Risperidone compared with olanzapine in a naturalistic clinical study: a cost analysis

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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
Two atypical antipsychotics for the first-line treatment of schizophrenia or schizoaffective disorders are compared: risperidone and olanzapine. Mean (+/- SD) doses were 5.5 (+/- 2.4) mg/day for risperidone and 14.1 (+/- 4.7) mg/day for olanzapine.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hospitalised patients aged 65 or younger with schizophrenia or schizoaffective disorder, for whom risperidone or olanzapine were the drug of first choice for long term management. The patients had a minimum follow-up period of 120 days or were discharged.

Setting
The setting was secondary care within the UK.

Dates to which data relate
Effectiveness and resource use data were collected between September and June 2000. The prices used appear to be from the same year.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Retrospective costing was carried out on the same sample of patients as in the effectiveness study.

Study sample
Eleven UK psychiatric units in hospitals participated in the RODOS-UK and 501 patients were included. Two patients were excluded because of insufficient data on study medications, leaving 240 in the risperidone group and 259 in olanzapine group. Patients fulfilling the inclusion criteria received prescription chart and medical note reviews. Power calculations were adequately reported.
Study design
This was a retrospective, multicentre, cohort study. Outcomes were assessed by an independent trained team. The duration of follow-up was not precisely reported, but the maximum was 120 days.

Analysis of effectiveness
The analysis was based on intention to treat. The primary outcome of the study was the mean daily inpatient drug cost. Some secondary outcomes included mean daily dose, treatment efficacy, and time to first documented effectiveness. A predefined analysis plan using analysis of covariance was conducted to correct for imbalances between groups, which occurred only in the number of previous antipsychotics used.

Effectiveness results
Clinical outcomes were similar in the two groups.

Treatment effectiveness was 78% for risperidone and 74% for olanzapine, (p=0.39).

The mean time to documented onset of effectiveness (+/- SD) was shorter for risperidone than for olanzapine (17.6 +/- 17.9 days compared to 22.4 +/- 20.1 days; p=0.01).

The proportion of patients who discontinued treatment was similar in both groups (20% in both groups), as was the percentage of patients documented as experiencing adverse events (22% risperidone, 19% olanzapine; p=0.32).

The risperidone group stayed a mean of 9 fewer days in the hospital than olanzapine group (49 versus 58 days; p=0.007). The mean (+/- SD) doses of risperidone and olanzapine received were 5.5 (+/- 2.4) mg/day and 14.1 (+/- 4.7) mg/day, respectively.

Clinical conclusions
Both risperidone and olanzapine had similar effectiveness and tolerability, although risperidone was tentatively associated with faster speed of onset. The possibility that observed differences were a result of different baseline characteristics could not be entirely discounted.

Measure of benefits used in the economic analysis
Outcomes were left disaggregated and no single measure of benefit was reported, thus the study was classified as a cost-consequences analysis.

Direct costs
The only cost category evaluated included inpatient drug use discriminated by study drugs and concomitant medications. The estimation of quantities and costs were based on actual data from patients' charts. Discounting was, appropriately, not carried out due to the short time horizon of the study. Quantities and costs were analysed separately. Although inpatient stay was also evaluated and reported, its costs were not included in the analysis, which biases results against risperidone. The quantity/cost boundary adopted appears to be that of the hospital, and the price year was 2000. Resource use was evaluated in the last semester of 2000.

Statistical analysis of costs
Costs were treated in a stochastic way, and compared through analysis of variance with stratification for centre and using log-transformed data. Analysis of covariance was used to adjust for baseline differences.

Indirect Costs
Indirect costs were not included.
Currency
UK pounds sterling (£). 1 equalled Euro 1.61 and US$ 1.44 at the time of the study.

Sensitivity analysis
No sensitivity analysis was reported.

Estimated benefits used in the economic analysis
The reader is referred to the effectiveness results reported above.

Cost results
The geometric mean daily inpatient drug costs were significantly higher for olanzapine than for risperidone: 5.63 (CI 95%: 5.32 - 5.96) versus 3.92 (CI 95%: 3.70 - 4.16) (p<0.0001).

Geometric mean total costs of all inpatient drugs were also significantly higher for olanzapine than for risperidone: 163.8 (CI 95%: 141.3 - 190.0) versus 96.2 (CI 95%: 82.4 - 112.3), (p<0.0001). This is partly due to the longer mean treatment duration for olanzapine (44 versus 37 days).

Other costs (daily costs of other neuroleptics or other relevant comedication) were similar across the groups. Neither adjustment for baseline group differences or analysing by centre significantly changed the results.

Synthesis of costs and benefits
Costs and benefits were not combined.

Authors' conclusions
Both risperidone and olanzapine had comparable clinical outcomes in this cohort of hospitalized patients, but risperidone had significantly lower drug treatment costs.

CRD COMMENTARY - Selection of comparators
The justification for the comparators used was clear: there was controversy about the relative efficacy of the two most widely prescribed agents. Nevertheless, other antipsychotics, both typicals and atypicals, could be used, and you should judge if they represent an adequate choice in your own setting.

Validity of estimate of measure of effectiveness
Although the retrospective observational study design could be prone to bias in the estimation of drug relative effects and costs, the authors reported a predefined analysis plan to correct imbalances between groups, and had an independent team for outcome assessment, which helps to reduce potential biases. The authors also stated that the possibility that observed differences were a result of different baseline characteristics could not be discarded. Another limitation stated by the authors was that the analysis of effectiveness relied on accurate recording by the clinician on the patient chart. Another possible confounding factor suggested by the authors was that risperidone was possibly prescribed to milder patients as it has dose limiting adverse events.

Validity of estimate of measure of benefit
As the study was based on a cost-consequences approach the reader is referred to the "Validity of estimate of measure of effectiveness" section above.
Validity of estimate of costs
The previous comment of potential problems arising from the choice of study design, applies to this section as well. The only cost category evaluated was inpatient drug use, and the perspective was not clearly stated. Quantities and costs, however, were analysed separately. Although inpatient stay was also evaluated and reported, its costs were not included in the analysis, which biases the results against risperidone. The exclusion of other non-drug related costs could also have altered the results, although probably only marginally compared to inpatient stay costs. As costs had a skewed distribution, they were transformed and then compared and reported using log-transformed data. This is an approach that is currently not widely recommended to inform decision makers. Although the price year was not specifically reported, resource use was evaluated in the last semester of 2000, and the source of prices appears to have been the recruiting centres.

Other issues
The authors compared the UK study results with the international study results and with those of other studies, and cited contradictory results about the cost-effectiveness of risperidone and olanzapine. Generalisability to the UK was assessed by reporting study results in each of the 11 centres, which showed results to be similar among them.

Implications of the study
In this naturalistic non-randomised study, risperidone was tentatively associated with faster speed of onset, shorter hospital stay, and about half the drug costs of olanzapine for hospitalised patients with schizophrenia or schizoaffective disorder. Although confounding factors cannot be totally discarded, the study suggests risperidone may offer a meaningful advantage over olanzapine in this patient population. These findings relate only to short term treatment of hospitalised patients, and further studies with randomised designs are needed to better evaluate the relative cost-effectiveness of these drugs in other settings and in the long term.

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Other publications of related interest


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