The cost-effectiveness of herpes simplex virus-2 suppressive therapy with daily aciclovir for delaying HIV disease progression among HIV-1-infected women in South Africa


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 daily acyclovir to suppress the herpes simplex virus type two and to slow HIV-1 disease progression in women who were not eligible for antiretroviral therapy. The authors concluded that suppressive therapy might be cost-effective and affordable for these women, if the price of acyclovir was low and it encouraged patients to return for care. The study was well performed and various areas of uncertainty were assessed. The authors’ conclusions seem to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of daily acyclovir therapy to suppress the herpes simplex virus type two (HSV2) and prevent HIV-1 disease progression, in women who were not eligible for antiretroviral therapy (ART) as their cluster of differentiation (CD4) count was not below the ART initiation threshold.

Interventions
Acyclovir 400mg was given twice daily for five days to all HIV-1 seropositive women who had a CD4 count of over 200 cells per microlitre (μL). The intervention included initial counselling with health care professionals. The comparator was standard care with no active therapy.

Location/setting
South Africa/primary care.

Methods
Analytical approach:
The analysis was based on a Markov model, with a lifetime horizon and a cohort of 300 women. The authors stated that it was carried out from the perspective of the health service provider. Two scenarios were considered with patients eligible for ART at a CD4 count of less than 200 cells per μL, or at the World Health Organization (WHO) recommended CD4 count of less than 350 cells per μL.

Effectiveness data:
Most of the clinical data were from two trials: the Partners in Prevention HSV/HIV Transmission trial and the Johannesburg HSV-2 Suppressive Therapy trial. Other data were from published sources. The clinical trials provided the efficacy of acyclovir and the short-term disease progression, while a South African cohort study provided the long-term disease progression data. Most of the sources studied the South African setting. The primary input to the model was the efficacy of suppressive therapy, in reducing both the rate at which patients became eligible for ART and the HIV-related deaths.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years were the summary benefit measure and were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of acyclovir, the treatment of sexually transmitted infections, consumables associated with suppressive therapy, capital costs (such as equipment for the intervention, training the defaulter (patient who did not return for care) tracer, and nurses to provide clinical examination and management for HSV2 and other sexually transmitted infections), and the lifetime management of HIV. The price of acyclovir was based on the government’s procurement cost. Other economic data and the resource use came from the Johannesburg trial. All costs were in US dollars ($) and the price year was 2008. An inflation adjustment factor was used and a discount rate of 3% was applied to annualise the capital costs.

Analysis of uncertainty:
The uncertainty was investigated in a multivariate analysis, with random sampling, based on 95% confidence intervals for most model inputs. Other inputs were varied by ±50% of their baseline estimate. Alternative discount rates and diagnostic tests were assessed and the cheapest internationally available price for acyclovir was considered.

Results
For the cohort of 300 women, using a threshold CD4 count of 200 cells per μL, the projected life-years gained with suppressive therapy, over no intervention, were 142 and the additional costs were $224,000. The incremental cost-effectiveness ratio (ICER) was $1,558 per life-year gained. Using the cheapest international price for acyclovir, the ICER was $1,023 per life-year gained.

At a stringent cost-effectiveness threshold of $1,200 per life-year gained, suppressive therapy was cost-effective in 22% of simulations (67% with the lower price).

Using a threshold CD4 count of 350 cells per μL, the projected life-years with suppressive therapy, over no intervention, were 110 and the costs were $126,000. The ICER was $1,130 per life-year gained or $737 per life-year gained using the lower price. Acyclovir was cost-effective in 58% of simulations (86% at the lower price).

When including the additional cost and benefit of ART, the ICERs of suppressive therapy were higher with each CD4 threshold, and the likelihood of therapy being cost-effective was substantially lower.

The biggest impact on the model outcomes was from variation of the efficacy of suppressive therapy (without ART) and in the assumptions on the default rate (with ART). Variations in other inputs affected the model results, including the proportion of HIV-1-infected women who were HSV2 infected, the initial number of patients receiving suppressive therapy, the salary of the defaulter tracer, the HIV death rate, and the discount rate.

Authors’ conclusions
The authors concluded that HSV2 suppressive therapy might be cost-effective and affordable for women with HIV-1 before ART initiation, if the price of acyclovir was low and it reduced the number of patients who did not return for care.

CRD commentary
Interventions:
The selection of the comparators was appropriate. No clear definition of standard care was given, but the authors stated that there was little that could be offered to these patients.

Effectiveness/benefits:
Most of the treatment efficacy data were from two clinical trials, which should have had high internal validity, but few details were provided. No systematic review was reported to identify the relevant sources of evidence, but most of the data were from country-specific sources that reported the implementation of HIV treatments and this was appropriate. The possibility of fully judging the validity of the clinical estimates was limited by the lack of information on these studies. Survival was an appropriate benefit measure that not only captured the impact of the intervention on a patient’s health, but also will allow cross-disease comparisons.

Costs:
The categories of costs reflected the perspective of the health care provider, and the unit costs and resource use were provided. Most of the cost data were varied in the sensitivity analysis, which showed the strong impact of the price of acyclovir on the cost-effectiveness results. The sources of data seem to have been appropriate for South Africa. Other details, such as the price year, discount rate, and inflation adjustments, were given.

Analysis and results:
The results were partly presented; only the incremental findings were reported. An appropriate incremental analysis was used to synthesise the costs and benefits of the two strategies. The authors used valid approaches to investigate the uncertainty and the key findings were clearly presented. The details of the decision model were reported in an online appendix. The authors justified their use of a stringent cost-effectiveness threshold. They stated that their findings were specific to the South African population and might not be transferable to other settings, especially those with a different prevalence of HSV2 in HIV-1 patients or with different health care structures.

Concluding remarks:
The study was well performed and various areas of uncertainty were addressed. The authors’ conclusions seem to be robust.

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