Projecting the cost-effectiveness of adherence interventions in persons with human immunodeficiency virus 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
Interventions aimed at promoting adherence to combination therapy in persons with human immunodeficiency virus (HIV) infection were under evaluation. The interventions included beeper, counselling and directly observed therapy.

Type of intervention
Other: treatment adherence programme.

Economic study type
Cost-utility analysis.

Study population
Three different hypothetical study populations were considered. The first was a cohort of patients with a mean CD4 count of 350 cells/L and a median log10 HIV RNA of 4.8 (cohort with early disease). The second was a cohort of patients with a mean CD4 count of 87 cells/L and a median log10 HIV RNA of 5.0 (cohort with late disease). The third was a cohort of patients with a mean CD4 count of 217 cells/L and a median log10 HIV RNA of 4.6 (urban cohort).

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

Dates to which data relate
The effectiveness data were derived from studies published between 1993 and 2001. The dates relating to resource use were unclear. The price year was not reported.

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

Modelling
A computer-based mathematical model of HIV infection was used to simulate the impact of different adherence interventions on (quality-adjusted) survival and the lifetime costs in a hypothetical cohort of patients with HIV infection. This was a state-transition model in which the patients moved across the health states at monthly intervals. The model was constructed on a first-order, Monte Carlo simulation, which was repeated until the cohort of one million patients had passed through the model. The health states were descriptive of the patient’s health. The health states considered were HIV RNA levels, CD4 lymphocyte count, opportunistic infections, antiretroviral therapy, and prophylaxis against opportunistic infections. The patients could die of an acute clinical event, chronic acquired immunodeficiency syndrome (AIDS), or non-HIV-related causes. The patients received up to four antiretroviral
regimens and every 3 months stable patients were tested. Other treatment and testing decisions were made on the basis of national guidelines. Details of the model had been published.

Outcomes assessed in the review
The outcomes estimated from the literature were:

- the rate of initial HIV RNA,
- the mean monthly CD4 cell decline,
- the rate of monthly risk of opportunistic infections, and
- the efficacy of prophylaxis against opportunistic infections.

Study designs and other criteria for inclusion in the review
It was unclear whether a review of the literature was carried out. The design of the primary studies was not reported.

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
Thirteen primary studies were used in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The rate of initial HIV RNA was 36.2% for >100,000 copies/mL, 31.3% for 30,001 to 100,000 copies/mL, 20.7% for 10,001 to 30,000 copies/mL, 9.5% for 3,001 to 10,000 copies/mL, 2.2% for 501 to 3,000 copies/mL, and 0.1% for 0 to 500 copies/mL.

The mean monthly CD4 cell decline (in cell/microL) was 6.375 for >30,000 copies/mL, 5.400 for 10,001 to 30,000 copies/mL, 4.600 for 3,001 to 10,000 copies/mL, 3.733 for 501 to 3,000 copies/mL, and 3.025 for 0 to 500 copies/mL.

The rate of monthly risk of opportunistic infections was reported for Pneumocystis carinii pneumonia, Mycobacterium avium complex, toxoplasmosis, cytomegalovirus, and fungal infection by CD4 stratum.

The efficacy of prophylaxis against opportunistic infections (i.e. percentage of decrease in incidence) was 97.32%.
(range: 94 - 98) with trimethoprim-sulfamethoxazole (against Pneumocystis carinii pneumonia), 87.20% (range: 81 - 91) with dapsone (against Pneumocystis carinii pneumonia) and 63.60% (range: 58 - 66) with azithromycin (against Mycobacterium avium complex).

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

The summary benefit measure was the quality-adjusted life-years (QALYs). Mortality data were estimated from US life tables. Utility weights were derived from a published study (data not reported), which used the Short-Form 6D health state classification for HIV individuals. The QALYs were discounted at an annual rate of 3%.

**Direct costs**

The lifetime costs were discounted at an annual rate of 3%. The unit costs were not presented separately from the quantities of resources used. A microcosting approach was used to identify the relevant costs, but not all the cost items were reported. The categories of costs considered were the monthly costs of chronic medical care for HIV patients, costs associated with death (depending on the cause), prophylaxis against opportunistic infections, antiretroviral therapy, diagnostic tests and adherence interventions. The perspective adopted was not reported. Both the unit costs and resources used were estimated from published studies. The price year was not reported.

**Statistical analysis of costs**

Statistical analyses of the costs were not performed.

**Indirect Costs**

The indirect costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

Sensitivity analyses were carried out to test the robustness of the estimated cost-effectiveness ratios to variations in several model inputs. The ranges over which the model inputs were varied were derived from the literature or authors' assumptions. The type of analysis was not reported.

**Estimated benefits used in the economic analysis**

In the cohort with early disease, the expected quality-adjusted life expectancy was 116.4 months with no intervention, and from 119.6 to 153.9 months with the intervention. More specifically, 119.6 months with an adherence programme with 10% reduction in failure rate (AP10), 123.4 months with 20% reduction (AP20), 131.4 months with 40% reduction (AP40), 141.6 months with 60% reduction, 151.2 months with 80% reduction (AP80), and 153.9 months with 100% reduction (AP100).

In the cohort with late disease, the expected quality-adjusted life expectancy was 55.5 months with no intervention, 58.1 months with AP10, 61.0 months with AP20, 68.4 months with AP40, 79.2 months with AP60, 98.2 months with AP80, and 128.9 months with AP100.

In the urban cohort, there were 73.80 quality-adjusted life-months in the absence of the intervention. The quality-adjusted life expectancy ranged from 9.8 months with AP20 to 33.4 months with AP80.

**Cost results**

In the cohort with early disease, assuming a monthly cost of $100 for the intervention, the expected lifetime costs were
$132,600 with no intervention, $144,300 with AP10, $151,600 with AP20, $169,200 with AP40, $196,600 with AP60, $238,900 with AP80, and $260,500 with AP100.

In the cohort with late disease, assuming a monthly cost of $100 for the intervention, the expected lifetime costs were $91,500 with no intervention, $98,200 with AP10, $102,900 with AP20, $115,600 with AP40, $136,300 with AP60, $180,200 with AP80, and $253,900 with AP100.

The costs increased under the assumption of a more costly intervention.

The costs in the urban cohort were not reported.

**Synthesis of costs and benefits**

In the cohort with early disease, the incremental cost per QALY (compared with the next least costly strategy) when assuming a monthly cost of $100 for the intervention was $40,300 with AP10, $30,100 with AP20, $27,100 with AP40, $28,200 with AP60, $33,900 with AP80, and $40,900 with AP100.

In the cohort with late disease, the incremental cost per QALY (compared with the next least costly strategy) when assuming a monthly cost of $100 for the intervention was $31,000 with AP10, $25,100 with AP20, $22,400 with AP40, $22,700 with AP60, $25,000 with AP80, and $26,600 with AP100.

The cost-effectiveness ratios became less favourable when more costly interventions were used and very high efficacy rates were required for the cost per QALY to be below the benchmark value of $50,000.

In the urban cohort, even very expensive interventions were cost-effective (cost-effectiveness ratio below $50,000).

These conclusions remained stable over a wide range of variations explored in the sensitivity analysis.

**Authors’ conclusions**

The implementation of an adherence programme for human immunodeficiency virus (HIV) patients receiving antiretroviral therapy was effective in improving quality-adjusted survival. However, the cost of the programme represented a key variable. An acceptable cost-effectiveness ratio was obtained among patients with advanced disease and those with low levels of baseline adherence.

**CRD COMMENTARY - Selection of comparators**

The basic comparator was the strategy of no intervention, which represented the usual approach offered to most HIV patients. The interventions considered in the adherence programme were not described. You should decide whether they represent valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The measure of effectiveness was derived using data coming from the literature. However, details of the methods used to identify primary studies, select and combine relevant estimates, and ensure the validity of the sources used, were not reported. Therefore, it is difficult to estimate the validity of the effectiveness measure.

**Validity of estimate of measure of benefit**

The authors used QALYs as the summary benefit measure. This choice was appropriate since the interventions under examination had an impact on both the length and quality of life. The quality of life adjustments were derived from an earlier study. The benefits were discounted.

**Validity of estimate of costs**

The authors stated that a societal perspective was adopted, but the indirect costs were not included. The unit costs,
quantities of resources used, price year and source of resource use data were not reported. Most of the data were estimated from published studies. Sensitivity analyses were performed on economic inputs, which were varied within reasonable ranges. However, statistical tests were not carried out on the costs.

**Other issues**
The authors did not compare their results with other economic evaluations. To increase the generalisability of the study results to other settings, three different target populations were considered. Sensitivity analyses were also performed. A state-transition model was used to estimate the long-term costs and benefits of the adherence programme. Most details of the model had been published elsewhere. The authors reported some of the limitations of the study. In particular, it was stated that several conservative assumptions were made, presumably among the data extracted from the literature.

**Implications of the study**
Interventions that aimed to improve adherence to antiretroviral therapy and to reduce failure rate by 10 to 20% were cost-effective in HIV patients with low baseline adherence levels.

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