusion criteria for the review were clearly reported. A meta-analysis was used to combine the effectiveness estimates and the methodology used was clear. The authors noted the limitations about incorporating all the relevant data. They did not consider the impact of differences between the primary studies when estimating the effectiveness. It was assumed, for example, that psychologists and psychiatrists have equal efficacy, but this has not been proven. For the SSRI intervention, the authors assumed equal efficacy of the different types of SSRIs, although the evidence was limited to fluoxetine and paroxetine.

**Validity of estimate of measure of benefit**

The measure of benefit used was the DALYs. The derivation of disability weights for the different health states was adequately explained. The authors acknowledged the lack of overall quality of life data in the calculation of the effect size, which was limited primarily to symptom measures, and the measurement of severity in the DALY disability weights.
Validity of estimate of costs

All the categories of cost relevant to the perspective adopted were included in the analysis, and most of the costs relevant to each category were included. The authors acknowledged that the cost offsets for CBT were considered as being very conservative, as they did not include the impact of reduced use of medication on the Pharmaceutical Benefits Scheme, or resource savings resulting from reduction in relapse and severity of depression. On the other hand, costs associated with implementation, such as training, were not factored in. The authors stated that the costs and the quantities were reported separately. A sensitivity analysis of the quantities was conducted, and the ranges used appear to have been appropriate as they were based on expert opinion. A sensitivity analysis of the prices was also conducted. Discounting was unnecessary because of the short timeframe of the study. The date to which the costs referred was reported.

Other issues

The authors stated that there were no cost-effectiveness analyses of the health technology in the Australian children and adolescent population. Consequently, they could not compare the results with those from other studies. The authors considered the issue of generalisability to different groups of patients, particularly those with very severe depression, but acknowledged that patient heterogeneity had not been sufficiently evaluated in the results. The authors did not present their results selectively. The study investigated the impact of CBT and SSRIs on children and adolescents, and this was reflected in the authors' conclusions.

The authors reported a number of further limitations to their study, which related to the assumptions adopted and the data sources used. Some of these have been highlighted in earlier fields. Another limitation was the use of mean values to describe the natural history of MDD. Also, the use of an episode-based analysis of MDD, which prevented the longer term health benefits due to the prevention of new episodes or delay in relapse from being measured.

Implications of the study

The authors noted that, as not all patients can currently access CBT provided by a public psychologist, it will require a change in policy to allow more widespread uptake. It will also require "start-up" costs, and attention to ensuring an adequate workforce. The authors considered that, should no action be taken, SSRIs may become the first-line treatment by default because of their greater affordability for consumers and easier access. The authors noted that further data on the treatment of depression in children and adolescents in Australia should be collected, as estimates of the proportion treated with CBT, SSRIs and non-EBM are uncertain.

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