Cost-effectiveness of risperidone, olanzapine, and conventional antipsychotic medications

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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 study examined the use of two novel antipsychotic medications, risperidone and olanzapine, to treat people diagnosed with schizophrenia and schizoaffective disorder.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 54 years old with a diagnosis of schizophrenia or schizoaffective disorders using the DSM-IV criteria. Patients who had had two or more acute psychiatric hospitalisations in the last twelve months and were noncompliant with outpatient treatment were included in the study, as were those who had not taken a novel antipsychotic medication for at least 6 weeks in the 3 months prior to recruitment into the trial. Patients who had a primary diagnosis of organic brain syndrome, mental retardation, or a substance-related disorder were excluded from the patient population.

Setting
The setting was the community and outpatient care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were collected between October 1997 and November 1998. The resource use data related to the same time. The price year was not stated.

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

Link between effectiveness and cost data
The resource use data were taken retrospectively from the same patient sample that provided the effectiveness data.

Study sample
The patients were recruited into the study at the point of hospitalisation for an acute episode of schizophrenia or schizoaffective disorder. The exact recruitment process was not reported. A total sample of 343 patients who met the inclusion criteria were screened and randomly assigned to the study groups. Of those assigned, 74 (21.6%) patients refused to participate and in 146 (42.5%) cases the patient's physician refused participation, either because they did not
want to change the treatment or because of patient-related concerns. Overall, 108 patients were included in the study. Of these, 30 were allocated to receive olanzapine, 36 received risperidone and 42 were treated with conventional medication. The mean age of the patients was 34.10 (+/- 9.29) years in the olanzapine group, 37.56 (+/- 9.29) years in the risperidone group and 38.36 (+/- 7.55) years in the conventional medication group. The proportions of males were 56.7% (olanzapine), 63.9% (risperidone) and 66.7% (conventional), respectively.

The authors reported that the baseline characteristics of those who refused to participate were not statistically significantly different from those who took part in the study. The authors did not comment on whether their sample was representative of all patients with schizophrenia or schizoaffective disorders. No power calculations were reported in the paper.

**Study design**

This was a prospective, non-blind, randomised controlled trial that was conducted in two state acute care psychiatric hospitals. The patients were randomised using an adaptive randomisation procedure. This stratified individuals on the basis of patient demographics, whether they were diagnosed with schizophrenia or schizoaffective disorder, the number of hospitalisations in their lifetime, and the number of days hospitalised in the preceding 6 months. The paper did not report the actual process by which patients were allocated to the treatment groups, or who performed this action. Once patients had been allocated to the treatment group, attending physicians prescribed the randomised treatment and adjusted the dose and supplementary medication as they saw fit. The study aimed to follow up patients for 12 months. Twenty-four (22.2%) patients were lost to follow-up at 12 months. Of these, 5 (16.7%) were in the olanzapine group, 9 (25.0%) were in the risperidone group and 10 (23.8%) had been allocated to receive conventional treatment.

**Analysis of effectiveness**

The primary outcomes assessed in the study were the effectiveness of the treatments in terms of compliance with the allocated drug, and the prescription of supplementary antipsychotic medications or mood stabilisers. Secondary outcomes were symptomatology, side effects, time to discharge for index hospitalisation, survival in initial re-hospitalisation, and client satisfaction. Changes in symptoms were assessed using:

- the Positive and Negative Syndrome Scale (PANSS),
- the Brief Psychiatric Rating Scale (BRPS),
- the Dyskinesia Identification System Condensed User Scale (DISCUSS),
- the Simpson-Angus Extrapyramidal Symptoms Scale (S-A EPS),
- the Barnes Akathisia Scale (BAS),
- the Diagnostic Interview Schedule (DIS),
- the Role Functioning Scale (RFS),
- the Social Adjustment Scale - Severely Mentally Ill (SAS-SMI), and
- the Chemical Use, Abuse and Dependence Scale (CUAD).

The groups were shown to be similar in terms of demographic information, primary diagnosis, the number of times the patient had been hospitalised in the past 6 six months, and most aspects of drug history. Patients allocated to the olanzapine group had been hospitalised for a statistically significantly greater number of days than those allocated to the risperidone group, followed by those in the conventional treatment group. Of the patients in the risperidone group, 33.3% had atypical antipsychotic use compared with 41.7% in the olanzapine group and 9.5% in the conventional treatment group. The analysis was undertaken on an intention to treat basis.
Effectiveness results
At the 12-month follow up, 96% of patients in the olanzapine group, 70.4% of patients in the risperidone group, and 68.8% of patients in the conventional treatment group were classed as being compliant with their antipsychotic medication. The results of the logistic regression showed a significant group effect, with the odds ratio (OR) of compliance being six times higher for the olanzapine group than with the conventional medication group (OR 6.08, 95% confidence interval, CI: 2.47 - 15.01). There was also a significant negative time effect, with the OR reflecting an overall decrease in compliance during the 12-month follow-up period (OR 0.44, 95% CI: 0.20 - 0.97).

The prescription of supplementary medications was significantly higher in the olanzapine and risperidone groups than in the conventional medication group (OR 2.70, 95% CI: 1.60 - 4.55 and OR 4.13, 95% CI: 2.48 - 6.85, respectively).

The prescription of mood stabilisers was significantly higher in the olanzapine and risperidone groups than in the conventional medication group (OR 2.61, 95% CI: 1.58 - 4.31 and OR 3.59, 95% CI: 2.19 - 5.88, respectively).

There were no statistically significant differences between the groups in the symptoms of schizophrenia, side effects, time to discharge for index hospitalisation, survival to initial re-hospitalisation or client satisfaction with the services.

Over time, across medication groups, symptoms of schizophrenia were decreasing, affective symptoms were increasing, side effects were decreasing, and rated psychosocial functioning was increasing, (p<0.05).

Clinical conclusions
The author concluded that compliance in taking the assigned medication was significantly higher in the olanzapine group than in the conventional group during the study period. Risperidone and olanzapine were no more effective in controlling the symptoms of schizophrenia, or improving psychosocial function, repeat hospitalisation and client satisfaction, than conventional medication.

Measure of benefits used in the economic analysis
No summary benefit was used in the economic analysis. In effect, a cost-consequences analysis was performed.

Direct costs
The study included the average costs incurred by the health care purchaser. Three categories of costs were calculated. More specifically, the costs of hospital care, outpatient care and medication.

Medical records were used to establish the number of mental health inpatient nights and the use of mental health outpatient facilities. The unit cost of inpatient nights were obtained from each of the hospitals at which the patients were treated. No details of how this figure was calculated were reported. The average unit cost for providing outpatient care was taken from the state department of mental health (DMH) database. The methods used to calculate this average cost were not reported. The quantity of medication was taken from the patient's medical notes. This quantity was adjusted to reflect compliance with prescriptions (no details of how this was done were provided). The unit cost for medication was taken from the DMH database.

The resource quantities and the unit costs were not reported separately. Discounting was not reported in the paper although, methodologically, it would not have been required as the time span of the study was one year. No price year was reported.

Statistical analysis of costs
The author reported the mean and standard deviation (SD) for each of the three categories of costs. The existence of a statistically significant difference between the costs of the three groups was assessed using multiple logistic regression models and t-tests.
Indirect Costs
No indirect costs were included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis of the cost data was undertaken.

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

Cost results
The total costs for the 12 months covered by the study were $7,173 (SD=9,234) for the olanzapine group, $7,178 (SD=8,925) in the risperidone group and $3,805 (SD=7,592) for the conventional medication group. The difference between the cost of olanzapine treatment and conventional treatment was statistically significant, (t=2.84, p=0.02). The difference in costs between risperidone treatment and conventional treatment was also statistically significant, (t=3.17, p=0.005).

The inpatient costs for the 12 months covered by the study were $4,788 (SD=8,857) for the olanzapine group, $5,773 (SD=9,284) in the risperidone group and $3,004 (SD=7,576) for the conventional medication group. The difference between these costs was not statistically significant.

The outpatient costs for the 12 months covered by the study were $1,837 (SD=3,624) for the olanzapine group, $906 (SD=1,120) in the risperidone group and $747 (SD=933) for the conventional medication group. The difference between these costs was not statistically significant.

The medication costs for the 12 months covered by the study were $886 (SD=623) for the olanzapine group, $541 (SD=458) in the risperidone group and $225 (SD=314) for the conventional medication group. The difference between these costs was statistically significant, (F=6.33, p<0.0001).

Synthesis of costs and benefits
The estimated benefits and costs were not combined.

Authors' conclusions
The psychiatric medication costs increased more over time in both the olanzapine and risperidone groups than in the conventional medication group. The olanzapine group demonstrated better compliance over time than the conventional medication group.

CRD COMMENTARY - Selection of comparators
This study used treatment with conventional antipsychotic medication as the comparator. This appears to have been chosen because it represented current practice in the author's setting. However, the lack of clear information on the conventional antipsychotic medication (predominantly haloperidol but also fluphenazine) means that it would be difficult to apply the results to other settings. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a randomised controlled trial, which was appropriate for the study question. However, as the author acknowledged, there were several aspects of the trial that raised questions about its quality. First, there were no statistically significant differences in symptoms of schizophrenia, side effects, time to discharge for index hospitalisation, and survival to initial re-hospitalisation between the groups, which might have been due to the small sample size and lack of power of the study. Second, there was a lack of blinding in the study. Third, the paper reported that physicians refused permission for 70 patients to be included in the study because they did not wish to alter their treatment. It appears that these withdrawals occurred after the patients had been randomised to a particular treatment. This has the potential to introduce substantial bias into the results. The study design also handed all decisions relating to patient care to their attending physician who were able to make any alterations to the medication that they considered appropriate. Consequently, there was the potential for a considerable degree of discrepancy between the treatments received within each treatment group. Finally, there was no information on how the study sample represented the patient population. On a more positive note, the three treatment groups were shown to be comparable at baseline and the analysis was performed on an intention to treat basis.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of health benefit. The health benefits were, therefore, those associated with the effectiveness outcome.

Validity of estimate of costs
The study was undertaken from the perspective of the health care purchaser. Although the author reported the categories of costs included in the analysis, there were no details of the cost components that were considered in each cost category. Thus, it was not possible to assess whether all the relevant costs were included in the analysis. For example, it was unclear whether the costs associated with the treatment of side effects were included in the analysis. The lack of a clear price year limits the generalisability of the study and would hinder any future attempts at reflation. The generalisability of the study is also limited by the fact that the resource use and unit costs were not reported separately, and there was a lack of sensitivity analyses. Discounting was not relevant, as all of the costs were incurred during a short time, and hence was not performed.

Other issues
The author compared the effectiveness results with those from other studies, noting that the data from this study would appear to contradict other studies. There was no discussion about how the results of this study could be applied to other settings. The author does not appear to have presented the results selectively and the conclusions reflected the scope of the analysis. As there was no discussion of how the study sample represented the study population, it is not possible to assess the appropriateness of the study conclusions. The author highlighted the limitations of the analysis (see 'Validity of estimate of measure of effectiveness' field above) and made appropriate references to other studies in this area.

Implications of the study
Whilst the author did not make any specific recommendation for changing policy or practice, further research in usual practice settings was suggested. This should employ more rigorous research designs with larger samples to draw more specific conclusions about the comparative costs and effectiveness of these medications.

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