Economic analysis of initial HIV treatment: efavirenz- versus indinavir-containing triple therapy
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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 comparison of triple therapy with zidovudine, lamivudine and either 600 mg efavirenz once daily or 800 mg indinavir every 8 hours, for the treatment of human immunodeficiency virus (HIV).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of HIV-positive people with limited exposure to nucleoside reverse transcriptase inhibitors. The average time since diagnosis was 3.2 years.

Setting
The setting involved secondary and community care of HIV-positive patients. The economic study was carried out in the USA.

Dates to which data relate

Source of effectiveness data
The effectiveness data were derived from a synthesis of published studies, and one unpublished study.

Modelling
The authors designed a 5-state Markov model. This used a Monte Carlo simulation to estimate the clinical and economic outcomes for up to 15 years from the initiation of treatment. Progression from one state to another was based on viral load levels and CD4+ cell counts.

Outcomes assessed in the review
The outcomes assessed were:
the proportions of patients in each study arm responding to first-line and second-line treatment;
the probability of treatment failure after initial response, second and third-line treatments; 

the rate of progression to acquired immune deficiency syndrome (AIDS) following treatment failure; and 

the rate of AIDS-related death.

**Study designs and other criteria for inclusion in the review**
The short-term viral load data were obtained from a randomised clinical trial. The probabilities of treatment failure after initial success were derived from data supplied by a commercial partner. The other data were obtained from published studies, no details of which were provided.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Eleven primary studies were included in the review.

**Methods of combining primary studies**
The authors appear to have used only one source per baseline parameter estimate. Thus, there was no need to combine the results of the separate studies.

**Investigation of differences between primary studies**
The authors discussed differences between the primary studies briefly.

**Results of the review**
The initial response rate of patients on efavirenz-containing triple therapy was 75.3%.

The initial response rate of patients on indinavir-containing triple therapy was 54.7%.

The response rate was 67.9% on second-line therapy and 27.0% on third-line therapy.

The probability of viral rebound was 39.6% on second-line therapy and 75.8% on third-line therapy.

**Methods used to derive estimates of effectiveness**
The authors made assumptions about some of the parameters used in the model.

**Estimates of effectiveness and key assumptions**
Three main assumptions were made. First, that reversion from the AIDS state is not possible. Second, that patients can switch regimens up to two times. Third, that an undetectable viral load implies an interruption of the progression from
HIV to AIDS.

Measure of benefits used in the economic analysis
The summary benefit measure was survival.

Direct costs
The costs considered were relevant to a health service or health-care payer. These covered the costs of acute inpatient, emergency room, nursing home, home health, outpatient care, counselling, social services, drug therapy and viral load monitoring. The resource use quantities were not reported separately. The costs associated with side effects (such as nausea and headaches) were excluded from the analysis but were thought to be low.

The cost data for the inpatient acute care were derived from the databases of six American states and related to 1996 and 1997. The drug costs were derived from average wholesale prices published in 1998. Other resource use data were derived from studies and national sources published between 1991 and 1999. Other price data related to 1998.

The costs incurred beyond one year were discounted at a baseline rate of 3%. The authors have translated the charges to costs where necessary, but did not report the conversion ratio. All of the costs were reported in 1998 dollars, and were adjusted for inflation using a medical prices index.

Indirect Costs
The indirect costs were not included in this analysis.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were carried out on some of the effectiveness and cost parameters. These analyses investigated the impact of the extrapolation of primary data used in the model, and the generalisability of the results across patient subgroups. In addition to varying the parameters listed in the 'Results of the Review' section, the drug acquisition costs and the discount rate were also varied. The authors suggested that both one- and multi-way sensitivity analyses were carried out, but did not specify which combinations they used. In some cases, the ranges over which the variables were tested were derived from the literature.

Estimated benefits used in the economic analysis
The model estimated that 11.0% more patients on the efavirenz-containing regimen would be alive at 5 years, compared with those on the indinavir-containing regimen.

Cost results
The total costs of the interventions were not stated precisely but were presented graphically in the article. The efavirenz option was estimated to cost $2,696 ($2,672, discounted at 3%) less than the indinavir option at the end of the first year. The estimated savings were $7,706 ($7,436) at 3 years and $10,923 ($10,326) at 5 years.

Synthesis of costs and benefits
Since the efavirenz-containing regimen was shown to be both cost-saving and better from a survival point of view, the costs and the benefits were not formally combined. This dominance of efavirenz was shown to hold over reasonable ranges of the parameters varied in the sensitivity analysis.
Authors’ conclusions
According to the authors' model, the short-term clinical benefits of efavirenz-containing triple therapy will lead to economic and survival benefits for approximately a decade after the initiation of therapy.

CRD COMMENTARY - Selection of comparators
Although not explicitly stated, the authors suggested that the indinavir-containing triple therapy (with zidovudine and lamivudine) has been the widely used option for the initial treatment of HIV. You should compare this with the current treatment in your own settings.

Validity of estimate of measure of effectiveness
The structure of the model was well described and could be adapted to other settings. However, there were few details of the review of the literature, which was undertaken to populate the model. The authors did not state that a systematic review was performed.

Validity of estimate of measure of benefit
The model estimated survival as the measure of benefit. While this is an appropriate measure, it does not capture the quality of life implications of the two treatment alternatives.

Validity of estimate of costs
The cost analysis included all the relevant categories of costs. The resource use quantities were not reported in this article but may have been described in the primary sources. The authors converted the charges to costs where appropriate, although they did not state the method they used. Only the drug acquisition costs were subjected to the sensitivity analysis. It would have been useful to have seen if the study’s findings were robust to changes in the costs of other items.

Other issues
This study's main strength is that it acknowledged the need for a long-term perspective in estimating the costs associated with triple therapy. This is important because successful treatment means that patients survive longer, and thus incur high drug costs for a longer period of time. This study aimed to weigh these costs against the reduced need for acute care in patients who are less ill on the triple therapies.

The authors discussed their contribution to the cost-effectiveness literature in this treatment area. They explained that other studies have used shorter term, or simpler models, or have addressed different treatment questions.

The authors mentioned, as a possible limitation of their study, the fact that the AIDS progression rates were derived from a more specific patient population than that considered in this study. However, they speculated that likely errors would not adversely affect their conclusion.

Implications of the study
The authors suggest that the adoption of efavirenz-containing triple therapy should continue as it is predicted to be both cost-saving and life-extending.

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