Modeling the cost-effectiveness of granulocyte colony-stimulating factor use in early-stage breast cancer

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
Granulocyte colony-stimulating factor (G-CSF) use in early-stage breast cancer.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with early-stage breast cancer. The population of patients was assumed to be similar to the population presented in a companion report.

Setting
The practice setting was a secondary care institution and the economic study was carried out in the United States.

Dates to which data relate
It was not clear during which years data were collected for the effectiveness analysis. Effectiveness estimates were based on a study published in 1994. It was not clear which price years were used.

Source of effectiveness data
The estimates for final outcomes (3-year disease-free survival) were based on a review of previously completed studies. Estimates of the future events of neutropenia, chemotherapy dose reduction or dose delay were based on opinion.

Modelling
A conditional cost-effectiveness model was developed for the use of G-CSF based on a ranking of patient need as determined by patient blood counts during the first cycle of chemotherapy. The model integrated estimates of outcome and costs and projected effectiveness and cost estimates beyond the timescale of direct observation.

Outcomes assessed in the review
Disease-free survival (DFS) at three years was assessed by literature review.

Study designs and other criteria for inclusion in the review
Randomised studies with a population of patients similar to the patients used to construct the authors' predictive model
of neutropenia were identified.

**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**
The judgement criteria used were not stated. Summary statistics from the study were used to extract the data.

**Number of primary studies included**
One randomised clinical trial was included in the review. Four other studies were also referred to although no details of their design were provided.

**Methods of combining primary studies**
This was not relevant as the results of only one study were used.

**Investigation of differences between primary studies**
The authors reported that three other studies had shown similar results while one had disagreed. The authors suggest that these inconsistencies arose from difficulties in estimating dose-response in non-randomised, retrospective studies.

**Results of the review**
The study demonstrated an 11% reduction in 3-year DFS with a 50% reduction in dosage. The 3-year DFS was 74% versus 63%.

**Methods used to derive estimates of effectiveness**
Authors’ assumptions were used to derive estimates of likely future events of neutropenia, chemotherapy dose reduction, and dose delay.

**Estimates of effectiveness and key assumptions**
These estimates were reported in a companion paper and are not presented here.

**Measure of benefits used in the economic analysis**
Life years saved was the outcome measure used in the economic analysis. A conditional cost-effectiveness model was developed for the use of G-CSF based on a ranking of patient need, as determined by patient blood counts during the first cycle of chemotherapy. The model integrated estimates of outcome and costs and projected effectiveness and cost estimates beyond the timescale of direct observation.

**Direct costs**
Costs were discounted at a rate of 4%. Quantities and costs were not analysed separately. The health service costs of treatment measured were expenditures for G-CSF, chemotherapy, hospitalisation for fever and neutropenia, and outpatient administration of salvage chemotherapy and obtaining blood counts. The estimation of quantities and costs was derived using a modelling study. Seven doses of G-CSF per cycle were assumed, with a maximum of five cycles of
G-CSF. Payment per hospital episode of febrile neutropenia was based on reimbursement rates for the Health Care Financing Administration's Diagnostic group 399 with a mean hospitalisation rate of 4.7 days. Costs of salvage therapy were based on paclitaxel as salvage therapy if cyclophosphamide, doxorubicin and fluorouracil (CAF) was the primary therapy, or CAF as the salvage therapy if cyclophosphamide, methotrexate and fluorouracil (CMF) was the primary therapy.

Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
One-way simple sensitivity analyses were performed for a range of model assumptions: discount rates, effectiveness data and cost data. A three-way sensitivity analysis of the influence of the dose-reduction assumptions on the results was also performed.

Estimated benefits used in the economic analysis
The incremental gains in life expectancy were not reported separately in the paper: only graphical illustrations of gains in life expectancy were provided. The authors reported that the gain in life expectancy was greater in the patients who received G-CSF than in those who had to wait until an event occurred. The group that received G-CSF would have less chance of dose reduction. Side effects of treatment were considered in the economic analysis.

Cost results
The total intervention cost was not reported separately in the paper: only graphical illustrations of total cost of treatment per patient and incremental cost per patient were provided. The authors noted that the cost savings of G-CSF (with respect to lowered hospitalisation and salvage costs) were less than the costs of giving G-CSF to all patients from cycles 2 through 6. On an incremental basis, as initial patient risk increases, incremental cost in the group starting on G-CSF in cycle 2 was declining, because the higher average hospitalisation expenditures of high-risk patients were reduced by G-CSF.

Synthesis of costs and benefits
At a threshold of risk of an event above which the decision-maker administers G-CSF equal to 0.48 (at which 50% of patients would receive G-CSF), the cost per life year saved was $34,297. If all patients were given G-CSF starting in cycle 2, the cost-effectiveness ratio increased to $254,925 per life year saved. If patients were not permitted to use G-CSF unless preceded by an event, the cost fell to $21,673 per life year saved.

These estimates were relatively insensitive to in-patient hospital cost estimates. However, the model was sensitive to assumptions about the shape of the relationship between dose reduction and disease-free survival at 3 years.

Authors' conclusions
Even with the limited data analysed, it seems reasonable to say that selective use of G-CSF for those patients who are most in need of the drug can achieve cost-effectiveness ratios comparable to those of other medical technologies. It helps avoid the use of expensive drugs for patients where benefit is small, while not denying an expensive drug to that subset of patients who can benefit substantially from it.

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

**Validity of estimate of measure of benefit**
As the authors indicated, the greatest imprecision in their analysis was associated with the sensitivity of their results to the shape of the dose-response curve, which, at the time of the study, was not known with precision. The thoroughness of the authors’ attempts to identify relevant studies was not reported. Therefore, it is difficult to judge whether biases could have been introduced into the model.

**Validity of estimate of costs**
Resource quantities were not reported separately from prices and only partial details of the methods of quantity/cost estimation were provided. Cost results might not be generalisable outside the US setting. Furthermore, a discount rate of 4% was used in the cost analysis, which might not be relevant to other settings.

**Other issues**
To account for the uncertainties in the data the authors carried out extensive sensitivity analyses. Appropriate comparisons were made with other studies.

**Implications of the study**
The authors suggested that better prospective data on the influence of small dose reduction of DFS is required and that this could be achieved by routinely randomising patients inside dose ranges to receive varying doses of agents.

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**Other publications of related interest**


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