Cost-effectiveness of psychological and pharmacological interventions for generalized anxiety disorder and panic disorder


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 technologies assessed were cognitive behavioural therapy (CBT) and serotonin and noradrenalin reuptake inhibitors (SNRIs) for the treatment of generalised anxiety disorder (GAD); and CBT, selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants (TCAs) for the treatment of panic disorder (PD). CBT was considered as 12 one-hour consultations plus one general practitioner (GP) consultation for referral to 4 different providers: psychologists and psychiatrists, working either in the private or public sector. SNRIs were defined as 12 months of venlafaxine (at 75mg or 150mg per day). SSRIs were expressed as 12 months of paroxetine (40mg per day). TCAs were represented by imipramine (225mg per day). All pharmacological interventions also included 9 doctor consultations per year.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population consisted of adults (18 years or older) with ICD-10 defined GAD or PD in the Australian population in the year 2000 who sought health care for their mental health disorder but would not have received evidence-based medicine (EBM) under current practice. Of those with GAD, 55% reported a consultation, 27% received EBM and 28% received non-EBM. Of those with PD, 65% reported a consultation, 47% received EBM and 19% received non-EBM. Consultation was defined as seeking care during the past 12 months from a GP, psychiatrist, psychologist, physician, surgeon, social worker, mental health team worker, or an admission to a hospital. EBM was defined as 3 or more consultations with a GP, psychiatrist or psychologist plus CBT and/or drug treatment.

Setting
The study was conducted in various settings, but primarily primary care. The economic study was conducted in Australia.

Dates to which data relate
Effectiveness evidence was based on data reported in studies published between 1991-2003. Resources used were derived from a survey published in 1998 and further assumptions. The price year was not reported. Although not explicitly reported, the price year appears to have been 2000.

Source of effectiveness data
The source of effectiveness data was a review of the literature and estimates made by the authors.
Modelling
A model was developed in order to estimate costs and benefits associated with interventions for the treatment of GAD and PD. Costs and benefits were estimated by modelling different states of the patient (symptomatic or not) and different courses of treatment (in the case of current treatment, patients might receive EBM or non-EBM; in the case of the interventions assessed treatment might be characterised by patient adherence or non-adherence).

Outcomes assessed in the review
The outcomes assessed in the review were the prevalence of GAD and PD and the number of prevalent cases in the Australian population; the percentage of time over which patients with GAD or PD were symptomatic; the proportion of patients with GAD or PD who consulted and received non-EBM under current practice; the effectiveness of the interventions under assessment; the baseline disability weights for GAD and PD; and the adherence of GAD and PD patients with the interventions examined.

Study designs and other criteria for inclusion in the review
Effectiveness of and adherence with the interventions examined were based on the results of published meta-analyses of randomised clinical trials (RCTs) in the case of PD, or individual RCTs, in the case of GAD. The inclusion criteria for RCTs were: subjects aged 18 years or older, and a diagnosis of GAD according to DSM-III-R or DSM-IV, and reporting of continuous measures (with both means and standard deviations). The prevalence of GAD and PD, the percentage of symptomatic time, and the percentage of patients receiving non-EBM were based on the Australian national mental health survey. The rest of the input parameters were based on other published 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
Eight primary studies were included in the review.

Methods of combining primary studies
The results of RCTs on effectiveness of the interventions assessed were combined in meta-analyses. Regarding TCAs, results from individual RCTs reported in two published meta-analyses were combined in a new meta-analysis.

Investigation of differences between primary studies
Potential differences between primary studies were not discussed. It was only reported that the effect size in the case of TCAs differed markedly between two published meta-analyses.

Results of the review
The one-year prevalence of GAD was 3.03%, with 437,417 prevalent cases; the percentage of GAD time symptomatic over 12 months was 63%.

The one-year prevalence of PD was 1.34%, with 193,641 prevalent cases; the percentage of PD time symptomatic over
12 months was 48%.

The proportion of patients with GAD or PD who consulted and received non-EBM under current practice was 28.2% and 18.6% respectively.

The mean effect size for GAD interventions was: CBT 0.77, and SNRI (venlafaxine) 0.44; the mean effect size for PD interventions was: CBT 0.66, SSRIs 0.32, and TCAs 0.53.

The baseline disability weights for GAD were 0.17 for mild and moderate cases and 0.60 for severe cases; the disability weights for PD were 0.16 for mild and moderate cases, and 0.69 for severe cases.

The adherence of patients with treatment, based on published evidence, for GAD interventions was: CBT 95%, and SNRI (venlafaxine) 73%; and for PD interventions was: CBT 85%, SSRIs 67%, and TCAs 69%.

These percentages were used as the maximum values of adherence in the model.

**Methods used to derive estimates of effectiveness**

Some estimates of effectiveness were based on authors' opinion.

**Estimates of effectiveness and key assumptions**

The minimum adherence for all interventions assessed was assumed to be 50%.

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

The measure of benefit used in the economic analysis was the number of disability-adjusted life-years (DALYs) saved due to treatment. The disability weights were based on published Dutch weights. The reduction in disability weights due to treatment was modelled by translating effect sizes of the interventions examined, using a disability weight conversion factor method, and also a survey severity method. Benefits were assessed by a two-stage process. In the first stage, the health benefit from the interventions in the form of DALYs was assessed. The second stage involved the assessment of issues that either influenced the degree of confidence that could be placed in the incremental cost-effectiveness ratios (ICERs) (such as the level of available evidence), or broader issues that would need to be taken into account in decision-making about resource allocation (such as equity and acceptability to stakeholders).

**Direct costs**

Costs consisted of government and patient costs. Costs included medication, GP visits, and psychologist and psychiatrist consultations. Costs and quantities were analysed separately. Resources used were based on treatment guidelines, the pharmaceutical benefits scheme, and further assumptions. It was assumed that the cost associated with non-adherence under the interventions assessed was equal to the cost of providing non-EBM. Unit costs were derived from national sources (such as the Australian Department of Health and Ageing, the 'Victorian Hospitals' Industrial Association, etc.). Total costs were derived using modelling. The price year appears to have been 2000. Discounting was not applied, since costs were incurred over a period of one year.

**Statistical analysis of costs**

Costs were presented as median values, with the 95% uncertainty intervals (UI) provided; these results were based on simulation modelling techniques.

**Indirect Costs**

Indirect costs were not included in the analysis.
**Currency**
Australian dollars (Aus$)

**Sensitivity analysis**
Simulation modelling techniques were used to investigate the uncertainty range around the costs, benefits and cost-effectiveness ratios. Monte Carlo simulations allowed the calculation of median values, as well as uncertainty intervals representing ranges within which the true results lay within 95% certainty. Uncertainty intervals were derived from standard errors and ranges for effectiveness data presented in the published literature, as well as from further assumptions regarding the distribution of cost and effectiveness data.

**Estimated benefits used in the economic analysis**
The incremental benefits in the patient population of the interventions used for the management of GAD compared to current practice were (median, 95% UI in parentheses): psychologist 7,200 (4,300 - 12,000) DALYs saved; psychiatrist 7,200 (4,300 - 12,000) DALYs saved; SNRI 3,300 (1,900 - 5,100) DALYs saved.

The incremental benefits in the patient population of the interventions used for the management of PD compared to current practice were (median, 95% UI in parentheses): psychologist 1,200 (630 - 1,900) DALYs saved; psychiatrist 1,200 (630 - 1,900) DALYs saved; SSRIs 590 (250 - 840) DALYs saved; TCAs 870 (340 - 1,500) DALYs saved. Benefits were estimated over a period of one year.

**Cost results**
The incremental total costs (in millions) in the patient population of the interventions used for the management of GAD compared to non-EBM were (median, 95% UI in parentheses): private psychologist Aus$140 (Aus$100 - Aus$190); public psychologist Aus$50 (Aus$34 - Aus$69); private psychiatrist Aus$170 (Aus$130 - Aus$210); public psychiatrist Aus$160 (Aus$120 - Aus$220); SNRI Aus$77 (Aus$60 - Aus$96).

The incremental total costs (in millions) in the patient population of the interventions used for the management of PD compared to non-EBM were (median, 95% UI in parentheses): private psychologist Aus$27 (Aus$18 - Aus$38); public psychologist Aus$7.0 (Aus$3.2 - Aus$12.1); private psychiatrist Aus$33 (Aus$24 - Aus$41); public psychiatrist Aus$31 (Aus$20 - Aus$46); SSRIs Aus$23 (Aus$18 - Aus$27); TCAs Aus$15 (Aus$11 - Aus$19).

Total costs were estimated over a period of one year.

**Synthesis of costs and benefits**
Costs and benefits were combined in the form of ICERs, expressing incremental cost-effectiveness of the interventions assessed compared to current treatment. In addition, cost-effectiveness ratios (CERs) by dividing intervention costs by the number of DALYs saved by each intervention were also provided.

The ICERs of GAD interventions compared to current practice were (median, 95% UI in parentheses):
- private psychologist Aus$20,000 per DALY saved (Aus$12,000 - Aus$33,000 per DALY saved);
- public psychologist Aus$6,900 per DALY saved (Aus$4,000 - Aus$12,000 per DALY saved);
- private psychiatrist Aus$23,000 per DALY saved (Aus$15,000 - Aus$38,000 per DALY saved);
- public psychiatrist Aus$23,000 per DALY saved (Aus$14,000 - Aus$38,000 per DALY saved);
- SNRI Aus$23,000 per DALY saved (Aus$16,000 - Aus$40,000 per DALY saved).

The ICERs of PD interventions compared to current practice were (median, 95% UI in parentheses):
private psychologist Aus$26,000 per DALY saved (Aus$15,000 - Aus$45,000 per DALY saved);

public psychologist Aus$6,800 per DALY saved (Aus$2,900 - Aus$14,000 per DALY saved);

private psychiatrist Aus$27,000 per DALY saved (Aus$19,000 - Aus$48,000 per DALY saved);

public psychiatrist Aus$30,000 per DALY saved (Aus$18,000 - Aus$55,000 per DALY saved);

SSRIs Aus$38,000 per DALY saved (Aus$27,000 - Aus$89,000 per DALY saved);

TCAs Aus$17,000 per DALY saved (Aus$9,700 - Aus$42,000 per DALY saved).

The CERs of GAD interventions were (median, 95% UI in parentheses):

private psychologist Aus$28,000 per DALY saved (Aus$17,000 - Aus$56,000 per DALY saved);

public psychologist Aus$12,000 per DALY saved (Aus$7,000 - Aus$25,000 per DALY saved);

private psychiatrist Aus$32,000 per DALY saved (Aus$20,000 - Aus$63,000 per DALY saved);

public psychiatrist Aus$31,000 per DALY saved (Aus$19,000 - Aus$63,000 per DALY saved);

SNRI Aus$30,000 per DALY saved (Aus$20,000 - Aus$51,000 per DALY saved).

The CERs of PD interventions were (median, 95% UI in parentheses):

private psychologist Aus$32,000 per DALY saved (Aus$21,000 - Aus$58,000 per DALY saved);

public psychologist Aus$15,000 per DALY saved (Aus$10,000 - Aus$29,000 per DALY saved);

private psychiatrist Aus$36,000 per DALY saved (Aus$23,000 - Aus$66,000 per saved);

public psychiatrist Aus$36,000 per DALY saved (Aus$26,000 - Aus$65,000 per DALY saved);

SSRIs Aus$78,000 per DALY saved (Aus$48,000 - Aus$147,000 per DALY saved);

TCAs Aus$30,000 per DALY saved (Aus$18,000 - Aus$73,000 per DALY saved).

For both GAD and PD, the major contributors to uncertainty around the ICERs for all interventions were: the effect size; the reduction in disability weights; and (for CBT only) the variation around the cost of consulting private psychologists, private psychiatrists, and GPs. Regarding the second-filter criteria, a main outcome was the elucidation of issues surrounding the availability and distribution of an adequate workforce for CBT. The drug interventions were likely to be more feasible, although possibly less acceptable due to concerns about side effects.

Authors' conclusions
CBT, in particular by a public psychologist, was the most effective and cost-effective intervention for GAD and PD. However, its implementation would require policy change to enable more widespread access to a sufficient number of trained therapists for the treatment of anxiety disorders.

CRD COMMENTARY - Selection of comparators
The comparator of the interventions assessed was 'current practice' as reflected in the Australian national mental health survey. You, the user of the database, should consider whether 'current practice', as described by the authors, reflects routine practice in your own setting.
Validity of estimate of measure of effectiveness
Although it was not explicitly stated that a systematic review had been undertaken, it is likely that this was the case. Effectiveness estimates from primary studies were combined appropriately by meta-analyses. The methods and conduct of meta-analyses were not clearly described. Potential differences between primary studies were not discussed.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The model used was appropriate for this purpose, since it examined benefits for various patient states (symptomatic or not, severity of illness) and course of treatment (EBM versus non-EBM, adherence in intervention versus non-adherence).

Validity of estimate of costs
It was stated that the study adopted the health sector perspective. All categories of cost relevant to this perspective were included in the analysis. Costs and quantities were analysed separately and this improves the reproducibility of the results. A sensitivity analysis of costs examining the uncertainty surrounding the results by using simulating modelling techniques was conducted. Discounting was not undertaken, but this was not required, since costs were incurred within a period of one year. Although not explicitly reported, the price year appears to have been 2000.

Other issues
The authors made appropriate comparisons of their findings to those of other studies, although they acknowledged restrictions in their comparisons due to a lack of other economic evaluations assessing interventions for anxiety disorders. The issue of generalisability to other settings was not addressed. However, the authors discussed the generalisability of their results to patient populations with comorbidities. The authors reported a number of limitations of their analysis, such as the methodological difficulty in the calculations of health benefits, and the lack of data on long-term effectiveness of interventions, treatment patterns, and health service utilisation among GAD and PD patients. The results of the analysis were fully reported. The authors’ conclusions reflected the scope of the analysis.

Implications of the study
The authors recommended future research in order to estimate the effect of CBT relative to pharmacological interventions alone and in combination with psychological interventions. In addition, they suggested that, if cost-effective CBT was to be widely adopted as a treatment option for anxiety disorders, then attention should be given to ensure an adequate workforce of publicly funded psychologists, since this was the most cost-effective option for provision of CBT. Alternatively, they suggested funding of a mix of providers including other suitably trained health professionals (social workers, GPs), with attention being paid to their training and accreditation, although in this case, effectiveness and cost-effectiveness of CBT might be different from that reported in the study. Finally, they stated that conclusions drawn from the economic evaluations should be considered within the context of the second stage filter process, which qualified the results taking into account issues of equity, feasibility, strength of evidence, and acceptability to stakeholders, before any implementation of changes in actual service practice.

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Bibliographic details

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