Etude medico-economique du Leponex (clozapine) au centre hospitalier Charles Perrens de Bordeaux [Medico-economic study of Leponex (clozapine) in the Bordeaux Charles Perrens Hospital Center]

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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 clozapine, an atypical neuroleptic, in the treatment of neuroleptic-resistant schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of both male and female patients diagnosed as suffering from resistant schizophrenia, and who had been treated with standard antipsychotics.

Setting
The setting was secondary care (Hospital). The economic study was conducted in Bordeaux, France.

Dates to which data relate
Data were derived from a retrospective study conducted in 1996. The dates of the resource and price data were not stated.

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

Link between effectiveness and cost data
The costing was undertaken retrospectively on 44 patients from the same patient group as that used in the effectiveness study.

Study sample
72 patients with resistant schizophrenia and treated with clozapine for more than 18 weeks formed the study sample. These patients had been treated firstly by standard antipsychotics before administration of clozapine.

The characteristics of the patient sample were as follows:
48 male and 24 female patients;  
mean age: 38.6 years;  
mean age at disease diagnosis: 22 years;  
65.3% patients suffered from comorbidities;  
mean length of clozapine treatment: 2 years and 10 months.  

Power calculations to determine the sample size were not used. Data from 34 patients were not included in the quality of life estimation and economic analysis as self-administrated questionnaires were not returned or were incomplete.  

Study design  
The study was a before and after study using the same cohort, and conducted in a single centre. Two periods of schizophrenia treatment were investigated: before clozapine treatment (patients had been treated with standard antipsychotics) and at the time of the survey (in which patients had been treated for at least 18 weeks with clozapine).  

Analysis of effectiveness  
The basis for the analysis of the clinical study was not specifically stated but it is likely to have been treatment completers only (at least 18 weeks of clozapine treatment). The primary health outcomes used in the analysis were the results of a clinical questionnaire using the Clinical Global Impression scale (completed by psychiatrists), and of two questionnaires evaluating the impact of therapy on the patient's quality of life. The patient-completed scales used to measure quality of life were the Subjective Well Being under Neuroleptic Treatment (SWN) scale and a quality of life evaluation table (TEAQV). Clinical information and quality of life were evaluated retrospectively before the administration of clozapine treatment and at the time of the survey.  

Effectiveness results  
The clinical gravity score with clozapine treatment was improved (4.35 versus 6.08, p<0.0001). No adverse effects were observed in 33.3% of patients and no agranulocytosis was found. One case of neutropenia and 4.2% of neurologic adverse effects were observed. However, the patients' weight increased in 36% of patients and usage of some psychiatric drugs increased with clozapine. The quality of life score, measured by the TEAQV self-rating scale, was statistically significant between both periods, (p<0.0001). A statistically significant decrease in the length of full-time hospitalisation was observed: an annual mean of 214 days per patient with standard treatment versus 135 days after two years of Clozapine, (p<0.0005).  

Clinical conclusions  
Clozapine treatment resulted in improved psychopathology, social functioning and quality of life in treated patients.  

Measure of benefits used in the economic analysis  
The authors did not develop a summary benefit measure. Primary health outcomes, as reported earlier, were expressed as benefits. As such, a cost-consequences study was carried out.  

Direct costs  
Discounting was not applied. Costs and quantities were reported separately only for the ambulatory cost estimation and the number of days of hospitalisation. Estimates of the quantities and costs were based on data available at the time of the economic study. Hospitalisation costs were estimated from the hospital records, and ambulatory costs were estimated from the French reimbursement system. Ambulatory costs included consultations with psychiatrists and psychiatric nurses, nurse visits, biological tests and median treatment costs. In-patient costs were based on two types of
hospitalisation: full-time or daily hospitalisation. Total costs and costs per patient per year were measured. The price year was not stated.

Statistical analysis of costs
Statistical analyses were performed on costs using the Student t test. Tests for differences in characteristics from patient samples were carried out using ANOVA analysis.

Indirect Costs
No indirect costs were estimated.

Currency
French francs (Ffr).

Sensitivity analysis
Sensitivity analysis was not carried out.

Estimated benefits used in the economic analysis
Primary health outcomes were expressed as benefits. The reader is referred to the effectiveness results reported above.

Cost results
The average cost per patient per year was Ffr373,295 for standard treatments and Ffr363,200 after one year of clozapine treatment. The estimated total cost of clozapine treatment decreased from Ffr363,200 per patient per year during the first year to Ffr275,357 during the two-years treatment (a decrease of 26.2%). The direct costs reduction was mainly related to shorter length of stay in hospital associated with clozapine treatment: Ffr9,418 versus Ffr5,410 days per year of full-time hospitalisation in standard and clozapine treatment respectively, p<0.0005.

Synthesis of costs and benefits
The authors did not produce a summary measure that combined costs and effectiveness.

Authors' conclusions
The authors concluded that the use of clozapine may confer clinical benefits, as well as an improvement in quality of life, and led to a drop in global direct costs per patient. This was achieved by reducing the number of days of full-time hospitalisation, although the acquisition cost of clozapine is high. Consequently, the authors argued in favour of the extension of the use of clozapine.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of comparators was clear: the comparator reflected standard practice in France. You, as a user of this database, should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a before and after study, a design which is susceptible to a number of biases and confounding variables. No evidence was presented to support the validity and relevance of the estimate of the retrospective measures of the clinical effectiveness and quality of life (scores interpretation). This makes it difficult to judge the validity of the results: the quality of life measure before clozapine treatment was based on retrospective data relying on the patients’ memory. Thus, the assessment of clinical functioning, tolerance and quality of life, retrospectively and at the time of
the survey, could bias the interpretation of the results. The degree to which the study sample was representative of the study population was not stated. Outcomes were analysed for treatment completers and patients currently being treated. Ideally, quality of life and tolerance should have been assessed prospectively on the same treatment periods (before, during, or/and after treatment) for each patient.

**Validity of estimate of measure of benefit**
The estimates of benefit used in the study were the primary health outcomes. No summary benefit measure was developed. The analysis was therefore a cost-consequences study.

**Validity of estimate of costs**
The perspective adopted was not clearly reported but is likely to have been the third party payer. Although costs were estimated from a societal perspective, indirect costs were not included. Some relevant costs were omitted from the analysis. For example, the costs of corrective drugs and associated psychiatric drugs were not included. Quantities and costs were reported separately for ambulatory care estimates. The source of the data on quantities was taken from the authors' setting. The source of price data was the authors' organisation and the French reimbursement system. No statistical analysis of quantities or prices was performed. The price date was not reported. These features of the cost analysis tend to limit the generalisability of the results to other settings.

**Other issues**
Although appropriate comparisons were made with other studies in terms of clinical and economic results, the difficulty of generalising to other settings or countries was not addressed. The authors' conclusions that clozapine treatment for resistant schizophrenia was more effective than standard treatments may need to be supported by a prospective study based on treated and non-treated patients (a point acknowledged by the authors themselves). The absence of sensitivity analysis, particularly around cost parameters, weakens the results of the study.

**Implications of the study**
A prospective study is required in order to carry out a more relevant analysis of quality of life. The authors' recommendations expressed the need to facilitate the use of clozapine by hospitals in creating a resource allocation for this drug.

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None stated.

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**Other publications of related interest**

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