The cost effectiveness of combination antiretroviral therapy for HIV disease

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
Combination antiretroviral therapy for HIV disease.

Type of intervention
Treatment.

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

Study population
The study population consisted of a hypothetical cohort of 1 million patients infected with HIV.

Setting
The setting was Hospital. The economic study was conducted in the USA.

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1993 and 2000. Cost data were taken from sources relating to 1994-1998. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a literature review.

Modelling
A simulation model was used to determine the cost-effectiveness of antiretroviral therapies. A random effects model was used to estimate missing CD4 cell counts at the time of an opportunistic infection or death.

Outcomes assessed in the review
The review assessed monthly probabilities of clinical events, the development of opportunistic infections, adverse reactions to medications, and death.

Study designs and other criteria for inclusion in the review
Three large randomised trials and one cohort study were included in the review.

Sources searched to identify primary studies
Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Summary statistics from individual studies were used.

Number of primary studies included
At least 17 primary studies were included in the review.

Methods of combining primary studies
The narrative method was used to combine studies.

Investigation of differences between primary studies
Not stated.

Results of the review
The initial mean CD4 cell count ranged from 217 to 377 per cubic millimetre. The rate of HIV RNA suppression was 44% at 24 weeks. The rate of viral suppression at 52 weeks was 53% in the three-drug group. The rate of viral suppression at 48 weeks ranged from 48% to 70%. The mean monthly decline in the CD4 cell count ranged from 6.375 to 3.025 cells per cubic millimetre.

The probability of pneumocystis carinii pneumonia (PCP) ranged from 0.037 to 0.00041. The probability of mycobacterium avium complex (MAC) ranged from 0.0122 to 0.000059. The probability of toxoplasmosis ranged from 0.0027 to 0.000029. The probability of cytomegalovirus ranged from 0.01857 to 0.000059. The probability of fungal infection ranged from 0.01123 to 0.000088. The probability of other infections ranged from 0.003940 to 0.000470.

The efficacy of prophylaxis against PCP and MAC infections was 97.32% and 63.35%, respectively. Immunologic efficacy of regenerated CD4 cells was similar to that of the cells that predated the HIV-associated decline in the CD4 cell count.

Antiretroviral therapy ceased to confer benefits after two years.

Measure of benefits used in the economic analysis
Life years and quality-adjusted life years (QALYs) were used as the measures of benefit. Quality of life estimates were derived from a questionnaire item about overall health status used in several AIDS Clinical Trials Group studies. Patients' responses were converted to quality of life scores by the method of Torrance. Benefits were discounted at an annual rate of 3%.

Direct costs
Direct costs were discounted at an annual rate of 3% (time horizon greater than one year). Quantities and costs were reported separately. Direct costs included costs of treatment for acute illnesses and of routine medical care, costs for CD4 cell counts and HIV RNA tests, and drug costs. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Costs and quantities were obtained from the AIDS Cost and Services Utilization Survey, the Payment Office at Boston Medical Center, and the Red Book. Charges were converted into costs using a national cost-to-charge ratio. Costs were converted to 1998 values using the medical-care
component of the Consumer Price Index.

**Statistical analysis of costs**
The authors provided estimates of total lifetime costs.

**Indirect Costs**
Indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were conducted using reasonable variations of cost estimates, initial CD4 cell count, initiation of treatment at higher CD4 cell counts, duration of efficacy and toxicity of first-line therapy, and chronic toxic effects.

**Estimated benefits used in the economic analysis**
Life expectancy for a patient receiving no antiretroviral therapy was 1.97 years or 1.53 QALYs. Life expectancy for a patient receiving three-drug antiretroviral therapy was 3.51 years or 2.91 QALYs.

**Cost results**
Total lifetime costs were $45,460 for a patient receiving no antiretroviral therapy and $77,300 for a patient receiving three-drug antiretroviral therapy.

**Synthesis of costs and benefits**
The incremental cost per QALY of three-drug versus no antiretroviral therapy ranged from $13,000 to $23,000. Two-drug therapy was superior to no therapy but less cost-effective than three-drug therapy. Therapy initiated when the CD4 cell count was 500 per cubic millimetre had cost-effectiveness ranging from $11,000 to $15,000 per QALY. The cost-effectiveness ratio of three-drug therapy was sensitive to the cost of antiretroviral drugs.

**Authors’ conclusions**
Treatment of HIV infection with a combination of three antiretroviral drugs is a cost-effective use of resources.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparators used namely no therapy. You, as a user of the database, should decide if these health technologies are relevant to your setting.

**Validity of estimate of measure of effectiveness**
The authors undertook a literature review to derive estimates for the model which seemed appropriate, although they did not state that a systematic review of the literature had been undertaken. More information about the methods of the review could have been provided. The validity of the results was, however, enhanced by sensitivity analyses to account for variability in the estimates over plausible ranges. The authors noted that the rate of adherence to the treatment regimen might be lower, and the rates of viral resistance and drug toxicity higher, in other populations of patients.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis. Estimation of QALYs was modelled. The instrument used to derive benefits, the method of Torrance, was appropriate. By including QALYs as one of their benefit measures, the authors have enhanced the comparability of the intervention with respect to those in other clinical domains.

**Validity of estimate of costs**

Good features of the cost analysis were that all relevant direct cost categories were included, quantities and costs were reported separately, the price year was reported, and charges were converted to costs. The validity of the cost results was further enhanced by appropriate sensitivity analyses over reasonable ranges. The authors did not include indirect costs, such as lost wages arising from time spent obtaining care, which would be relevant if the perspective of interest was that of society.

**Other issues**

This was a methodologically sound and comprehensive economic evaluation using modelling techniques. The authors did make appropriate comparisons of their findings with those from other studies and the issue of generalisability to other settings was addressed. The authors did not present their results selectively. The study considered HIV-infected patients and this was reflected in the authors’ conclusions.

**Implications of the study**

The authors’ findings suggest that three-drug antiretroviral therapy is highly cost-effective and should be made available to all patients who can benefit from it. As the intervention was both more costly and more effective, however, this statement should be viewed within the context of a decision-maker's willingness to pay threshold. Better data on the long-term effects and toxicity of combination antiretroviral therapy, the costs of routine care with current regimens, and the effects of interventions designed to improve adherence to the regimens and decrease the rate of treatment failure, are needed.

**Source of funding**

Supported in part by grants from the National Institute of Allergy and Infectious Diseases (R01-AI42006) and the Centers for Disease Control and Prevention (U64/CCU 114927) to the Cost-Effectiveness of Preventing AIDS Complications project, and by a grant from the Adult AIDS Clinical Trials Group (UO1 AI38838). Dr Cohen has been a paid consultant to Glaxo Wellcome and Roche.

**Bibliographic details**


**PubMedID**

11248160

**DOI**

10.1056/NEJM200103153441108

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

AIDS-Related Opportunistic Infections /economics /prevention & control; Anti-HIV Agents /economics /therapeutic use; CD4 Lymphocyte Count; Computer Simulation; Cost-Benefit Analysis; Direct Service Costs /statistics & numerical data; Disease Progression; Drug Costs /statistics & numerical data; Drug Therapy, Combination; HIV
Infections /drug therapy /economics; Health Care Costs /statistics & numerical data; Humans; Life Expectancy; Models, Biological; Quality-Adjusted Life Years; RNA, Viral /blood; United States; Value of Life

AccessionNumber
22001008051

Date bibliographic record published
31/10/2001

Date abstract record published
31/10/2001