A cost-utility analysis of second-line antibiotics in the treatment of acute otitis media in children

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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
Second-line antibiotic treatment used to treat acute otitis media in children.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Male and female children with acute otitis media. Ages ranged from 2 months to 18 years, but the majority of patients were between 6 months and 12 years of age.

Setting
The setting was primary and secondary care (family physicians offices and paediatric clinics). The economic study was carried out in Ontario, Canada.

Dates to which data relate
The effectiveness data related to the period 1979 to 1994. The drug acquisition costs were obtained from the 1994 Ontario Drug Benefit Formulary. Information about the costs of drugs, dosing, paediatric visits and laboratory studies were taken from the 1994 Schedule of Benefits, Physicians Services under the Health Insurance Act. The dates for the resource use data collection were not reported.

Source of effectiveness data
The estimate of final outcomes was obtained from a synthesis of previously completed studies.

Modelling
A decision tree analytic model was used to estimate both the cost and the benefits associated with the treatment strategies for acute otitis media. The model estimated total costs and benefits for a 30-day period and included initial treatment success and failure, adverse event/no adverse event, and second antibiotic treatment success and failure points. Monte Carlo simulations were performed to estimate average cost and benefit values by using the same number of replications as the number of patients pooled from the primary clinical studies.

Outcomes assessed in the review
The outcomes considered in the review were:
(1) improvement or cure without adverse events;
(2) improvement or cure with adverse events;
(3) initial failure and second antibiotic treatment without adverse events, and
(4) initial failure and second antibiotic treatment with adverse events.

Improvement was defined as the resolution of signs and symptoms with or without complete disappearance of middle ear effusion, such that no further antibiotic therapy was required, whilst failure was defined as persistence of signs and symptoms necessitating a further course of antibiotic therapy.

**Study designs and other criteria for inclusion in the review**

Only randomised controlled trials involving a 7 - 14 day course of CEF (40mg/kg per day in three divided doses), AMX-CLA (40/10mg/kg per day in three divided doses) or ERY-SULF (50/150mg/kg per day in three divided doses) were included in the analysis.

**Sources searched to identify primary studies**

A MEDLINE search was used to identify studies between January 1970 and December 1994. The bibliographies of the articles generated by this search were then reviewed to identify further relevant papers.

**Criteria used to ensure the validity of primary studies**

Not stated

**Methods used to judge relevance and validity, and for extracting data**

Original data from the primary studies were pooled.

**Number of primary studies included**

Nine, 4 and 2 studies were included for the efficacy of CEF, AMX-CLA and ERY-SULF respectively.

**Methods of combining primary studies**

Studies were combined using the DerSimonian and Laird method of meta-analysis.

**Investigation of differences between primary studies**

Not stated.

**Results of the review**

The probability of improvement (and 95% confidence intervals) for the three antibiotics were estimated as follows;

CEF, 0.927 (95% CI: 0.899 - 0.954);
AMX-CLA, 0.904 (0.857 - 0.951),
erythromycin-sulfisoxazole, 0.947 (0.848 - 1.0).

**Measure of benefits used in the economic analysis**

Quality-adjusted life-days were used in the economic analysis. These were derived from physicians' preferences for
each of three possible health states, measured using a visual analogue scale on which 1 represented perfect health and 0 represented death.

**Direct costs**
Some quantities of resource use were analysed separately from the costs. Quantities of resource use for both operating and complication costs were included and were derived by a panel of physicians, the perspective used being that of a specific third party payer (the Ontario Ministry of Health). The costs of adverse events were estimated from a mail survey of physicians who indicated their own management strategies for possible adverse events. The source of unit costs was the Ontario Drug Benefit Formulary and the Ontario Health Insurance Plan (OHIP) fee schedule. The price year was not clearly reported. The total costs were estimated for a 30-day period based on a model.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
All costs were varied over the range Can$0 - Can$500, all probabilities were varied over the 95% confidence interval defined by the meta-analysis and all quality-adjusted life-days (QALD) were varied over the range 0 - 30 days. Monte Carlo simulation was used.

**Estimated benefits used in the economic analysis**
The QALD figures were 28.15 for CEF, 27.98 for AMX-CLA and 28.03 for ERY-SULF.

**Cost results**
Total costs were estimated as follows:
- CEF, Can$108.00;
- AMX-CLA, Can$119.00;
- ERY-SULF, Can$120.00.

The mean costs estimated for the management of adverse reactions were as follows:
- gastrointestinal, Can$57.98;
- dermatological, Can$41.81;
- and serum-sickness-like reaction, Can$80.83.

**Synthesis of costs and benefits**
The cost per cure (and cost per quality-adjusted-life-day) was calculated for each antibiotic:
- CEF, Can$116.50 (3.83);
- AMX-CLA, Can$131.64 (4.26);
- ERY-SULF, Can$126.72 (4.26).

Incremental analysis was undertaken comparing CEF and ERY-SULF to give an incremental cost-effectiveness ratio for CEF of Can$600 per additional treatment success.
Authors' conclusions
The authors concluded that, from the three antibiotics considered, CEF was the most cost-attractive. The acquisition cost of CEF was higher than the other two but it had the greater gastrointestinal tolerability.

CRD Commentary
As the authors themselves state, the limitations of the study include:

(1) The model was based on efficacy rather than effectiveness data.

(2) The analysis was restricted to a short time period and longer follow up may have revealed more data regarding relapse and recurrence rates.

(3) The clinical data used did not uniformly report adverse events and their consequences, and the physician survey carried out to supplement that data had a response rate of only 59% from a relatively small sample.

(4) The utility measurements used were derived by physicians and therefore may be improved by the inclusion of values from patients, families or other health care providers using more rigorous techniques.

Implications of the study
More information is required about the incidence and management of adverse drug reactions. Information about the impact of treatment on quality of life of patients is also required.

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