Prophylaxis for disseminated Mycobacterium avium complex (MAC) infection in patients with AIDS: a cost-effectiveness analysis
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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
Prophylaxis for disseminated Mycobacterium avium Complex (MAC) infection in patients with AIDS: rifabutin (300 mg/day), azithromycin (1200mg/week) and clarithromycin (500 mg twice per day) were compared with no prophylaxis.

Type of intervention
Treatment; secondary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
Hypothetical HIV-infected patients at various CD4 levels <200 cells. No further details were given.

Setting
Hospital. The economic study was carried out in Boston, Massachusetts, USA.

Dates to which data relate
The main effectiveness data were derived from randomized controlled studies conducted between 1993 and 1996. Resource and cost data were taken from 1994 sources. The price year was 1994.

Source of effectiveness data
The efficacy and toxicity data were derived from a series of previously published studies.

Modelling
A decision analysis model was used to compare the cost per quality-adjusted life year (QALY) of rifabutin, azithromycin, and clarithromycin, against no prophylaxis.

Outcomes assessed in the review
The outcomes assessed were the efficacy (in terms of the probability of preventing MAC) and toxicity data associated with each strategy.

Study designs and other criteria for inclusion in the review
No specific study designs were stipulated by the authors as inclusion criteria although all were randomised controlled trials.
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
3 primary studies were included in the review.

Methods of combining primary studies
Narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
The probabilities of preventing MAC for rifabutin, azithromycin and clarithromycin were 0.5146, 0.6335 and 0.7199, respectively. The probabilities of major symptoms or toxicity for rifabutin, azithromycin and clarithromycin were 0.2833, 0.2243 and 0.2564, respectively. The overall likelihood of developing MAC was 18% with placebo and 9% with rifabutin over a mean of 222 days. Minor toxicity or symptoms developed in 42% of patients receiving placebo and 46% of patients receiving rifabutin. Major toxicity occurred in 17% and 22% of patients.

Measure of benefits used in the economic analysis
The outcome measures of benefit were life years gained and quality-adjusted life expectancy. These were estimated from a global quality of life question from AIDS Clinical Trial Group Protocols. The QOL estimates were 0.8700 (no MAC), 0.5610 (acute MAC), 0.7720 (history of MAC and 0.0054 (major toxicity or symptoms) (decrease in QOL).

Direct costs
Total direct medical costs included the cost of prophylaxis, the cost of treating toxicity related to prophylaxis, the cost of evaluation for suspected MAC and the cost of treating diagnosed MAC. The source of costs was a nation-wide survey reported in Physicians’ Fee Reference 1994. The charges were converted to costs by a cost-to-charge ratio. Resources were reported separately from the prices. The quantity/cost boundary adopted was that of the payer. Discounting was not undertaken. The price year was 1994.

Currency
US dollars ($).

Sensitivity analysis
A series of sensitivity analyses was carried out on all model parameters, including initial CD4 count for beginning prophylaxis, to determine the impact on the cost-effectiveness results of changing parameter values. Although there is no broad consensus on what cost-effectiveness ratios may be acceptable from a clinical policy perspective, parameter
values which had incremental cost-effectiveness ratios < $20,000/QALY and $100,000/QALY were identified.

**Estimated benefits used in the economic analysis**
Quality-adjusted life expectancies were 1.6068, 1.6239, 1.6186 and 1.6255 for no prophylaxis, azithromycin, rifabutin and clarithromycin, respectively.

**Cost results**
For patients with AIDS and those having CD4 counts <75 cells/mm3, azithromycin, clarithromycin and rifabutin prophylaxis increased lifetime per person MAC-related costs by $994, $2,117 and $2,185, respectively.

**Synthesis of costs and benefits**
The cost/QALY utilities ratios were $58,200, $116,000 and $179,000/QALY saved for azithromycin, clarithromycin and rifabutin prophylaxis, respectively (each compared with no prophylaxis). When compared with each other, azithromycin was the most cost-effective. Clarithromycin had an incremental cost-utility ratio of $744,400/QALY saved compared with azithromycin. Rifabutin is a dominated, or not cost-effective, strategy. Results were mainly dependent on the annual cost of prophylaxis, the initial CD4 count when starting prophylaxis and any survival benefit with prophylaxis. For each type of prophylaxis, strategies beginning with CD4 counts <25 or 50 cells/mm3 were substantially more cost-effective than those beginning in patients with higher CD4 counts.

**Authors' conclusions**
The authors concluded that "MAC prophylaxis is likely to cost society an additional $99 million to $219 million per 100,000 patients treated. In the context of Centers for Disease Control and Prevention (CDC) recommendations to use prophylaxis in patients with CD4 counts <75 cells/mm3, azithromycin represents the best value and is most cost-effective when used in patients with CD4 counts <25 cells/mm3".

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparators is clear. Strategies to prevent MAC infection have assumed increasing importance as they are likely to increase the life expectancy of HIV-infected patients. You, as a user of this database, should consider whether these are widely used health technologies in your own setting.

**Validity of estimate of measure of benefit**
The estimate of measure of benefit used in the economic analysis is likely to be internally valid as a review of recent trials was undertaken in determining baseline data within the normal limitations of a modelled solution. The data have not been used selectively.

**Validity of estimate of costs**
The resources were reported separately from the prices. Adequate details of methods of quantity/cost estimation were given. Important cost items do not appear to have been omitted.

**Other issues**
The authors' conclusions are likely to be justified given the uncertainties in the data. The modelled solutions were tested using sensitivity analysis in order to validate the robustness of the findings. The issue of generalisability to other settings/countries was not addressed. However, appropriate comparisons were made with other studies in terms of the cost-effectiveness of prophylaxis for other conditions such as Pneumocystis carinii Pneumonia. Results do not appear to have been presented selectively.
Implications of the study
As the authors noted, better data on costs of care could be obtained by including cost studies in parallel with clinical trials as they are conducted. Furthermore, more research is required in which patients are directly comparable with each other in terms of concomitant medications and other characteristics. Better data on drug interactions and clinical outcomes might be included in the cost-effectiveness model. Other important factors such as drug toxicity, patient-specific quality-of-life considerations, the likelihood of drug interactions and geographic or environmental MAC exposure risk should be included in future research.

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