Assessing the cost-effectiveness of HAART for adults with HIV in England

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
The study examined highly active antiretroviral therapy (HAART). Specific details of the therapy were not reported.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The target study population comprised adults (aged 18 years at the time of entering the model) in England who were infected with the HIV.

Setting
The setting was tertiary care (HIV treatment centres in England). The economic study was carried out in the UK.

Dates to which data relate
The effectiveness evidence was collected between March 1992 and December 1998 and between October 1994 and March 1999. The costs were estimated between January and June 1997 and were reported in 1999/2000 prices.

Source of effectiveness data
The effectiveness data were derived from a single study with two patient cohorts and some authors' assumptions.

Link between effectiveness and cost data
The costing was carried out retrospectively on a different sample of patients to that used in the effectiveness study.

Study sample
The authors did not report whether power calculations were carried out to estimate the influence of chance on the results. The initial sample for the antiretroviral naïve alternative was selected by including patients who started treatment with either two NRTIs or with two NRTIs plus at least one protease inhibitor (PI) or non-NRTI. The patients also had to have CD4 counts of less than 500 cells/microL in the 6 months before starting treatment. This group comprised 172 individuals who started treatment between March 1992 and December 1998. The initial sample for the HAART alternative was selected by including 243 individuals who started antiretroviral treatment with at least three drugs (including at least one PI or non-NRTI) between October 1994 and March 1999. These initial samples were appropriate for the clinical questions as they included patients suffering from AIDS who began relevant treatments.
Study design
The basis of the study was a cohort design, with the cohorts determined by exposure to one of the treatments of interest. Data from the cohorts were then included in the Markov model. The authors reported that the study was set in multiple English HIV treatment centres, but specific details of each centre were not reported. The follow-up for the NRTI patients ended at death, or when the patient started treatment with a PI or non-NRTI. For HAART patients, the follow-up ended at the time of the last visit or death. No loss to follow-up was reported.

Analysis of effectiveness
The analysis was based on the treatment received. The primary health outcomes were the risk of death and the risk of progression between AIDS-related states. These variables entered the model as transition probabilities. A distinction was made between events in year one and later years, as initial responses to treatment were expected to differ from longer run responses. The authors did not report summary statistics of the individuals in the two treatment groups, or make any statements concerning their comparability.

Effectiveness results
For dual NRTI in year one, the annual transition probability from a CD4 count of at least 200 cells/microL was 0.15 to a CD4 count of less than 200 cells/microL, 0.05 to AIDS and 0 to death.

For dual NRTI in subsequent years:
from a CD4 count of at least 200 cells/microL, the annual transition probability was 0.16 to a CD4 count of less than 200 cells/microL, 0.04 to AIDS and 0.04 to death;
from a CD4 count of less than 200 cells/microL, the annual transition probability was 0.11 to a CD4 count of at least 200 cells/microL, 0.11 to AIDS and 0.05 to death; and
from AIDS, the annual transition probability was 0.13 to a CD4 count of at least 200 cells/microL, 0.50 to a CD4 count of less than 200 cells/microL and 0.25 to death.

For HAART in year one, the annual transition probability from a CD4 count of at least 200 cells/microL was 0.02 to a CD4 count of less than 200 cells/microL, 0.01 to AIDS and 0 to death.

For HAART in subsequent years:
from a CD4 count of at least 200 cells/microL, the annual transition probability was 0.05 to a CD4 count of less than 200 cells/microL, 0.02 to AIDS and 0 to death;
from a CD4 count of less than 200 cells/microL, the annual transition probability was 0.43 to a CD4 count of at least 200 cells/microL, 0 to AIDS and 0.03 to death; and
from AIDS, the annual transition probability was 0 to a CD4 count of at least 200 cells/microL, 0.49 to a CD4 count of less than 200 cells/microL and 0.5 to death.

In each case, the transition probability of remaining in the same health state was the residual probability.

Clinical conclusions
The authors did not draw clinical conclusions independently from the cost conclusions. The transition probabilities indicated that HAART reduced the likelihood of progressing to worse AIDS-related health states.

Modelling
A Markov model with 20 one-year periods was used to simulate four acquired immune deficiency syndrome (AIDS)-related disease states. More specifically, CD4 count of at least 200 cells/microL and no AIDS, CD4 count of
less than 200 cells/microL and no AIDS, AIDS, and death. The model used hypothetical cohorts of 1,000 individuals. It was used to estimate the cost, effects and cost-effectiveness of the treatment options.

Methods used to derive estimates of effectiveness
The effectiveness estimates were supplemented by authors’ assumptions.

Estimates of effectiveness and key assumptions
For the purposes of the analysis, the authors assumed that individuals who died during follow-up died due to an HIV-related event.

Measure of benefits used in the economic analysis
The summary measures of benefit used were the quality-adjusted life-years (QALYs) and the life-years. To derive the utility weights for the QALYs, Health Utilities Index mark II utility weights were used from a study of 203 members of the Canadian general population. The participants completed visual analogue scales and these were transformed into standard gamble values to give an estimate of the QALYs (see Other Publications of Related Interest).

Direct costs
Costing was carried out from the perspective of UK public finance. The baseline analysis discounted costs at a rate of 6%. The annual per patient costs were based on estimates derived from the National Prospective Monitoring System - HIV Health Economics Consortium study. This study estimated health care resource requirements of patients with HIV across nine treatment centres in England. It was not clear what elements of costs were included in these estimates, although the authors reported that the estimates included opportunistic infections. Resource use was linked to unit costs from a further study. Therefore, the costing was calculated from actual data in published sources. The authors assumed that the incremental costs of treating people with HAART, compared with NRTIs, was the cost of the third drug. The costs and the quantities were not reported separately, although this breakdown can presumably be viewed in the source studies. The costs were measured from January to June 1997 and were inflated to 1999/2000 prices.

Statistical analysis of costs
The authors reported 95% confidence intervals (CIs) for the costs.

Indirect Costs
The authors did not report that the indirect costs were estimated.

Currency
UK pounds sterling (£).

Sensitivity analysis
A one-way sensitivity analysis was carried out to assess the importance of the additional cost of the third drug in determining the cost-effectiveness.

Estimated benefits used in the economic analysis
Life expectancy was 11.6 years with dual NRTI and 14.5 years with HAART.

The QALYs were 9.3 with dual NRTI and 11.7 with HAART.
Cost results
The annual costs per patient were 8,743 (95% CI: 7,815 - 9,905) for a CD4 count of 200 cells/microL, 9,597 (95% CI: 8,479 - 10,695) for a CD4 count of less than 200 cells/microL, 19,139 (95% CI: 16,941 - 21,294) for AIDS and 0 for death.

The total discounted costs of treatment per patient were 77,135 with dual NRTI and 119,190 with HAART.

Synthesis of costs and benefits
For HAART compared with dual NRTI, the incremental cost per life-year gained was 14,602 and the incremental cost per QALY was 17,698. The sensitivity analysis showed that the incremental cost-effectiveness ratio was very sensitive to the discount rate and the duration of the cost of the additional third drug.

Authors' conclusions
Compared with two nucleoside reverse transcriptase inhibitors (NRTIs), highly active antiretroviral therapy (HAART) was, at the very least, a moderately cost-effective method for treating individuals infected with human immunodeficiency virus (HIV).

CRD COMMENTARY - Selection of comparators
The authors chose to compare HAART with NRTI. HAART was assessed due to the authors' concern that HAART was in widespread use despite the lack of a cost-effectiveness analysis. Although the reasons for using NRTI as a comparator were not explicitly stated, it seems that NRTI has been used since it was a component of HAART. HAART was standard practice in the authors' setting at the time of the study.

Validity of estimate of measure of effectiveness
The basis of the analysis was a cohort study with cohorts from different time periods. A randomised study with treatment groups at the same point in time would have improved the internal validity of the study. However, the authors seemed to be making use of evidence already available. The cohort analysis presented an excellent basis for comparison purposes and for highlighting further work. Further, if HAART is accepted as standard practice and NRTI is no longer used, it may be deemed unethical to then randomise patients to what is seen as a less effective treatment, irrespective of the cost-effectiveness. The study sample was representative of the study population. The patient groups were not compared at baseline, thus it is unclear whether differences in the results between the groups were due to differences in the treatment received or due to differences between the groups. This factor significantly reduces the internal validity of the results. The assumptions made were well justified and their implications were discussed.

Validity of estimate of measure of benefit
The estimation of benefits was modelled using QALY data taken from a published study that used responses from a Canadian HIV infected population. The authors used the Canadian study as they felt this data were the most suitable. They also highlighted the lack of utility weights for individuals infected with HIV. This method allows comparisons of cost-effectiveness on a broad basis.

Validity of estimate of costs
The costs were estimated from the perspective of UK public finance. The authors provided very few details of the cost estimates, thus making it impossible to comment on the quality of these estimates. Providing greater detail would have significantly increased the quality of the study itself, as this would have enabled future readers to assess whether the results would be transferable to their own setting. This is especially true since the authors appropriately stated the price year and perspective of the study, and indicated that discounting was used.

Other issues
The authors made appropriate comparisons of their results with those from other studies by reporting published cost-effectiveness results. The authors did not present their results selectively. They also gave a thorough discussion of the impact of their sensitivity analyses without presenting detailed tabulated results. The issue of generalisability to other settings was not discussed. However, the authors’ conclusions accurately reflected the scope of the analysis. Several limitations were presented that centred on the assumptions made. For example, the 5-year treatment effect for HAART and changes in CD4 count being exclusively due to treatment. The authors also considered the implications of relaxing these assumptions.

**Implications of the study**
The authors suggested that the use of HAART for adults should be recommended on economic grounds. Further work was explicitly discussed. This focused on addressing the limitations of the current study, as well as acquiring longer-term data on the relative effectiveness of HAART.

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**Bibliographic details**

**Medline ID**
11737376

**Other publications of related interest**
Reisbrough N, Oh P, McMurchy D, Bast M, Dowsell M. Economic evaluation of triple ART with indinavir or abacivir and ZDV+3TC compared to dual therapy ZDV+3TC. 6th Conference on Retroviruses and Opportunistic Infections; 1999, Jan 31-Feb 4, Chicago (IL), USA.

**Indexing Status**
Subject indexing assigned by NLM

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