Cost-effectiveness of current and optimal treatment for schizophrenia
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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
This study compared services currently provided (current treatment (CT)) for schizophrenia with those that could be achieved with wider implementation of evidence based interventions (referred to as optimal treatment (OT)). CT was defined according to local epidemiological and practice pattern data, and OT was defined by recommendations in the clinical practice guideline literature, primarily the PORT study recommendations (see "Other Publications of Related Interest" below). The authors presented the different treatment strategies as different population proportions that received typical, atypical or clozapine pharmacological treatment and family therapy, social training skills or cognitive-behavioural therapy. The study also provided estimates of what would be the state of schizophrenia patients without any treatment (natural history).

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The target population was that of schizophrenic patients and those with schizoaffective disorder in the general population.

Setting
The setting was a combination of community care, primary care, secondary care and institution, due to the complex treatments. The economic study was carried out in Australia.

Dates to which data relate
Effectiveness evidence was derived from studies published between 1995 and 2000. Resource use data were derived from the 1997-98 survey. The price year was 1997-1998.

Source of effectiveness data
The effectiveness evidence was derived from a review of the literature, as well as estimates based on expert opinion.

Modelling
An epidemiological model was developed, firstly, to calculate the total health burden due to schizophrenia, the total burden avoided by the different treatment strategies and the related costs within the Australian population, and secondly to derive cost-effectiveness ratios for the different treatment strategies. The following is a brief description of the steps of the model. First, the prevalence of disease was established through a cross-sectional survey of a catchment area. Second, the distribution of current treatments within the Australian population was derived from the same survey.
Third, the distribution of optimal treatments within the Australian population was derived from the PORT study recommendations (see "Other Publications of Related Interest" below). Fourth, a composite disability weight was derived for the prevalence of disease given current treatment. Fifth, the effectiveness of each type of treatment relative to no treatment was derived from the published literature, mostly meta-analyses, and expressed as an effect size. Sixth, a subsidiary study estimated the average shift in disability weight with an effect size shift in symptoms and functioning, called a transfer factor (see Sanderson et al, in press, for a full explanation of this method). Seventh, a multiplication of the effect size for each intervention by the transfer factor, applied to each person who received that intervention, provided the average shift in disability weight under current treatment. Steps 5-7 were repeated, this time with the distribution of treatments given optimal treatment from Step 3, to derive a summary disability weight for optimal treatment.

**Outcomes assessed in the review**
Inputs to the model were schizophrenia prevalence, incidence, disability weightings in different states, percentage of time spent in a psychotic episode, and effectiveness of CT and OT.

**Study designs and other criteria for inclusion in the review**
Prevalence, incidence and disease states were taken from a catchment area cross-sectional study for current treatment. Effectiveness of treatments was taken from published meta-analyses. The authors did not describe any other study designs or inclusion criteria.

**Sources searched to identify primary studies**
Not stated by the authors.

**Criteria used to ensure the validity of primary studies**
For effectiveness studies, the authors used meta-analysis with analyses chosen for their methodological rigour and ability to code overall effect sizes of treatment benefits.

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

**Number of primary studies included**
Eight primary studies were included to derive effectiveness evidence.

**Methods of combining primary studies**
The authors incorporated results from published meta-analysis for some effectiveness data but did not combine the results of individual studies.

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

**Results of the review**
One month prevalence was 0.29%, and the distribution of cases were as follows:

- 2% new incident cases,
- patients with complete or partial remission 30%,
- negative symptoms between episodes 23%,
- and continuous psychotic symptoms 45%.
Apart from the last category, an estimated 23% of a person's time would be spent in a psychotic episode.

Disability weights were 0.82 for acute psychosis, 0.34 for patients with complete or partial remission, and 0.46 if negative symptoms between episodes, giving a composite weight of 0.638.

A transfer factor of 0.181 was derived and used to transform effect size superiority over placebo due to treatment into preference weighting change due to treatment.

Disability weighting changes attributed to pharmaceutical and psychosocial interventions of OT derived from the weighted effect size by the transfer factor were an improvement of 0.121 (0.097 when accounting for treatment resistance, see "estimates of effectiveness & key assumptions").

Effects sizes were as follows: for typical: 0.47, atypicals: 0.50, clozapine: 1.17, family therapy: 0.56; social skills training: 0.44; and cognitive behavioural therapy: 0.76.

**Methods used to derive estimates of effectiveness**
The methods used to derive estimates based on opinion were not specifically reported but the assumptions were based on the literature.

**Estimates of effectiveness and key assumptions**
Treatment resistance was assumed to be 20% and it was backed by a reference. Other model assumptions are detailed in the modelling field above.

**Measure of benefits used in the economic analysis**
Although the authors evaluated disability-adjusted life-years (DALYs) (which comprise years of life lost (YLLs) plus years lived with the disorder (YLDs) weighted by the disability weighting associated with the disorder), the study focussed on YLD, as YLLs are a minor contributor to schizophrenia burden. Disability weights taken from the literature were used to derive these, but neither the methods used nor whose values were used were reported. See "results of the review" above for the disability weights.

**Direct costs**
Discounting was, appropriately, not performed given the short-term perspective of the study. Resources used in the previous 12 months for a mental health problem were estimated from surveys. The unit cost of each service or procedure was obtained from published sources. Categories of costs included were mental health sector (acute and chronic in-patient, visits to psychiatrists and psychologists, and mental health team), pharmaceuticals and general health sector. The authors excluded out of pocket costs. Two additional calculations were included for the cost of CT to ensure consistency with other Australian studies: these were the total treatment costs for other contacts for a mental health problem (including radiologist, pathologists, general medical specialists and other counsellors); and an adjustment of the number of general practitioner contacts not specifically related to mental health taken from one survey by the proportion that were mental health related taken from a national survey. The cost-quantity boundary adopted was that of the health service. The price year was 1997-1998 and prices were deflated using the health component of the consumer price index. Dates of resource use ranged from 2000 to 2002. Unit costs and resources were reported separately. Further details about the calculations were not provided by the authors but are available in the Carr et al study (see "Other Publications of Related Interest" below).

**Statistical analysis of costs**
95% confidence intervals of costs were calculated using Monte Carlo simulation approach.

**Indirect Costs**
The study did not include indirect costs.

**Currency**
Australian dollars (Aus$)

**Sensitivity analysis**
A multivariate stepwise linear regression was conducted to identify the most important contributors to cost and effects variances. Univariate sensitivity analysis was carried out for variables identified by investigators and experts.

**Estimated benefits used in the economic analysis**
The actual burden of disease in the Australian population was: YLL attributed to schizophrenia: 402, YLDs 24,913.

Outcome with CT was: 3,774 YLDS averted (95% CI: 2908 - 4691).

Outcome with no treatment (natural history) was: 28,671 YLDs, and only 13.2% of disability burden averted by CT.

Outcome with OT was: 6,217 YLDs averted (95% CI: 4326 - 8382), or 21.7% of baseline YLDs.

**Cost results**
The costs of CT were:

average cost of a person with schizophrenia: Aus$18,949; and

total direct governmental costs; Aus$740 millions (95% CI: 484.7 - 1020.2).

For OT the average costs per person are Aus$17,113 and a total population cost of Aus$668 million (95% CI: 408.5 - 1133.3).

Bed day costs accounted for half of this expenditure, down from 85% from CT.

**Synthesis of costs and benefits**
Average cost-effectiveness ratios were calculated, which compared the cost and effects of the intervention to "do nothing". The average cost-effectiveness (cost per YLD averted) was Aus$196,070 for CT (95% CI: 123,827 - 297,516) and Aus$107,482 for OT (95% CI: 59,714 - 205,418). The authors did not perform an incremental analysis, however, it is apparent that OT dominates CT: it is cheaper and more effective.

Influential parameters from the multivariate analysis that contributed to the estimated variability of YLDs averted were cognitive behavioural therapy and haloperidol effect sizes, and the transfer factor to convert this to disability weightings.

OT was most influenced by cognitive behavioural therapy and risperidone effect sizes and the transfer factor.

The most important predictors of cost per YLD averted were acute and non-acute bed day unit costs, the cognitive behavioural therapy effect size for CT, and standard case manager unit costs, intensive case management contacts and cognitive behavioural therapy effect sizes for OT.

Univariate sensitivity analysis showed that, although some investigator assumptions did have an impact, they did not affect the overall conclusions.

**Authors' conclusions**
Only 13% of the present burden of schizophrenia and schizoaffective disorder is being averted from current treatment, in part because the best existing interventions are not widely enough used for the right cases. YLDs averted increased by two thirds with OT but cost remained stable, so the Aus$/YLD averted was reduced and efficiency improved with OT. Optimal treatment is affordable within the present budget and should be implemented.

CRD COMMENTARY - Selection of comparators
The selection of comparator (the current practice pattern in Australia) was clearly justified as the study tried to evaluate the burden of disease it averted, as well as whether the move towards a more evidence-based scenario would improve cost-effectiveness.

Validity of estimate of measure of effectiveness
Although the authors did not report undertaking a systematic review to derive input for the model parameters, they use meta-analytical published studies to derive effect sizes of most interventions. Although prevalence data were taken from a mostly urban population, the authors stated that most of the Australian population is urban. As the survey was conducted in subjects in contact with health services, this may have led to an underestimation of prevalence and an overestimation of treatment coverage. All the assumptions used were transparently reported by the authors, and references were given to their sources. The authors conducted an extensive sensitivity analysis to estimate the impact of input variations on results, both those based on the literature and those based on assumptions. Other limitations reported by the authors report were that modelling atypical antipsychotics in favour of typicals is controversial, and that the evidence for the efficacy of social skills training has recently been questioned (although a sensitivity analysis showed that their impact on the model was modest).

Validity of estimate of measure of benefit
As the authors stated, the study focussed on YLDs as a measure of DALYs, and YLLs are poorly represented by the data, especially those due to suicide. This may overestimate the proportion of the burden averted. The method for estimating change in disability weighting and the transfer factor to translate effect sizes to disability were developed on an ad hoc basis for the project, and the authors stated that they gave comparable results with the few prospective studies that evaluate health status and health state preferences concurrently.

Validity of estimate of costs
Most relevant categories of costs were included for the perspective adopted, and, within each category all the relevant costs seem to have been included. An important exclusion, as stated by the authors, was the costs of implementing the evidence-based treatment, which may alter the results. Costs and quantities were, in part, reported separately. Indirect costs were not considered as the perspective was not societal, and this may have had a major impact on cost estimates. Resource use data were derived from national surveys to subjects of 12-month resource use. A statistical analysis as well as a sensitivity analysis was conducted on resource use. Unit costs data came from published sources and their impact was evaluated in the multivariate analysis.

Other issues
The authors did not make appropriate comparisons of their findings with those of other studies, but the issue of generalisability was explicitly tackled. Although prevalence, service use and unit cost data were from Australia, the authors stated that the finding that optimal care is no more expensive but twice as efficient is likely to be transferable to other settings.

Implications of the study
Although the cost-effectiveness of schizophrenia treatment is well above the affordable price in Australia, OT at the same level of coverage as in CT and with compliance similar to efficacy trials would not increase total costs to the health system, and will increase health gains by 65%. As it is not always possible to carry out that which is optimal, it is likely therefore that the attainable cost-effectiveness in real practice will lie somewhere between the CT and OT
figures. Nevertheless, it is of serious concern that three quarters of the burden seems unavoidable with existing best interventions, so new strategic research is required to improve the knowledge base.

**Source of funding**
Supported by the Australian National Health and Medical Research Council (project no. 113807).

**Bibliographic details**

**PubMedID**
14594918

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aged; Cost of Illness; Cost-Benefit Analysis /methods; Evidence-Based Medicine; Financing, Organized /methods; Humans; Mental Health Services /economics; Prevalence; Psychotherapy /methods; Quality-Adjusted Life Years; Schizophrenia /drug therapy /therapy; Treatment Outcome

**AccessionNumber**
22003008305