Modelling the impact of clozapine on suicide in patients with treatment-resistant schizophrenia in the UK

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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 clozapine in treatment-resistant schizophrenia to reduce the rates of suicide.

Type of intervention
Primary prevention and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients with treatment-resistant schizophrenia in the UK (n=30,000).

Setting
The setting was not clearly stated but it is likely to have been community services. The economic analysis was carried out in the UK.

Dates to which data relate
The effectiveness data were derived from studies published in 1999. The dates to which the resources and price data relate were not stated.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies.

Modelling
A 40-year time series, based on a static prevalence and current UK population trends, was modelled to compare current levels of clozapine prescribing with a scenario in which all suitable patients with treatment-resistant schizophrenia received clozapine.

Outcomes assessed in the review
The outcomes assessed in the review were the prevalence of schizophrenia, the percentage of patients with treatment-resistant schizophrenia, the annual incidence of suicide in patients with schizophrenia, and the cumulative number of suicides avoided with clozapine. Clinical effectiveness, and positive and negative symptoms of schizophrenia were not reported.
Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
The prevalence of schizophrenia was taken from systematic reviews conducted by the Cochrane Schizophrenia Group, 1999.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
One study was reported for each outcome assessed in the review.

Methods of combining primary studies
The annual incidence of suicide in people with schizophrenia was combined with the findings of Munro et al. (see Other Publications of Related Interest), in order to calculate the suicide rates for patients prescribed clozapine and those treated with other drugs. The resulting number of suicides was combined to give a total figure for each year.

Investigation of differences between primary studies
Not applicable.

Results of the review
The authors did not report all the results of the review. A total of 30,000 patients with treatment-resistant schizophrenia would be suitable for and compliant with clozapine therapy. This equated to an additional 16,330 patients in the UK. By prescribing clozapine to these patients, 53 suicides would be avoided each year, 154 over three years and 518 over ten years.

Measure of benefits used in the economic analysis
The measure of benefits was the number of life-years saved (LYS) over 20 years. The LYS were calculated on the assumption that the life expectancy of a person with schizophrenia at diagnosis was 37 years. It was assumed that the average life expectancy of a patient at any one time was half of this figure. The outcomes were discounted at 1.5%.

Direct costs
The costs were restricted to patient support and suicide costs. The costs and the quantities were not reported separately. The costs were discounted at 6%. The costs were calculated for two scenarios, one in which clozapine was assumed to be cost-neutral and a second in which it was assumed to be cost-saving. In the latter scenario, the support costs were reduced by 10% for all patients taking clozapine. The annual support costs were calculated using weighted average costs, based on the proportion of 'incident' and 'prevalent' patients. Half-cycle correction was used to calculate the total annual support cost. The cost of suicide included only general hospital costs. Utilisation of acute bed days was calculated. The number of days hospitalised was reduced by 16.9% for people treated by clozapine.

Statistical analysis of costs
A statistical analysis was not performed.

**Indirect Costs**
Not estimated.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
A sensitivity analysis was carried out by varying the suicide risk reduction experienced by patients on clozapine treatment from 25 to 75%, the cost of patient support between 5,038 and 8,740, and the reduction in the support cost of patients receiving clozapine from a 0% cost-saving to 50%.

**Estimated benefits used in the economic analysis**
By prescribing clozapine, more than 10,250 life-years would be saved over the following 20 years.

**Cost results**
In the cost-neutral scenario, the current support costs were just over 1,300 million per year. The additional cost associated with keeping patients alive was approximately 3.8 million per year. Savings resulting from a reduction in the number of suicides totalled approximately 10,000 per year. The net discounted cost over 10 years was 9.2 million.

In the cost-saving scenario, the total cost of support fell by more than 8.7 million per year. The net annual saving totalled approximately 8,748,000. The net discounted saving over 10 years was 65.1 million. Modelling the reduction in hospitalisation among clozapine patients led to a saving of 167 acute beds in the UK per year.

**Synthesis of costs and benefits**
In the cost-neutral scenario, the cost per LYS was 5,108. In the cost-saving scenario, the authors did not produce a summary measure since it is likely that clozapine therapy was both more effective and generated lower costs. The sensitivity analysis generated 10,000 random scenarios using figures ranging between the lowest and the highest values of the parameters. The mean number of suicides avoided was 35 per year (95% confidence interval, CI: 34.96 - 35.09). The average number of LYS at 20 years was 6,833 (95% CI: 6,831.8 - 6,834.3). The average cost per LYS was 6,864 (95% CI: 6,863.4 - 6,864.7). Cost-savings occurred in 94.4% of the cases and averaged 29.8 million per year (95% CI: 29.79 - 29.82).

**Authors' conclusions**
The use of clozapine in treatment-resistant schizophrenia saves lives, frees resources and is cost-effective.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator (conventional neuroleptic therapy) used. You should consider whether this is a widely used technology in your own setting.

**Validity of estimate of measure of effectiveness**
It was unclear if the review was conducted in a systematic way to identify relevant research and minimise biases. The authors did not clearly report the data used to derive the estimates of effectiveness, and limited data on effectiveness were reported. The authors did not report the percentage of clozapine treatment compliance. No sensitivity analysis, either of compliance or prevalence of treatment-resistant illness, was reported. A randomised controlled trial would
have been a more appropriate study design with which to evaluate the effectiveness of clozapine and with which to eliminate bias.

**Validity of estimate of measure of benefit**
LYS were used as the benefit measure. A more appropriate measure of benefits, to compare widely the benefits of treatment alternatives and the findings with other cost-effectiveness studies of physical disorders, would have been relevant. For example, the evolution of positive and negative symptoms or the quality of life could have been included in the measure of benefits.

**Validity of estimate of costs**
The perspective adopted for the economic analysis was not clearly stated, but it is likely to have been that of the UK NHS. As the authors noted, suicides were associated with considerable consequences in terms of distress and lost productivity. However, the authors did not include these indirect costs in the analysis. The exclusion of indirect costs might have biased the results in favour of the standard treatment (in particular, in the “cost-neutral” approach). No details were given on the cost items included in the average cost of patient support. The costs of clozapine treatment were also not reported. Consequently, there is uncertainty as to whether all the relevant costs were included in the analysis. The justification given by the authors for conducting a cost-analysis for two scenarios with clozapine (cost-neutral or cost-saving) was unclear. The costs and the quantities were not reported separately. A sensitivity analysis on the costs was carried out.

**Other issues**
The above factors have implications for both the internal and external validity of the study. Therefore, the results provided in this article cannot easily be generalised to other settings or to other countries. The authors made appropriate comparisons of their findings with those from other studies. The study enrolled patients with treatment-resistant schizophrenia and this was reflected in the authors’ conclusions.

**Implications of the study**
The clinical and economic findings support the use of clozapine to reduce rates of suicide in treatment-resistant schizophrenia, by demonstrating more effectiveness and lower costs. For the authors, an analysis of the resource and cost impact of attempted suicide would strengthen the case put in this study.

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**Bibliographic details**

**PubMedID**
12777341

**Other publications of related interest**


Wahlbeck K, Cheine M, Essali A, et al. Evidence of clozapine's effectiveness in schizophrenia: a systematic review and


Indexing Status
Subject indexing assigned by NLM

MeSH
Antipsychotic Agents /economics /therapeutic use; Clozapine /economics /therapeutic use; Cost-Benefit Analysis /economics /methods; Great Britain /epidemiology; Health Resources /economics; Hospitalization /economics; Humans; Life Tables; Models, Statistical; Prevalence; Risk Factors; Schizophrenia /drug therapy /epidemiology; Schizophrenic Psychology; Suicide /economics /prevention & control

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