Cost-effectiveness of outpatient management for febrile neutropenia in children with cancer
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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.

CRD summary
This study examined the cost-effectiveness of in-patient versus out-patient treatment strategies for children with cancer, who were experiencing episodes of low-risk febrile neutropenia. The authors concluded that the higher costs of in-patient care could not be justified on the basis of efficacy or preferences, but it was uncertain whether intravenous was better than oral out-patient treatment. Some critical assumptions were made, but uncertain areas were investigated and all the methods were valid. The authors' conclusions appear to be robust.

Type of economic evaluation
Cost-utility analysis

Study objective
This study examined the cost-effectiveness of in-patient versus out-patient treatment strategies for children with cancer, who were experiencing episodes of low-risk febrile neutropenia.

Interventions
Four treatment strategies were considered: hospital treatment, with intravenous antibiotics; early discharge after 48 hours of in-patient observation, with intravenous antibiotics, followed by oral out-patient treatment; out-patient management, with intravenous antibiotics; and out-patient management, with oral antibiotics. The first-line intravenous antibiotics in hospital were gentamicin plus the combination of piperacillin and tazobactam, while for out-patients they were ceftriaxone plus amikacin. Oral treatment consisted of ciprofloxacin plus the combination of amoxicillin and clavulunate. Treatment lasted for six days.

Location/setting
Canada/in-patient, out-patient, and home.

Methods
Analytical approach:
The analysis was based on a decision-tree model, with a one-month time horizon. The authors stated that the perspective of the health care payer was adopted.

Effectiveness data:
The clinical data were identified by a systematic review of the literature in commonly used electronic databases, including MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search identified six randomised controlled trials. Authors’ opinions were used where there were no estimates available. The rates of treatment failure and hospital re-admission were the key inputs.

Monetary benefit and utility valuations:
The utility values were elicited from 149 parents of children who were receiving active treatment for cancer at a Canadian institution (the Hospital for Sick Children). Scores on a visual analogue scale (VAS) were converted into utilities, using a specific conversion algorithm.

Measure of benefit:
The summary benefit measure was the number of quality-adjusted febrile neutropenia episodes (QAFNEs).

Cost data:
The economic analysis included the costs of hospitalisation, initial consultation, out-patient visits, laboratory tests, home care nursing, and medication. These costs were from the Ontario Health Insurance schedule of benefits and fees, and from the local finance offices at the Hospital for Sick Children. A hypothetical 20kg child was considered for the calculation of the drug costs. The costs were in Canadian dollars (CAD) and the price year was 2009.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on all the model inputs. The ranges of values were from published sources. A probabilistic sensitivity analysis was carried out to investigate the overall uncertainty in the model parameters, using a second-order Monte Carlo simulation. Cost-effectiveness acceptability curves were generated, for a range of willingness to pay (WTP) from zero to CAD 20,000, and a threshold of CAD 4,000 per QAFNE.

Results
The projected costs were CAD 2,732 with intravenous out-patient treatment, CAD 2,757 with oral out-patient treatment, CAD 5,579 with early discharge, and CAD 14,493 with hospital treatment. The QAFNEs were 0.6632 with intravenous out-patient, 0.5534 with oral out-patient, 0.6841 with early discharge, and 0.6496 with hospital treatment.

The incremental analysis showed that both oral out-patient and hospital treatment were dominated as they were less effective and more expensive than another strategy. Intravenous out-patient treatment was the reference strategy, with an average cost per QAFNE of CAD 4,119. The incremental cost per QAFNE with early discharge over intravenous out-patient treatment was unacceptably high at CAD 136,148.

The most influential inputs were the cost for a home care nurse visit, the duration of out-patient treatment, and the utility for intravenous and oral out-patient treatment. Beyond certain thresholds, the most cost-effective strategy was oral out-patient treatment, but under no scenario was either out-patient strategy inferior to hospital treatment or early discharge.

At a WTP threshold of CAD 4,000 per QAFNE, intravenous out-patient treatment was the preferred strategy in 57% of simulations and oral out-patient treatment was preferred in 35% of simulations.

Authors' conclusions
The authors concluded that the higher costs of in-patient care could not be justified on the basis of efficacy or preferences, but it was uncertain whether intravenous was better than oral out-patient treatment.

CRD commentary
Interventions:
The selection of the comparators was appropriate as all the feasible management strategies for these patients were considered.

Effectiveness/benefits:
A systematic search of the published literature was a valid way to identify the relevant sources of evidence. It appears that all the clinical data were from randomised controlled trials which should have ensured high internal validity. Limited information on the methods of the source studies was provided, and this reduces the possibility of objectively assessing the quality of the clinical inputs. The authors did not report the methods used to synthesise the values from more than one study. They justified their use of QAFNEs as the summary benefit measure, rather than the more commonly used quality-adjusted life-years (QALYs) on the basis that death was not an outcome in the model, and the survival component of QALYs would not substantially alter the preference for any strategy.

Costs:
The categories of costs reflected the perspective of the health care payer. Most of the unit costs and some resource quantities were presented in an appendix, improving the transparency of the study. Typical Canadian sources were used and appear to have been appropriate. The costs were varied in the deterministic and in the probabilistic sensitivity analyses. The price year was reported and there was no need for discounting given the short time horizon of the study.

Analysis and results:
The total costs and benefits results were clearly presented. Both average and incremental cost-utility ratios were calculated and the incremental analysis allowed the exclusion of inferior (dominated) strategies. Extensive and appropriate sensitivity analyses were carried out to investigate the key areas of uncertainty and the results were clearly presented. The authors acknowledged some limitations of their analysis, such as the limited number of clinical studies retrieved, the use of a VAS to elicit the preferences from parents, and the lack of a standard threshold for QAFNEs. The generalisability of the analysis was not explicitly addressed, but the results might be transferable to settings with a similar cost structure.

Concluding remarks:
Some critical assumptions were made, but uncertain areas were investigated and all the methods were valid. The authors’ conclusions appear to be robust.

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