Comparing olanzapine and ziprasidone in the treatment of schizophrenia: a case study in modeling

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 use of olanzapine and ziprasidone for the treatment of schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with acute-episode schizophrenia. Further inclusion and exclusion criteria were not reported. The baseline characteristics of the samples from four of the published studies used in the model were presented.

Setting
The setting appears to have been a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence and resource use data were derived from studies published between 1995 and 2000. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from published studies, supported by the authors' assumptions.

Modelling
A decision analytic model was used to estimate the annual medical costs and health outcomes for individuals treated with olanzapine and ziprasidone. The analysis was conducted on an intention to treat basis, over a one-year period. Patients entered the model when they experienced an acute-psychotic episode that required hospitalisation, and were initially treated with olanzapine or ziprasidone (first drug treatment). People not responsive to the initial treatment were allowed to switch to the alternative drug (second drug treatment). The two study groups considered were olanzapine as first drug followed by ziprasidone as second drug (olanzapine group), and ziprasidone as first drug followed by olanzapine as second drug (ziprasidone group).

Outcomes assessed in the review
The primary health outcomes used as model inputs were response rates, based on following percentages:
patients achieving a 30% improvement in the Brief Psychiatric Rating Scale (BPRS), relapse rate, the rate of suicide attempts per relapse, the rate of suicide completions per relapse, and the rate of people taking anticholinergic drugs for extrapyramidal symptoms (EPS).

**Study designs and other criteria for inclusion in the review**
Four of the primary studies used as the main source of the effectiveness evidence were clinical trials. The populations considered were described.

**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**
The effectiveness evidence was mainly obtained from eight primary studies.

**Methods of combining primary studies**
The effectiveness data were combined using narrative methods, and conservative estimates were selected.

**Investigation of differences between primary studies**
The authors selected studies that had similar populations, used standard drug doses, and were of similar length.

**Results of the review**
The 30% improvement in the BPRS was achieved by 55.4% with olanzapine and by 48.8% with ziprasidone. The relapse rate was 28.6% with olanzapine and 35.0% with ziprasidone. The rate of suicide attempts per relapse was 13.1% with both drugs. The rate of suicide completions per relapse was 3.01% with both drugs. The rate of people taking anticholinergic drugs for EPS was 19.8% with olanzapine and 19.0% with ziprasidone.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions to support the data used in the decision model.
Estimates of effectiveness and key assumptions
The patients were assumed to have, at most, one relapse per year. Those who did not respond to the first drug treatment were all switched to a second drug, requiring additional days in the hospital. The rest of the treatment process was assumed to be similar to the treatment of those who responded to the first drug treatment. People who did not respond to both the first and second drugs were assumed to experience an extended episode, and to switch to clozapine for the rest of the year. Similar suicide attempt and completion rates were assumed. For people experiencing acute episodes, a compliance rate of 85% was assumed for both drugs. Finally, it was assumed that the response of an individual to the second drug was not dependent on the responsive to the first drug.

Measure of benefits used in the economic analysis
The outcomes assessed using the decision model were overall relapse rate, hospital stay, and EPS days. However, no summary benefit measure was used in the economic analysis. A cost-consequences analysis was therefore carried out.

Direct costs
Discounting was not performed as the costs were incurred over one year. The unit costs and the resource quantities were reported in full. The costs included in the analysis were for inpatient services (acute hospital services) and drug acquisition expenses. The cost/resource boundary appears to have been that of the hospital. The unit costs and the resource use were estimated from published data. The total costs of each treatment were obtained from modelling. All costs were inflated to 2001 using the US Consumer Price Index.

Statistical analysis of costs
Statistical analyses of the costs were not performed.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were performed to determine the impact on the study results of several variables. These included the daily drug costs, relapse rates, response rates for the second drug treatment, hospital length of stay, and the costs of switching treatments. In addition, the impact of using risperidone as a second drug treatment was tested. This assumed a response rate of 45.5%, a relapse rate of 17%, an EPS rate of 29%, and a daily cost of $6.88.

Estimated benefits used in the economic analysis
Overall, the relapse rate was 23.5% with olanzapine and 25.2% with ziprasidone. Hospital stay was 36.7 days with olanzapine and 37.4 days with ziprasidone. The number of EPS days was 60 with olanzapine and 60.1 with ziprasidone.

Cost results
The one-year treatment costs were $48,676 with olanzapine and $48,873 with ziprasidone. Consequently, olanzapine resulted in cost-savings of $197. The inpatient costs accounted for 74 to 75% of the total annual medical costs for both treatment pathways, while the outpatient costs accounted for about 19% of the total costs. The contribution of drug costs was 6.3% for olanzapine and 5.4% for ziprasidone. The estimated costs were fairly sensitive to variations in the relapse rate for ziprasidone, changes in the drug costs, and changes in the response rates for the second drug.
Synthesis of costs and benefits
Not applicable.

Authors' conclusions
The annual treatment costs were similar for both treatments. The significantly lower acquisition cost for ziprasidone did not result in a significant reduction in the total costs of the treatment. In terms of effectiveness, the health outcomes slightly favoured olanzapine.

CRD COMMENTARY - Selection of comparators
The authors did not justify their rationale for the choice of the comparator. Olanzapine represented a commonly used antipsychotic treatment, which was launched in the USA in 1996. The Food and Drug Administration approved ziprasidone in February 2001. You should assess whether olanzapine represents a widely used technology in your own setting, and whether other drugs might have been used as comparators.

Validity of estimate of measure of effectiveness
The effectiveness estimates were derived from published studies. The authors selected primary studies that were similar in terms of their study populations, to minimise differences in the outcome measures. Authors’ assumptions were also used in the decision model. Sensitivity analyses were appropriately carried out to assess the robustness of the study results to variations in the estimated data. The authors noted that there was no information on adverse events, such as weight gains and QTc interval prolongation, which would have highlighted substantial differences between the two drugs.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis. As a result, the costs and the benefits were not combined. Only the outcomes of the decision model were reported. A discussion of the quality of life issues related to the treatments would have been interesting. In addition, this would have enabled a better comparison with technologies for other conditions.

Validity of estimate of costs
The perspective adopted in the study was not stated, but referred presumably to the hospital. The unit costs and the resource quantities were reported and the price year was given, thus improving transparency and allowing an analysis of generalisability. No statistical analyses were performed on the costs or quantities. However, several sensitivity analyses were carried out and illustrated.

Other issues
The authors made few comparisons of their findings with those from other studies. In addition, the issue of the generalisability of the study results was not explicitly addressed. Sensitivity analyses were carried out and the unit costs were reported separately, thus enhancing the external validity of the analysis. The authors presented their results in detail. The authors noted a potential limitation of the analysis, in that the patients in the model were assumed to switch to the alternative drug as second treatment, which may not represent current practice. However, the impact of a different treatment was assessed in the sensitivity analysis.

Implications of the study
The main implication, as identified by the authors, was that the greater proportion of the total treatment costs is attributable to hospitalisation, thus "drug efficacy, rather than acquisition cost, appears to have the greatest impact on total costs". "The model suggests that the choice of the antipsychotic treatment should not be made strictly on acquisition cost considerations." The authors recommend that future research should focus on head-to-head trials comparing the effectiveness, safety, tolerability and cost-effectiveness of the two treatments.
Source of funding
None stated.

Bibliographic details

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Subject indexing assigned by CRD

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