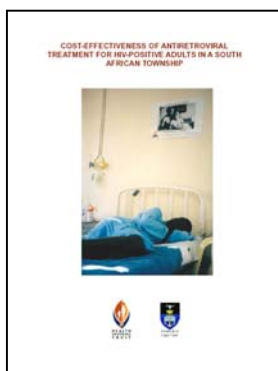


COST-EFFECTIVENESS OF ANTIRETROVIRAL TREATMENT FOR HIV-POSITIVE ADULTS IN A SOUTH AFRICAN TOWNSHIP



Research conducted by:

Susan Cleary¹, Andrew Boulle², Di McIntyre¹ and David Coetzee²

¹ Health Economics Unit, ² Infectious Diseases Epidemiology Unit, School of Public Health and Family Medicine, University of Cape Town

Summary

Contents

Introduction	2
Study Design and Methodology: Use of Economic Evaluation and Markov Modelling	2
The South African experience	2
Key Findings	3
1. Lifetime and annual cost estimates	3
2. Cost-effectiveness of different starting times of ART	5
Discussion	5
Conclusion	6



Introduction

This study aims to establish the costs and effectiveness of antiretroviral therapy (ART) for HIV positive adults in a resource-constrained public-sector setting. The research compares ART to the current status quo for HIV-positive adults who are dependent on the public sector for care in South Africa – i.e the treatment of opportunistic and HIV-related infections and events (e.g. wasting) in the absence of ART. This research is clearly important in the developing country context, where the HIV epidemic is expected to have a dramatic impact on life expectancy and to lead to early mortality for a large proportion of the population (Dorrington, Bourne et al. 2001).

This study presents the first cost-effectiveness results derived from a public sector clinic-based treatment programme. Cost, effectiveness and quality of life data have been collected from a single cohort receiving care in three HIV-dedicated clinics in Khayelitsha, a township on the outskirts of Cape Town. This setting is similar to what will be encountered in the public sector ART rollout.

Study Design and Methodology: Use of Economic Evaluation and Markov Modelling

Economic evaluations use commonly accepted methodology to establish the costs and the outcomes of different courses of action, in order to provide clarity to the decision-making process. This research uses both cost-utility and cost-effectiveness analyses.

The cost-effectiveness analysis uses an outcome measure that has only one dimension (the Life Year (LY), for instance). The cost-utility analysis is a far more appropriate form of economic evaluation when comparing ART to no ART. It uses a multi-dimensional outcome measure, and can capture the different effects of ART and no ART in terms of both quantity and quality of life for example by using the Quality Adjusted Life Year (or QALY). Given that the cost-utility analysis is merely a specialised form of the cost-effectiveness analysis, for simplicity this report uses the terms cost-effectiveness and cost-utility interchangeably.

One of the key difficulties in predicting the cost-effectiveness of ART is that data are not yet available for the full course of patients' lifetimes on ART in the public sector in South Africa, although there is much less uncertainty for patients who are not on ART. This is a common problem in the economic evaluation of long-term interventions and chronic diseases, and has led to the widespread adoption of Markov modelling, which is a technique that allows current data to be extrapolated forward into future health states in order to predict future costs and future effects. Sensitivity analyses are used in clarifying the degree of variability in the estimates.

This study uses Markov Modelling to calculate the cost per Life Year gained and Quality Adjusted Life Year gained from each treatment option. The model also calculates total costs, total LYs and total QALYs.

The South African experience

In South Africa and in Africa in general, there are no published studies based on existing programmes examining the cost-effectiveness of ART versus no ART and there are no published Markov models of HIV.

While no economic evaluations based on primary research have been conducted, a number of spreadsheet models have estimated the lifetime cost of ART (AbtAssociates 2000; Boule, Kenyon et al. 2002; Marseille, Hofmann et al. 2002; Geffen, Natrass et al. 2003). Furthermore, the National Departments of Health and Treasury developed a cost model of ART in 2003.

In addition, a small number of studies have undertaken primary costing of inpatient and outpatient care for HIV-positive people who are not on ART (Karstaedt, Lee et al. 1996; Kinghorn, Lee et al. 1996; Govender, McIntyre et al. 2000; Haile 2000)

Key Findings

1. Lifetime and annual cost estimates

The costing of ART and no ART includes all recurrent costs required to deliver ART, to treat opportunistic and HIV-related infections, to encourage adherence and to minimize transmission of the virus (including viral load, CD4 count and other laboratory testing, co-trimoxazole prophylaxis, ongoing palliative care, extensive counselling of patients, referrals for tuberculosis treatment and inpatient care, nutritional supplementation, and the provision of male and female condoms). The capital costs associated with infrastructure, medical equipment, furniture and staff training were also included (annualized using a real discount rate).

The cost results are shown graphically in Figure 1.

Figure 1: Breakdown of costs across the average patient's lifetime

(a) ART

(b) No ART

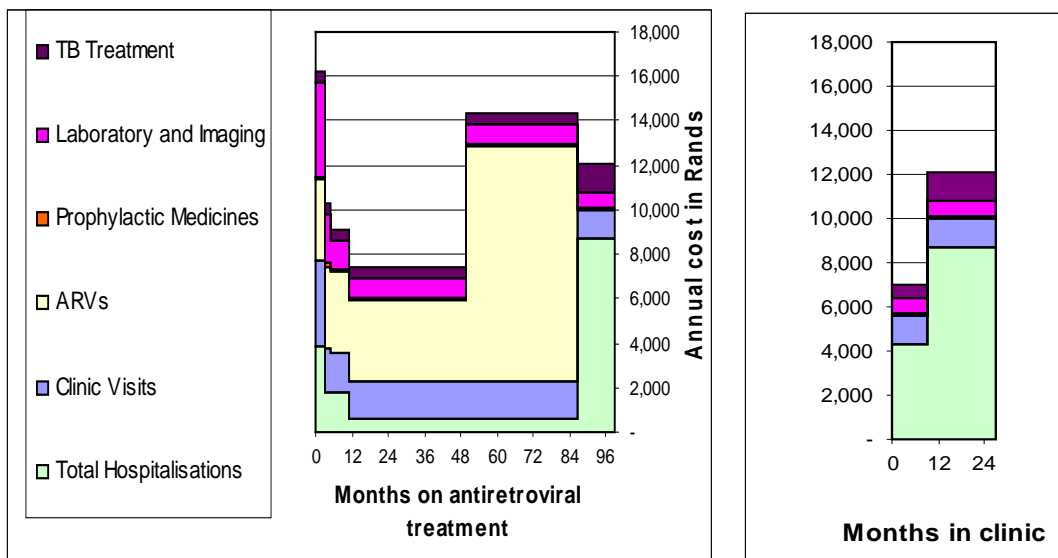


Figure 1 (a) highlights the following points:

- ARVs make up a large proportion of the cost of the ART option
- Second Line ARVs (after month 48 in the diagram) are particularly important cost drivers
- Laboratory testing is an important cost item at baseline, but decreases in importance once patients are on treatment for longer than 3 months
- Inpatient costs are important at baseline (indicating morbidity and mortality due to the low CD4 counts at baseline in this cohort) but decrease in importance until cohort members go off treatment when they become the most important cost driver
- The costs associated with clinic visits are relatively unimportant. In all states other than the first 3 months on treatment (where there are almost 8 visits per client), the costs of ARVs (approx R257 per month for the first-line regimen and R880 for second-line) are more than double the costs of clinic visits (approx R162 per month).

Figure 1 (b) clearly shows that the most important cost driver off ART is inpatient care.

In terms of the overall efficiency of the intervention, this research has calculated that ART costs R13 754 per QALY versus R14 189 per QALY for patients who do not receive ART. The incremental cost per QALY gained on ART is R13 621. This result indicates that ART is efficient in economic terms, and ought to be pursued if economically feasible and desirable to society.

While the intervention has been shown to be efficient, the lifetime costs of treatment are not insignificant. For patients on ART, the lifetime cost was calculated to be just over R93 000, and off ART just under R24 000 (for patients with CD4 counts less than 200 cells/ μ l). The average life expectancy is 8.33 years on ART, and 2.27 years for patients not on ART. In other words, ART leads to an average gain in life expectancy of 6.06 years. This translates into 6.79 QALYs on ART or 1.59 QALYs for no ART. Patients reported higher Health Related Quality of Life (HRQoL) on ART than off ART.

The estimate of the lifetime cost of ART represents one of the first attempts to provide the economic costs of ART that is fully inclusive of all levels of care. Encouragingly, the results that have been obtained in this study when hospitalisations are excluded (R9359 per year) are similar to the theoretical costs produced by other South African studies which have not included hospitalisations. The recent study commissioned by the Treatment Action Campaign calculated a cost per year of almost R9,000 if viral loads were included (Geffen, Nattrass et al. 2003).

ARV medicines account for about 50% of the lifetime cost, therefore the most important factor in the cost-effectiveness of ART is the prices of ARVs. Fortunately, various recent changes have opened far more opportunities for the procurement of generic antiretrovirals.

Firstly, South African generic manufacturer Aspen Pharmacare has developed the capacity to manufacture generic versions of ddI, 3TC, AZT, Combivir and Nevirapine (through voluntary licenses) at a price of approximately \$1.00 per day for a first-line regimen (Meldrum and Smart 2003). Aspen has also recently entered into an

agreement with the Clinton Foundation to deliver Triomune (a fixed dose combination of 3TC, d4T and Nevirapine) at \$0.38 per day (Schoofs 2003).

A further welcome change in the market for antiretrovirals has been the decision by GlaxoSmithKline (2003) to extend its voluntary licenses (on AZT, 3TC and Combivir) to include sale to the private sector and to all countries in Sub-Saharan Africa, and to extend voluntary licenses to four generic manufacturers.

However, there are a number of ARVs that are still relatively expensive. These include Merck's Efavirenz (an essential component of the proposed first-line regimen in the public sector rollout), Abbott's Kaletra and Bristol Myers Squibb's ddI, both of which are recommended second-line drugs. If the prices of these drugs could be reduced in the coming years, the impact on the lifetime cost of ART could be highly favourable.

A further key cost driver for ART is viral load testing. This research has applied the same viral load testing schedule irrespective of regimen, whereas many experts would be happy to omit viral load tests if patients were on second-line. Further, WHO guidelines for delivering ART in developing countries accept that viral load testing may not be feasible in many settings (WHO 2002).

2. Cost-effectiveness of different starting times of ART

Although commenting on the relative cost-effectiveness of different starting times of ART was not initially an objective of this research, it has become an increasingly important issue now that the planning of the ART rollout has commenced. To clarify the importance in terms of efficiency of different starting times of ART, this study has assumed that patients start ART either with a CD4<50 or a CD4 50-199.

Table 1 below demonstrates the cost-effectiveness of different starting times of ART

	Lifetime Cost	LYs	Cost per LY	Incremental Cost per LY gained
ART Started with CD4<50	R 89,421.63	7.92	R 11,296.82	
ART Started with CD4 50-199	R 98,119.27	8.82	R 11,118.92	R 9,569.52

All costs in 2002 prices

As expected, it is more effective and more cost-effective for patients to start ART with CD4 50-199 than with CD4<50. Although patients will probably start ART with low CD4 counts during the initial phases of the rollout, hopefully in time it will be possible to enrol patients earlier, in order to take advantage of the extra gains in effectiveness and in efficiency.

Discussion

Strengths and limitations

A strength of this study is that hospital utilisation data have been derived from the same cohort as the primary care cost and effectiveness data. Results indicate an average of only 10 days in hospital for the year when a patient dies, which is considerably lower than found in earlier studies (see Karstaedt et al 1996). However,

increasing inpatient costs by 20% in sensitivity analysis (for both ART and no ART) indicated very little change in the Incremental Cost Utility Ratio (although the lifetime costs obviously increased for both patients on and off ART).

Furthermore, this study is a valuable contribution to existing work on the lifetime cost of ART and no ART, and presents the first cost-effectiveness results derived from a public sector clinic-based treatment programme.

However, a general limitation of many aspects of this study is that the follow-up duration on ART has been insufficient to capture the full benefit of ART with respect to service costs (although there is much less uncertainty regarding the no ART costing in this setting). The following is a list of examples of potential cost overestimates:

- Utilisation of just over one clinic visit per month throughout ART despite evidence to suggest that patients might visit less frequently once established on their regimens
- Assumption that patients remain on second-line treatment while treatment is failing
- Insufficient follow-up time to fully capture the reduction in the incidence of tuberculosis
- Insufficient follow-up time to fully capture the reduction in morbidity requiring inpatient care once immune systems have recovered on ART

Although there is less uncertainty surrounding the no ART costing, some care should be taken in applying the lifetime costs calculated in this setting to other settings. It is likely that a variety of factors could affect the demand for, and supply of, health services for HIV-positive patients who are not on ART in other settings.

Finally, this analysis does not include the utilisation of specialised forms of inpatient services, such as tuberculosis hospitals and hospices. Data for these admissions were insufficient for their inclusion. A further omission is the failure to adequately capture outpatient visits at hospitals. Both of these omissions are likely to have generally biased the results against the cost-effectiveness of ART.

Conclusion

This research contributes three key findings to the current state of knowledge in this area. Firstly, it provides an indication of the relative efficiency of ART compared to no ART in a setting that is similar to future ART service sites in South Africa. Secondly, this research is able to give a better indication of the costs of providing ART over a patient's lifetime than is currently available. Thirdly, it is able to give a solid indication of the current costs of treating opportunistic and HIV-related infections for patients who are not on ART. The latter two pieces of information are essential for budgeting for the ART rollout adequately, whilst the former gives an indication of the relative efficiency of ART versus no ART in similar settings.

ART has been shown to be cheaper per QALY and to lead to enhanced life expectancy. Furthermore, ART can prevent some of the devastation associated with the early mortality of breadwinners and caregivers that is currently being felt across the continent, and therefore offers immense benefits of the sort that are typically excluded from this type of analysis.

These findings have a number of immediate policy implications.

- The current focus on reducing the cost of antiretroviral drugs is warranted, as on the whole, ARVs still account for nearly 50% of the lifetime cost on ART. This is particularly important for the drugs that remain relatively expensive (such as Efavirenz, ddI and Kaletra). Although personnel costs are not a major cost driver, recruiting and training sufficient human resources to deliver ART will still be a major challenge.
- More emphasis should be placed on reducing the cost of HIV RNA (viral load) testing. Viral load testing makes up almost 50% of the cost of laboratory testing for ART. There should also be clarification of the role of this test in the provision of ART in South Africa.
- The clinical results on which this study is based are a clear demonstration of the potential for the intervention to extend life, and delay many of the individual and societal consequences associated with premature mortality.

It is hoped that these results will assist the planners of the ART rollout in the public sector in South Africa to anticipate the costs of the services and to implement ART in the most efficient manner.

This research was supported by a grant from the Health Systems Trust.

The full report (668kb, 66 pages) can be downloaded from <http://www.hst.org.za>