

The Costs of Anti-Retroviral Therapy in Low- and Middle Income Countries: Present Commitments and Future Needs

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Abstract

Background. Four million people were receiving antiretroviral therapy (ART) in low and middle-income countries by the end of 2008. At current survival rates most of these patients can expect to live another 13 years or more if they continue to receive treatment. The scale up of treatment today implies a long-term commitment to continue support well into the future.

Methods. We developed a model to project the number of people on ART and the costs of treatment through 2015. We examined several scenarios to understand the future financial resources required to maintain the current patients on ART and to expand ART coverage.

Results. About US\$ 2 billion will be required each year just to maintain current patients on ART through 2015. To continue the pace of scale up experienced from 2005-2007 will require expenditures rising to US\$ 8 billion by 2015. To reach universal access by 2010 would require US\$ 8 billion in 2010 and US\$ 10 billion in 2015. Total expenditures from 2008-2015 would range from US\$ 50 billion to US\$ 65 billion.

Conclusions. The financial commitment associated with the current scale up of ART coverage is substantial and will continue well into the future. Funders need to plan for this commitment to ensure

that resources are available to achieve and maintain the goal of universal access, and accelerate efforts to prevent new infections.

Introduction

The number of people receiving anti-retroviral therapy (ART) to treat HIV infection in low- and middle-income countries¹ has grown rapidly from about 100,000 in 2001¹ to 4 million in 2008², just over 40 percent of all those in need of treatment. This expansion has saved many lives and has contributed to a decline in AIDS deaths globally from a peak of 2.2 million in 2005 to 2.0 million in 2007.³

A number of factors have made this progress possible. First, significant reductions in the prices for anti-retroviral (ARV) drugs for low- and middle-income countries brought the annual cost of drugs down from over \$10,000 per person to as low as \$88 today. Second, strong political commitment has resulted in increased financing for ART. New funding mechanisms such as the US President's Emergency Fund for AIDS Relief (PEPFAR), the Global Fund to Fight AIDS, TB and Malaria and UNITAID coupled with other donors and national governments provided about US\$ 13.7 billion for AIDS programs in 2008⁴, a significant proportion of which supported treatment. Finally, revised treatment guidelines and a public health approach to treatment have simplified treatment programs, supporting expanded coverage even in countries with weak health systems.

ART is remarkably effective at delaying death from AIDS. It can provide 13 or more years of additional life. Since there is no cure for AIDS, patients starting on ART need to continue therapy for the rest of their lives. This means that the number requiring treatment grows each year as new patients starting ART are added to the patients that are continuing therapy.

¹ The World Bank defines low income countries as those with Gross National Income below \$935 and middle income countries as those with Gross National Income between \$936 and \$11,455.

The purpose of this paper is to examine the long-term commitment that is implied by the numbers of people receiving ART today and the international goals for achieving universal access. We address the following three questions:

1. What is the cost of maintaining one patient on ART?
2. What is the funding required to continue treatment for the 3 million patients currently on ART?
3. What is the funding required to scale up coverage to universal access?

Methods

We have developed a model for projecting future ART requirements that estimates new ART patients as a proportion of those newly needing treatment and unmet need from previous years and estimates continuing patients as those who successfully continue from the previous year. Costs are calculated on the basis of the number of patients and the costs of drugs, laboratory tests and service delivery per patient.

The projection of new and continuing patients is based on the methods used in the Spectrum software on the basis of recommendations from the UNAIDS Reference Group on Estimates, Models and Projections.⁵ Our projections of the future costs of treatment use the same approach as the UNAIDS global resource needs estimate but include updated prevalence estimates and reports of numbers of people receiving ART.⁶

Need for ART

The number of people newly eligible for ART in each year is based on new infections in previous years and the pattern of progression from infection to need for treatment. UNAIDS estimates prevalence

trends for all countries from national HIV surveys and surveillance data⁷. The Spectrum model estimates the number of new adult HIV infections from prevalence, population size and AIDS deaths:

$$I_t = P_t \times \text{Pop}_t - P_{t-1} \times \text{Pop}_{t-1} + D_{t-1,t}$$

Where:

I_t = New adult HIV infections during year t

P_t = Adult HIV prevalence in year t

Pop_t = Adult (15-49) population in year t

$D_{t-1,t}$ = Deaths due to AIDS and other causes among HIV+ population from year t-1 to t

New infections progress over time to need for treatment and AIDS death. Progression from new infection to AIDS death for adults is modeled as a Weibull distribution with a median time of 11 years based on data from the ALPHA network of cohort studies^{8,9}

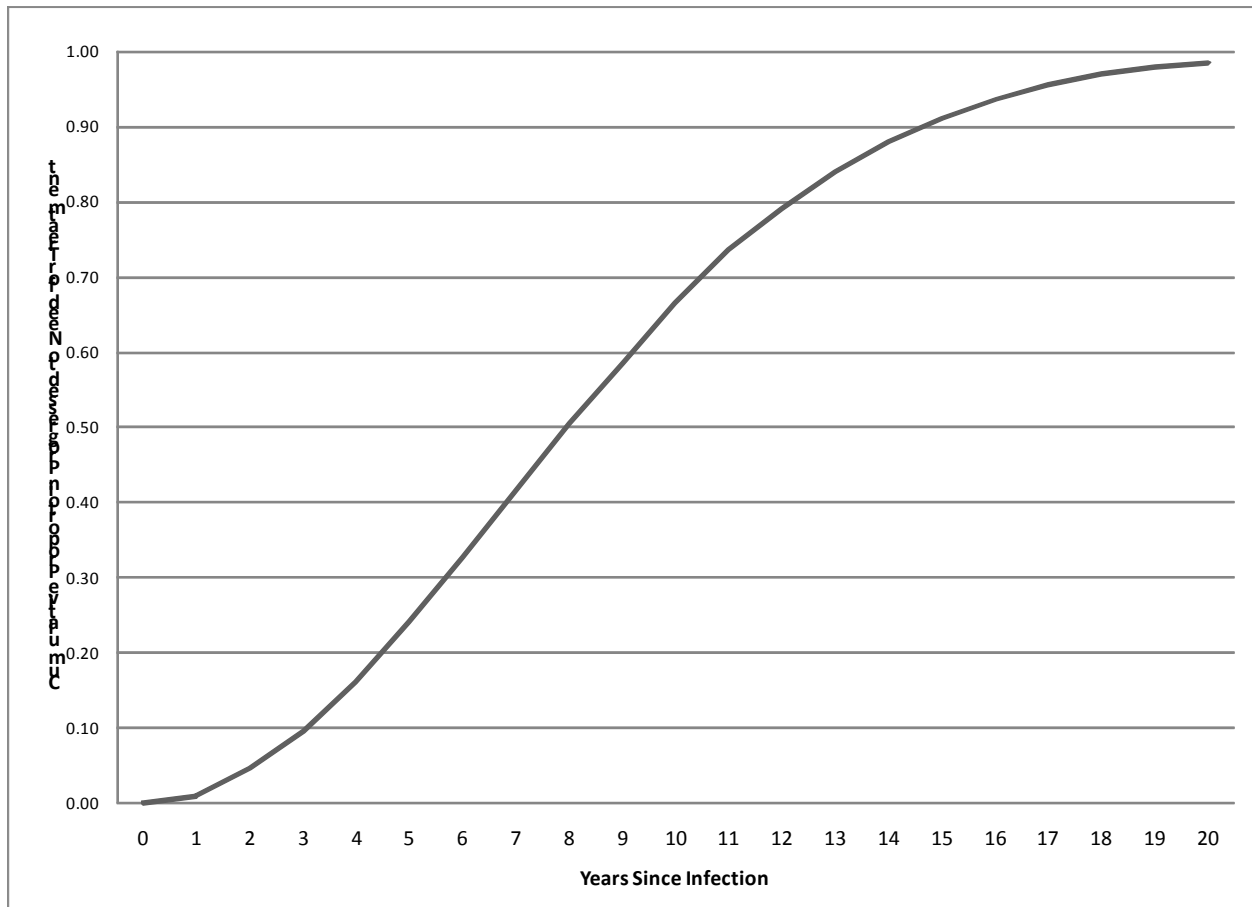


Figure 1. Proportion progressing to 'need for treatment' by number of years since infection

Before AIDS death occurs a person becomes eligible for ART. According to current WHO guidelines eligibility for ART among adults begins when the CD4 count drops below 200 cells/mm³ or the CD4 count drops below 350 and the patient exhibits WHO Stage III (Advanced) or IV (Severe) clinical stage.¹⁰ Our model does not estimate the decline in CD4 counts of patients to calculate those in need of ART but instead uses the time from infection to the point when CD4 counts meet the WHO criteria. We model this progression as a Weibull curve with a median of 8 years (Figure 1). This assumption is based on data from five cohorts in the e-ART-linc collaboration which indicate that the median time from new infection to a CD4 count of 200 is 7.6 (3.4-15.2) years and the median time from CD4 count of 200 to AIDS deaths is 2.7 (0.8-8.4) years and from CD4 count of 350 and WHO Stage III or IV is 3.0 (2.4-3.8) years.¹¹ People

who do not receive ART as soon as they become eligible remain eligible to start ART in subsequent years until they die.

New child infections are estimated from the prevalence of HIV among women giving birth and the probability of mother-to-child transmission. A review of studies of mother-to-child transmission suggests that the probability varies from 35% in cases of no drug prophylaxis and long duration of breastfeeding to as low as 2% when the mother is receiving triple ART and does not breastfeed⁴. The probability is 17-26% with single dose nevirapine and 10-29% with dual ART therapy assuming mixed feeding depending on the duration of breastfeeding. When replacement feeding is practiced transmission probabilities are 11% for single dose nevirapine and 4% for dual ART. For children progression to ART eligibility occurs much more rapidly than for adults. We use a progression pattern described by a double Weibull curve that recognizes that children infected perinatally progress very rapidly (median survival of about 10 months) while those infected through breastfeeding progress at slower rates similar to adults (median survival time of 8.3 years)¹².

Survival on ART

Once on ART most patients will live much longer than the three years of survival expected without ART, assuming that the drugs remain available. Data from the ART-LINC Collaboration from 17 cohorts of ART patients indicate that the proportion surviving on ART after one year is 0.939 (0.936-0.942) and 0.929 (0.926-0.932) after two years. However, these data ignore loss to follow-up which can be as high as 16% in the first six months. After adjusting for loss to follow-up we assume that 86% of ART patients will survive the first year on treatment and 90% will survive each subsequent year.⁵

Patients failing on first line ART are assumed to die unless they are started on second line ART. Little information is available on survival on second line ART in developing countries, so we assume that

survival on second line is the same as survival on first line. With these assumptions, median survival on first line is about 7 years and patients receiving immediate access to second line have a median survival of 13 years. (These estimates include the probability of mortality from non-AIDS causes.)

Costs of ART

We model the costs of four components of ART: first line drugs, second line drugs, laboratory tests and service delivery. Information on prices paid for ARV drugs has been collected by the Global Price Reporting Mechanism since 2004. Prices have declined by about half since 2004. Prices vary from country to country and by regimen. For low-income countries the median price paid for the most common first line regimen (d4T, 3TC and nevirapine) was US\$88 per person per year. The weighted average median price of the four most commonly used first line treatment regimens was US\$ 143 in 2008 in low-income countries and US\$162 in middle-income countries².

Prices for second line drugs are considerably higher than first line drugs and show more variation across countries. The median cost for the second line regimen that is the most expensive of the most commonly used regimens (didanosine, abacavir and ritonavir-boosted lopinavir) was US\$ 1105 in low-income countries and US\$2192 in lower middle income countries and US\$2634 in upper middle income countries. The median cost for the most commonly-used second line regimen (tenofovir, FTC and ritonavir-boosted lopinavir) was US\$819 in low-income countries, US\$1479 in lower-middle-income countries, and US\$1677 in upper-middle-income countries².

Laboratory tests, particularly those monitoring CD4 counts, become an important component of overall costs as drug prices have declined. Laboratory costs vary from country to country depending on national treatment guidelines. To estimate the global costs we calculated the annual median cost for laboratory

tests from published studies from eight countries (Cote d'Ivoire, Ethiopia, Mexico, Nigeria, South Africa, Thailand, Uganda, Zambia)^{13, 14, 15, 16, 17, 18, 19, 20, 21}. The median cost is \$191 per patient per year.

Our estimates of service delivery costs are based on a standard number of in-patient days and out-patient visits per patient per year and country specific costs for in-patient days and out-patient visits. These will also vary from country to country based on national guidelines. For this global analysis we used the same studies referenced above for laboratory costs (with the exception of Cote d'Ivoire and the addition of another South Africa study²²) to calculate the median number of out-patient visits per year as 9.5. Only three of these studies also had data on the number of in-patient days for ART patients^{15,17,22}; we used these to calculate the median number of in-patient days for ART patients per year as 1.56. Country-specific costs per in-patient day are the costs of one bed day at a primary-level hospital as reported in the WHO-CHOICE database of service delivery costs²³. The cost of an out-patient visit is for a 20-minute outpatient visit at a health centre, from the same WHO database. The result is annual service delivery costs that vary from US\$72 in sub-Saharan Africa, US\$94 in South-east Asia, US\$100 in East Asia, to US\$120-140 elsewhere.

Scale Up Scenarios

We calculated the future costs of ART for 133 low- and middle-income countries using two scenarios of future ART coverage (the percentage of those in need of ART who receive it). Due to the difficulty of identifying all those in need of ART as soon as they become eligible we adopt the UNAIDS definition that universal coverage of ART is defined as 80% of those in need. (In countries that already exceed 80% coverage the current level of coverage defines universal access.)

1. Historical growth. The number of people receiving ART in each county increases at the same rate as during the period 2005-2007.

2. Rapid scale up. ART coverage increases to achieve universal access by 2015.

The costs of ART drugs have been declining rapidly in the past few years and this trend is expected to continue for second line drugs as more patients require second line therapy and the Clinton Foundation and others work with manufacturers to lower second line prices. This may not be true for first line drugs, however, as prices are already low for the most popular regimens and many countries will be switching their primary first line regimen to drugs that perform better but are also more expensive such as efavirenz, tenofovir and FTC. We assume that the drug prices in each country will change from their current levels to US\$136 for low income countries and \$165 for middle income countries per patient per year for first line drugs by 2015. We assume that second line drug prices drop to US\$ 665 in low income countries and \$1,714 in middle income countries by 2015²⁴. The costs of laboratory tests and service delivery are assumed to remain constant.

Projections are done separately for each country and then aggregated to get totals for each region and for all low- and middle-income countries.

An interactive version of the model is available at the following web site: www.FutureARTCosts.org.

Results

For a single person in a low-income country starting on ART today the first year costs would be US\$ 380 (US\$ 88 for first line drugs, US\$ 190 for laboratory tests and \$102 for service delivery). That person could expect to survive on first line ART for 7 years by which time the annual costs would have risen to US\$ 143 because of increases in first line costs due to switches to new regimens. If that person then switches to second line therapy the annual costs will rise to US\$ 890 because of the higher cost of second line drugs. That patient would be expected to survive another 7 years on second line ART. During the course of the treatment the total costs would be US\$ 9,200. The present value of those future costs, discounted

at 3% per year, would be US\$ 7,485. Thus a funding agency paying for a patient to start on ART today will pay only US\$ 380 this year but should be prepared to fund an additional US\$ 8,820 for future treatment costs.

For the 4 million people in low- and middle-income countries on ART as of the end of 2008 the current funding requirements are higher than US\$ 380 per person since these patients represent a mixture of low-income and middle-income countries and about 2% of patients are on second line therapy. Total costs in 2008 were about US\$ 2 billion. (Note that the total funding for treatment is significantly higher as it includes non-ART care, research, monitoring and evaluation, facilities expansion and technical assistance costs that we do not consider here.) At the current rates of survival on ART the number of patients on first line therapy would decline from about 3.9 million in 2008 to 1.8 million by 2015. If all patients failing first line get second line drugs then the number of patients on second line therapy will increase from less than 100,000 today to 1.4 million by 2015. The total number of patients on ART in 2015 would be 3.2 million² and the cost in that year would be US\$ 2.2 billion (Table 1). Therefore about US\$ 2 billion will be needed each year through 2015 to maintain patients currently on ART without adding any new patients.

Maintaining current patients on ART will not be enough to address the global problem because current coverage is only 42% of those who need ART and more people will need ART in future years.

- Continuing Historical Growth in ART coverage would raise coverage to about 72% by 2015 at which time almost 9 million people would be receiving ART at an annual cost of US\$ 5.1 billion.

Cumulative costs from 2009 to 2015 would be US\$ 31 billion.

² Of the 4 million on ART in 2008 about 80,000 are on second line. At 90% annual survival 38,000 would still be alive in 2015. Of the 3.9 million on first line in 2008 1.9 million would still be alive and on first line therapy in 2015. The other 2.1 million would switch to second line and 1.5 million would still be alive in 2015. Non-AIDS mortality causes about 220,000 deaths during this period, so the total alive in 2015 is about 3.2 million.

- Rapid Scale Up would raise ART coverage to 60% by 2010 and to 80% by 2015 at which time 11.3 million patients would be on ART at an annual cost of US\$ 5.8 billion. Cumulative costs from 2008 to 2015 would be US\$ 34 billion.

Increasing ART coverage means that the annual costs of delivering ART will rise from about US\$ 2 billion in 2007 to US\$ 5.1 – 5.8 billion by 2015. Additional resources will be needed to support health system expansion, research, etc. This substantial rise in resources required will also bring substantial benefits. There were about 2 million AIDS deaths in 2007³. Under these two scenarios the annual number of AIDS deaths would decline to 1.7 million deaths in 2015 (Continuing Historical Growth) or about 1.3 million deaths (Rapid Scale Up). For the period 2008 to 2015 scaling up ART coverage would avert 7-11 million deaths compared to no scale up.

There is considerable uncertainty around these projections due to uncertainties around the number of people in need of treatment, the effects of treatment on survival and the costs of drugs, labs and service provision. When plausible variations in these factors are taken into account the plausibility bounds on resources needs for 2015 are: Current Scale-Up: US\$ 4.1-6.6 billion and Rapid Scale-Up: US\$ 4.4-7.2.

The incremental cost-effectiveness ratio is \$1750 per death averted for the Historical Growth scenario compared to Rapid Scale Up. The cost per disability-life-year (DALY) gained is about \$ 50. The WHO-Choice Project²⁵ and the Commission on Macroeconomics and Health²⁶ have suggested that any health intervention with a cost per DALY saved less than the gross national income (GNI) per capita is very cost-effective. These comparisons are typically made in international dollars. For low income countries GNI per capita in international dollars is \$2486²⁷.

Discussion

The resources required for ART in low- and middle-income countries go well beyond the costs of starting new patients on therapy. Each new patient represents a commitment to keep providing funds to continue that patient on ART for 13 years or more. Thus the present value of the commitment is about 11 times the first year cost. The current number of 4 million people on ART implies a commitment of about US\$ 2 billion a year to maintain them on ART through 2015.

Two-thirds of current ART patients are supported by funding from the Global Fund to Fight AIDS, TB and Malaria (GFATM) and the United States President's Emergency Program for AIDS Relief (PEPFAR). The US Congress has authorized additional funds for PEPFAR for 2009-2014 that will provide about US\$ 2 billion per year for treatment. Other donors may contribute additional resources to the GFATM. There should be more than enough resources available in the next five years to meet the commitment to those currently on ART, but the funds required to maintain the historical rate of scale-up may well exceed the funding available in just the next few years. An increase to annual funding of US\$ 5-6 billion will be needed to continue rapid scale up.

The need for ART is already determined for the near term future. The majority of those who will progress to needing treatment between now and 2015 are already infected. There is little we can do today to reduce the need for treatment by 2015. Beyond 2015, however, the need for ART will be determined by the number of new infections occurring now and in the future. Studies have shown that more forceful efforts in prevention today could reduce the treatment burden in 2020 by more than half²⁸.

Direct measures of incidence trends at the national level do not exist so we have estimated incidence from prevalence trends. The projections of the number of people needing treatment rely on these

incidence estimates. The accuracy of the estimates of people newly needing treatment depends on the accuracy of the prevalence estimates. While these estimates have been changed significantly in the past, most countries with the largest number of HIV infections have now had at least one population survey so the estimate of prevalence at the global level should be better now than it has been in the past.

It may be expanded ARV treatment will affect the incidence of new HIV infections. Incidence could decline if reductions in viral load result in reduced chances of transmission or incidence could rise if ready access to ART results in increases in risky behavior. In any case, changes in the number of new infections now will not affect the estimate of treatment costs by 2015 since few new infections today would progress to need for treatment by 2015.

In the next 6 years there may well be changes in drug prices, monitoring and testing technology and treatment approaches that we have not anticipated that would change these cost projections. However, some funding for this period has already been committed and others are making those decisions now, so it is important to make projections using the best available data.

It is important to recognize that successful efforts to increase the number of people on ART today carry with them a commitment to continued support for at least the next 13 years. While this commitment requires significant financial resources, the treatment it supports is a cost-effective use of resources. Treatment can significantly extend the lives of millions of people and bring additional benefits to their children, families and communities.

Authors Contributions

JS prepared the projection model. LB compiled the costs of treatment. JS and LB wrote the manuscript.

Conflicts of Interest

None.

Role of Funding Source

The Bill and Melinda Gates Foundation encouraged us to address the topic but did not participate in the analysis or influence the conclusions.

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