Multiple outcome assessment in a study of the cost-effectiveness of clozapine in the
treatment of refractory 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
Clozapine use in the treatment of refractory schizophrenia.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with refractory schizophrenia with at least 30-364 days of hospitalisation during the previous year.

Setting
The practice settings were Department of Veterans Affairs (VA) medical centres in the USA.

Dates to which data relate
Effectiveness and resource data were collected over a 12 month period between 1996 and 1998 (approximately). No price year was stated.

Source of effectiveness data
Clozapine effectiveness estimates in the treatment of refractory schizophrenia were derived from a single study.

Link between effectiveness and cost data
Cost estimates were derived from the study sample. It was not clear whether this information was obtained retrospectively or prospectively.

Study sample
423 patient were enrolled in the study (clozapine 205, haloperidol 218). No other patient characteristics were reported within this paper. No power calculations were reported. Details around entry criteria and pharmacological and psychosocial treatment have been presented elsewhere (Rosenheck, Cramer, Xu, et al. 1997). The 2 study groups were shown to be comparable at baseline.

Study design
This was a double-blind, multi-centre randomised controlled trial. The duration of follow-up was 12 months. No loss to
follow-up was recorded, although 82% of all assessments through all time points were completed.

**Analysis of effectiveness**
The analysis was based on an intention-to-treat basis as well as a crossover exclusion basis. The primary health outcomes used was a Composite Health Index for Schizophrenia (CHIS), developed from combining the weighted results of:

1. the Structured Clinical Interview for Positive and Negative Syndrome Scale (PANSS) for schizophrenia;
2. social relationships;
3. role functioning;
4. general daily activity and recreation;
5. family relationships (using a section of the Quality of Life Interview; and
6. medication side effects (using standard scales).

The CHIS evaluated a person's total time in good health through weighted (patient/provider) and non-weighted outcomes. The unweighted clozapine-haloperidol cumulative gain in CHIS was 49% (0-6 months) and 37% (0-12 months).

**Effectiveness results**
The effectiveness results were as follows:

The patient-weighted clozapine-haloperidol cumulative gain in CHIS was 50% (0-6 months) and 44% (0-12 months).

The provider-weighted clozapine-haloperidol cumulative gain in CHIS was 49% (0-6 months) and 41% (0-12 months).

Clozapine was significantly more effective than haloperidol in the measure of symptoms (p=0.02) and side-effects (p<0.0001), with nonsignificant trends in the positive direction on community role functioning (p=0.06), family relationships (p=0.23), social relationships (p=0.30), and daily activities (p=0.20).

Clozapine was also more effective than haloperidol on the one-year CHIS (p<0.0001).

**Clinical conclusions**
Clozapine offers clinical benefits in the measure of symptoms and side-effects, and is also more effective than haloperidol on the one-year CHIS.

**Measure of benefits used in the economic analysis**
QALYs were adapted from the primary health outcome findings, according to worst health-good health units (analogous to QALYs).

**Direct costs**
Discounting was not undertaken due to the short period of analysis (less than 1 year). Direct costs from a societal perspective included inpatient stays, medical/surgical costs, residential care costs, outpatient and treatment costs. No price year was stated.

**Statistical analysis of costs**
Costs were statistically analysed (t-test).

### Indirect Costs
Indirect costs from a societal perspective included lost productivity, benefits, criminal justice and family burden costs. No price year was stated.

### Currency
US dollars ($).

### Sensitivity analysis
Not reported.

### Estimated benefits used in the economic analysis
Intention-to-treat QALY gains (clozapine-haloperidol) at 0-6 months were 0.008, and over 0-12 months were 0.021. Crossover exclusion QALY gains (clozapine-haloperidol) at 0-6 months were 0.008, and over 0-12 months were 0.027.

### Cost results
the total societal costs were $58,151 for clozapine and $60,884 for haloperidol (t=0.83; p=0.409, non-significant).

### Synthesis of costs and benefits
The cost-effectiveness ratio results ranged from -$431,585 to $177,352 for clozapine over haloperidol. The change of direction is related to the uncertainty around the cost results and the small changes in benefit.

### Authors' conclusions
Clozapine is more cost-effective than standard treatment for use with patients suffering from refractory schizophrenia. Although the magnitude of its effect is small, there is considerable uncertainty around the cost results.

### CRD COMMENTARY - Selection of comparators
The rationale for the choice of comparator was clear.

### Validity of estimate of measure of benefit
The measure of benefit was a utility score appropriate for the patient sample. Conventional QALYs (which focus on physical pain and motor functioning) were not appropriate for patients with psychotic illnesses. It was not clear whether the study sample was representative of the study population due to lack of information provided around patient characteristics, although the authors state that, at baseline, the two groups were comparable. Appropriate statistical analyses were undertaken on the study findings.

### Validity of estimate of costs
All relevant categories of cost appeared to have been included in the analysis. Costs were not reported separately from quantities. Resource figures were taken from the VA Cost Distribution Report and computerised workload data. Non-VA health care costs were obtained from another study (Office of the Inspector General, 1992). No sensitivity analysis around costs was conducted and the price year was not given.

### Other issues
The authors made some reference to comparing their findings to those in other papers, although the issue of generalisability to other settings was not addressed. The authors do not appear to have reported their results selectively. The authors reported that the cost intervals found were uncertain and also that using summed weighted z-scores may have resulted in some double-counting.

**Implications of the study**
The study suggests that using clozapine is more cost-effective than haloperidol in the treatment of schizophrenia. However, further analysis is required in order to substantiate the cost findings therein as there is a very large confidence interval (which changes direction) which may or may not substantiate such claims.

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**Other publications of related interest**


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