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Aidspan Review of a Study on the Costs and Health Impact of Continued Global Fund Support for Antiretroviral Therapy

by
Dr David McCoy

This is a review of the following study:

Long-term costs and health impact of continued Global Fund support for antiretroviral therapy

by John Stover[1], Eline Korenromp[2,3], Matthew Blakley[2], Ryuichi Komatsu[2], Kirsi Viisainen[2], Lori Bollinger[1] and Rifat Atun[2,4]
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Preface

Aidspan (www.aidspan.org) is an NGO based in Nairobi, Kenya. Its mission is to reinforce the effectiveness of the Global Fund to Fight AIDS, Tuberculosis and Malaria. Aidspan performs this mission by serving as an independent watchdog of the Fund, and by providing services that can benefit all countries wishing to obtain and make effective use of Global Fund financing.

Aidspan and the Global Fund maintain a positive working relationship, but have no formal connection. *The board, staff and other structures of the Global Fund have no influence on, and bear no responsibility for, the content of this review or of any other Aidspan publication.*

The author of this review, Dr David McCoy (david.mccoy@aidspan.org), is a public health physician and honorary senior clinical research fellow at University College London. He serves as a consultant to Aidspan and also works part-time in the UK National Health Service.

While the authors of the original study have seen drafts of this review, the author of this review takes full responsibility for ensuring that the original study has been accurately and fairly represented, as well as for the opinions and recommendations expressed here. Aidspan is grateful for the comments and suggestions received from the authors of the original study.

Introduction

Questions about the feasibility of universal access to antiretroviral treatment (ART) and the sustainability of ART funding are increasingly being raised as aid budgets begin to shrink. Even the long term sustainability of existing ART programmes has been called into question. As a consequence, global health agencies and governments need to plan and budget the expansion of ART programmes with great care.

This review discusses a study that was conducted by John Stover and others to estimate the total cost of sustaining treatment until the year 2020 for the estimated 3.5 million persons who are currently on ART in Global Fund–supported programmes.[1] The study also computed the impact of the sustained provision of ART for this cohort in terms of deaths averted or postponed, and life-years saved.

The study is important not only because it estimated the cost and impact of Global Fund grants to support ART, but also because it described what may be done to minimise future costs while maximising health impact.

Study Design and Methods

The study consisted of a modelling exercise based on certain empirical data, as follows.

Survival rates

First, the annual survival rates of the cohort of 3.5 million patients were estimated. This was done by extrapolating from data submitted by the national AIDS programmes of 38 low- and middle-income countries in 2008, which reported that the proportion of patients (adults and children) remaining on treatment (i.e., not dying and not lost to follow-up) averaged 80% at 12 months after treatment initiation; 75% after 24 months; 74% after 36 months; and 73% after 48 months.[2]

Because there is considerable variation in treatment retention rates from region to region (as illustrated in Figure 1 below), a *weighted average*[3] from across the regional survival/retention data was used to assume an annual survival rate of 79.5% for the first year, and 96% for each subsequent year (i.e., cumulative survival rates for Years 2, 3 and 4 of 76.3%, 73.3% and 70.3% respectively).

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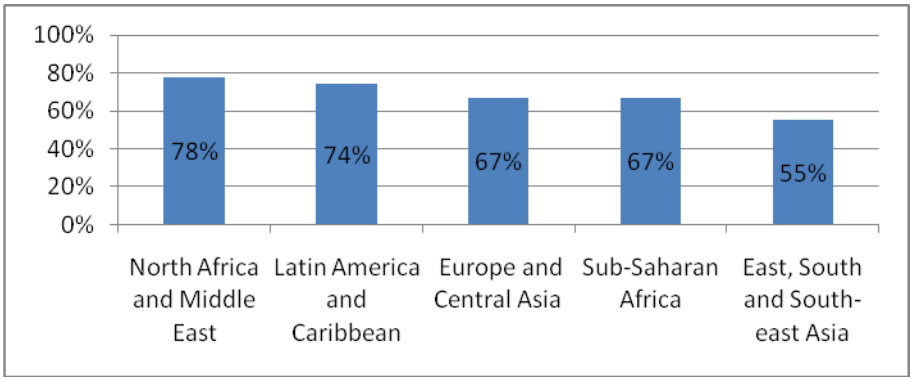
[1] J. Stover et al. Long-term costs and health impact of continued Global Fund support for antiretroviral therapy. *PLoS ONE* , 6(6): e21048 (June 2011). Available here.

[2] WHO, UNAIDS, UNICEF. Towards Universal Access: Scaling up Priority HIV/AIDS Interventions in the Health Sector: Progress Report 2009. Available here.

[3] Note: The published paper mentions use of an unweighted average, which was an error.

Figure 1: 48 month antiretroviral (ARV) treatment retention rates by region, 2008



(Derived from figures supplied in journal paper)

First- and second-line treatment regimens

The study estimated the number of patients on first- and second-line treatment regimens for each year from 2011 to 2020, basing this on the same data from the 38 national AIDS programme reports mentioned earlier. It estimated that the proportion of patients on second-line regimens in 2011 was 2.5% and assumed that for subsequent years, 1.9% of surviving patients on first-line regimens would switch to second-line regimens each year.[4]

Health impact

Health impact was calculated by comparing the survival and cumulative life-years of the cohort of 3.5 million patients with an imaginary counterfactual cohort for whom no treatment was available. In doing so, it was assumed that all patients initiating ART met WHO's 2006 treatment eligibility criteria.

For the imaginary counterfactual cohort, mortality rates were calculated using data from various cohort studies in Africa.[5, 6] The proportion of a cohort currently on ART who would die *if ART were stopped* was estimated to be 18% after one year; 46% after two years; 64% after three years; 76% after four years; 84% after five years; and 97% after six years.

Cost

The estimated average cost of ART per patient was based on a number of components.

The costs of medicines were based on country-reported procurements reported through the Global Fund's Price and Quality Reporting system and the WHO's Global Price Reporting Mechanism. These indicated that the median annual cost across Global Fund–supported countries was $204 for first-line drugs and $1,238 for second-line drugs as of 2011.

But drug prices change over time. From 2006 to 2009, the median price of the most commonly used first-line ARVs declined by an average 12% per year.[7] Because this rate of decline is unlikely to continue, the study assumed that the price of first-line drugs would

[4] WHO, UNAIDS, Futures Institute. Antiretroviral Medicines in Low- and Middle-Income Countries: Usage in 2008 and a Demand Forecast for 2010–2012, with a Special Focus on Sub-Saharan Africa, 2010.

[5] K. Todd et al. Time from HIV sero-conversion to death prior to ART: a collaborative analysis of eight studies in developing countries, *AIDS* 21 (suppl 6): S55–63 (2007).

[6] M. Marston et al. Estimating 'net' HIV-related mortality and the importance of background mortality rates, *AIDS* 21(suppl 6): S65-7.1 (2007).

[7] Global Fund. The Global Fund Results Report 2010: Innovation and Impact, 2010. Available here.

continue to drop, but only at an annual rate of 5%. For second-line ARVs, the study assumed that prices would reduce annually by 11% until 2015, after which prices would level off.

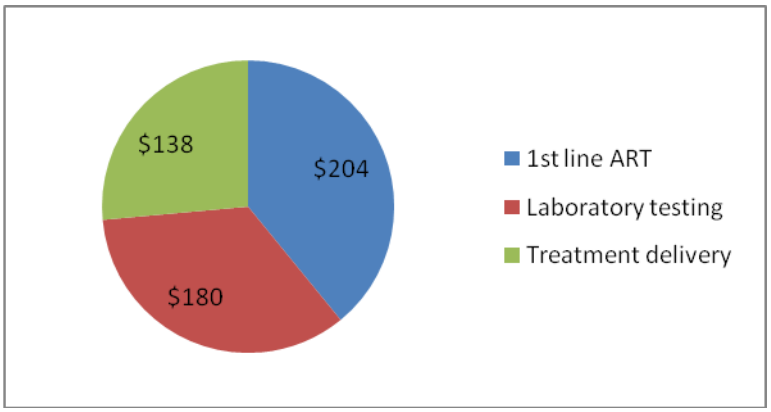
However, the average cost of ARVs per patient-year may yet rise because the revised 2009–10 WHO ART guidelines recommend phasing out stavudine (d4T) and replacing it with a more expensive drug. The study therefore also estimated costs on the assumption that a growing proportion of first-line treatment regimens will be more costly than most current treatment regimens.

The cost of laboratory tests was derived from a review of 15 published reports from low- and middle-income countries which found a median annual cost of $180 for monitoring each patient receiving ART.

The cost of inpatient and outpatient treatment was based on a review of studies from eight countries which reported a median of 9.5 out-patient visits and 1.6 in-patient days per ART patient per year. Country-specific estimates of the cost per in-patient day in a primary-level hospital and a 20-minute out-patient visit (extracted from the WHO CHOICE database) were then used to estimate a median annual cost of $138 per patient receiving ART (covering both inpatient and outpatient care).

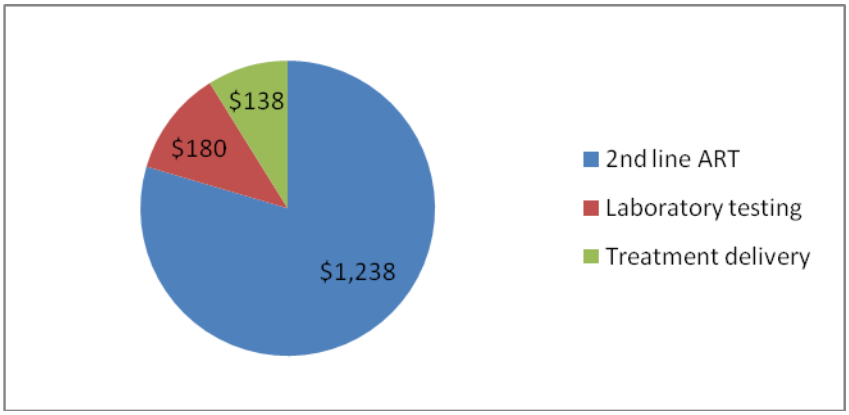
Figure 2 below shows the estimated costs and relative proportions of the different elements of the costing model for a single person on a first-line regimen in 2011. Approximately 39% of the cost is due to medicines ,while 34% is laboratory costs. The costs of actual service delivery accounts for only 26%. However, in the case of a person on second-line treatment, medicines make up 80% of the full costs, as shown in Figure 3.

Figure 2: Breakdown of first line treatment costs (with stavudine) for one person for one year ($US)



(Derived from figures supplied in journal paper)

Figure 3: Breakdown of second line treatment costs for one person for one year ($US)



(Derived from figures supplied in journal paper)

Finally, for patients on failing treatment regimens, it was assumed that costs would consist of 5.5 out-patient visits, 9.7 in-patient days and $49 worth of non-ARV drug costs per patient-year. This led to an estimated median health care cost of $320 per year. For patients dying on ART, the study added end-of-life care costs of $160 per patient.

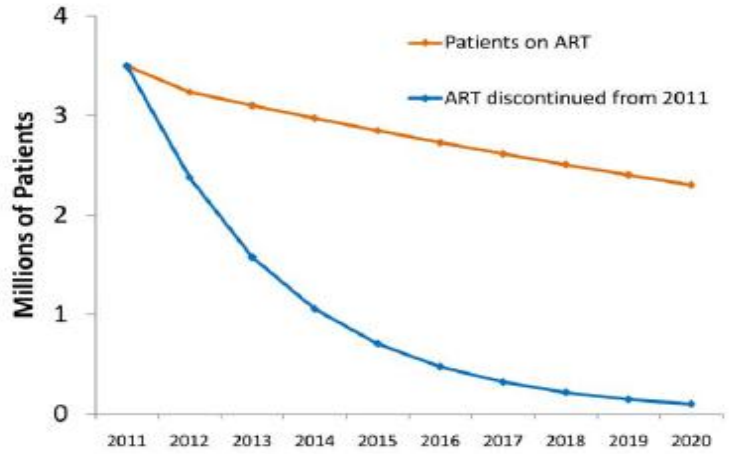
Although the study went to great efforts to calculate the various costs associated with ART, the following "above-facility-level costs" were not included: the human resource costs at drug distribution centres; district, provincial and national programme management; monitoring and evaluation costs; and the costs of health worker training in AIDS management and health system strengthening in general. Based on data from a recent evaluation of six African AIDS programmes, the study authors estimate that "above-facility-level costs" would add a further 20% of overall treatment costs.[8]

Results / Findings

The study estimates that of the 3.5 million people receiving ART in 2011, 2.3 million would still be alive and receiving treatment in 2020, a cumulative survival rate of 66%. Cumulatively, an estimated 17.7 million life-years would be saved. But if ART were to be discontinued, all 3.5 million people on ART would be dead by 2020 (Figure 4).

[8] Report to Congress on Costs of Treatment in the President's Emergency Plan for AIDS Relief (PEPFAR), July 2010, available for direct download here.

Figure 4: Survival curves of the 2011 cohort with and without ART



(Source: Stover et al, 2011)

The proportion of patients receiving second-line regimens would rise from 2.5% in 2011 to 24% by 2020, at which time patients on second-line regimens would account for about 50% of total costs.

If the price of medicines does not change over time, the full annual cost would decline from $1.9 billion in 2011 to $1.7 billion in 2020. This means that although patient numbers would reduce by 34%, there would only be a 10% reduction in costs – because of the higher proportion of patients on more expensive second-line treatment. Average per capita per year costs would therefore increase – from $543 in 2011 to $739 in 2020.

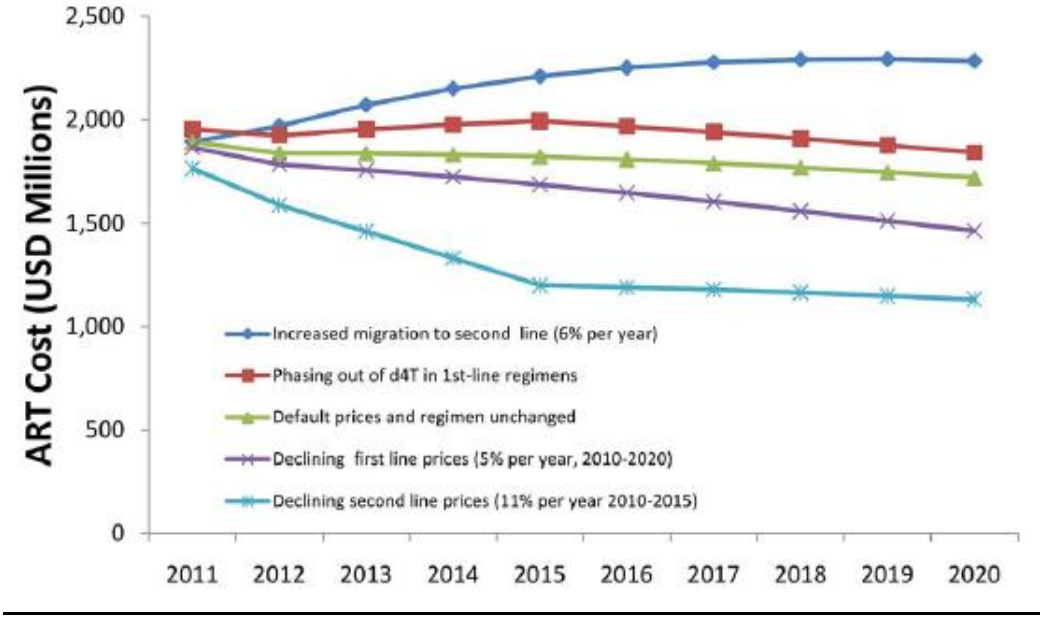
However, if first-line ARV prices continue to decline by 5% every year, the estimated cost in 2020 would be reduced by $260 million, down to a total annual cost of about $1.44 billion in 2020; and if, in addition, second-line treatment prices were to reduce by 11% annually until the year 2015, the overall costs would decline further to about $1.14 billion per annum in 2020.

However, if the phasing out of stavudine (d4T) from first-line regimens results in the median price of first-line ARVs per patient per year increasing (from $166 to $254 in 2015), financing needs in 2020 would consequently increase by $120 million (and possibly by more if the switch to non-d4T regimens leads to better adherence and survival).

The rates of migration to second-line treatment regimens used by the study are based on existing practices. However, more routine use of viral load monitoring leads to higher migration rates (around 6% compared to 2.6% in sub-Saharan Africa, Latin America and the Caribbean, and 1.1% in Asia). If this happens, and if all Global Fund–supported countries increase their annual migration rates to 6%, then the financing needs in 2020 would increase to about $2.3 billion per year, i.e., to a figure that exceeds the current estimated costs in 2011.

The annual costs and the trajectory of those costs over time under these different scenarios and assumptions are shown in Figure 5 below; and demonstrate the degree to which costs are sensitive to the price of medicines, the substitution of one drug for another, changes to clinical monitoring protocols, and the rate of migration from first- to second-line treatment.

Figure 5: Estimated costs under different ARV regimens and prices assumptions



(Source: Stover et al, 2011)

Discussion

The first step to take when discussing any research study is to understand its limitations. The results of this study are based on a range of assumptions about clinical practice, the quality of treatment and survival rates. Although these assumptions are derived from real data, they often come from a limited number of countries or research studies. And extrapolating the findings from one country to another, or from a research setting to a non-research context, is not easy. The study authors themselves highlight the need for better data on patient retention and survival, for both first- and second-line regimens.

The study is also based on very rough assessments of costs. For example, the costs of treatment varied only by the proportion of patients on first- and second-line treatment, when in reality, costs would differ according to (a) the number of patients who are pregnant, are children or have TB, (b) local laboratory testing policies, and (c) the efficiency of treatment delivery systems. Costs are also likely to vary from one country to another. As well, the lack of country-specific expenditure data is another source of error.

Finally, although the study examined costs under a number of different scenarios, other variables may affect the future cost of treatment. For example, it is possible that cost savings can be made by adopting lower-cost treatment models (e.g. shifting a greater proportion of ART to primary care and community-based approaches) or through the development of cheaper point-of-care diagnostics. Treatment retention rates may also change. For example, the low current treatment retention rates in the East, South and South-East Asia region (55% at 48 months) may improve and result in greater costs (although there would also be an increase in the number of lives saved).

However, despite these limitations, the study provides important and useful information, especially in terms of demonstrating the effects of changes in ARV prices, treatment regimens and clinical monitoring protocols. Such findings point to the need to press for a continued reduction in ARV prices, especially in relation to second-line treatments. They also emphasise the importance of optimising treatment quality and adherence so that patients

can be retained on first-line regimens for as long as possible, as well as the need for carefully constructed clinical monitoring protocols. (This last point is because recent studies in resource-constrained settings suggest that while CD4-based patient monitoring is generally more cost-effective compared to clinical monitoring alone, viral load monitoring may not always be cost-effective.)

This study's estimation of the future cost of ART was limited to the cohort of 3.5 million individuals on Global Fund–supported ART programmes. But of course, the global need for treatment and financing of HIV involves a far larger number of individuals. The study's authors quote UNAIDS estimates that funding for ART would require $7 billion to be spent in 2015 to achieve 80% coverage of those with CD4 counts under 200 cells/mL, and would need to increase by a further $3.5 billion to achieve 80% coverage under the WHO's current, expanded treatment eligibility criteria (covering all those with CD4 counts under 350 cells/mL).

If the number of patients on ART continues to increase by about one million patients per year through to 2020 and if the Global Fund's proportional contribution to overall ART financing continues as it is today, this would require the Global Fund to spend $5.2 billion on ART programmes alone in 2020, more than the $3 billion in total annual disbursements made by the Fund for all three diseases in 2010.

In light of the financial constraints that are already being imposed on donor programmes for ART, not to mention the inadequate levels of funding in many countries for basic and essential primary health care, this study brings to the surface a sobering picture in which the need for treatment is likely to increasingly outstrip the available supply of funding.[9]

It is therefore worth mentioning another recent study,[10] published in the *Lancet*. The *Lancet* study estimated all costs required to ensure an effective response to HIV/AIDS – i.e., not just the cost of providing ART, but also the costs of prevention, and care and support. And it dealt with the costs of providing such services to all who needed it, not just to the 3.5 million people currently under treatment in Global Fund–financed programmes.

A particularly important contribution from the *Lancet* study was the estimation of the costs of a set of critical social and programmatic enablers (required to ensure the cost-effective delivery of clinical and public health interventions) as well as broader developmental improvements (such as in the education and justice sectors) that are considered as important elements of a comprehensive response to HV/AIDS.

The *Lancet* study estimated that all these costs would total no less than $22 billion in 2015, rising from an estimated cost of $16.6 billion in 2011. The study predicted that, from 2015 onwards, annual costs would then decline for three main reasons: first, because target coverage rates will have been reached; second, because of efficiency gains through cost savings in treatment commodities, simplification of laboratory monitoring and a shift to community-based approaches in treatment and testing; and third, because of a decrease in new infections that will result from the earlier investment.

This is an important finding because it means that the pattern of rising costs associated with HIV/AIDS programmes need not be indefinite. There is a prospect that annual costs will reach a plateau, possibly at a level of about $20 billion per year. But it appears that the international health community will still need to campaign and lobby hard for every dollar

[9] This of course, was a central topic of discussion at the UN high-level meeting on HIV/AIDS that took place in June 2011.

[10] Schwartlander B, Stover J, Hallett T, et al. Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet* 2011; 377: 2031–41

required, while simultaneously lobbying for reductions in prices of medicines, and extracting maximum efficiency from their HIV/AIDS programmes and health systems.

With regard to the last point, the recent change in the Global Fund's grant-making architecture – to transition to one single stream of funding per recipient country per disease and per principal recipient (instead of multiple parallel grants) – is a potentially positive development, as it should make it easier to assess and improve activities at a programmatic level (rather than at a grant level), and should thereby identify opportunities for efficiency and quality improvements. The need to extract maximum efficiency from HIV/AIDS programmes and health systems also highlights the importance of health systems strengthening activities that improve the coherence and effectiveness of human resource planning and management, infrastructure development, and information and community systems strengthening – all of which will also enhance the effectiveness of the response to HIV/AIDS.