Changes in perceived health and functioning as a cost-effectiveness measure for olanzapine versus haloperidol treatment of 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
Olanzapine in the treatment of schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-consequences analysis.

Study population
The study evaluated patients with schizophrenia and related psychotic disorders. Male and female outpatients over the age of 18 were included in this study. All patients met the DSMR-III-R criteria for schizophrenia, schizophrenic disorder and schizoaffective disorder. Patients had a minimum brief Psychiatric Rating Scale score of 18 and were intolerant to current antipsychotic therapy (excluding haloperidol). Exclusion criteria were not provided.

Setting
The setting was a hospital and the community.

Dates to which data relate
The effectiveness and resource use data were from a study published in 1997, and the unit costs were from 1995.

Source of effectiveness data
The effectiveness data were based on a single study, the details of which were published elsewhere.

Link between effectiveness and cost data
Both cost and effectiveness estimates were based on the same study sample. Resource and clinical data were collected prospectively.

Study sample
This study was based on a large multinational randomised controlled trial comparing the efficacy, safety and cost-effectiveness of olanzapine versus haloperidol in the treatment of schizophrenia. The sample size was not based on power calculations. A total of 1,996 patients were included in the trial, and were randomised in a 2:1 fashion to olanzapine or haloperidol. The evaluation of health outcomes for the economic analysis was based on the English-speaking subgroup of patients in the trial (UK, US and Canadian patients): 772 taking olanzapine and 383 taking haloperidol. The analysis of cost data included only the US patients: a sample of 812 patients. The patient inclusion
criteria were broad and seem to have reflected the population for which the therapy would subsequently be used in clinical practice.

**Study design**
The study was a randomised, controlled trial (RCT) in which patients were the units of randomisation. The original study was multi-centred, with 174 centres in 17 countries in Europe and North America. Only patients who demonstrated a clinically significant treatment response after 6 weeks, according to predefined criteria, were included in the 52-week follow-up study; this was about 60% of the patients.

**Analysis of effectiveness**
The analysis of effectiveness was based on intention to treat analysis through imputation of missing data based on the whole study sample. The quality of life instrument SF-36 was used to evaluate the health status of the patients. The SF-36 instrument measures 8 domains of an individual’s perceived functioning and well being through 8 subscales. The authors aggregated the 3 subscales that focus on the physical health factor and the 3 subscales that focus on the mental health factor. The resulting two dimensions of "physical health" and "mental health" were used in the economic evaluation. The SF-36 questionnaire was administered at the end of the 6-week acute phase and, for those in the extension phase, every 8 weeks for an additional 46 weeks. Among patients completing the SF-36 at baseline there were no differences between the olanzapine and haloperidol groups with respect to baseline characteristics.

**Effectiveness results**
Patients receiving olanzapine experienced an incremental improvement of a mean of 5.75 points on the physical health scale as compared with patients receiving haloperidol. On the mental health scale, the olanzapine patients experienced a mean incremental improvement of 1.66 points as compared to haloperidol patients. Data on absolute improvement in each group were not provided.

**Clinical conclusions**
The authors concluded that olanzapine showed greater effectiveness than haloperidol and that olanzapine might offer "great promise for affecting the physical aspects of functioning".

**Modelling**
A model was used to present uncertainty in the cost-effectiveness estimates in cost-effectiveness planes.

**Measure of benefits used in the economic analysis**
The sub-scales of SF-36 were aggregated into a mental health scale and physical health scale. The authors used the number of points on the physical and mental health scales as a measure of benefit in the economic evaluation.

**Direct costs**
Only US patients were included in the cost analysis (n=812). Information on resource utilisation was collected through self-report forms and corroborative written records. A standardised list of prices for services was used to cost the resources, and references for these were provided. The authors reported that they included "hospital costs" in the analysis. These were, however, not reported separately, and it was not reported which costs were included or how they were measured in the trial. Discounting was not relevant and was not carried out. It appears that the authors have estimated a daily cost of hospitalisation of $599 per day. The price year was not reported.

**Statistical analysis of costs**
Bootstrap analysis was used to synthesise costs and effectiveness and to evaluate the stability of the incremental cost effectiveness ratios presented.
Indirect Costs
Indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Please see the "effectiveness results" section reported earlier.

Cost results
The authors reported that patients receiving olanzapine incurred a cost of $9,386 less than haloperidol patients over the 52-week follow-up period. Confidence intervals were not provided.

Synthesis of costs and benefits
Costs and benefits were combined to arrive at an estimate of cost savings per 1 interval point on the mental health scale and on the physical health scale. When comparing olanzapine with haloperidol, the saving for one point on the physical health scale was $1,632 and the saving for one point on the mental health scale was $5,654. The authors expressed the uncertainty in the incremental cost effectiveness ratio on cost-effectiveness planes. On both the physical and the mental health scales, less than one percent of the bootstrap replication results were in the "haloperidol less costly" quadrant. Olanzapine was less costly and more effective in 89% of the replications on the physical health scale, and less costly and less effective in 11% of the replications. Similarly, olanzapine was less costly and more effective in 62% of the replications on the mental health scale, and less costly and less effective in 38% of the replications.

Authors' conclusions
The authors concluded that the results of this study indicated that olanzapine is both more effective and less costly than treatment with haloperidol, and therefore is a cost-saving treatment option.

CRD COMMENTARY - Selection of comparators
The comparison with an active substance rather than placebo was appropriate and is an advantage in economic evaluation. The authors compared olanzapine, a second-generation antipsychotic drug belonging to the group of 'atypical antipsychotics' with haloperidol, a first generation 'typical' antipsychotic drug. The authors stated that the differing pharmacological profile of these drug classes have been demonstrated through an advantageous side effect and tolerability profile for the atypicals, but that cost-effectiveness remains to be established.

Validity of estimate of measure of effectiveness
The estimate of effectiveness was based on a subgroup of patients who completed the 52-week follow-up phase of the original 6-week study. Missing values were imputed in order to complete an intention to treat analysis, and this may have led to a more conservative estimate. Only patients in the US study centre were selected for the cost-effectiveness analysis.

Validity of estimate of measure of benefit
The choice of using intervals of improvement on an aggregated estimate of physical functioning was justified by the
authors. However as a measure of effectiveness it may not have great clinical significance for the purpose of economic evaluation. Only relative differences in functional scales were provided and not the absolute scores, and this makes assessment of the clinical outcomes difficult.

**Validity of estimate of costs**
Neither the components of the cost estimate nor the unit prices were reported in this paper. It is therefore very difficult to assess the relevance of the costs included and the validity of the estimate. Furthermore, only a subgroup of US patients who completed the 52-week follow-up period were included in the evaluation of costs.

**Other issues**
The issue of generalisability to other settings was not discussed, but only US patients were included in the economic evaluation. By only including US patients in the economic analysis, the authors did not make use of the opportunity that this multinational trial presented to look at transferability of cost-effectiveness results across countries. A sensitivity analysis of country-specific resource may have been appropriate.

**Implications of the study**
The authors comment that patient-centred measures such as quality of life measurement should be used more extensively in the evaluation of clinical outcome in cost-effectiveness analyses.

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None stated.

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**Other publications of related interest**

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