An economic model to assess the savings from a clinical application of haematopoietic growth factors

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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
Haematopoietic growth factors (HGF) to prevent, or to decrease the duration of, febrile neutropenic episodes in patients receiving chemotherapy.

Type of intervention
Treatment; primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Cancer patients, undergoing intensive or standard chemotherapy.

Setting
The practice setting was hospital. The economic analysis was carried out in Rotterdam, The Netherlands.

Dates to which data relate
Effectiveness and resource use data were from studies ranging from 1987 to 1994. The prices used were from a 1994 study.

Source of effectiveness data
Effectiveness data was derived from a review of previously completed studies.

Modelling
A decision tree was used to combine the estimates of effectiveness and costs. A Markov model was used to estimate the impact of additional chemotherapy cycles on costs, using the computer program ‘Quattro Pro for Windows’.

Outcomes assessed in the review
The two effectiveness outcomes assessed in the review were the probability of developing fever and neutropenia and the length of (hospital) stay.

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
Seven primary studies were used to derive default values for the model. Study designs were not explicitly stated, but the references include one phase I/II study; one double-blinded, controlled trial; one phase III, double-blinded, randomised, controlled study; one randomised trial; and three studies of unspecified design.

Methods of combining primary studies
A set of default values was derived from the review using the authors' judgement.

Investigation of differences between primary studies
Differences in hospital stay between the studies were examined and explained by differences in HGF dosage and in the definition of fever and neutropenia.

Results of the review
For category I, length of stay was 27 days in the intervention group and 33 days in the control group. For category II, the probability of developing fever and neutropenia in the comparator group was 57%; this probability was 50% lower in the HGF group. Length of stay was 10 days in both the control and intervention groups. For category III, length of stay was 10 days in the control group and 8 days in the intervention group.

Methods used to derive estimates of effectiveness
Clinical experts were interviewed to derive an estimate for the probability of a patient developing fever and neutropenia in subsequent chemotherapy cycles.

Estimates of effectiveness and key assumptions
Patients who had suffered an episode of fever and neutropenia during the initial chemotherapy cycles were assumed to have a 95% chance of developing an episode in a subsequent (standard chemotherapy) cycle. Patients who had not suffered fever and neutropenia during the initial chemotherapy cycles were assumed to have a 5% chance of developing an episode in a subsequent cycle.

Measure of benefits used in the economic analysis
Effectiveness estimates were not converted to a measure of health benefit.

Direct costs
Costs were not discounted. Quantities and costs were reported separately for inpatient days. The total cost was estimated from the perspective of the hospital and includes, for each therapy group, the cost of antibiotics, the cost of HGF, and the cost of inpatient days. It is unclear if the cost of outpatient visits was estimated. The cost of additional cycles of chemotherapy was also estimated. Quantities and costs were based on published studies from 1987 to 1994.
Prices were from a 1994 study. The cost of side effects was not considered in the study.

**Statistical analysis of costs**
A statistical analysis of costs was not performed.

**Indirect Costs**
Not considered in this study.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and two-way sensitivity analyses were carried out. For category I, the length of stay for the control group and the cost per hospital day were varied in a two-way analysis. The length of stay of the intervention group was varied unilaterally. For category II, the probability of developing fever and neutropenia and the cost per hospital day were varied in a two-way analysis. For category III, the length of stay (the group(s) to which this relates was not specified) and the cost per hospital day were varied in a two-way analysis. When three cycles of chemotherapy were modelled, the effect on costs of changing HGF therapy from treatment to prophylaxis was considered. The probability of developing fever and neutropenia was also varied.

**Estimated benefits used in the economic analysis**
Estimated benefits were proxied by the effectiveness estimates.

**Cost results**
After one cycle of chemotherapy, the total intervention cost for category I was $21,550 and the comparator cost was $22,510, yielding an incremental cost saving of $960. For category II, total cost of the intervention was $2,890 and the comparator cost was $3,020, yielding an incremental cost saving of $130. For category III, the total intervention cost was $5,028 and the comparator cost was $5,300, yielding an incremental cost saving of $272. When three chemotherapy cycles were considered for the case of category III, the intervention cost was $8,496 and the comparator cost was $8,955 (cost saving = $459). In category I, length of stay in the comparator group was varied from 25 to 40 days. Sensitivity analysis showed that when the cost per hospital day was $400, HGF treatment was cost saving only if the length of stay in the comparator group was 35.8 days, or greater. When the cost per hospital day was $800, HGF therapy was cost saving, whatever the length of stay. Increasing the length of stay of the intervention group, relative to the control group, decreased cost savings. In category II, the risk of developing fever and neutropenia was varied from 0 to 100%. When the cost per hospital day was $450, HGF therapy was cost saving only if the risk of developing fever and neutropenia was greater than 52%. When the cost per hospital day was $300, then this break-even risk point rose to 72.7%; if the cost was $600 (the default value), the figure was 38.4%. In category III, the incremental cost of the intervention was not found to be sensitive to changes in the length of stay. When the cost per hospital day was increased to $600 ($150 above the default value for category III), HGF was always cost saving. If the cost per hospital day was $300, HGF was cost saving only if length of stay was nine days or less. Prophylactic use of HGF in additional chemotherapy cycles was found to be cost saving only when given to patients who had previously suffered an episode of febrile neutropenia. HGF can only be cost saving for other patients if the risk of an episode is greater than 80%.

**Synthesis of costs and benefits**
A synthesis of costs and benefits was not performed.

**Authors' conclusions**
HGF therapy can produce cost savings in intensive and standard chemotherapy following neutropenic fever. Prophylactic administration is also cost-effective if the risk of infection is considerable.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparator is clear. You, the user of the database, should decide if this is a widely used practice in your own setting.

**Validity of estimate of measure of benefit**
The estimates of effectiveness do not appear to be based on a systematic review of the literature and may therefore be subject to bias. Moreover, the statistical significance of estimates used in the model, when comparing groups, was not reported. However, sensitivity analyses were conducted to investigate changes in these variables and it was acknowledged that the cost saving potential of HGF therapy was sensitive to these changes.

**Validity of estimate of costs**
Derived from the same review, the cost estimates may also be subject to bias and, since they appear to be taken from Dutch studies, may not be generalisable to other settings. Only the unit cost of a hospital day was either reported or investigated by sensitivity analysis. There is an explanation of costing methodology, but it is unclear if the cost of outpatient visits was included.

**Other issues**
The authors have not established the cost effectiveness of HGF therapy, since no attempt was made to synthesise cost results with effectiveness. Moreover, the uncertainty surrounding the cost and effectiveness estimates used in the analysis suggests that the authors' conclusions concerning the cost saving potential of HGF therapy may not be justified.

**Implications of the study**
Evidence from a systematic review of randomised controlled trials is needed to establish the effectiveness of HGF therapy in reducing the risk of febrile neutropenic episodes in patients undergoing chemotherapy. The impact of HGF therapy on length of stay also needs to be established if cost-effectiveness is to be known.

**Source of funding**
Not stated.

**Bibliographic details**

**PubMedID**
8695242

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Antineoplastic Agents /adverse effects /therapeutic use; Drug Costs; Fever /economics /prevention & control; Hematopoietic Cell Growth Factors /economics /therapeutic use; Hospital Costs; Humans; Markov Chains; Models, Economic; Neoplasms /drug therapy; Netherlands; Neutropenia /chemically induced /prevention & control

**AccessionNumber**
NHS Economic Evaluation Database (NHS EED)
Produced by the Centre for Reviews and Dissemination
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21996000398

Date bibliographic record published
31/01/1999

Date abstract record published
31/01/1999