The costs and cost-effectiveness of unrelated donor bone marrow transplantation for chronic phase chronic myelogenous leukemia


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
Unrelated donor bone marrow transplantation for chronic phase chronic myelogenous leukemia.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
A hypothetical population of 35-year-old patients transplanted within 1 year of diagnosis.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data were collected from studies published in 1997. Cost data were based on patient records collected between 1991 and 1996 and on studies published between 1994 and 1997. The price year was 1996.

Source of effectiveness data
Effectiveness data were derived from a literature review.

Modelling
A 5-year Markov model was used to determine the cost-utility of non-T-cell depleted unrelated donor bone marrow transplantation for chronic phase chronic myelogenous leukemia (CML).

Outcomes assessed in the review
The review assessed survival and mortality rates, and the proportion of patients entering blast crisis.

Study designs and other criteria for inclusion in the review
Data on alpha-interferon and hydroxyurea therapy were based on the results of a meta-analysis of seven randomised trials analysed on an intention to treat basis. Data on transplantation were obtained from a previous cohort study.
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
At least two studies were included.

Methods of combining primary studies
The narrative method was used to combine primary studies.

Investigation of differences between primary studies
Not stated.

Results of the review
Effectiveness data were based on the records of 157 patients.

During the six months of peri-transplant 48 patients died and 109 patients survived.

100% of untransplanted patients would eventually enter blast crisis unless they died of a cause unrelated to CML, and 50% of patients entering blast crisis would undergo one induction chemotherapy cycle.

27 patients died in the period 6 to 12 months after bone marrow transplantation (BMT). 21 died in the period 12-18 months post BMT. 19 died 18-24 months post BMT, 16 died 24-30 months post BMT, 12 died 30-36 months post BMT and 8 died 36-42 months post BMT. 6 patients died 42-48 months post BMT, 4 died 48-54 months post BMT and 3 died 54-60 months post BMT.

The overall survival of the patients who were 50 years old or less and transplanted from fully matched unrelated donors within 1 year of diagnosis was 77% at 3 years.

Measure of benefits used in the economic analysis
Quality-adjusted life years (QALYs) were used as the measure of benefit. Benefits were discounted at an annual rate of 3%. Utilities were derived from physicians using the standard gamble methodology.

Direct costs
Direct costs were discounted at an annual rate of 3%. Quantities and costs were reported separately. Direct costs included the cost of treatment peri-transplant and post-transplant, the cost of treating CML blast crisis, the cost of outpatient alpha-interferon and hydroxyurea therapy and the cost of an outpatient phlebotomy appointment. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Cost estimates were based on the records of 49 patients transplanted at the Brigham and Women's Hospital (BWH), and 108 patients transplanted at the Fred Hutchinson Cancer Research Centre (FHCRC). Medication costs were based on prices listed in the Red Book. Charges were adjusted by the institutional ratio of costs to charges. Costs were adjusted using the medical care component of the consumer price index. The price year was 1996.
Statistical analysis of costs
Multiple linear regression was used to assess the association between peri-transplant costs and patient age, patient gender, whether a patient was mismatched, site, length of stay during the transplant hospitalisation and whether a patient died during the transplant hospitalisation or after hospital discharge but before 6 months.

Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed on cost estimates, patient age, discount rate, utilities, the handling of unusually high post-transplant hospitalisations, and long-term medical costs more than 5 years post-transplant. Ranges for testing were identified from the medical literature and the recommendations of the Panel of Cost-Effectiveness in Health and Medicine.

Estimated benefits used in the economic analysis
A patient transplanted within 1 year of diagnosis would attain 9.95 QALYs. A patient treated with alpha-interferon or hydroxyurea therapy would attain 4.7 or 4.5 QALYs, respectively.

Cost results
The most significant predictors of costs within the first six months were initial hospital length of stay and death. Post-transplant care costs remained high during months 6 to 18 and then decreased and plateaued except for a single hospitalisation 3 years after transplantation. Patients dying within 6 months of transplantation were significantly more costly in the first 6 months than those surviving beyond 6 months ($211,000 versus $189,700, p=0.03). Transplantation cost $333,600, alpha-interferon cost $61,800 and hydroxyurea therapy cost $31,400.

Synthesis of costs and benefits
The incremental cost-effectiveness of BMT over alpha-interferon was $51,800/QALY. The results were sensitive to changes in patient age and other variables that influenced the effectiveness of transplantation. Most results varied between $50,000/QALY and $100,000/QALY. The incremental cost-effectiveness of BMT over hydroxyurea therapy was $55,500/QALY.

Authors' conclusions
In appropriate populations, unrelated donor transplantation has a cost-effectiveness ratio comparable to that of other accepted medical interventions used in the prevention, screening or treatment of both malignant and non-malignant disease.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used, namely current therapy. You, as a user of the database, should decide if these health technologies are relevant to your own setting.

Validity of estimate of measure of benefit
The authors did not state that a systematic review of the literature had been undertaken and more details could have
been provided about the design of the review and the method of combining primary effectiveness estimates. The estimation of benefits was modelled. The instrument used to derive the measure of health benefit, the standard gamble, was appropriate. More details on the effectiveness of the comparators would have been helpful.

Validity of estimate of costs
All relevant cost categories were included and quantities and costs were reported separately. Sensitivity analyses were conducted on costs and on quantities. Charges were converted to costs. The price year was reported. Costs did not include the costs of establishing the unrelated donor registry or donor searches for patients unable to locate a donor. The inclusion of professional fees was expected to increase the costs of transplantation. The costs of cytogenetic studies and palliative care for patients electing non-transplant therapy were not considered. These costs would improve the cost-effectiveness of transplantation. The authors intended to include indirect costs, but the retrospective design of the cost analysis made this impossible.

Other issues
The authors made appropriate comparisons of their findings with those from other studies but did not address the issue of generalisability to other settings. The authors did not present their results selectively. The study considered patients with chronic CML and this was reflected in the authors' conclusions. The authors did not know if those cured of malignancy by transplantation would have more late medical complications and costs than the average population. Recent changes in transplantation practice such as better HLA matching or approaches to GVHD were not considered.

Implications of the study
Both non-transplant and transplant therapy are improving and their cost-effectiveness ratios will need to be continually re-evaluated. If transplant costs can be lowered while health outcomes improve, the cost-effectiveness ratio of unrelated donor transplantation will become more favourable than shown in this analysis.

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Other publications of related interest


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