Olanzapine versus risperidone: a prospective comparison of clinical and economic outcomes in 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
The use of olanzapine, compared with risperidone, for the treatment of schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 65 years who had been diagnosed with schizophrenia, schizophreniform disorder or schizoaffective disorder, according to the American Psychiatric Association's criteria (see Other Publications of Related Interest no.1). In addition, the participants had to exhibit a minimum score of at least 42 on the Brief Psychiatric Rating Scale extracted from the Positive and Negative Syndrome Scale (PANSS). Patients were excluded from the study if they had a documented treatment resistance to antipsychotic agents, or a co-morbid or other recent major axis I disorder, and/or serious unstable medical illness.

Setting
The study setting was a hospital and the community. The economic analysis was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were obtained from a study published in 1997. The cost data were taken from sources published between 1994 and 1997. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from a single study (see Other Publications of Related Interest no.2).

Link between effectiveness and cost data
The costing was carried out prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
The analysis was restricted to the 150 patients recruited in the USA (44% of the original study sample) who received either olanzapine (n=75) or risperidone (n=75). The baseline demographic and clinical characteristics were given, thus allowing comparison with the population. No power calculations were performed to determine sample size.
Study design
The study took the form of a randomised, double-blind prospective study carried out in 13 clinical centres in the USA. The patients were followed-up for 28 weeks. Fifty-nine patients did not complete the study.

Analysis of effectiveness
The analysis was based on intention to treat. The primary health outcome was the PANSS total score. The other outcomes measured were the Clinical Global Impressions-Severity of Illness Scale (CGI-S), extrapyramidal symptoms (EPS), akathisia, dyskinesia, visit-wise response rates, time maintaining response, and the use of anticholinergic agents. EPS, akathisia and dyskinesia were assessed using the Simpson-Angus Scale, the Barnes Akathisia Scale, and the Abnormal Involuntary Movement Scale (AIMS).

Maintained response was defined as a 20% or greater worsening in the PANSS total score, along with a CGI-S score of at least 3, after 8 weeks' therapy. The treatment emergent EPS was defined by scores of at least 4 on the Simpson-Angus scale, of at least 2 on the Barnes Akathisia scale, and of at least 3 on the AIMS.

The two groups did not generally differ in terms of patient demographic characteristics. The exception was that risperidone-treated patients had greater baseline PANSS total scores, \( p=0.043 \) and greater PANSS positive scores, \( p=0.037 \). The authors stated that the differences were not clinically significant.

Effectiveness results
The survival analysis revealed that olanzapine-treated patients were more likely to have a maintained response than risperidone-treated patients, \( p=0.048 \).

There were no differences between treatment groups in terms of the proportion of patients demonstrating a response based on the PANSS total scores.

The number of patients defined as having treatment emergent EPS was:
- for the Simpson-Angus Scale, 5 (7.5%) for the olanzapine group versus 8 (13.1%) for the risperidone group, \( p=0.290 \);
- for the Barnes Akathisia Scale, 17 (28.3%) for the olanzapine group versus 18 (32.7%) for the risperidone group, \( p=0.609 \); and
- for the AIMS, 2 (3.0%) for the olanzapine group versus 9 (13.0%) for the risperidone group, \( p=0.055 \).

The use of anticholinergic agents was higher among the risperidone-treated patients (34 patients or 45.3%) than among the olanzapine-treated patients (19 patients or 25.3%), \( p=0.016 \).

Clinical conclusions
Olanzapine-treated patients were significantly more likely to have a maintained response than risperidone-treated patients. Also, a higher proportion of risperidone-treated patients suffered treatment emergent EPS, although this was not statistically significant. A significantly higher proportion of risperidone-treated patients used anticholinergic agents.

Measure of benefits used in the economic analysis
The authors did not report a summary health benefit and left clinical outcomes disaggregated. Hence, a cost-consequences analysis was conducted.

Direct costs
The direct costs were not discounted due to the short timeframe of the study (less than one year). The authors reported the unit costs but did not report the resource use. The direct costs were broken down into categories: the length of hospital stay; the number of emergency department visits; the number of hospital treatment sessions; the number of out-
patient visits to psychiatrists, other physicians, or other mental health care provider services; and the number of home visits by health professionals. The quantity/cost boundary adopted was that of the health service. The prices for the in- and out-patient physician services were based on Healthcare Financing Administration data. The prices for the length of hospital stay were taken from the Monroe-Livingston Mental Health Capitation Programme and inflated using the medical care component of the consumer price index. The drug prices were taken from the Red Book (see Other Publications of Related Interest no.3). The price year was 1997.

Statistical analysis of costs
An ordinary least-squares regression was used to ascribe missing cost data, based on the observed in-trial costs for those patients who did not complete the study. Given that cost distributions were asymmetrical and included outliers, the authors reported medians, trimmed means (10, 15 and 20%), tri-means, and Gastwirth means. One-way analysis of variance (ANOVA) models were used to determine differences between the groups in terms of the cost estimates. Median regression models were used to estimate the total costs, medication costs, and in- or out-patient service costs. The reduced models were formed by removing those independent variables (excluding treatment and intercept) with t-statistics of less than 1.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
One-way ANOVAs were conducted to evaluate the cost impact of more typical dosage regimens for olanzapine (10 and 13 mg) and risperidone (5 and 6 mg).

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The median total medical costs per patient were $2,843 lower in the olanzapine group ($5,141) than in the risperidone group ($7,984), (p=0.342).

The medication costs were $2,513 in the olanzapine group and $1,581 in the risperidone group, (p<0.001).

The in- or out-patient service costs were $3,774 lower in the olanzapine group ($3,516) than in the risperidone group ($7,291), (p=0.083).

The median regression model estimating medication costs predicted a significant saving of $793 for the risperidone-treated patients, (p=0.001).

The median regression model estimating in- or out-patient service costs predicted a significant saving of $3,644 for the olanzapine-treated patients (p=0.094).

The median regression model estimating total costs predicted a non significant saving of $3,569 for olanzapine (p=0.212).

The sensitivity analyses showed that the estimates of the potential savings achievable with olanzapine at the doses studied were conservative.
Synthesis of costs and benefits
Not applicable.

Authors' conclusions
Olanzapine offered advantages over risperidone in terms of efficacy and tolerability. In addition, savings in the in- and out-patient service costs offset the higher acquisition cost of olanzapine, compared with risperidone.

CRD COMMENTARY - Selection of comparators
The comparator was justified on the basis that it represented a currently employed strategy. You should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of effectiveness
The analysis was based on a prospective randomised controlled trial, which was appropriate for the study question. The authors showed, by baseline characteristics, the extent to which the study sample was representative of the study population. The groups were shown to be comparable at analysis, except for the PANSS scores. The measure of effectiveness seems to have been appropriate for this technology. However, its validity depended on whether converting model scale information into categorical (“maintenance of response”) data was appropriate. Where the division was made into categories, bias could have been introduced, and information lost as a consequence. Parametric tests of differences between the scale values might have been useful.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit, thus making comparison with other technologies difficult in terms of cost-effectiveness. However, since olanzapine was both more effective and less costly, the decision on adoption was straightforward to make.

Validity of estimate of costs
There were several good features of the cost analysis. Firstly, all the direct cost categories relevant to the health service seem to have been included, and statistical analyses were conducted to account for the uncertainty of the cost data. Secondly, the price year was reported, which makes it possible to replicate the cost results in other settings. Thirdly, the authors conducted sensitivity analyses on the costs of dosage regimens that are more common in practice, thus increasing the generalisability of the results. However, the charges were used to estimate the unit costs, and the quantities were not reported separately from the unit costs. The authors also did not consider the costs per day for concomitant medications, and did not include the costs in terms of informal and formal care.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings. The authors did not seem to present their results selectively. The study considered patients with schizophrenia and this was reflected in the authors’ conclusions. The authors noted that there was a loss of statistical power that resulted from restricting the sample. They also noted that the generalisability of the results to community practice was unclear, because the trial used doses higher than those seen in clinical practice.

Implications of the study
The authors argued that the advantages in the clinical outcomes experienced by olanzapine-treated patients translate into savings in the in- and out-patient costs, which more than offset any increase in medication costs relative to risperidone.

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Other publications of related interest


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