Clozapine for refractory schizophrenia: the Illinois experience

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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
Clozapine for refractory schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study consisted of hospitalised treatment-resistant schizophrenia patients.

Setting
Hospital and community. The economic study was carried out in the USA.

Dates to which data relate
Data about the effectiveness of clozapine for refractory schizophrenia were collected between 1990 and 1995. Cost data were obtained from estimates over the five-year period, according to activity data recorded on the Illinois Department of Mental Health and Developmental Disabilities (IDMHDD) information system. No price year was stated.

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

Link between effectiveness and cost data
Estimated retrospective costings were undertaken on the effectiveness study sample.

Study sample
518 hospitalised patients were selected over the period of analysis. No power calculations were stated around sample sizes. Subjects were chosen from all over the state of Illinois. 129 patients were not included in the analysis due to waiting for laboratory tests to determine whether or not they were eligible for clozapine treatment.

Study design
This was a before-and-after multi-centre study. Patients were followed up for 5 years. There appears to have been no loss to follow-up.
**Analysis of effectiveness**

The analysis of the study was based on clozapine consuming, refractory schizophrenia patients. Primary health outcomes assessed at the end of the 5 year period were the effects of treatment with clozapine: successfully treated patients, patients discharged from hospital, patients still in hospital but improving, and patients who discontinued the therapy. A subgroup of 189 patients was closely observed for 1 year and the following health outcomes were evaluated: side-effects, brief psychiatric rating scale (BPRS), remaining hospitalisations after clozapine initialisation, and decline in injury frequency between patients.

**Effectiveness results**

The effectiveness results were as follows:

Of the initial sample of 518 patients, 403 (78%) had their symptoms controlled due to the therapy.

Of these 403 patients, 243 (60%) were successfully treated and were discharged from the hospital back to the community.

62 (15%) were successfully treated and were waiting to be discharged, and 99 (25%) had improved substantially but were still hospitalised.

A total of 115 (22%) patients discontinued the therapy for various reasons.

There was a 0.9% incidence of agranulocytosis in the total study population.

The effectiveness results of the subgroup were as follows:

In the subgroup of 189 patients the average admission BPRS score was 64, and the average discharge score was 37.

From admission values, BPRS scores were reduced after 2 months of therapy (22%), 3 months (28%), 6 months (33%), and 12 months (42%).

After 12 months of clozapine therapy, only 55 (29%) of the original 189 hospitalised patients remained in hospital.

The number of injuries resulting from aggressive behaviour declined in 1 hospital location between 1990 and 1994 as the number of patients on clozapine therapy increased.

**Clinical conclusions**

Clozapine was well tolerated, with a very low incidence of agranulocytosis, 47% of patients were treated successfully and discharged to the community and only 22% were treatment failures.

**Measure of benefits used in the economic analysis**

The authors did not introduce a summary measure of benefit in the economic analysis and as such a cost-consequences analysis was performed.

**Direct costs**

Costs were not discounted, although some were incurred within a 5-year period and discounting would have been appropriate. Quantities and costs were analysed separately. Only direct costs were considered in the analysis (thus adopting a health service provider perspective) and these included hospitalisation costs and the costs of maintaining a community discharged schizophrenic patient on clozapine treatment (no other details were provided). These costs were estimated from the activity recorded on the IDMHDD information system. No price year was given.
Indirect Costs
Indirect costs were not included.

Currency
US dollars (§).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
Total intervention costs were not recorded. The total cost of institutionalising patients prior to initiating clozapine was $45,041,949 (for a 5-year period). With clozapine therapy this was reduced to $20,847,967. Cost savings from discharging 243 clozapine-treated patients amounted to $20 million per year (approximately), as the cost to maintain a community discharged schizophrenic patient on clozapine treatment was about $1 million per year.

Synthesis of costs and benefits
Not applicable.

Authors' conclusions
The study provides evidence that it “is economically prudent to treat and stabilize all eligible schizophrenic patients with clozapine”.

CRD COMMENTARY - Selection of comparators
The comparator used within the study was that of normal treatment in the form of continued hospitalisation for treatment-resistant schizophrenics, although this was not explicitly expressed and followed-up as a comparator throughout the study.

Validity of estimate of measure of benefit
Effectiveness data were derived from a before-and-after study and may thus have been prone to biases. It would have been helpful had the baseline study sample characteristics reported. The authors did not derive a summary measure of benefit and the analysis was therefore of cost-consequences design.

Validity of estimate of costs
Costs were not documented and were reported in a general manner, from the perspective of a health service provider. No price year was stated. More details about the methods of cost estimation would have been helpful. Discounting was not applied although it was relevant given the 5-year time frame of the study.

Other issues
The issue of generalisability of the results was not addressed nor were any appropriate comparisons with other studies made by the authors. Cost results might not apply to other settings or countries.
Implications of the study
The findings of this study were used to encourage physicians to comply with existing treatment algorithms for chronic refractory schizophrenia suggested by the State of Illinois. The increased drive by many hospitals to reduce the number of inpatient beds within their services to more appropriate levels would further benefit from long-term well-designed randomised controlled trials involving the use of clozapine in the treatment of refractory schizophrenia in the community, and using appropriate comparators.

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