Reducing the global burden of depression: population-level analysis of intervention cost-effectiveness in 14 world regions
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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
Seven treatments for depression were examined. These were:

older antidepressants such as tricyclic antidepressants (e.g. imipramine, amitriptyline) (1);
newer antidepressants such as selective serotonin re-uptake inhibitors (e.g. fluoxetine) (2);
brief psychotherapy (brief cognitive therapy or problem-solving treatment) (3);
older antidepressants plus brief psychotherapy (4);
newer antidepressants plus brief psychotherapy (5);
proactive collaborative care with older antidepressants (6); and
proactive collaborative care with newer antidepressants (7).

Interventions 1 to 5 followed guideline-level therapeutic dosages or number of sessions over the average duration of an untreated depression episode. Maintenance treatment for recurrent depression was incorporated into strategies 6 and 7.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients suffering from depression.

Setting
The setting was primary care. The economic study was conducted in the 192 member states of the WHO. These member states were grouped into 14 epidemiologic world regions on the basis of their levels of child and adult mortality. There were two regions in Africa (Afr D and E), three in the Americas (Ame) A, B and D), two in the Eastern Mediterranean (EMed B and D), three in Europe (Eur A, B and C), two in South-east Asia (SeAs B and D), and two in the Western Pacific (WPac A and B).

Dates to which data relate
The resource use and effectiveness data were gathered from 1997 to 2004. The price year was 2000.
Source of effectiveness data
The effectiveness evidence was derived from a review of published studies.

Modelling
A state transition population model, which had been published, was constructed to trace the development of sub-regional populations. It considering births, deaths and the disease in question. Depression was defined as an episodic disorder with a high rate of remission and subsequent recurrence, and with excess mortality from unnatural causes (suicide). Persons not currently depressed became cases at an instantaneous transition rate (incidence, including recurrence). Persons with a depressive episode went back to being susceptible at determined remission rates. Cases were subject to the instantaneous case-fatality rate. Both susceptible persons and cases were subject to the general mortality rate. All data used to populate the model were derived from the literature. The time horizon of the model was lifetime. The cost-effectiveness of the treatment strategies was assessed as the difference between two scenarios. The first scenario was an epidemiological situation representing the natural history of depression (no intervention). The second scenario was an epidemiological situation reflecting the population-level impact of each specified intervention implemented for a 10-year period.

Outcomes assessed in the review
The outcomes assessed were:

- the prevalence of depression by age group and gender in each world region;
- the composite health state valuation (HSV) for an untreated depressive episode;
- the incidence and remission rates;
- the case-fatality rates; and
- the efficacy of the interventions under evaluation. This was assessed in terms of improvement in HSV and remission rates, after considering the rates of coverage, adherence and partial response.

Study designs and other criteria for inclusion in the review
A systematic review of the literature does not appear to have been conducted. Most of the primary studies were clinical trials or of WHO data. Some information was obtained through personal communication.

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
Fifteen studies provided the evidence.

Methods of combining primary studies
Investigation of differences between primary studies
Not stated.

Results of the review
The prevalence of depression (rates per 1,000 population), according to age group, is reported here for Eur A (e.g. France, Norway) only. For males (females), the prevalence was:

0 (0) for the 0- to 4-year age group,
11 (11) for the 5- to 14-year age group,
19.3 (41.2) for the 15- to 29-year age group,
19.2 (44.7) for the 30- to 44-year age group,
17.8 (39.2) for the 45- to 59-year age group,
14.7 (34.3) for the 60- to 69-year age group,
6 (14.9) for the 70- to 79-year age group, and
4.6 (10.5) for the over 80-years age group.

The weighted average HSV for an untreated depressive episode was 0.62 (where 1 equated to full health), giving 23% severe (HSV=0.24), 47% moderate (HSV=0.65) and 30% mild (HSV=0.86).

The rate of incidence was calculated from the estimates of 6 months as the mean duration of an untreated depressive episode.

The remission hazard rate was 2. This was calculated as the inverse of the untreated episode duration (i.e. 1/0.5 years).

The case-fatality rate was 9% for age groups between 15 and 45 years. This was reduced to 3% for age groups over 45 years.

No excess risk of mortality from natural causes was attributed.

The coverage rates were 50%.

The rates of adherence ranged from 60% for strategy 1 (older antidepressants) to 75% for strategy 7 (proactive collaborative care with newer antidepressants).

The rate of partial response ranged from 15 to 20%.

The improvement in HSV was 4.5, 5, 5.8, 6.3, 6.3, 7.3 and 7.3%, respectively, with programmes 1 to 7.

The range of improvement in remission rates was:

9 to 10.5% for strategy 1,
9.5 to 11% for strategy 2,
7 to 8.8% for strategy 3,
10.5 to 12.3% for strategy 4,
10.5 to 12.3% for strategy 5,
13.1 to 15% for strategy 6, and
13.1 to 15% for strategy 7.

Measure of benefits used in the economic analysis
The summary benefit measure was the expected number of disability-adjusted life-years (DALYs) averted. These were estimated using the decision model. An annual discount rate of 3% was applied and age-weighted estimates were calculated. The percentage of current burden of depression averted and the disability-free days were also reported.

Direct costs
Discounting was relevant. An annual rate of 3% was applied since the costs were incurred during a long time period. The unit costs were not presented separately from the quantities of resources used, but resource use was reported for the majority of items. The health services included in the economic evaluation were identified at patient-level and at programme-level. The patient-level costs comprised all services relating to the treatment of depression episodes. For example, drug dosage and frequency, psychotherapy, case management, primary care visits, outpatient visits and inpatient stay. The programme-level costs were for central administration and training. The cost/resource boundary of the study was unclear. Resource use was estimated on the basis of authors' assumptions and published studies. The costs were estimated from a multi-national data-set for primary and secondary care services and from the International Drug Price Indicator Guide for drugs. The source of the other costs was not reported. All the costs were presented in year 2000 values.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered.

Currency
International US dollars (IS).

Sensitivity analysis
Sensitivity analyses were conducted to assess whether the estimated cost-effectiveness ratios were robust to variations in the model inputs. Univariate sensitivity analyses were conducted on discount rates and age-weighting. The best- and worst-case scenarios were also considered by varying key cost drivers and treatment effectiveness. The ranges used were derived from the literature. Finally, a probabilistic sensitivity analysis was performed using a Monte Carlo simulation with 2,000 runs.

Estimated benefits used in the economic analysis
The total estimated DALYs averted per year ranged from:

243,409 (programme 1) to 477,102 (programme 7) in region Afr D,
268,381 to 525,494 in region Afr E,
503,869 to 1,031,234 in region Ame A.
564,188 to 1,105,894 in region Ame B,
87,249 to 171,151 in region Ame D,
173,568 to 340,530 in region EMed B,
406,517 to 797,291 in region EMed D,
503,574 to 1,029,952 in region Eur A,
260,119 to 532,555 in region Eur B,
239,342 to 489,201 in region Eur C,
257,055 to 502,500 in region SeAs B,
1,619,708 to 3,175,356 in region SeAs D,
95,459 to 195,202 in region WPac A, and
1,759,925 to 3,447,334 in region WPac B.

In general, interventions 1 to 3 could avert between 9 and 15% of current burden, interventions 4 and 5 averted 11 to 18%, and strategies 6 and 7 averted 18 to 29% of depression burden.

The disability-free days were between 18 and 23 with strategies 1 to 3, between 23 and 28 days with strategies 4 and 5, and between 24 and 29 days with strategies 6 and 7.

Cost results

There was a high variability in the average cost per treated episode.

The lowest patient-level costs per treated episode related to older antidepressants (strategy 1). These costs ranged from IS50 to IS80 in high-mortality developing sub-regions (Afr D, Afr E, Ame D, EMed D and SeAs D) to approximately IS1,400 in the most economically developed sub-regions (Ame A, Eur A and WPac A).

The cost per treated episode with strategy 7 ranged from IS130 to IS150 in high-mortality developing sub-regions to IS700 to IS750 in developed sub-regions.

The costs of the programme accounted for only 1 to 10% of the total costs.

The total population costs per year are reported here for Eur A (e.g. France, Norway) only. The total population costs per year (in millions) were:

IS3,207 with programme 1,
IS3,480 with programme 2,
IS4,958 with programme 3,
IS5,555 with programme 4,
IS5,862 with programme 5,
IS10,596 with programme 6, and
IS11,244 with programme 7.
**Synthesis of costs and benefits**

Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the interventions under evaluation.

The most cost-effective strategy (with a lower average cost-effectiveness ratio) in all sub-regions was that of older antidepressants (strategy 1). The average cost per DALY averted was:

- I$700 to I$1,000 in high-mortality developing sub-regions (Afr D, Afr E, Ame D, EMed D and SeAs D),
- I$1,100 to I$1,800 in low-mortality developing sub-regions (Ame B, EMed B, SeAs B and WPac B), and
- I$1,600 to I$7,100 in developed sub-regions (Ame A, Eur A, Eur B, Eur C and WPac A).

The incremental analysis showed that the most cost-effective single intervention was therapy with older antidepressants, while the most cost-effective combined intervention was strategy 6 (proactive collaborative care with older antidepressants). The incremental cost per DALY averted for strategy 6 was I$1,650 to I$1,850 in high-mortality developing sub-regions, I$2,000 to I$3,000 in low-mortality developing sub-regions, and I$2,300 to I$14,000 in developed sub-regions.

In all sub-regions, with the exception of the lowest-income sub-regions, the incremental cost per DALY averted of strategy 6 was considerably less than the average yearly income per capita, which was an international threshold value proposed for accepting an intervention as very cost-effective.

The sensitivity analyses showed that variations in the discount rate altered the cost-effectiveness ratio by 14% and -11%.

The removal of age-weighting resulted in an increase of 19 to 34% in the average cost-effectiveness ratios.

The best-case scenario lowered the average cost per DALY averted by 50 to 60%. The worst-case scenario led to substantial increases in the average and incremental cost-effectiveness ratios.

The probabilistic sensitivity analysis (run only for SeAs D) showed that, when resources were limited, older antidepressants were the most cost-effective strategy. More resource-consuming interventions could only be affordable with higher budgets.

**Authors' conclusions**

Primary care strategies for the treatment of depression were cost-effective since the incremental cost-effectiveness ratio was below the yearly average per capita income. The use of old antidepressant strategies was more cost-effective than the use of newer, more intense strategies.

**CRD COMMENTARY - Selection of comparators**

The selection of the comparators appears to have been appropriate since old and newer strategies for the treatment of depression were considered. Standard dosages and guideline sessions were considered. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis of effectiveness was based on a synthesis of published studies. However, it appears that a systematic review of the literature has not been undertaken. Presumably, the primary studies were identified selectively. Most of the evidence came from clinical trials, but limited information on the study design and patient samples was reported. The methods used to extract and combine the primary studies were not reported. Some of the estimates were then varied in the sensitivity analysis in order to address the issue of uncertainty.
Validity of estimate of measure of benefit
The summary measure of benefit was the DALYs. This was appropriate since it represents a valid instrument for assessing the impact of the interventions on patient health using WHO methods. Discounting was applied, and variations in the discount rate were investigated in the sensitivity analysis. The disability weights were obtained from the literature.

Validity of estimate of costs
The perspective adopted in the study was unclear since the authors stated that costs relevant to society were adopted but the indirect costs, which could have been relevant, were not considered. However, the authors stated that the inclusion of the indirect costs would have further enhanced the cost-effectiveness of the antidepressant strategies. The unit costs and the quantities of resources used were not reported separately. The price year was reported, thus simplifying reflation exercises in other settings. The costs were treated deterministically but key cost inputs were varied in the sensitivity analysis. The source of the data was reported for some items only. The costs were not broken down, which limits the possibility of replicating the study.

Other issues
The authors compared some of their results with those from other studies, stating that similar results were observed. Several sensitivity analyses were conducted and the results were clearly reported. This enhances the external validity of the analysis. The authors acknowledged some limitations to the validity of the analysis. First, the countries were grouped in sub-regions, which was not always appropriate. Second, the complex issue of co-morbidity in depression was not explicitly addressed. Third, most of the evidence came from data obtained from trials conducted in developed countries.

Implications of the study
The authors suggested that, as the price of antidepressants falls, the cost-effectiveness of treatment strategies for depression should improve in developing countries.

Source of funding
Supported in part by the WHO's Global Programme on Evidence for Health Policy, and the Spanish Fondo de Investigacion Sanitaria.

Bibliographic details

PubMedID
15123502

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH