Clinical impact and cost-effectiveness of antiretroviral therapy in India: starting criteria and second-line therapy

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.

CRD summary
The study assessed the cost-effectiveness of different strategies for starting and stopping first- and second-line antiretroviral therapy (ART) in people infected with the human immunodeficiency virus (HIV). The authors concluded that first-line ART was a cost-effective strategy, while second-line therapy increased survival but its cost-effectiveness depended on the relative cost of therapy compared with first-line regimens. The quality of the study methodology was satisfactory, and the authors’ conclusions appear valid and are enhanced by the extensive use of sensitivity analysis.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of different strategies for starting and stopping first- and second-line antiretroviral therapy (ART) in people infected with the human immunodeficiency virus (HIV).

Interventions
The starting/stopping strategy depended on the CD4 cell count. Three thresholds were considered: CD4 count <200, <250 or <350 cells/μL. For the first-line therapy, the study considered a combination of non-nucleoside reverse transcriptase inhibitor (nevirapine) and nucleoside reverse transcriptase inhibitors (stavudine and lamivudine), as recommended by the Indian National AIDS Control Organization and the World Health Organization (WHO). The second-line therapy consisted of ritonavir-boosted indinavir, and didanosine and lamivudine. The use of co-trimoxazole for prophylaxis was also considered.

Location/setting
India/primary care.

Methods
Analytical approach:
This economic evaluation was based on an international state-transition model of HIV disease (Cost-effectiveness of Preventing AIDS Complications). A lifetime horizon was considered. The authors did not explicitly state the perspective adopted in the study.

Effectiveness data:
The clinical data were derived from a selection of known, relevant studies. For example, the baseline characteristics of the hypothetical cohort of patients were derived from a cohort of 6,918 patients treated at an acquired immune deficiency syndrome (AIDS) research centre in Chennai (India) from 1996 to 2005. This source was also used to derive the incidence of opportunistic infections and disease progression in the absence of ART. The effectiveness of ART was based on data derived from randomised clinical trials (RCTs). Given the lack of Indian data, AIDS-related mortality was taken from the placebo arm of an RCT performed in Cote d’Ivoire, while age- and gender-adjusted mortality for other causes was obtained from Indian life tables. The key clinical outcome was the treatment effect on increase in CD4 count.

Monetary benefit and utility valuations:
None.
**Measure of benefit:**
The summary benefit measure was the life-years (LYs). These were estimated using the decision model. An annual discount rate of 3% was applied.

**Cost data:**
The health services included in the analysis were ART (co-trimoxazole prophylaxis and first- and second-line therapy), treatment of drug toxicity, monitoring, treatment of severe opportunistic infection, treatment of chronic care, terminal care, and visits to the hospital or clinic. These costs were derived from published studies. Resource use was mainly gathered from a sample of 1,913 patients treated at the AIDS research centre in Chennai in 2005 and 2006. The costs were in US dollars ($). The price year was 2005. Future costs were discounted at an annual rate of 3%.

**Analysis of uncertainty:**
A one-way sensitivity analysis was carried out on most model inputs to identify the most influential parameters. The sources of alternative values were not explicitly reported. All model inputs not obtained from Indian sources were also investigated.

**Results**
For first-line therapy, the LYs were 34.5 with no therapy, 34.9 with co-trimoxazole prophylaxis alone and 62.4 with ART started at CD4 cell count <200 cells/μL; 63.7 with ART started at CD4 cell count <250 cells/μL; and 64.7 with ART started at CD4 cell count <350 cells/μL. The expected costs were $530 with no therapy, $580 with co-trimoxazole prophylaxis alone and $1,540 with ART started at CD4 cell count <200 cells/μL; $1,580 with ART started at CD4 cell count <250 cells/μL; and $1,630 with ART started at CD4 cell count <350 cells/μL.

The incremental analysis showed that, after excluding dominated strategies (less effective and more costly) or weakly dominated strategies (less cost-effective than the next most effective strategy), the incremental cost per LY gained was $430 with ART started at CD4 cell count <250 cells/μL (over no ART) and $550 with ART started at CD4 cell count <350 cells/μL (over ART started at CD4 cell count <250 cells/μL).

When two lines of ART were available, the LYs were 34.5 with no therapy, 34.9 with co-trimoxazole alone and 84.8 with ART started at CD4 cell count <200 cells/μL; 86.7 with ART started at CD4 cell count <250 cells/μL; and 88.9 with ART started at CD4 cell count <350 cells/μL. The expected costs were $530 with no therapy, $580 with co-trimoxazole alone and $4,980 with ART started at CD4 cell count <200 cells/μL; $5,140 with ART started at CD4 cell count <250 cells/μL; and $5,430 with ART started at CD4 cell count <350 cells/μL.

The incremental analysis showed that, after excluding (weakly) dominated strategies, the incremental cost per LY gained was $1,060 with ART started at CD4 cell count <250 cells/μL over no ART and $1,530 with ART started at CD4 cell count <350 cells/μL over ART started at CD4 cell count <250 cells/μL. When compared with first-line ART only, second-line ART therapies resulted in cost-effectiveness ratios ranging from $1,850 to $1,880 per LY gained.

The sensitivity analysis indicated that the most influential model inputs were the relative efficacy and the cost of second-line ART regimens. The results were also sensitive to the assumption about stopping treatment after immunological failure.

**Authors' conclusions**
The authors concluded that, using the criteria set by the WHO, first-line ART was a cost-effective strategy in India for the treatment of HIV. Second-line therapy increased survival, but the cost-effectiveness of these regimens depended on their relative cost compared with first-line regimens.

**CRD commentary**
**Interventions:**
The selection of the comparators appears to have been appropriate within the authors' setting. However, these therapies might not be relevant for other health care systems, especially in developed countries.

**Effectiveness/benefits:**
The sources of clinical evidence may have been selectively identified since the authors did not report details of a review of the literature. Nevertheless, the selected sources appear to have been appropriate. The use of RCTs to derive treatment effectiveness should have ensured the validity of these estimates, given the robustness of the study design. The use of a longitudinal database was appropriate as it reflects patterns of disease in the authors' setting. Furthermore, the uncertainty surrounding these estimates was investigated in depth in the sensitivity analysis.

Costs:
The authors did not state the perspective used in the study, but only the costs relevant to the health care system appear to have been adopted. The unit costs were reported for some items, but details of resource use consumption were not given. The sources of the costs were not fully described. Resource use was based on the real consumption of health services in a large sample of Indian patients. Other aspects of the analysis, such as the price year and the use of discounting, were reported.

Analysis and results:
The synthesis of the costs and benefits was appropriately presented. The issue of uncertainty was addressed using an extensive deterministic sensitivity analysis that investigated key uncertain areas. The results of both the base-case and the sensitivity analyses were presented clearly and discussed. The authors pointed out some advantages of the study (use of recent data and a validated decision model) as well as some weaknesses (unavailability of Indian data and non-inclusion of economies of scale in the model). It was also highlighted that the results of the study might have been conservative as HIV transmission was not considered in the model.

Concluding remarks:
The quality of the study methodology was satisfactory, and the authors’ conclusions appear valid and are enhanced by the extensive use of sensitivity analysis.

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Bibliographic details

Other publications of related interest


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