Cost-effectiveness of nucleoside reverse transcriptase inhibitor pairs in efavirenz-based regimens for treatment-naive adults with HIV infection in the United States

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CRD summary
The study assessed cost-effectiveness of three first-line treatments for treatment-naive individuals with HIV-1 infection: once-daily tenofovir DF plus emtricitabine (TDF/FTC), twice-daily zidovudine plus lamivudine and once-daily abacavir plus lamivudine, all in combination with efavirenz. The authors concluded that TDF/FTC was likely to improve clinical outcomes at lower cost than the alternative regimens. The study used valid methods that enhanced the robustness of the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The study assessed the cost-effectiveness of three first-line treatments for treatment-naive individuals with HIV-1 infection: once-daily tenofovir DF plus emtricitabine (TDF/FTC), twice-daily zidovudine plus lamivudine (ZDV/3TC) and once-daily abacavir plus lamivudine (ABC/3TC), all in combination with efavirenz.

Interventions
The three first-line regimens under examination were once-daily TDF/FTC, twice daily ZDV/3TC and twice-daily ABC/3TC, all in combination with efavirenz. Subsequent lines were based on USA clinical guidelines.

Location/setting
USA/secondary care.

Methods
Analytical approach:
The analysis was based on a Markov model that considered up to four lines of treatment and was based on CD4+ cell count. A lifetime horizon was considered. A societal perspective was adopted.

Effectiveness data:
MEDLINE and scientific conference abstracts were searched for clinical trials of the three treatments. Four trials were identified. Two trials were excluded, so evidence on efficacy of the treatments was derived from two studies (144-week results and 48-week results) that compared two of the three regimens head-to-head. Neither trial included all three first-line regimens. The trials had comparable virologic efficacy endpoints (time to regimen failure), which allowed for an indirect comparison of TDF/FTC and ABC/3TC. Data for subsequent lines of treatment and transition probabilities were derived from other published sources, which included clinical trials and observational studies. Mortality was obtained from USA life tables.

Monetary benefit and utility valuations:
Utility valuations were derived from a study that used community based preferences.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were the summary benefit measures and were discounted at an annual rate of 3%.
Cost data:
Drug costs were derived from average wholesale prices. Non-drug costs (in-patient, outpatient and emergency department utilisation, additional laboratory tests, resistance assay and a clinician visit) were derived from published USA studies and expert opinions. Costs of treating adverse events were derived from published sources. Costs were in USA dollars. The price year was 2009. A 3% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on selected inputs using plausible ranges of values derived from the published literature where possible. A probabilistic sensitivity analysis was performed using a Monte Carlo simulation by simultaneously sampling all input parameters from appropriate probability distributions.

Results
Lifetime costs, life-years and QALYs were $747,327, 17.22 and 15.75 with TDF/FTC plus efavirenz, $777,090, 17.14 and 15.68 with ABC/3TC plus efavirenz, $778,287, 17.06 and 15.44 with ZDV/3TC plus efavirenz. TDF/FTC was the dominant treatment as it was more effective and less expensive than the other regimens.

The most influential inputs were efficacy parameters for first-line regimens, annual change in CD4+ cell count in later therapy lines and antiretroviral drug costs in later therapy lines. TDF/FTC remained dominant in all simulations when compared with ZDV/3TC.

In comparison with ABC/3TC, TDF/FTC dominance no longer held when CD4+ cell count increases were higher for ABC/3TC. In this scenario the incremental cost per QALY gained with ABC/3TC over TDF/FTC remained above $96,000. Probabilistic sensitivity analysis showed that at a threshold of $50,000 per QALY gained TDF/FTC was the preferred strategy in 88.1% of simulations.

Authors' conclusions
The authors concluded that TDF/FTC was likely to improve clinical outcomes at reduced cost compared with the alternative regimens.

CRD commentary
Interventions:
Selection of the comparators was appropriate as the available first-line treatment strategies were considered. Later lines of therapies were based on regimens recommended by the USA treatment guidelines. The authors stated that comparisons with other regimens were beyond the scope of the analysis.

Effectiveness/benefits:
Clinical data were retrieved by a systematic review of the literature of the most relevant sources. Efficacy data were taken from two clinical trials with head-to-head comparisons of two of three regimens. An indirect comparison of TDF/FTC and ABC/3TC used ZDV/3TC as common comparator. The studies selected were generally similar and were characterised by a long-term follow-up. Other effectiveness data came from valid published sources and included a UK cohort study. Extensive sensitivity analysis was conducted on all clinical parameters. There was limited information on the derivation of utility valuations. QALYs and life-years enabled comparisons with the benefits of other health care interventions.

Costs:
The economic analysis was carried out from a societal perspective. Indirect costs (such as productivity losses) were not included in the model and were assumed to have been captured in the QALY estimates. Extensive information on assessment of drug costs was reported; details on other cost categories were less clear. Costs associated with each model health state were taken from a previous study conducted in USA that was likely to provide relevant estimates for the authors' setting. The price year was given, which allowed reflation exercises in other time periods. Variations in cost estimates were tested in the sensitivity analyses.

Analysis and results:
The study results were clearly presented for both the base case and the alternative scenarios. An incremental approach was used to combine the costs and benefits of the treatments. The issue of uncertainty was satisfactorily investigated.
using various approaches and the results were illustrated and discussed. There was an extensive description of the model and its pathways. Conventional discounting was applied to clinical and economic outcomes. Transferability of the results was not addressed explicitly, but the findings might be relevant to other settings with similar drug prices.

Concluding remarks:
The study used a valid methodological approach that considered various areas of uncertainty and enhanced the robustness of the authors' conclusions.

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