A Monte Carlo simulation of advanced HIV disease: application to prevention of CMV infection

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
Oral ganciclovir (1,000 mg, three times a day) for prevention of cytomegalovirus (CMV) infection in HIV-infected patients versus no primary prophylaxis for CMV infection.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Hypothetical HIV-infected patients. No further details were given.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
The main effectiveness data were derived from a variety of cohort studies, randomized clinical trials and national resource utilization surveys dated 1982-1996. Resource and cost data were derived from 1991-92 sources. The price year was 1995.

Source of effectiveness data
The estimates of transition rates, drug efficacy, toxicity and adherence were derived from a variety of cohort studies, randomized clinical trials and national resource utilization surveys. The quality of life status estimates were obtained through the use of a questionnaire.

Modelling
A state-transition model of the natural history of late-stage HIV disease and AIDS was used and implemented as a Monte Carlo simulation.

Outcomes assessed in the review
The outcomes assessed were the monthly transition probabilities for primary infection, relapse infections and acute infection survival.
Study designs and other criteria for inclusion in the review
No specific study designs were stipulated by the authors as inclusion criteria.

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
7 primary studies were used in the review.

Methods of combining primary studies
Narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
The monthly transition probability for (primary infection) cytomegalovirus were 0.0580% (high CD4 counts), 0.2140% (medium CD4 counts), 0.5230% (low CD4 counts) and 1.8570% (very low CD4 counts). The monthly transition-probabilities for cytomegalovirus were 5% and 89.47% for relapse infections and acute infection survival, respectively.

Methods used to derive estimates of effectiveness
A questionnaire was used to derive quality of life measures.

Estimates of effectiveness and key assumptions
The quality of life for patients with no prior infections and CD4 counts in excess of 200/mm3 was estimated to be 0.82 (very good) and for patients with CD4 counts below 50/mm3 was 0.62 (good). The average rating-scale scores were converted to average time-trade-off (TTO) values. The TTO estimate for the health state for no prior infections and CD4 counts in excess of 200/mm3 was estimated to be 0.94 (nearly excellent) and for CD4 <50/mm3 state was 0.79 (very good).

Measure of benefits used in the economic analysis
The measure of benefits was quality-adjusted months of life expectancy. A 30-item questionnaire (MOS-HIV) was used to elicit quality of life scores from patients taking part in 3 clinical trials.

Direct costs
Resource consumption costs were included in the analysis. The quantities were reported separately from the prices (in the appendix). The analysis was carried out from the societal perspective. A discount rate of 3% was applied to all outcomes (clinical and economic). The price year was 1995.
Sensitivity analysis
A one-way sensitivity analysis was performed on economic costs, drug efficacy, incidence of infections and patient assessment of quality of life.

Estimated benefits used in the economic analysis
Ganciclovir prophylaxis confers an additional 0.7 quality-adjusted month of life.

Cost results
The ganciclovir prophylaxis confers an additional quality-adjusted month of life at a net cost of $10,700.

Synthesis of costs and benefits
The incremental cost-effectiveness ratio was $173,000 per quality-adjusted life year (QALY) gained. Sensitivity analysis reveals that this baseline result is stable over a wide range of input data estimates including quality of life and drug efficacy but it is sensitive to CMV incidence and drug price assumptions. Specifically, a costless drug produces a small net cost saving while, at a price of $500 per year, the cost per additional QALY is roughly $63,000. When the factor representing an across-the-board reduction of 50% in CMV incidence, by which the risk of infection is multiplied, assumes values of 1.0, 2.0 or 3.0, the baseline result becomes $173,000, $112,000 and $87,000 per QALY, respectively.

Authors’ conclusions
Compared with alternative interventions, CMV prophylaxis does not appear to be a cost-effective use of scarce HIV clinical care funds. However, targeted prevention in patients identified to be at higher risk for CMV-related disease may warrant consideration.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear. CMV infection is a serious condition detectable in over 50% of patients in the latter stages of HIV illness and which has been found in roughly 90% of AIDS patients at autopsy. It has been suggested that the risk of primary CMV infection may be reduced with oral ganciclovir or valacyclovir prophylaxis. 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 systematic review of the literature was undertaken in determining baseline data within the limitation of a modelled solution. The data have not been used selectively.

Validity of estimate of costs
Resource quantities were reported separately from the prices. Adequate details of methods of quantity/cost estimation were given. Important cost items do not seem 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 or countries was not addressed. However, appropriate comparisons were made with other studies in terms of cost-effectiveness of alternative prophylaxis. Results do not appear to have been presented selectively.

Implications of the study
Further research is required to introduce more than a single parameter to measure the impact of prophylaxis and to include some important developments in the science and art of HIV patient care such as the emergence of combination antiviral therapy as the standard of care or the use of HIV viral load as an independent predictor of prognosis.

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