First-line antiretroviral therapy after single-dose nevirapine exposure in South Africa: a cost-effectiveness analysis of the OCTANE trial


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 combined lopinavir and ritonavir, compared with nevirapine, as first-line antiretroviral therapy, using data from a recent clinical trial of women who had received one dose of nevirapine to prevent mother-to-child HIV transmission. The authors concluded that first-line lopinavir and ritonavir-based antiretroviral therapy was very cost-effective, for these South African women. Nevirapine was very cost-effective compared with no antiretroviral therapy. The cost-effectiveness methods were robust and should have ensured the validity of the authors' conclusions.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of combined lopinavir and ritonavir compared with nevirapine as antiretroviral therapy, using data from a recent clinical trial of women who had been given one dose of nevirapine to prevent mother-to-child HIV transmission.

Interventions
Three strategies were examined: no antiretroviral therapy, first-line nevirapine followed by second-line lopinavir and ritonavir, and first-line lopinavir and ritonavir followed by second-line nevirapine.

Location/setting
South Africa/secondary care.

Methods
Analytical approach:
The analysis was based on a published state-transition model of HIV infection, namely the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) International model, for South Africa. A lifetime horizon was considered. The authors stated that a modified societal perspective was adopted, which excluded the patients' costs for time, transport, and child care.

Effectiveness data:
The clinical data were from a selection of studies. The key evidence on the efficacy of the two antiretroviral therapies and the patients' characteristics were from the Optimal Combination Therapy After Nevirapine Exposure (OCTANE) trial, which was a randomised controlled trial (RCT) of women with a cluster of differentiation (CD) 4 cell count below 200 per microlitre, who had received a dose of nevirapine. The data for the natural history of disease were from the Cape Town AIDS Cohort study, the Multicenter AIDS Cohort Study, and other studies. The key clinical input was treatment efficacy, measured as the percentage HIV ribonucleic acid suppression at 24 weeks and the gain in CD4 count.

Monetary benefit and utility valuations:
Not considered.
Measure of benefit:
Life-years were the summary benefit measure and they were discounted at an annual rate of 3%.

Cost data:
The economic analysis included the monthly costs of antiretroviral therapy, clinical care (opportunistic infections, drug toxicity, chronic care, and terminal care), and laboratory monitoring (CD4 test, and viral load test). The economic data were from the Clinton Foundation, Medecins Sans Frontieres, the Cape Town AIDS Cohort study, and a Health System Trust. The costs were in US dollars ($) and the price year was 2008. A 3% annual discount rate was applied.

Analysis of uncertainty:
A deterministic approach was used to assess the uncertainty. Single- and multi-variate analyses were carried out and best- and worst-case scenarios were considered. The alternative ranges were based on data from published reports. Various subgroup analyses based on trial data were carried out.

Results
The projected life-years were 1.6 with no antiretroviral therapy, 15.2 with first-line nevirapine, and 16.3 with first-line lopinavir and ritonavir. The costs were $2,980 with no therapy, $13,990 with first-line nevirapine, and $15,630 with first-line lopinavir and ritonavir. The incremental cost per life-year gained was $810 with first-line nevirapine over no antiretroviral therapy and $1,520 with first-line lopinavir and ritonavir over nevirapine.

The cost-effectiveness ratio of lopinavir and ritonavir rose to $5,650 for OCTANE participants with no detectable non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance at baseline. Nevirapine was dominated for women with baseline NNRTI resistance, as it was less effective and more expensive, and for women who received the dose of nevirapine six to 12 months before antiretroviral therapy initiation. Lopinavir and ritonavir became dominated with increasing time from the dose of nevirapine to antiretroviral therapy initiation.

The 24-week suppressive antiretroviral therapy efficacy and the risk of late virologic failure after 24 weeks of lopinavir and ritonavir were the most influential inputs. Lopinavir and ritonavir remained cost-effective at a threshold of $5,700 (the South African per capita Gross Domestic Product) per life-year gained as long as its efficacy was higher than 89% (97% in the base case).

In general, the base-case findings were robust to variations in the other inputs. Lopinavir and ritonavir ranged from being dominated in the worst-case scenario to an incremental cost per life-year gained of $813 in the best-case scenario.

Authors' conclusions
The authors concluded that first-line lopinavir and ritonavir-based antiretroviral therapy was very cost-effective, compared with nevirapine, for South African women, who had received nevirapine. First-line nevirapine was very cost-effective, compared with no antiretroviral therapy.

CRD commentary
Interventions:
The authors provided a justification for their selection of the comparators. No antiretroviral therapy was considered as a comparator, while the two antiretroviral therapies were the interventions considered in the OCTANE trial.

Effectiveness/benefits:
A selective approach appears to have been used to identify the relevant sources of data. The bulk of the evidence came from a pivotal RCT, and the rigour of its methods should have ensured the validity of the clinical data. Other inputs were from sources that were not described, limiting the possibility of judging their validity. They were mainly cohort studies and these are often used to project the natural history of a disease. Life-years were an appropriate benefit measure, given the importance of survival for these patients. They also permit cross-disease comparisons to be made. The authors pointed out the limited availability of HIV-related quality-of-life data in Africa, which precluded the calculation of quality-adjusted life-years (QALYs).

Costs:
The cost categories reflected the perspective stated. The resource quantities and unit costs were not presented separately, limiting the reproducibility of the analysis. The sources of data were reported and appear to have been appropriate for the authors’ setting. More details on these sources might have been available in an online appendix. Some cost categories were varied in the sensitivity analysis. Other details, such as the price year and discounting, were appropriately reported.

**Analysis and results:**
The results were extensively presented. An incremental approach was used to synthesise the costs and benefits of the strategies. A deterministic approach was used to consider the uncertainty in the model inputs, and simultaneous variations of these parameters were considered in alternative scenarios. The analysis was based on a well-known model and the findings were validated using real-world data. The results should be transferable to settings with a similar epidemiology, income level, and cost structure.

**Concluding remarks:**
The cost-effectiveness methods were robust and should have ensured the validity of the authors’ conclusions.

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