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 either risperidone or olanzapine for the treatment of patients with schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hospitalised patients aged 65 years or younger, who were diagnosed with schizophrenia or schizoaffective disorder. To be included in the analysis, the patients had to be 65 years or younger, have been diagnosed with schizophrenia or schizoaffective disorder, have been discharged from hospital or, if not discharged, have spent at least 120 days in hospital.

Setting
The setting was secondary care. The study was performed at 61 centres in nine countries (i.e. Australia, Austria, Denmark, Great Britain, Germany, The Netherlands, Norway, Spain and Sweden).

Dates to which data relate
The dates to which the effectiveness and resource utilisation data related were not reported. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a single study (see Kasper et al., Other Publications of Related Interest).

Link between effectiveness and cost data
The costing was performed retrospectively on the same patient population as that used in the effectiveness analysis.

Study sample
No power calculations to assure a certain power were reported. The authors reported that a sample size of 33 patients was the target for each centre, although the final sub-samples differed from this target value. The records of 2,339 patients were reviewed and 438 did not meet the inclusion criteria, mainly because schizophrenia or schizoaffective disorder was not their primary diagnosis (415 patients). The final study sample was composed of 1,901 patients, of which 924 received risperidone and 977 were administered olanzapine. The sample was selected in a methodological manner. The most recent admissions in which either risperidone or olanzapine was the drug of first choice for long-
Study design
The study was a multi-centred, retrospective cohort study (61 centres from nine countries were included in the effectiveness analysis). The effectiveness data were obtained from a retrospective chart review. The follow-up was during hospitalisation, up to a maximum of 120 days of hospitalisation. A total of 145 risperidone and 165 olanzapine patients discontinued treatment.

Analysis of effectiveness
All the patients included in the study were accounted for in the analysis of most outcomes. The primary outcomes used in the effectiveness analysis were treatment efficacy, time to efficacy (not assessed in German centres), time to discharge, treatment discontinuation, spontaneously reported side effects, and the number of patients considered as responders (i.e. those for whom the treatment was effective and for whom it was not discontinued unless no longer needed). The sample used for time to efficacy included patients whose efficacy was established.

The patient groups were shown to be comparable at analysis in terms of age of onset of first symptoms, age at admission, gender and diagnosis, although olanzapine patients had a greater number of prior hospitalisations and a higher number of them used antipsychotics in the year before the study. Logistic regression was used to correct for potential baseline differences between the comparison groups, adjusting by age at onset, age at admission, gender, number of prior hospitalisations and antipsychotic use in the previous year. The baseline characteristics were also analysed for responders only in order to examine whether any bias was introduced into the data by differences in the study sample.

Effectiveness results
The number of patients for whom the treatment was considered to be effective was higher among the risperidone patients (765 patients; 84%) than among the olanzapine patients (766 patients; 79%), (p=0.01).

The average number of days before efficacy was established was significantly shorter for risperidone patients (13.6 days; 95% confidence interval, CI: 12.7 - 14.5) than for olanzapine patients (18.6 days, 95% CI: 17.4 - 19.8), (p<0.01).

The number of olanzapine patients who discontinued treatment due to lack of efficacy (107 patients; 11%) was significantly higher than the number of risperidone patients (77 patients; 8%), (p=0.05).

The number of patients who discontinued treatment because they experienced side effects was significantly higher among risperidone patients (36 patients; 4%) than among olanzapine patients (23 patients; 2%), (p=0.05).

There were no statistically significant differences between risperidone and olanzapine patients in terms of the number who experienced an adverse event, (p=0.10), and the number who discontinued treatment either because it was no longer needed, (p=0.40), or for other reasons, (p=0.70).

A total of 1,287 patients were classified as responders, 658 of them receiving risperidone (71% of risperidone patients) and 629 olanzapine (64% of the olanzapine patients).

The results were adjusted to assess the effect of differences in the baseline characteristics of the study groups, but there was no change in the magnitude of the differences and statistical significance of the key findings of the study. The analysis of the responders' baseline characteristics showed that the key findings were also maintained within this patient group.

Clinical conclusions
Risperidone was shown to be statistically significantly more effective than olanzapine in terms of a significantly higher number of patients achieving efficacy and a significantly shorter time taken to achieve efficacy. However, a
significantly higher number of risperidone patients had to discontinue treatment due to adverse effects.

**Measure of benefits used in the economic analysis**
No summary measure of benefit was used in the economic analysis. The study was therefore categorised as a cost-consequences analysis.

**Direct costs**
The cost/resource boundary was not stated. However, the direct costs considered in the economic analysis were those related exclusively to the inpatient drugs used. These included the drug costs of risperidone and olanzapine, and the concomitant medication (anti-epileptics, anti-Parkinsonians, anxiolytics, hypnotics or sedatives, psychoanaleptics, antihistamines and others). The Spanish centres did not contribute cost data for the concomitant therapies. Therefore, they were excluded from the calculation of inpatient costs. The source of the costs was the National IMS data. The hospital pharmacy purchase prices were used as an estimation of the drug costs. Therefore, the costs were estimated on the basis of actual data. Some resource quantities (in terms of the dosage characteristics for both risperidone and olanzapine) were reported separately from the costs. The study reported the unadjusted and adjusted (by baseline characteristics) average drug costs per day for each of the therapies. Discounting was not performed, but was not relevant since the period considered at analysis was less than two years. The price year was 1998.

**Statistical analysis of costs**
The costs were treated in a stochastic manner. However, the statistical tests used were not reported.

**Indirect Costs**
No indirect costs were included in the economic analysis.

**Currency**
The authors reported that all the costs were expressed in local currency and then converted into US dollars ($), based on a moving average for each relevant currency at the end of the 1998 calendar year.

**Sensitivity analysis**
No sensitivity analyses were reported.

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

**Cost results**
The unadjusted mean daily costs of treatment drugs were $3.7 (95% CI: 3.6 - 3.8) for risperidone and $6.5 (95% CI: 6.4 - 6.6) for olanzapine, (p<0.001).

The unadjusted mean daily costs of all inpatient drugs were $4.6 (95% CI: 4.4 - 4.8) for risperidone and $7.7 (95% CI: 7.4 - 8.0) for olanzapine, (p<0.001).

The adjusted mean daily costs of treatment drugs were $3.5 (95% CI: 3.4 - 3.6) for risperidone and $6.3 (95% CI: 6.2 - 6.5) for olanzapine, (p<0.001).

The adjusted mean daily costs of all inpatient drugs were $4.4 (95% CI: 4.2 - 4.5) for risperidone and $7.5 (95% CI: 7.2 - 7.7) for olanzapine, (p<0.001).
The authors presented plots of the 95% CI for the treatment costs and the total inpatient drug costs by countries. The countries showed similar cost patterns, and larger variations were observed for the costs related to olanzapine. The costs of the adverse events were not dealt with in the analysis, although they were relevant since there were patients experiencing adverse events and even discontinuing treatment due to these adverse events.

**Synthesis of costs and benefits**
The costs and benefits were not combined due to the cost-consequences approach adopted.

**Authors' conclusions**
Risperidone may offer an advantage over olanzapine as a first-line drug treatment in schizophrenia, because it is more effective at a lower cost.

**CRD COMMENTARY - Selection of comparators**
None of the therapies analysed was stated to be the comparator. Risperidone and olanzapine were compared because they were the most commonly prescribed atypical antipsychotics, although there were other new agents and older neuroleptics available. You must decide whether these health technologies are widely used in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis used a retrospective cohort study, which the authors justified on account of the national clinical setting. The authors stated that, as the study was naturalistic, it reflected everyday clinical practice and it may have avoided the protocol-induced treatment bias related to the clinical trials. However, it may have been subject to bias due to the lack of randomisation. No power calculations were reported so it is possible that the results were due to chance. Selection bias was minimised by the independent, methodological approach to patient selection. The study sample was likely to be representative of the study population since patients from 61 sites (9 different countries) were included in the effectiveness analysis.

Measurement bias may have been a problem for the following reasons. The efficacy of the treatment was evaluated according to the clinicians' ratings, and not by means of a validated questionnaire. This may have introduced uncertainty into the reliability of the conclusions. Moreover, the retrospective nature of the study may have led to the loss of some important information. In addition, the follow-up period was quite short. This may have affected the outcomes obtained since schizophrenic patients are likely to experience recurrences in the long term.

In terms of the possibility of confounding, the patient groups were shown to be comparable in terms of some important baseline characteristics, although they also presented some systematic differences in the number of prior hospitalisations and antipsychotic drug use before the study. However, the authors made adjustments to take account of baseline characteristics. These did not affect the results obtained.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

**Validity of estimate of costs**
The perspective adopted was not reported. However, it was very limited since it considered only the drug costs and not those related to, for example, hospitalisations. The authors stated that the inclusion of the hospitalisation costs would have increased the cost difference between risperidone and olanzapine, not only because olanzapine was more expensive but because olanzapine patients also presented greater lengths of hospitalisation. However, the authors did not consider the costs of the adverse effects, and a larger number of patients in the risperidone group discontinued treatment due to adverse effects than did the olanzapine patients. The price year was stated, which allows the reproduction of the results. Some of the resource quantities were reported separately from the costs, but the unit costs...
applied were not reported. A statistical analysis of the quantities was not reported, only the mean daily costs, which introduces uncertainty into the reliability of the conclusions.

**Other issues**
The results were compared extensively with those obtained by other studies. The authors stated that the study presented advantages in terms of extrapolation of results, since the data were obtained from 61 sites in nine different countries. The study enrolled patients diagnosed with schizophrenia or with a schizoaffective disorder, and this was reflected in the authors’ conclusions.

**Implications of the study**
There were positive aspects of this study, such as the possibility of the extrapolation of the effectiveness results, since the study sample was taken from a large number of sites in different countries. However, there were also some limitations in both the effectiveness and the economic analyses, which must be considered.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
11459332

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adult; Benzodiazepines; Cost-Benefit Analysis; Cross-Cultural Comparison; Drug Costs /statistics & numerical data; Europe; Female; Humans; Male; Middle Aged; National Health Programs /economics; Pirenzepine /adverse effects /analsogs & derivatives /economics /therapeutic use; Retrospective Studies; Risperidone /adverse effects /economics