Cost-effectiveness of clozapine monitoring after the first 6 months
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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
White blood cell (WBC) monitoring to detect agranulocytosis in schizophrenia patients treated with clozapine.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Patients with schizophrenia receiving clozapine treatment.

Setting
Psychiatric outpatient care. The economic analysis was carried out in Arkansas, USA.

Dates to which data relate
Dates for effectiveness, costs and resource use data, and for the prices used were not stated.

Source of effectiveness data
The effectiveness data were based on previous published literature and on opinion.

Link between effectiveness and cost data
The costing was undertaken retrospectively, and was not based on the same patient sample as that used in the effectiveness study.

Outcomes assessed in the review
The cumulative incidence of agranulocytosis at 6, 12, and 18 months in patients taking clozapine, and mortality rates from detected and undetected agranulocytosis were assessed.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.
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
Four studies were included in the review.

Methods of combining primary studies
Results were not combined.

Investigation of differences between primary studies
Differences were not investigated.

Results of the review
The cumulative incidence of agranulocytosis after 6, 12, and 18 months was 0.75%, 0.80%, and 0.91%, respectively. Mortality from agranulocytosis was found to be 35% in the period before regular monitoring and 2/73 (3%) under the current monitoring scheme.

Methods used to derive estimates of effectiveness
Effectiveness estimates were also based on the authors’ assumptions.

Estimates of effectiveness and key assumptions
Due to lack of reliable published information, the authors assumed that the mortality rate among agranulocytosis patients would be reduced by 20% as a result of weekly WBC monitoring scheme.

Measure of benefits used in the economic analysis
Quality adjusted life years (QALYs) were the measure of benefit in the economic analysis. The health state utilities were obtained from the published literature.

Direct costs
The monitoring costs included health service costs (technician time to draw the blood sample, the costs of WBC count determination itself, and the physician time to read the results) and the costs to the patient and relatives (patients time travelling to and from the laboratory, a family members travelling time if accompanying the patient, and transportation costs). The cost estimates for WBC tests were based on charges obtained from 4 local laboratories. The costs to the patient and relatives were based on the authors’ assumptions. Costs were not discounted. Quantities and costs were not reported separately. The price date was not stated.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analysis was carried out to evaluate more conservative scenarios by varying costs per WBC test, mortality rate among agranulocytosis patients, age at onset of agranulocytosis, and QALYs for each year without clozapine. Also, a scenario in which all four parameters were changed simultaneously, was analysed.

**Estimated benefits used in the economic analysis**
The incremental QALYs lost per patient without monitoring (or gained because of monitoring) for the first, second and third 6-month periods were $12.90 \times 10^{-3}$, $0.86 \times 10^{-2}$ and $1.892 \times 10^{-3}$, respectively.

**Cost results**
The total 6-month cost per patient for weekly WBC monitoring was $795.86$, which was assumed to be the same for all three consecutive 6-month periods. The costs of treating for agranulocytosis were not included. Costs were not discounted.

**Synthesis of costs and benefits**
The estimated benefits and costs were combined as costs per QALY saved. Incremental analysis was performed. In the benchmark case the cost-effectiveness ratio was $61,694$ per QALY for the first 6-month period, $925,418$ per QALY for the second 6 month period and $420,644$ per QALY for the third 6-month period. Neither the costs nor QALYs were discounted. The results of the sensitivity analysis for the 5 more conservative scenarios showed that the costs per QALY gained ranged from $7,923$ to $46,056$ for the first, from $118,857$ to $690,850$ for the second and from $54,025$ to $314,023$ for the third 6-month periods.

**Authors' conclusions**
While the costs of monitoring patients with schizophrenia in the first 6-month period of clozapine treatment seem to be justifiable, monitoring thereafter may not be cost-effective because of the very low incidence of agranulocytosis in the later periods.

**CRD Commentary**
Selection of comparator:

A justification was given for the comparator used. Weekly monitoring over the first 6 months period was chosen as a comparator based on the fact that agranulocytosis is rare after the first 6 months and, in many European countries, a lower frequency of monitoring is used thereafter. You, as a user of this database, should consider whether this common practice in your setting.

Validity of estimate of measure of benefit:

The estimated benefits were based on very limited evidence from published literature complemented by authors’ assumptions. Hence, the possibility of bias cannot be ruled out. The data were not used selectively.

Validity of estimate of costs:

The costs and resource quantities were not reported separately. The method of estimations used in cost analysis was described in adequate detail. The cost of treating detected cases of agranulocytosis were not included in the analysis.

Other issues:

The authors’ conclusions seem to be justified. The robustness of the model to changes in key parameters was demonstrated in the sensitivity analysis. The cost estimates are specific to the US health care system, and hence, the results may not be directly generalisable to other countries.
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