Cost and cost-effectiveness of switching from stavudine to tenofovir in first-line antiretroviral regimens in South Africa

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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.

CRD summary
This study examined the cost-effectiveness of switching from stavudine to tenofovir disoproxil fumarate (TDF) as first-line antiretroviral therapy, focusing on toxicity events. The authors concluded that, at the current price of $17 per month, TDF appeared to be cost-effective and even slight reductions in the TDF acquisition costs would make it highly cost-effective for South Africa. There were a few limitations to the study, which might reduce the validity of the authors' conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of switching from stavudine (d4T) to tenofovir disoproxil fumarate (TDF) as first-line antiretroviral therapy (ART), focusing on the changes in toxicity events.

Interventions
The d4T scenario, which consisted of d4T-lamivudine (3TC)-nevirapine or d4T-3TC-efavirenz, was compared with the TDF scenario where the d4T was substituted with TDF in the same two regimens.

Location/setting
South Africa/hospital.

Methods
Analytical approach:
The economic evaluation was based on a state-transition model, which simulated the management of a hypothetical cohort of patients under the two treatment strategies, focusing on the discontinuation due to toxicity. The time horizon of the analysis was two years. The authors stated that the perspective of the national health care budget was adopted.

Effectiveness data:
The clinical data were derived from multiple sources including primary data, published studies (details of which were not given), and experts' opinions. The primary data for the d4T scenario were taken from the medical record database of the Themba Lethu Clinic of Helen Joseph Hospital in Johannesburg, South Africa. This database contained data for 5,766 adult patients. The data for the TDF scenario were all based on published sources which were not described. The primary clinical outcome was the risk of toxicity related to the two strategies.

Monetary benefit and utility valuations:
The utility valuation, and other data required to determine the duration of a health condition, were derived from the literature or were based on clinical experience (details of which were not given).

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure.

Cost data:
The two main cost categories considered were medical expenditures for antiretrovirals, and treatment of ART-related...
toxicities. Specifically, the analysis included the costs of drugs, laboratory test, outpatient visits, inpatient stay, infrastructure, and other fixed costs. The unit costs and quantities of resources used were presented for most items. Except for inpatient stay, which was based on a published study, the resource use and costs were derived from the primary data of the Themba Lethu Clinic of Helen Joseph Hospital. Discounting was not relevant given the two-year time horizon. All costs were in US dollars ($) and the price year was not explicitly reported.

Analysis of uncertainty:
A deterministic sensitivity analysis investigated the impact of variations in the treatment-related loss to follow-up on the cost-effectiveness results.

Results
Over two years, the total cost, in a cohort of 1,000 individuals, was $1,067,408, in the d4T scenario, and $1,323,445, in the TDF scenario. The TDF scenario cost $128 more per patient per year than the d4T strategy. At a monthly TDF price of $17, savings on d4T toxicity would offset only 20% of the higher price of TDF.

Over two years, the QALYs lost, in a cohort of 1,000 individuals, were 29.15 with d4T and 0.61 with TDF. Thus, the incremental cost per QALY gained with TDF over d4T was $9,007, which is far lower than three times South Africa's annual per capita gross domestic product (GDP) of $5,632, which is commonly used to define a cost-effectiveness threshold in developing countries.

At a TDF monthly price of $6.17, TDF would be cost-neutral, while at a monthly price of $12.94, TDF would be very cost-effective (it would equal the per capita GDP).

The sensitivity analysis showed that total costs of the d4T scenario and the cost-neutral price of TDF decreased with the increasing rate of loss to follow-up associated with d4T, as expected.

Authors' conclusions
The authors concluded that, at the current price of $17 per month, TDF appeared to be cost-effective and even slight reductions in the TDF acquisition costs would make it highly cost-effective for South Africa.

CRD commentary
Interventions:
The authors justified their selection of the comparators. Specifically, d4T represented the recommended drug in the South African national treatment programme, while TDF was one of the treatments with the lowest rate of drug-related toxicities, especially in comparison with d4T. However, given its high price, TDF was not available through public sector procurement.

Effectiveness/benefits:
The use of primary data to derive the clinical evidence is usually considered to be an appropriate approach, but the use of an administrative database might present some drawbacks due to incomplete or inappropriate reporting. Furthermore, data from the database referred to a single treatment strategy (that for d4T). Other inputs for the model were derived from published evidence, the details of which (types of studies, patients' characteristics, follow-up, etc.) were not provided. This prevents an objective assessment of the validity of the clinical data. Further, the assumptions based on experts' opinions were not tested in the sensitivity analysis. Similarly, little information on the derivation of the utility values was provided. QALYs are a validated measure and allow cross-disease comparisons.

Costs:
The categories of costs were appropriate given the study perspective. A breakdown of cost items was provided together with extensive data on resource consumption and unit costs. This enhances the transparency of the analysis and the possibility of replicating it in other settings. The sources of data were reported for most items. No statistical approaches were used for the economic data. The price year was not explicitly reported although some costs (such as drug prices) referred to 2007. However, the authors pointed out the wide variability in the prices of ART agents.

Analysis and results:
The synthesis of the costs and benefits was appropriately performed by means of an incremental analysis. The results were clearly presented, with extensive information on the epidemiological findings. The issue of uncertainty was only partially addressed since the sensitivity analysis considered only the impact of treatment-related loss to follow-up. The uncertainty underlying other inputs of the model was not investigated. Overall, the study reflected the programme implementation in a specific setting, thus caution will be required when extrapolating these findings to other health care systems. The authors acknowledged some potential limitations to their analysis, which have been reported in the relevant fields above. It was also noted that a longer time horizon would have been useful to capture the long-term differences between treatments.

Concluding remarks:
There were a few limitations to the study validity, so the authors’ conclusions should be considered with a degree of caution.

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