The cost-effectiveness of preventing AIDS-related opportunistic infections

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 AIDS-related opportunistic infections.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
A hypothetical cohort of HIV infected and AIDS patients whose CD 4 lymphocyte counts declined to less than 0.300x10^9

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

Dates to which data relate
The main effectiveness data were derived from studies published during 1993-96. Resource use data were collected for the period March 1991 through August 1992. The price year was 1995.

Source of effectiveness data
Effectiveness data were derived from a review of previously completed studies.

Modelling
A Markov simulation model was used to compare different strategies for prophylaxis of pneumocystis carinii pneumonia (PCP), toxoplasmosis, mycobacterium avium complex (MAC) infection, fungal infections and cytomegalovirus (CMV) disease in HIV-infected patients. The model started from a chronic state, and allowed progression to an acute state, with the associated transition being triggered by the development of an acute opportunistic infection. The survivors returned to a chronic state capturing the opportunistic infection history, whilst all others proceeded to the death state. The model allowed for the risk of drug-related toxicity, death from AIDS related causes and non-AIDS-related causes, and was used to estimate total lifetime costs and benefits.

Outcomes assessed in the review
The outcomes assessed in the review were the efficacy (reduction in the incidence of opportunistic infections), and toxic reactions to medications.
Study designs and other criteria for inclusion in the review
Randomized controlled trials were identified. The inclusion/exclusion criteria were not stated.

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
A total of 8 studies (including 1 meta-analysis) were included for the estimate of efficacy, whilst 1 study was used for the estimates of toxicity.

Methods of combining primary studies
Whilst one of the studies included was already a meta-analysis, the method of combination of primary studies was not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
Not stated except for the case of CMV prophylaxis, which used one study to derive the baseline ganciclovir efficacy estimate of 49%.

Measure of benefits used in the economic analysis
Life years gained and quality-adjusted life months (QALMs) gained. The utility weights used in the analysis were derived from the literature; Torrance’s power transformation method was used to convert rating scale scores to time trade-off values. Patient values were used to assess health states.

Direct costs
Quantities of resource use were not analysed separately from costs. Whilst the costs included were those associated with evaluation, workup, and treatment for acute opportunistic infections, the sources of costs data were the hospital billing data from a US national AIDS data set (ACSUS) and 1995 Red Book data. Charges were converted to costs using city-specific cost-to-charge ratios for each of the 10 cities included in the data set weighted by their contribution to total AIDS-related inpatient admissions in 1991. Costs were discounted. Costs were reflated to 1995 prices by using the medical care component of the consumer price index. Total costs were estimated using a model. Non-AIDS-related disease costs were omitted.

Currency
US dollars ($).
Sensitivity analysis
A one way sensitivity analysis was performed on the cost-effectiveness results. The parameters varied were the mortality rate (accounting for differences in mortality between patients with a history of opportunistic infection and those without), quality weights (results without any weighting of life expectancy), incidence rate of opportunistic infections and the timing of prophylaxis, and medication cost. A scenario analysis was used for antiretroviral medications, CD4 cell count decline, and differential mortality between patients with a history of opportunistic infection and those without.

Estimated benefits used in the economic analysis
Quality-adjusted life months were estimated to range from 39.08 with no prophylaxis to 42.56 months with the use of trimethoprim-sulfamethoxazole prophylaxis for PCP and toxoplasmosis for patients with CD4 cell counts of 0.200x10^9/L (200/microL) or less. The life expectancy was estimated to range from 45.67 months with no prophylaxis to 49.80 months with the use of TS for pneumocystis carinii pneumonia/toxoplasmosis. The QALMs were:

43.4(TSA);
43.1(TSF);
43.60(TSAF);
43.20(TSG);
43.83(TSAG);
43.80(TSFG),
and 44.62 (TSAFG).

Cost results
The no prophylaxis option yielded expected total lifetime costs of $40,288. The corresponding figure for prophylaxis for PCP and toxoplasmosis with trimethoprim-sulfamethoxazole was estimated to be $44,786. In turn, TSA, TSF, TSAF, TSG, TSAG, TSFG, TSAFG were associated with figures of $45,944, $47,046, $48,596, $54,628, $56,812, $58,082, and $61,119, respectively.

Synthesis of costs and benefits
The costs and benefits were combined in terms of an incremental cost-per-QALY-gained (relative to no prophylaxis) measure, using a discount rate for costs and benefits of 3% and 1995 prices. As for MAC prophylaxis, figures ranged from $35,000 per QALY saved for azithromycin, through $58,000 per QALY saved for clarithromycin, to $74,000 per QALY saved for rifabutin; fluconazole was $100,000 per QALY saved, and oral ganciclovir was $314,000 per QALY saved. The incremental cost-effectiveness ratio for PCP prophylaxis using TS was estimated to be $16,000 per QALY saved, compared with no prophylaxis. The corresponding figures for TSA, TSAF, and TSAFG were, respectively, $29,000, $59,000, and $147,000. All other combination strategies were found to be dominated. The most influential parameters were the risk of developing an opportunistic infection, the impact of opportunistic infection history on long-term survival, and the cost of prophylaxis.

Authors' conclusions
The cost-effectiveness of prophylaxis against HIV-related opportunistic infections varies widely, but prophylaxis against PCP or toxoplasmosis and against MAC delivers the greatest comparative value. These results can be used to set priorities and explore new alternatives for improving HIV patient care.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparators was not clearly stated. Given the multiple options now available for prophylaxis of AIDS-related opportunistic infections, the authors argued that, because of differences in incidence rates as well as drug efficacy, toxicity, and costs, the role of different prophylactic strategies remains uncertain.

**Validity of estimate of measure of benefit**
Given the lack of information with regard to the methodology used in the review, one can not assess whether the measure of benefit used in the economic analysis is likely to be valid.

**Validity of estimate of costs**
The resource quantities were not reported separately from the prices. Adequate details of methods of quantity/cost estimation were given. Important cost items were not omitted.

**Other issues**
The authors’ conclusions were justified on the grounds of the results of the sensitivity analysis. However, the analysis does not appear to have considered the variation in the efficacy rate of prophylaxis. The issue of generalisability to other settings was not clearly addressed. Appropriate comparisons were made with other studies. In all but one case, the underlying estimates of efficacy of prophylaxis were not stated.

**Implications of the study**
Further information is needed on the methodology used in, and the estimates obtained from, the review of the literature of the effectiveness study in order to consider whether the corresponding study results are valid.

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**Other publications of related interest**

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