Model to assess the cost-effectiveness of new treatments for 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 study examined a hypothetical new treatment for depression. The new antidepressant therapy was assumed to have a 50% relative improved remission rate in comparison with standard care.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of individuals with depression (mild, moderate and severe).

Setting
The setting was primary care. The economic study was carried out in Sweden.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1997 and 2006. The price year was 2005.

Source of effectiveness data
The clinical data used in the decision model were the transition probabilities. These were defined in terms of the relapse rate (every 6 months), remission rate, recurrence rate, increased risk of recurrence with previous episodes, suicide risk and duration of treatment.

Modelling
A Markov model was used to simulate the clinical and economic outcomes in a hypothetical cohort of 10,000 patients with depression. The time horizon of the model was 5 years and monthly cycles were considered. However, the analysis was also carried out for alternative time horizons (from 6 months to 5 years). The health states of the model were well, remission, episode and death. Patients started the simulation with a current episode from depression and then moved across the possible health states according to transition probabilities. For example, patients could remit from an initial episode and, once remitted, either relapse or remain remitted. After 6 months from remission, patients were considered to be free of depression. The model allowed for multiple depressive episodes.

Sources searched to identify primary studies
Much of the clinical data were derived from the HEADIS study, which was a naturalistic observational study in which
447 patients with depression were followed for 6 months. Patient characteristics at baseline were also taken from the HEADIS study. In view of the short follow-up period of the HEADIS study, the relapse risk of a new episode was estimated from a published meta-analysis. Data on mortality were obtained from general population life tables. Details of other sources were not explicitly stated.

**Methods used to judge relevance and validity, and for extracting data**

The process used to identify the data was not reported. No inclusion criteria were specified for any of the parameters. The primary studies appear to have been identified selectively. The method used to select the estimates was not reported and the approach used to combine the primary estimates was not discussed. The HEADIS study was probably chosen as being representative of the Swedish population, while the use of a meta-analysis to obtain long-term risks is likely to have ensured high internal validity.

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

The summary benefit measure used was the quality-adjusted life-years (QALYs). The utility weights were derived from several sources, including the HAEDIS study and a health-related quality of life study in the general population. The utility weights were combined with mortality rates through the Markov model. An annual discount rate of 3% was used.

**Direct costs**

A societal perspective was adopted in the study. The categories of direct costs included in the analysis were those related to care delivered in both inpatient and outpatient settings, such as primary care visits, hospital visits and visits to other health care professionals (psychologists and counsellors). Total costs were associated with the model health states. No cost was assigned to the new hypothetical treatment in the base-case. The unit costs and resource quantities were not presented separately. The estimation of resource consumption was mainly based on data from the HEADIS study, while costs were estimated using unit prices for Sweden. Discounting was relevant, as 5-year costs were evaluated, and an annual discount rate of 3% was used. The price year was 2005.

**Statistical analysis of costs**

Probabilistic distributions were assigned to each cost input in the model, but no details on the type of distributions used were given.

**Indirect Costs**

Productivity costs due to sickness absence were included in the analysis. The unit costs were derived using unit prices for Sweden. Days off work were estimated from the HEADIS study. The price year was 2005. An annual discount rate of 3% was used. The unit costs and the quantities of resources used were not presented separately.

**Currency**

Sweden kronor (SEK). The exchange rate from SEK to US dollars ($) and euros (EUR) was $1 = SEK 7.5 and EUR 1 = SEK 9.3.

**Sensitivity analysis**

A probabilistic sensitivity analysis was carried out by assigning stochastic distributions to all inputs. A univariate sensitivity analysis was also performed to assess the impact of changes in key model inputs on the expected costs and benefits. The model inputs under examination were relapse risk reduction, relapse and recurrence risk reduction, mortality risk reduction, additional cost of adverse events with new treatment, time horizon, increased mortality risk, and the discount rate for costs and benefits. The sources of the alternative values were not explicitly reported. The results were presented for different time horizons and for different values of treatment effect.
Estimated benefits used in the economic analysis
The 5-year QALYs associated with standard care were 3.62.

Assuming a 50% relative improved remission rate, the new treatment generated an additional 0.073 QALYs over the 5-year time horizon.

Variations in the relative effect of treatment showed that the QALYs gained ranged from 0.002 to 0.12 depending on the time horizon adopted and assumptions of relative treatment effect.

The sensitivity analysis showed that, in all scenarios, the new intervention led to more QALYs over standard care. Higher QALYs gained were observed, particularly when the same relative treatment effect of 50% was assigned to the risk of relapses but a longer time horizon was adopted (up to 30 years), or when the new therapy led to reductions in the mortality risk. However, there was a slight reduction in QALYs in comparison with the base-case estimate when drug-related adverse events were considered.

Cost results
The total accumulated 5-year costs with standard care were SEK 157,700.

Assuming a 50% relative improved remission rate, the new treatment led to cost-savings of SEK 20,100 over the 5-year time horizon, the greatest cost-savings being observed in the indirect costs (SEK 13,200).

With a relative improved remission rate of only 10%, the 5-year cost-savings with the new intervention were SEK 5,200. The cost-savings amounted to SEK 31,600 with 100% improved effect. Even when using a very short time-horizon (6 months), the new treatment led to cost-savings (SEK 2,300).

The analysis showed that even a small relative effect size or a short time horizon allowed for rather high premium prices for the hypothetical intervention. For example, in the base-case (50% treatment effect), the premium price for the new treatment would be SEK 17 per day with a 6-month time horizon and SEK 100 per day when assuming a 5-year timeframe.

The sensitivity analysis showed that the new intervention remained the cheapest option in all scenarios considered. The cost-savings increased when the time horizon was increased to 15 or 30 years, and decreased when additional costs of adverse events for the new treatment were considered.

Synthesis of costs and benefits
An incremental cost-utility ratio was not calculated since the new therapy dominated standard care, which was both less effective and more expensive.

Authors’ conclusions
New treatments for depression, having a relatively better effect, have the potential to produce cost-savings for society in comparison with standard care for depression.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The new hypothetical treatment was compared with usual care in the authors’ setting, which reflected actual treatment patterns in Sweden where a combination of treatments is available for patients with depression. Specifically, the combination of treatments included as a comparator was taken from a longitudinal Swedish study. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
No systematic search for data was reported. The parameters for the model were mainly derived from a published clinical study. Much of the clinical data were taken from the HEADIS study, the naturalistic design of which should
have ensured that the effectiveness data used reflected actual clinical practice. Patient characteristics were also taken from this study and represented the Swedish population. Finally, information on disease progression was taken from a published meta-analysis and this should ensure high internal validity.

Validity of estimate of measure of benefit
The estimation of QALYs was modelled using a Markov model. The methods used to estimate the utility weights were not described, but were mainly taken from the HEADIS study which should have been representative of the Swedish population. Discounting was appropriately performed and the impact of using different discount rates was investigated. QALYs are an appropriate measure since they capture the impact of the intervention on both quality of life and survival. They can also be compared with the benefits of other health care interventions.

Validity of estimate of costs
The perspective of the economic analysis was appropriate as all costs were included regardless of the payer. The unit costs and the quantities of resources used were not presented separately, which might limit the possibility of replicating the analysis in other settings. The source of the costs and resource use was reported. The costs were treated stochastically. The impact of changing the base-case economic assumptions was explicitly considered in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises in other time periods.

Other issues
The authors reported the results from other published economic evaluations of new treatments for depression. However, they made no formal comparison with the findings from the current study since the intervention assessed in this study was hypothetical. The authors stated that the generalisability of the study results to other settings was limited given the use of data derived mainly from a Swedish study. However, it was noted that the modelling approach used in the current study can be easily applied to other countries. The authors pointed out the strengths of the analysis, such as the adoption of a societal perspective and the use of a valid modelling approach. Several alternative scenarios and assumptions were also considered and these reinforce the transferability of the results to other settings.

Implications of the study
The study results provide a framework to evaluate the clinical and economic impact of new treatments for depression.

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Other publications of related interest
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