Early and late determinants of direct costs in a Southern African antiretroviral programme

Rory Leisegang[1], Susan Cleary[2], Michael Hislop[3], Alistair Davidse[1], Leon Regensberg[3] and Gary Maartens[1]
1. Division of Clinical of Pharmacology, Department of Medicine, University of Cape Town, Cape Town, South Africa
2. Health Economics Unit, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa
3. Aids for AIDS, Medscheme, Cape Town, South Africa

Introduction

With access to combination antiretroviral therapy (ART) rapidly expanding in resource-limited settings, data on the costs of providing HIV health care, including access to ART, is important to aid decisions to improve outcomes and efficiency where resources are constrained. There are few good quality studies of the direct health care costs of HIV infection, as illustrated by a recent systematic review that found only 9 studies from the ART era that fulfilled their inclusion criteria[1]. All of these studies were from resource-rich settings and extrapolating cost estimates from resource-rich to resource-limited settings is problematic[2].

Our objectives were to describe the direct heath care costs and establish the cost determinants over time in an HIV managed care programme in Southern Africa. Although the private sector is a relatively resource-rich setting, we argue that most aspects of the managed care guidelines are very similar to the WHO guidelines[11], and that many of the patient characteristics are similar to those of ART programmes in resource-limited settings.

Methods

Data for this study were extracted from a database of patients enrolled with Aid for AIDS (AfA), a group that manages HIV-related care for a number of medical insurance funds and companies in the private sector in Southern Africa. We analysed the direct costs of treating HIV-infected adults enrolled from 3 years before starting non-nucleoside reverse transcriptase inhibitor-based ART up to 5 years afterwards. The CD4 cell count criterion for starting ART was <350 cells/µL on two occasions or an AIDS defining illness.

In a multiple regression model to describe the time course impact of the variables on mean costs[3], we regressed the average cost in 4 month periods against patient variables using a generalised linear model with a log-link function and a gamma distribution from 4 months before starting ART to 60 months on ART.

Results

Our cohort consisted of 10,735 patients (59.4% women) with 594,497 months of follow up data (50.9% of months on ART). Median baseline CD4+ cell count and viral load were 125 cells/µL and 5.16 $\log_{10}$ copies/ml respectively. The most common first line and second line antiretroviral regimens were AZT/3TC/EFV and LPV/RTV/AZT/DDI respectively. CD4 and viral load monitoring were done 1.5 times per annum on average. Hospitalisation rates were 441 days per 100 patient years of observation (PYO) in the first 6 months of ART and 179 days per 100 PYO subsequently. Hospitalisation incidence was highest in patients in the lowest CD4 count stratum.

Exploratory Cost Analysis

The cost data was highly skewed with 10% of the population accounting for 90% of the costs. Looking at the mean cost over time (Figure 1), costs peaked in the period around ART initiation (from 4 months before until 4 months after starting ART) driven largely by hospitalisation, and thereafter were largely stable for the remaining period.

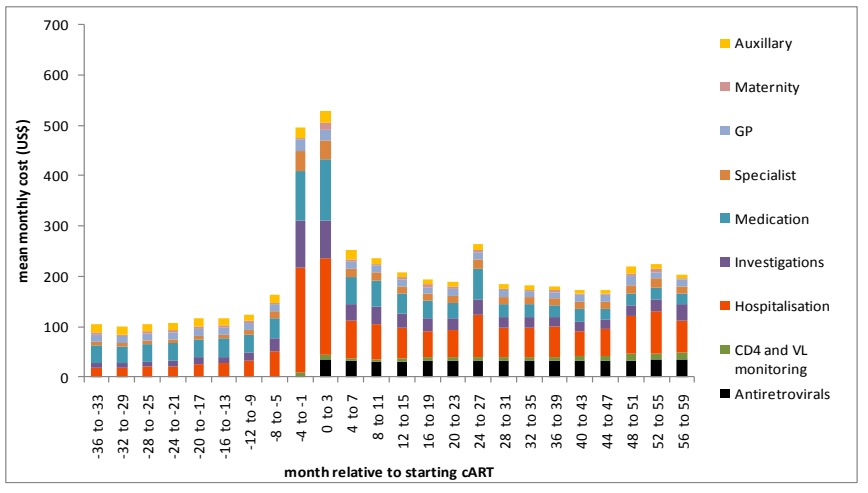
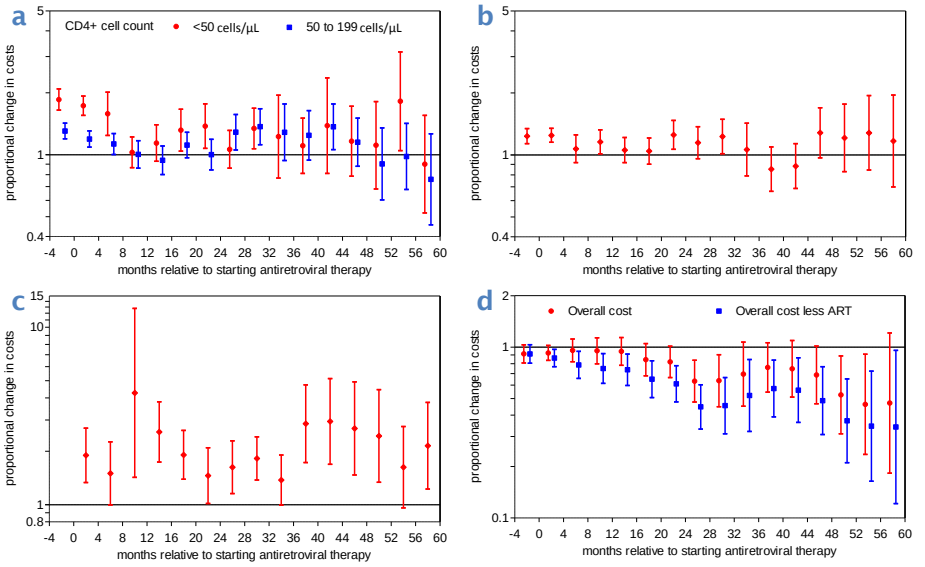


Figure 1: Mean monthly direct health care cost

Determinants of cost over time

We evaluated the following variables to assess if they were determinants of cost: baseline CD4+ cell count, HIV viral load, ART adherence, age, sex, NNRTI as well as NRTI combination used in patients on first line therapy, whether the patient switched to protease inhibitor-based second line ART and the duration of CD4+ cell count monitoring (as a proxy for being in HIV care) prior to starting ART. No statistically significant differences between the characteristics of this subgroup and the full cohort were found (data not shown). Age and sex we excluded from the final model as no significant effect was found in any time period.



(a) the baseline CD4+ cell count (referent group CD4+ cell count 200 to 349 cells/µL)
(b) baseline viral load (referent group baseline viral load < 100,000 copies/ml)
(c) second line ART (referent group first line ART)
(d) highest overall adherence quartile (referent group lowest adherence quartile)

Figure 2: The proportional change in mean costs attributable to variables from 4 months before starting ART to 60 months on ART

Discussion

We identified lower baseline CD4+ cell count, higher baseline viral load and duration of CD4+ cell count monitoring (as a proxy for HIV care before starting ART) as independent early determinants of costs until about 8 months on ART. ART adherence and being on second line ART were independent determinants of costs from as early as 4 months on ART, and remained important for 5 years on ART. ART adherence increased in importance as a cost determinant over time.

The peak in costs in the peri-ART period we observed was largely driven by the high proportion of patients requiring hospitalisation. High rates of early morbidity, often resulting in hospitalisation or death, are characteristic of antiretroviral programmes in resource-limited settings. Patients on ART in low-income countries have higher early mortality compared with high-income countries, even after correcting for baseline differences in CD4+ cell counts.

There are a number of limitations to this analysis. First, our cohort consisted of private sector patients when the majority of patients in resource-limited settings are treated in the public sector, though baseline characteristics were similar. Second, the impact of specific AIDS defining illnesses on outcomes and costs was not included in this analysis as these data were not available. Finally, we chose to use the tariff amount as opposed to the amount claimed or reimbursed so that similar services would take the same monetary value and have further assumed that these tariffs are a suitable proxy for opportunity costs.

In conclusion, we have described the temporal trends of costs of a large private sector HIV disease management programme in Southern Africa and shown that cost determinants change over time. Interventions that would reduce early costs include starting ART at higher CD4 counts and being in HIV care for longer periods before starting ART. Systems to detect sub-optimal adherence and interventions to effectively improve adherence would reduce later costs. The increasing impact of ART adherence on costs over time suggests that this variable should be incorporated in economic models of ART.

References

1. Levy AR, James D, Johnston KM, et al. The direct costs of HIV/AIDS care. *Lancet Infect Dis.* 2006;6(3):171-177.
2. Evans DB, Adam T, Edejer TT, Lim SS, Cassels A, Evans TG. Time to reassess strategies for improving health in developing countries. *BMJ.* Nov 12 2005;331(7535):1133-1136
3. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? *BMJ. Apr 29 2000;320(7243):1197-1200*

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