The health economic implications of treatment with quetiapine: an audit of long-term treatment for patients with chronic schizophrenia


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 quetiapine ('Seroquel'), a new atypical antipsychotic, in patients with chronic schizophrenia. The dosage was 150 to 750 mg/day.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised male and female patients with schizophrenia, as defined by the DS III R classification.

Setting
The setting was a hospital. The economic study was conducted in St. Luke's Psychiatric Hospital, Clonmel, Republic of Ireland.

Dates to which data relate
The effectiveness and resource data were collected retrospectively for the 12 months before quetiapine treatment was initiated (between 28 July 1994 and 23 December 1994) and for the 12 months after. The price year was 1999.

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

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample population as that considered in the study.

Study sample
Power calculations were retrospectively performed on the basis of the existing sample size. The study sample comprised 21 patients with schizophrenia, who were treated at the hospital in which the economic evaluation was performed. There were 15 men and 6 women, and the mean age was 39 years (range: 24 - 58 ). Thirteen of the patients had participated in a 6-week, randomised double-blind study of quetiapine in acute schizophrenia. The other 8 were entered directly without having taken part in the randomised phase. The authors did not provide any evidence that the initial study sample was representative of the study population.
Study design
This was a before-and-after case series study using the patients’ case notes and other routine information sources of a single institution. The duration of follow-up was two years (one year before and one year after). The patients were assumed to have received thioridazine (average daily dose of 200 mg) during the year prior to quetiapine treatment, and they received quetiapine during the second year of the study. The authors assumed that all patients treated with quetiapine received the recommended maintenance dose of 400 mg/day. Three patients did not complete the 12-month treatment with quetiapine, one because of a perceived lack of efficacy, and two because they decided by themselves not to continue in the study.

Analysis of effectiveness
The basis for the analysis (intention to treat or treatment completers only) was not reported, but it appears to have been intention to treat. The primary health outcomes assessed in the analysis were:

the symptoms and severity of neurological disturbance at baseline (before treatment with quetiapine started) and after 12 months, and the difference between them; and

the number of days of inpatient hospitalisation per patient treated with quetiapine, and the mean difference in the inpatient days compared with the previous year (when patients were assumed to be treated with thioridazine).

As four patients were institutionalised for the full period of the study, the authors also reported the number of days of inpatient hospitalisation per patient treated with quetiapine, and the mean difference in the inpatient days compared with the previous year for non-institutionalised patients.

The symptoms were rated using the Brief Psychiatric Rating Scale (BPRS), and the Clinical Global Impression (CGI) Severity of Illness Item. The severity of neurological disturbance was measured by the Abnormal Involuntary Movement Scale (AIMS) and the Simpson-Angus Scale. Seventeen patients (80.9%) showed partial responsiveness to prior antipsychotic medications, and only one patient (4.8%) had poor responsiveness. The remaining patients showed full responsiveness to prior antipsychotic medications. Final scores were used for the three patients not completing the 12-month treatment with quetiapine.

Effectiveness results
The BPRS scores were 37.9 at baseline, and 21.1 after 12 months of treatment with quetiapine. The difference between them was -16.8 (95% confidence interval, CI: -11.9, -21.6; p<0.001). The CGI scores were 4.6 at baseline and 3.5 at 12 months. The difference between them was -1.14 (95% CI: -0.78, -1.5; p<0.001). The AIMS scores were 24.3 at baseline and 20.7 at 12 months. The difference was -3.6 (95% CI: -1.8, -5.4; p<0.001). The Simpson-Angus scores were 14.9 at baseline and 12.3 at 12 months. The difference was -2.6 (95% CI: -0.9, -4.2; p<0.005).

The mean numbers of inpatient hospitalisation days, considering the whole sample population, were 109 at baseline and 97 at 12 months. The mean difference between them was 12 days (95% CI: -34, 58; p=0.58). The mean numbers of inpatient hospitalisation days, considering the non-institutionalised patients, were 45 at baseline and 30 at 12 months. The mean difference was 15 days (95% CI: -43, 74; p=0.58).

Clinical conclusions
After one year of treatment, patients treated with quetiapine showed improvements in the symptoms and severity of schizophrenia, compared with those treated with conventional antipsychotics. The number of inpatient hospitalisation days was lower for both the whole sample population and for the non-institutionalised patients, when treated with quetiapine, but the difference was not statistically significant. Therefore, the study did not provide statistically significant evidence that the use in health care resources was lower when patients were treated with quetiapine than when they were treated with the conventional antipsychotic.

Measure of benefits used in the economic analysis

NHS Economic Evaluation Database (NHS EED)
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A cost-consequences analysis was performed. Therefore, no summary measure of benefit was used in the economic analysis.

**Direct costs**
The resource quantities and the costs were reported separately. The costs included in the analysis were those of the hospital. These were for inpatient hospitalisation and medication. The data on the patients’ hospitalisation were obtained from the patients’ case notes and other routine information sources. The medication costs and dose were not collected. Therefore, to obtain the costing, the authors assumed that patients were treated during the first year with thioridazine (200 mg/day) at an annual cost of €140 per patient per year, and during the second year with quetiapine (400 mg/day) at an annual cost of €1,601 per patient per year. The assumption relating to the use and cost of thioridazine was based on the available market research data and clinical experience. The assumption about the costs of quetiapine was based on a recommended maintenance daily dosage for this medication.

The costing was performed on 20 patients since the data were unavailable for one patient, who was transferred to another hospital. The data were collected in natural units and then valued using 1999 prices, which were obtained from the St. Luke’s Hospital finance department. Discounting was not carried out, but it was irrelevant because the costs for each alternative treatment were incurred over less than 2 years. The study reported the average costs.

**Statistical analysis of costs**
Continuous variables were analysed using the t-test, while categorical variables were analysed using Wilcoxon's matched-pair rank sign test. Two-tailed tests of significance were used.

**Indirect Costs**
The indirect costs were not considered due to the perspective adopted. If researchers wish to adopt a societal perspective, the indirect costs (primarily productivity losses and care by relatives) should be considered.

**Currency**
Irish punts (€).

**Sensitivity analysis**
None reported.

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

**Cost results**
When the whole sample population was analysed, the annual inpatient hospitalisation costs were €20,809 for thioridazine and €18,451 for quetiapine. The difference in inpatient hospitalisation costs between the first and the second year (with thioridazine or quetiapine treatment, respectively) was €2,359 (95% CI: -€6,439, €11,157; p=0.58).

When the estimated cost of medication was included, the annual inpatient treatment costs were €20,843 for thioridazine and €19,827 for quetiapine. The difference between them was €1,017 (95% CI: -€7,781, €9,815; p=0.81).

When the non-institutionalised patients were analysed, the annual inpatient hospitalisation costs were €8,583 for thioridazine and €5,635 for quetiapine. The difference between them was €2,949 (95% CI: -€8,302, €14,199; p=0.58).

When the estimated cost of medication was included, the annual inpatient treatment costs were €8,617 for thioridazine and €7,011 for quetiapine. The difference between them was €1,607 (95% CI: -€9,644, €12,857; p=0.77).
Synthesis of costs and benefits
The costs and benefits were not combined due to the cost-consequences approach undertaken.

Authors’ conclusions
The patient population showed significant improvement in measures of schizophrenia symptom severity following treatment with quetiapine. These improvements were reflected in a lower utilisation of resources. After one year of treatment with quetiapine, the cost-savings from reduced hospitalisation were sufficient to offset the greater costs of quetiapine medication.

CRD COMMENTARY - Selection of comparators
The comparator was chosen because it represented one of the current conventional antipsychotics used to treat patients with schizophrenia.

Validity of estimate of measure of effectiveness
The analysis used a retrospective, before-and-after case series study. The authors reported that the use of this study design rather than a randomised controlled trial, coupled with the fact that it was conducted in only one centre, may have resulted in some degree of bias. In addition, the presence of confounding variables between the two periods of analysis cannot be ruled out. The authors also stated that the small sample size limited the statistical significance of the findings. The sample population was representative of the study population, as standard classifications were used to classify the patients.

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 analysis.

Validity of estimate of costs
Only the costs related to hospitalisation and medication were included in the analysis. However, the authors reported evidence that these data were likely to be strongly indicative of the total treatment costs for these patients. They stated that the inclusion of other resources might have altered the results, but with very low probability. No data on the use and dose of antipsychotic medications were collected, and some assumptions had to be made. These were likely to have led to an underestimation of the costs for thioridazine and an overestimation of the costs of quetiapine. The authors reported that, as quetiapine had associated lower extrapyramidal symptoms than conventional antipsychotics, the exclusion of additional medication costs may have underestimated the costs in favour of thioridazine.

The costs and the quantities were reported separately, which enhances the generalisability of the results to other settings. However, caution has to be exercised due to the study design used in the analysis (see ‘Validity of Estimate of Measure of Effectiveness’ section), and the assumptions about the dosage and costs of the drugs. The reliability of the conclusions is dependant on the accuracy of such assumptions. A statistical analysis of the quantities was only performed for the inpatient hospitalisation days, and not for the dosage of medication (because this was assumed). The price year was reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, in terms of the resource savings obtained with the new atypical antipsychotic.

Implications of the study
Quetiapine improves clinical outcomes of patients with schizophrenia. It seems to reduce the total health care cost by means of savings in inpatient hospitalisation, which offset the high costs of the drug treatment. However, as the authors
recommend, further investigation involving randomised clinical trials is required to strengthen these conclusions.

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Not stated.

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**Other publications of related interest**


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