Sustaining and Leveraging AIDS Treatment

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ABSTRACT

The international donor community has succeeded in supporting a vast expansion of access to subsidized AIDS treatment, from a few thousand patients in 2003 to approximately 4 million in 2010. If ethical or reputation concerns bind the donors to continue this support, these patients are the beneficiaries of the first international entitlement program. The AIDS treatment entitlement, like any entitlement, engenders dependency among its beneficiaries and restricts the flexibility of the donors and governments that assume its burden. This essay presents original estimates of the magnitude of the future fiscal burden of AIDS treatment under alternative assumptions about treatment quality and scale up and then proposes policy options to harmonize the incentives among donors, recipient governments, and AIDS patients to sustain treatment quality while leveraging treatment demand for the prevention of future cases.

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I. Donor supported AIDS treatment: the first international entitlement

At the 2005 summit meeting of the Group of Eight (G8) in Gleneagles, Scotland, the assembled heads of state pledged "to develop and implement a package for HIV prevention, treatment and care, with the aim of as close as possible to universal access to treatment for all those who need it by 2010." Furthermore, they promised that, "We will work to meet the financing needs for HIV/AIDS.[1]" When the International AIDS Society—a professional organization whose members include both AIDS researchers and AIDS patients—convened in November 2009, it referred to this commitment and then said, "Five years later, major donors and domestic governments appear to be pulling back on this commitment. While significant progress has been made toward expanding access to HIV prevention and treatment since 2005, the universal access goal is far from being met.[2]"

The "significant progress" referred to by the International AIDS Society is that the number of patients receiving subsidized AIDS treatment in poor countries, mostly in Sub-Saharan Africa, has risen from a few thousand in 2003to about 4 million in 2009. Of these patients, about 2.5 million are supported by the U.S. government's AIDS program, entitled the President's Emergency Program for AIDS Relief (PEPFAR). Thanks to this unprecedented international effort, the percentage of those needing treatment who were receiving it increased from less than 5 percent in 2003 to about 43 percent in 2009. Although the term "universal access" has been defined in many ways—ranging from 100 percent coverage to the more typical 80 percent coverage—all observers agree that 43 percent falls far short of that goal. Making matters more complicated, WHO has recently shifted the goalpost. At end-2009, it announced new treatment guidelines[3], which increased by a factor of two or three the number of people in need, and thus reduced the measured coverage rate from a hopeful

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[1] Paragraph 18. D) in the section of the G8 Communiqué on Africa entitled "Investing in People", available at http://www.g8.utoronto.ca/summit/2005gleneagles/communique.pdf (Accessed 4/25/2010.)
[2] http://www.iasociety.org/Web/WebContent/File/IAS_GC%20Backgrounder_%2019%20Nov%202009.pdf
[3] The definition of "needing treatment" continues to change. An important measure of the progression of HIV disease is the number of CD4 counts per milliliter of the patient's blood, a count that declines from close to a thousand for uninfected people to zero as the person's immune system is destroyed by HIV. After years of consensus that the threshold for AIDS treatment should be 200 cells per microliter (World Health Organization, 2006), which would be about eight years after HIV infection, evidence is accumulating that starting treatment a year or more earlier, when the CD4 count is 350, would improve the effectiveness of treatment (When to start Consortium and Jonathan Sterne, 2009). The WHO revised its guidelines on December 1, 2009 to recommend that treatment begin at a CD4 count of 350.

looking 43 percent to a dismal 10-20 percent. The attempt to provide treatment to all who need it looks more and more like the labor of Sisyphus, whom the Greek gods set the task of pushing a boulder to the top of a hill, only to see it roll back to the bottom each time it got close.

US funding for AIDS:
2004 - 2010: Enacted by US Congress
2011: Requested by administration
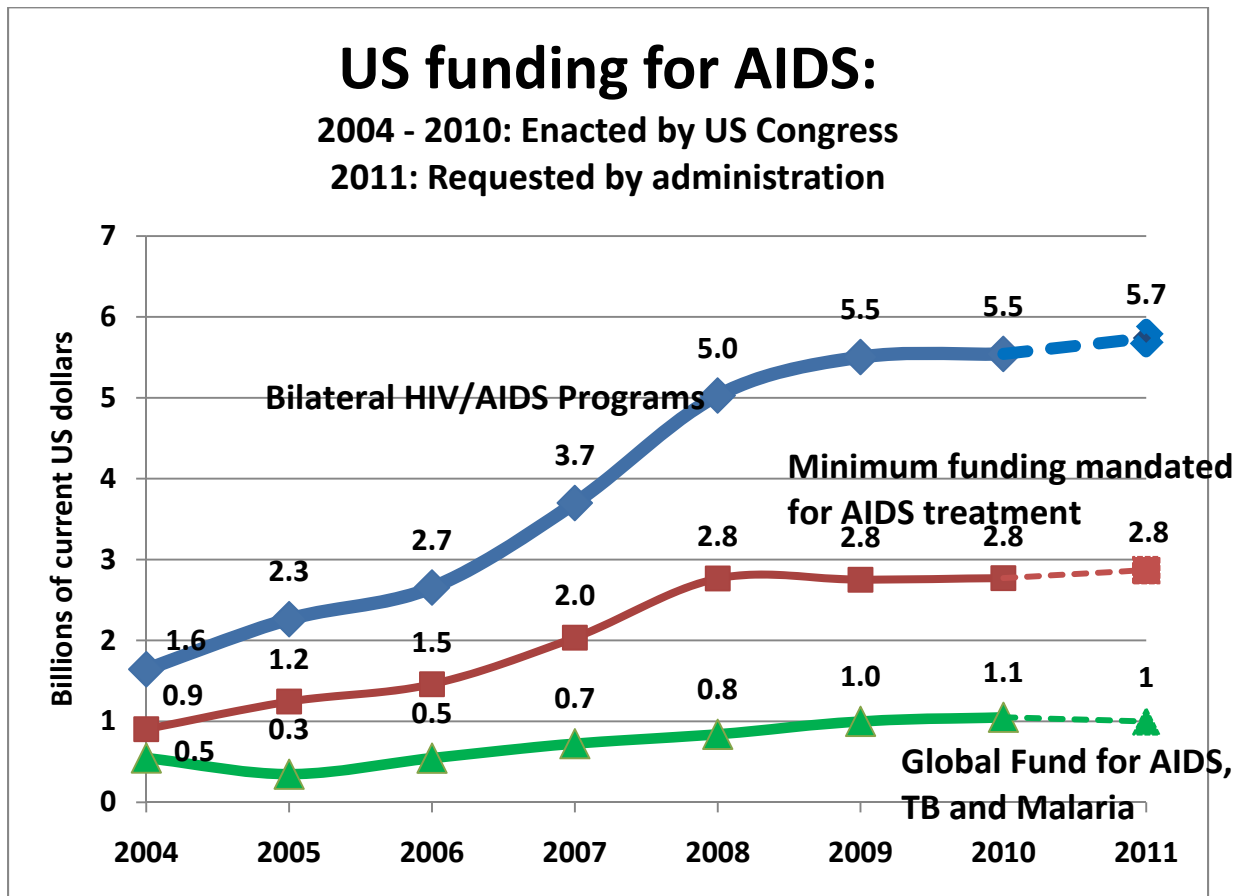
Figure 1. Universal treatment not on track
After a growth spurt, U.S. funding for AIDS treatment is flatlining
 (Source: http://www.pepfar.gov/documents/organization/80161.pdf accessed April 25, 2010.)

To support the view that donors are "pulling back" from their 2005 universal treatment commitment, one need look no further than the United States, the world's larger contributor.   The bill to reauthorize PEPFAR passed Congress in 2008, before the end of President Bush's second term. That bill authorized $63 billion in new spending from 2009 through 2014 of, which $39 billion is for HIV/AIDS treatment. Figure 1 shows the growth of PEPFAR funding for AIDS as enacted by Congress from 2004 through 2010 and as requested by the Obama Administration for 2011.   The uppermost line shows the total amount for bilateral AIDS support, while the second line applies to that total the minimum amount that PEPFAR was required by Congress to spend on AIDS

treatment, which was 55 percent under the original 2003 authorization bill and 50 percent under the 2008 authorization. From these lines it is evident that the rapid growth of U.S. funding for AIDS, at about 25 percent per year through 2008, has halted since that date, with the minimum amount mandated for treatment actually leveling off in recent years. Nor has the leveling off of the United States bilateral funding for AIDS been offset by its funding through other channels. The bottom line in Figure 1 shows that U.S. funding for the major multilateral route for funding AIDS treatment—the Geneva-based Global Fund for AIDS, Tuberculosis and Malaria—has also flattened in recent years.

In view of this "flatlining" of AIDS spending by the largest donor at a time when the number of people on treatment falls far short of universal access, one might ask whether the United States and the other G8 governments are committed to anything at all with respect to AIDS treatment. On April 11, 2010, Farah Stockman of the *Boston Globe* quoted a letter from the American embassy in Kampala, Uganda, to PEPFAR-supported AIDS treatment facilities in that country as saying: "While the U.S. government is committed to continuing treatment for those individuals already enrolled . . . funding for HIV programs is not expected to increase in the near future. As a result, PEPFAR Uganda cannot continue to support scale up of antiretroviral treatment without a plan from the Government of Uganda on how these patients will be sustained.'' According to Ambassador Goosby, the U.S. global AIDS coordinator and head of the PEPFAR program, the letter did not mean that U.S.-supported enrollment of new patients has stopped yet in Uganda. However, Stockman quotes him as saying, "People are struggling to find resources to honor the commitments we have made. … We're not at a cap point yet. If it gets worse, we'll have another discussion.''[4]

These statements by Ambassador Goosby and others by PEPFAR staff in Uganda suggest that the United States draws a sharp distinction between patients whose antiretroviral therapy (ART) it is currently supporting and those with equal need who have not yet enrolled in treatment at a U.S.-supported site. Supporting the first group is an existing "commitment" to be "honored." For patients not yet on treatment, the U.S. government will seek assurances that it alone will not bear all the future costs.

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[4] Farah Stockman, "US seeks to rein in AIDS program," Boston Globe, April 11, 2010
http://www.boston.com/news/nation/washington/articles/2010/04/11/us_seeks_to_rein_in_aids_program/ as accessed April 25, 2010.

Although called an "emergency plan," the U.S. PEPFAR initiative has already endured longer than most emergency programs and, unless the United States either abandons or hands over its patients to other funders, PEPFAR is likely to persist longer than most foreign assistance projects. As *The Economist* has pointed out,

> The problem with AIDS is that the more successful you are at treating it, the more you end up paying. That is because, unlike malaria and tuberculosis (TB), it is incurable. Once someone is infected with HIV, the virus that causes it, they will end up requiring treatment for life. Good news for drugmakers, but bad news for both the poor who make up the overwhelming majority of the 40m people infected and for the taxpayers of the rich world who will be expected to find much of the money (The Economist (2007)).

To the extent that donors and their constituents agree that continued treatment is sacrosanct, donor financed support of AIDS treatment in poor countries has created a new kind of international "entitlement." Although the donors are not required by law to continue AIDS treatment, as would be true for domestic entitlements like the U.S. Social Security program, I believe that the international community and the voting public in democratic countries will constrain donors from dropping patients from treatment rolls. As the largest national donor, the U.S. will be seen as particularly accountable for sustaining this life-giving therapy, especially in the 15 original PEPFAR focus countries. If the strength of this reputation effect is sufficient to prevent donors from reneging on implicit obligations to provide lifetime support for patients currently receiving treatment, then AIDS treatment can be treated as an entitlement—and all other types of international assistance financing, including HIV prevention, by contrast, discretionary.

Discretionary spending is whatever is left in a budget after entitlements are funded. From the donors' perspective, the downside of growing entitlements—in the absence of a very large increase in the total aid budget—is that the proportion of discretionary spending in donors' AIDS budgets will decline as donors place more and more patients on treatment. From the recipients' side, the downside of entitlements is dependency. Those who receive entitlements typically become dependent on them, and never more starkly than in the case of

expensive life-giving drugs. There may be medium- and long-term negative repercussions from the extreme form of aid dependency that AIDS treatment represents.[5]

Because support for AIDS treatment converts foreign assistance from discretionary to entitlement spending, past treatment expenditure has already locked the United States and the other donor countries into a new aid paradigm. Advocates point to the unmet need for care and call for ever-increasing funding levels.[6] To the extent that the international community heeds the advocates' call for more resources, entitlement spending will greatly increase in the next few years. The increase will be both absolute and, unless total assistance expands at the same phenomenal rate, relative to total assistance.

Are voting taxpayers of the United States and other industrial countries ready for this new entitlement paradigm? Growing funding for AIDS treatment suggests this possibility. But there is reason for concern. Historically, when budgets expand less quickly than planned, growing entitlements often squeeze out discretionary programs. In comparison to the moral imperative to continue funding AIDS treatment, HIV prevention and all other assistance programs will appear to be discretionary. So if the requested additional AIDS funds are not forthcoming, the discretionary assistance will be squeezed out. By one calculation, the $50 billion a year requested by UNAIDS from all donors to meet "universal access" objectives for treatment and prevention could squeeze out spending on all eight of the United Nations Millennium Development Goals (MDGs), which are aimed at boosting living standards worldwide .[7]

In a companion essay, I propose a new framework for addressing the AIDS epidemic, which I call the "AIDS Transition." I define the AIDS transition as a dynamic process that holds AIDS mortality down—that is,

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[5] For example, AIDS patients or their governments could begin to resent their dependency. Elsewhere, I have suggested that dependency for their day-to-day existence by the citizens in a poor country on the benevolence of foreign donors might be characterized as "post-modern colonialism."(Over, 2008)

[6] On September 26, 2007, UNAIDS published "Financial Resources required to Achieve Universal Access to HIV Prevention, Treatment, Care and Support" to request $50 billion a year in AIDS funding, up from the current level of about $10 billion a year.

[7] A 2002 World Bank study (Devarajan et al, 2002) in support of the UN-mandated Millennium Development Goals estimated that the cost of achieving all eight of the goals by the year 2015 would be between $40 and $60 billion a year.

preserves recently achieved mortality reductions while lowering the number of new infections even further—so that the total number of people living with HIV/AIDS will begin to diminish.

In this essay, we discuss policy options for AIDS treatment that can sustain current patients on treatment while at the same time hastening the AIDS transition. In conformity with the view that patients currently on treatment have an entitlement to continued treatment, none of the scenarios considers the possibility of reducing support for those patients. However, many other options are on the table. We project the cost of a range of new patient recruitment options from the "flatline" option in which no new patients are added to existing treatment rolls up to the option of recruiting 80 percent of those in need. We also contrast the cost of a policy that offers only the less expensive "first-line" therapy to the cost of a policy that continues patients onto second-line therapy when they fail first-line. And we show how a general move to initiate each patient's treatment earlier in the course of the illness will not only improve the efficacy of AIDS treatment and prevent a portion of new HIV infections but also greatly increase the fiscal burden of treatment. In a world of scarce financial resources, all of these options involve tradeoffs between expenditures and years of healthy life for the patients. While the calculations presented cannot determine how to choose among the alternative policies, they can elucidate the foregone opportunities implied by any choice and thus help policymakers and their constituencies choose wisely.

II. AIDS treatment successes

A. Numbers of patients on treatment

A number of influential players have contributed to increase the number of people in poor countries receiving antiretroviral treatment (ART) from less than 100,000 in 2003 to approximately 4 million in 2009. Among those most responsible for this dramatic change are President Jacques Chirac of France and President George W. Bush of the United States.

From 1981, when the human immunodeficiency virus (HIV) was discovered and identified as the cause of AIDS until 1997 when President Chirac of France made a dramatic proposal at that year's African AIDS conference, AIDS treatment was considered far too ineffective, complicated, and costly for governments or donors to fund in low- or even in middle-income countries. For example, in 1988, one year after the first antiretroviral drug, AZT, had been patented, and before it was widely available, a global review of the cost of AIDS treatment found that a single patient-year of treatment in some representative rich countries cost $19,000-$147,000 in the United States., $21,000 in France, $40,200 in Germany, $13,400-46,000 in the United Kingdom, and $15,800 in Australia, and rarely gave the patient more than a few months of healthy life (Scitovsky and Over, 1988). In subsequent years, as medical research introduced new classes of drugs to directly attack the HIV retrovirus and "triple-drug therapy" became accepted, the effectiveness of treatment dramatically improved but its potential cost per patient-year also rose. In the mid-1990s, the government of Thailand evaluated the cost-effectiveness of the new therapeutic combinations and concluded that "providing free antiretroviral therapy for symptomatic HIV infection, even with cost sharing, was unaffordable for both the public sector and the majority of patients" (Prescott, 1997; van Praag E. and Perriens, 1996).

Writing in 1996 and 1997 on the priorities for government and donor intervention in the AIDS epidemic, my co-author Martha Ainsworth and I recognized the human tragedy unfolding as AIDS deaths climbed in AIDS-affected countries. But we were persuaded that, given the high costs and still limited effectiveness of ART, spending $10,000 to $20,000 per patient year on treatment would alleviate much less of that tragedy than would

the same resources spent on prevention. So we argued that, while governments have a fundamental responsibility to assure and to finance effective HIV prevention, especially among those with the riskiest behavior, donor or government subsidies for AIDS treatment were hard to justify in poor or even middle-income countries. (Ainsworth et al, 1997). We hoped that our book's argument for a dramatic increase in the most cost-effective types of HIV prevention would be used by donors and governments to invigorate prevention efforts, especially in Africa. To that end we launched our book during the opening session at the 1997 African AIDS conference, which was held that November in Abidjan, Cote d'Ivoire.

At that 1997 AIDS conference, Ainsworth and I received a bracing lesson in the politics of AIDS treatment. President Chirac of France made a surprise appearance to give the keynote address, which immediately preceded our session. The contrast between his message and ours could not have been starker. While making only passing reference to the need for HIV prevention, President Chirac used his talk to issue a clarion call for donor funding of AIDS treatment and proposed the first global AIDS treatment initiative.[8] Neither donors nor governments immediately responded to Chirac's proposal. Indeed the European Commission, the World Bank, and the United States Agency for International Development all continued to emphasize prevention, though without scaling-up to full coverage of high-risk populations as Ainsworth and I had recommended. However, in retrospect, Chirac's proposal is the historical precursor of subsequent much more successful efforts to expand AIDS treatment, including the World Health Organization's 2003 initiative to place 3 million people in poor countries on AIDS treatment by 2005 (called the "3 by 5" initiative) and U.S. AIDS initiative called PEPFAR.

With President Bush's 2003 State of the Union address, the United States began a process that led to the creation of PEPFAR. While PEPFAR's objectives included not only treatment (2 million on treatment by 2007 in the 15 focus countries) but also prevention and care, the political emphasis and the difficulties of measuring the achievement of these last two objectives led to a focus on expanding of AIDS treatment. And ART did

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[8] According to Reuters' Mathew Bunce [http://www.aegis.com/news/ads/1997/AD972244.html], "French President Jacques Chirac addressed Africa's top AIDS conference on Sunday [December 7, 1997] and called on the world's richest nations to create an AIDS therapy support fund to help Africa. According to Chirac, Africa struggles to care for two-thirds of the world's persons with AIDS without the benefit of expensive AIDS therapies. Chirac invited other countries, especially European nations, to create a fund that would help increase the number of AIDS studies and experiments. AIDS workers welcomed Chirac's speech and said they hoped France would promote the idea to the Group of Eight summit of the world's richest nations."

expand! By the end of Bush's presidency in December, 2008, PEPFAR was reporting approximately 3 million directly or indirectly supported on ART, and during 2008, another 1 million were added. As Figure 2 shows, most of the 2.5 million people whose treatment is being directly supported by PEPFAR reside in Sub-Saharan Africa. Although the percentages of people infected are much smaller in Asia than in many African countries, the populations of China and India are so large that initial expansion of treatment there also contributes many people to the worldwide total.

Cumulative Number of People Receiving ARV Treatment from Programs Supported by PEPFAR
As of September 30, 2009
(Go to Table or Notes and Sources below)

☐ NA	☐ 100,000 - 200,000	☐ 300,000 - 400,000	☐ 500,000 - 600,000
☐ 0 - 100,000	☐ 200,000 - 300,000	☐ 400,000 - 500,000	☐ 600,000 - 700,000
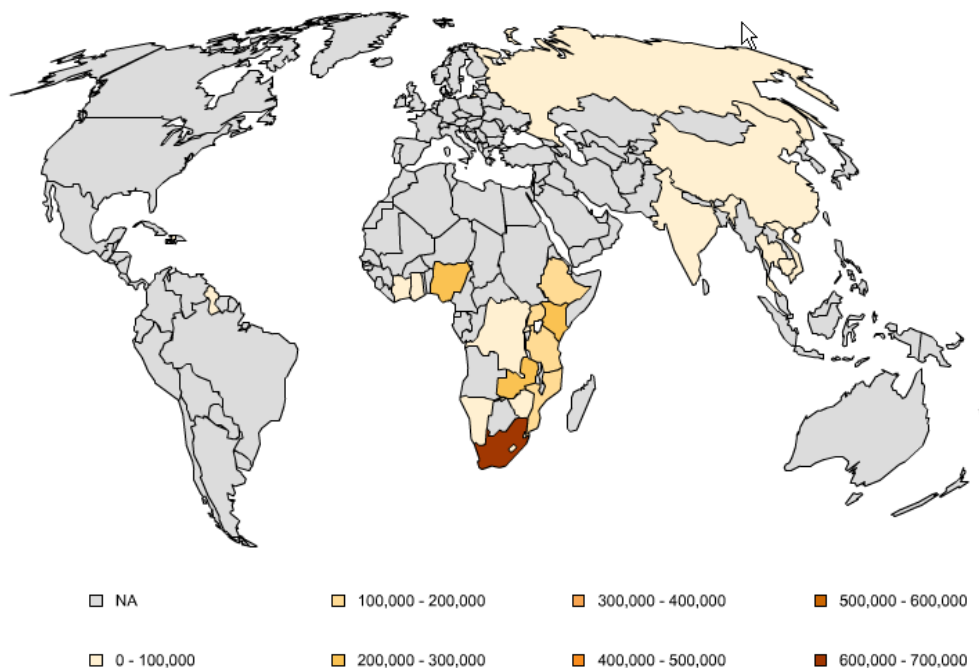
Figure 2. A lopsided burden
Most people receiving ART through PEPFAR are in Sub-Saharan Africa
(Source: Kaiser Foundation, http://www.globalhealthfacts.org/topic.jsp?i=55&col=ghf)

While these achievements have been prodigious, few countries are managing to absorb a large percent of all who need treatment into their treatment programs. In fact, as Figure 3 (panel a) shows, only about 20 of the world's low- and middle-income countries have achieved access—defined as the ratio of those on treatment to those needing treatment—of 80 percent or above. All the rest are reaching a minority of patients that need treatment. On a regional basis, as Panel B shows, countries with at least 80 percent access include two in East Asia and the Pacific (EAP), eight in Europe and Central Asia (ECA), three in Latin America and the Caribbean (LAC), five in the Middle East and North Africa (MENA), two in South Asia (SAS), and two in Sub-Saharan

Africa (SSA). However, most of these are small countries. The only countries with more than 1,500 people

needing treatment that have managed to treat more than 80 percent of those in need are Chile, Cost Rica, and

Namibia. In all six regions the majority of countries fall well behind these top performers.
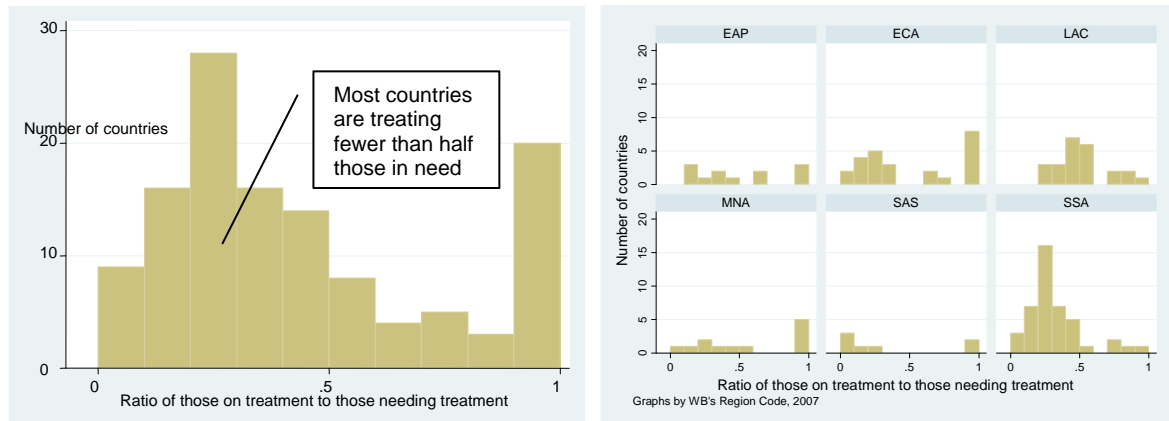
Figure 3. Huge numbers lack access
Ppanel a: *Most countries are treating fewer than half those in need …*
Panel b: … *in all regions*
(distribution of low and middle income countries by the ratio of those on treatment to those needing treatment).
Source: Author's construction based on data from UNAIDS and WHO

How about each country's rate of treatment uptake—that is, the ratio of the number who are newly recruited

during a year divided by the gap between those currently under treatment and the total needing it that year?

This measure, which is a more dynamic way of viewing treatment success, captures the ability of a country

program to absorb new patients as fast as people are developing the need for treatment. As Figure 4 shows,

here, too, developing countries are split into two groups, with most at the low end rather than at the high end.

And most of the good performers again are countries with small AIDS burdens (with the same few exceptions

of Chile, Costa Rica, and Namibia.

Figure 4. Not treating enough patients
Panel a: *Few countries are recruiting more than a quarter of those in need each year …*
Panel b: *… in all regions.*
(distribution of low- and middle-income countries by annual uptake rates for AIDS treatment by country)
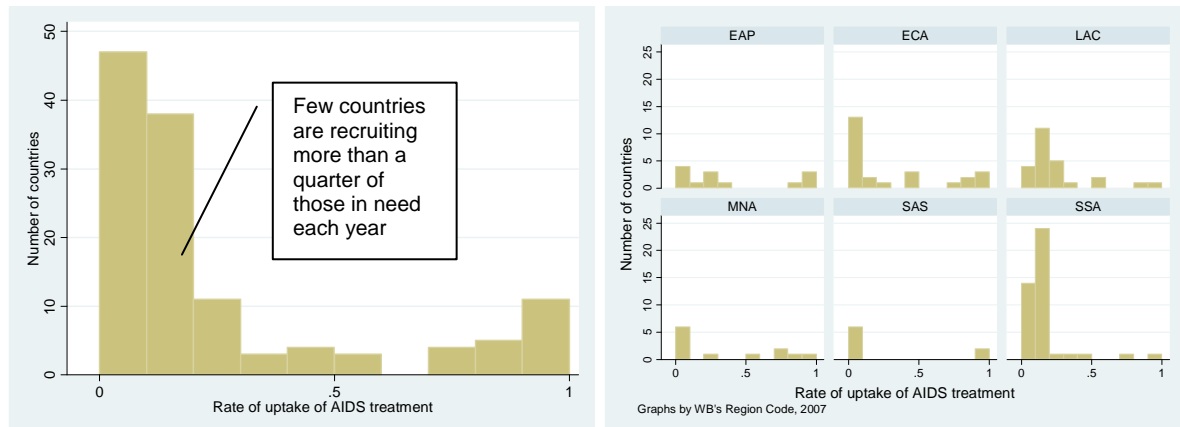Source: Author's construction based on data from UNAIDS and WHO.

histogram uptake, ytitle(Number of countries) xlabel(0 .5 1) start(0) width(.1) xtitle(Rate of uptake of AIDS treatment) frequency by(rgn) ylabel(0 5 10 15 20 25)

Thus the complement to the optimistic story of increasing numbers of people on treatment is the increasing amount of unmet need—essentially a death sentence for those left untreated. AIDS typically takes from 9 to 11 years from HIV infection until the individual feels the effects of the disease (eART-linc, 2008). But once symptoms appear, lack of treatment means half will die within a year and almost all within three years. PEPFAR and its partners succeeded in slowing the growth of unmet need, but not yet in reducing it in the world at large. This current and projected future persistence of unmet need despite the enormous effort and resources spent on treatment is one sign of the need to shift the policy objective from treatment access to the achievement of an AIDS Transition.

B. Indicators of the quality of treatment

The expansion of the numbers on treatment is one measure of treatment success; the survival of people on treatment is another. How well have treatment programs been able to prolong the lives of those who begin treatment?

Although the ART drugs currently used by poor patients in poor countries are far superior to those available a few years ago, achieving sustained health benefits from ART remains a substantial challenge to both the health care provider and the patient. ART drugs must be taken for the rest of the patient's life, once, twice, or more

frequently each day, at specific times in relation to the consumption of food or liquids. Failure to adhere closely to the prescribed timing and dosages leads to the patient's development of a drug resistant strain of HIV that leads within months to treatment failure and either death or the shift to a new and typically much more expensive drug combination. ART drugs have noxious side-effects like diarrhea, indigestion, or worse for varying proportions of patients, which sometimes recede after a few months of treatment, but can then reappear and prevent the necessary adherence[9]. Socioeconomic obstacles to patient adherence include cultural and employer acceptance of AIDS, distance between the patient's home and the treatment facility, cost and availability of transportation, user fees at the health facility, and compensation for "treatment buddies" or other treatment support personnel.

In view of the challenge that ART adherence represents, how well have ART programs done? This question is harder to answer than it might seem for two reasons. First, in the early years of implementation, treatment programs have focused more on expanding access than on patient retention. Thus, they have neither reported, nor always kept track of, the information required to measure ART patient retention. This failure is perhaps understandable during the early years of such a novel and difficult initiative. Second, even with good record-keeping, clinics have difficulty knowing whether a patient who stops coming has failed treatment or simply changed treatment providers. Prior to the push to expand ART, few providers in these countries had either the training or the resources to systematically track patients suffering from other chronic illnesses, like diabetes or high blood pressure. So the need to track ART patients required providers to develop follow-up and outreach systems from scratch for this class of illnesses.

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[9] Depending on their drug regimes and their individual sensitivity to those drugs, some patients experience alterations in weight or appearance due to the atrophy or displacement of fat deposits in their face, back or abdomen. One Thai patient in a focus group interview said "I am confused about ART. I do not understand why my weight went up and I am disturbed by the fact that the fat growth is misplaced. If I could go back, I would not join ART until my health was at its worst." (Revenga et al, 2006)
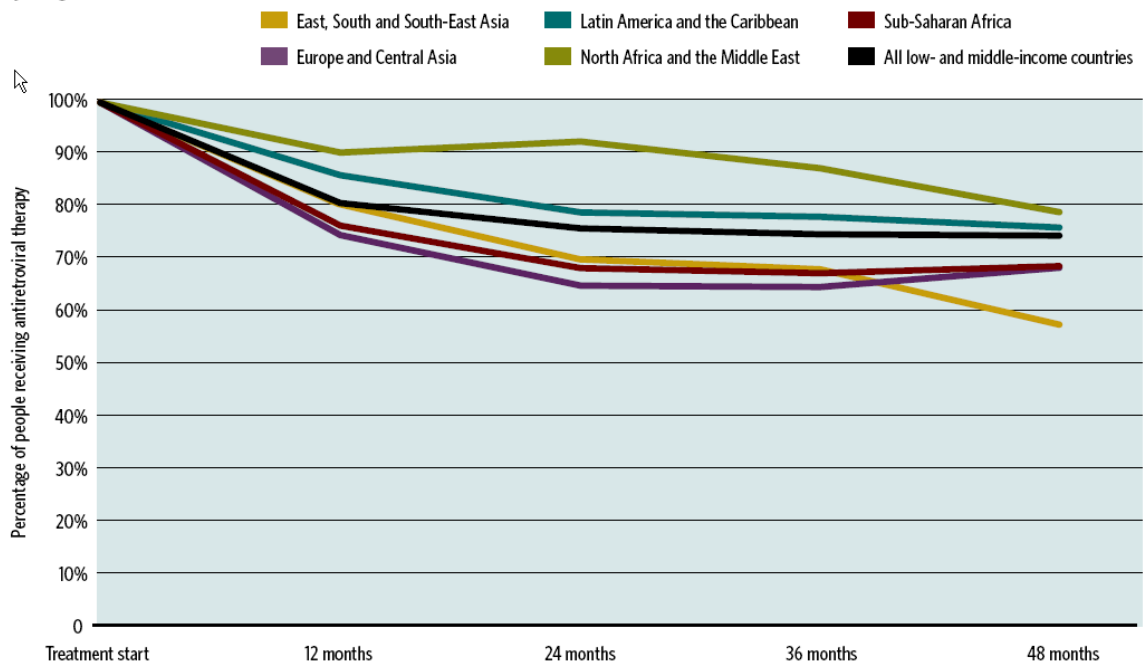
Figure 5. A tough medicine
The record for sticking to ART is not encouraging for the first two years of treatment
(Trends in retention on ART in low- and middle-income countries by region, 2008)
Source: Figure 4.5 from (UNAIDS, 2009)

Given these difficulties, a conservative approach is to focus on patient retention as a measure of the quality of

treatment programs. In response to a survey distributed by UNAIDS, 61 countries reported the number of

patients remaining in treatment at 12, 24, 36, and 48 months after treatment initiation. Figure 5 shows that only

countries in the Middle East and North African region, where there are very few patients, reported more than 80

percent retention after 24 months. For Sub-Saharan African countries—along with East, South, and South-East

Asian countries—retention at 24 months was less than 70 percent. Reviews of the literature on retention (Rosen

et al., 2007) (Rosen, et al, 2009, forthcoming) (Wester et al., 2009) often point to the first six to twelve months

as the critical period in a patient's treatment, during which ART treatment programs lose somewhere between

10 and 30 percent of those starting treatment. But Figure 5 leads to a more pessimistic assessment, suggesting

that retention typically continues to drop for two full years, before leveling off to a more moderate rate.

Treatment programs will be under constant pressure to spread resources more thinly so as to enroll a larger

number of patients while accepting lower patient retention rates. We would argue that poor countries with

multiple health threats cannot afford to spend scarce public health system resources on ART programs with low

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patient retention rates. Thus, an urgent question of operations research is how any given treatment budget can be allocated to maximize patient retention in AIDS treatment programs.

C. Foreign assistance for AIDS treatment

Given the huge resources thrown at HIV/AIDS in recent years, are we unduly pessimistic to even worry about future funding? A look at the historical trend of health aid in general, and AIDS in particular—and the motivations behind the increases—suggest the answer is no.

Since 1990 official development assistance (ODA) for health-related objectives has grown rapidly, at a compound rate of 8 percent a year, according to the Institute for Health Metrics and Evaluation (Ravishankar et al., 2009), However, the portion of total health assistance allocated to HIV/AIDS has grown even faster, at an average rate of about 20 percent a year. This extremely rapid growth of HIV/AIDS funding has fueled the growth in the numbers of people receiving ART and greatly expanded the scope of other HIV/AIDS interventions, including, HIV prevention and support for orphans and vulnerable children. But has it also come at the expense of other health sector funding? And can it, or even should it, continue at such a high growth rate in the coming years?

An examination of the growth trend of total funding for HIV/AIDS reveals a surprising discontinuity, not in the level of funding, but in its rate of increase. For the period 1990 to 2007, Figure 6 superimposes on the data a smooth growth trend at 20 percent per year and a second growth path consisting of two rates of growth, one prior to 1999 and a second from 1999 to the present. The dashed line representing constant growth clearly fits much less well than the "kinked" trend line. The data suggests that prior to 1999 the growth of HIV/AIDS spending in constant 2007 dollars was steady at about 13 percent per year. This growth rate was about twice as fast as the 5.8 percent growth of non-AIDS health assistance during that period and, if continued, would have steadily increased the share of HIV/AIDS in total health ODA. But then in 1999, something happened. The rate of growth of HIV/AIDS funding more than doubled, from 13 to 28 percent per year, an accelerated rate that

The growth of donor assistance for HIV/AIDS accelerated in 1999
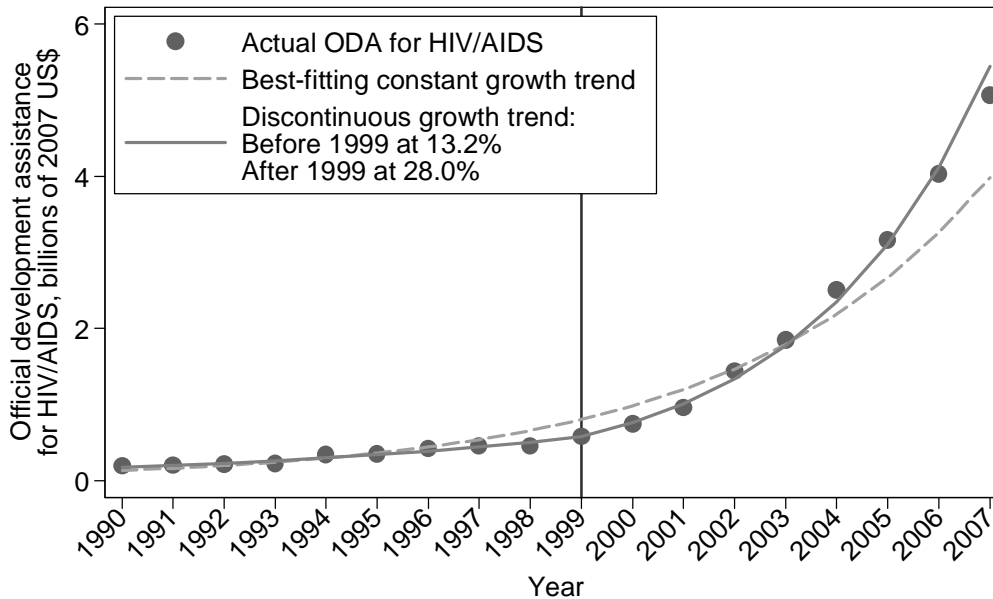
Source: Author's construction from data in Ravashankar et al (2009)

Figure 6. A sudden windfall
Growth of donor assistance for HIV/AIDS took off in 1999

continued until the deceleration of PEPFAR funding that began after 2008[10]. (See Figure 1.) At the same time, the rate of growth of non-health assistance remained unchanged[11].

What could account for the dramatic acceleration in donor assistance for AIDS in comparison to all other health problems? The disaggregation of HIV/AIDS assistance by donor (see Figure 29 of (Ravishankar, Nirmala, Gubbins, Paul, Cooley, Rebecca J., Leach-Kemon, Katherine, Michaud, Catherine M., Jamison, Dean T., and Murray, Christopher J. L., 2009)) makes clear that the increased growth in 2000 was owing to increased contributions from several of the larger donors, but not from the United States. The World Bank increased its allocation to HIV/AIDS in 1999 and then followed by launching its Multi-Country AIDS Program in September,

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[10] The hypothesis that there is no change in the growth rate of HIV/AIDS assistance in 1999 can be rejected at a p-value of 10^-8.

[11] For non-HIV/AIDS health assistance, the point estimate of the growth rate from 1999 to 2007 is 7.4 percent, slightly higher than the 5.8 percent rate estimated prior to 1999. But the p-value on the test of a change in the trend in 1999 is 0.06, greater than the conventional threshold for statistical significance of 0.05.

2000. The Bill and Melinda Gates Foundation started spending on HIV/AIDS in 2000. UNAIDS funding also

jumped upward in that year. U.S. spending did not take a large jump until 2002 and then accelerated in 2004,

when the U.S. PEPFAR program kicked in (See Figure 1). U.K. spending took its first large jump in HIV/AIDS

assistance in 2004. And the Global Fund for AIDS, Tuberculosis and Malaria began disbursing in 2003, greatly

increasing its disbursements in 2004.
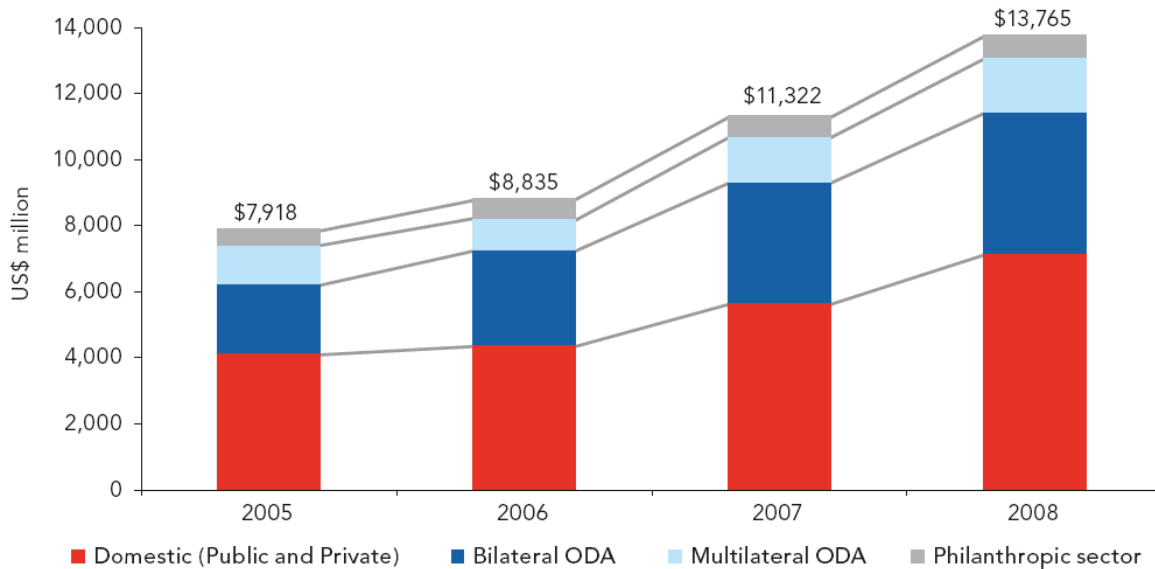
Figure 7. A full partnership
Domestic funding is keeping up with foreign funding for AIDS
(Domestic and foreign sources of AIDS funding in poor and middle income countries)
 Source: UNAIDS, 2009.

Looked at in this aggregate way, the trend since 1999 in HIV/AIDS assistance is remarkably smooth. All the

major donors have played their roles, some increasing their funding one year and others another year, so that on

average across all donors and recipients, the trend has been one of constant growth at 28 percent a year. Over

this period, the U.S. government's contribution has grown, but no more rapidly than that of other donors. The

result has been that the United States has maintained its share of total HIV/AIDS funding at slightly less than 50

percent throughout this historical period.

Furthermore, as Figure 7 shows, in recent years domestic spending has kept pace with donor spending, which

accounts for about half of total AIDS expenditures. Although a breakdown of domestic funding between AIDS

treatment and HIV prevention is not available, it seems likely that middle-income countries financed more than half of AIDS treatment through relatively developed health insurance and financing systems, while poorer countries probably depended more on donors.

What actually caused the acceleration of HIV/AIDS spending in 1999 can never be answered with certainty. As suggested above, there were many actors including organizations of AIDS activists and French President Chirac. That said, it is perhaps not a coincidence that the world had launched a new UN entity dedicated to prevention and control of the HIV/AIDS epidemic only two years before. Led by Dr. Peter Piot, this new organization called UNAIDS had the authority and prestige to command the attention of the international media and to marshal public opinion to a degree that has never been equaled by advocates for any other health problem. It seems likely that the accelerated growth of HIV/AIDS assistance from so many diverse sources throughout the world—sufficient to energize a decade-long sustained and remarkably constant growth of philanthropy for this single cause—can be attributed largely to the creation of UNAIDS and to the effective advocacy by Dr. Piot.

The question of whether this outpouring of assistance for HIV/AIDS has "crowded out" other types of donor assistance for health is impossible to answer in a definitive way, because it is impossible to know what would have happened had the HIV epidemic never appeared or had UNAIDS never been created. However, if starting in 1999, the sharp rise in HIV/AIDS assistance had been accompanied by a marked deceleration in the growth of non-HIV/AIDS health assistance, critics of HIV/AIDS spending would be justified in suggesting that there had been some crowding out. Indeed this pattern is visible in the aid trends from individual donors, such as the World Bank or the U.S. government. But for donors as a group, the trend of non-HIV/AIDS health assistance did not slow after 1999; it continued its growth at about 6 percent a year in real terms, twice as fast as other types of assistance, other than debt relief. If one believes that, in the absence of an AIDS epidemic or a UNAIDS to advance its cause, the rate of growth of health aid would have continued at its historical rate of 6 percent until the present, then there would be no grounds for the crowding out argument.

As for whether the high level of AIDS assistance will continue, the stage seems set for a slowdown in the growth of AIDS assistance. The World Bank has discontinued its special funding for AIDS. The Global Fund

for AIDS, Tuberculosis and Malaria is complaining of funding shortfalls. And the United States first moved to slow the growth of AIDS funding with the 2008 PEPFAR reauthorization bill and followed that up in 2009/10 (Figure 1) with folding AIDS into its new Global Health Initiative. Secretary of State Hillary Clinton, in her first major policy speech on foreign assistance in January 2010, said:

> One of our countries' most notable successes in development is PEPFAR, which has helped more than 2.4 million people with HIV receive life-saving anti-retroviral medications. Now PEPFAR will be the cornerstone of our new Global Health Initiative. We will invest $63 billion over the next six years to help our partners improve their health systems and provide the care their people need, *rather than* rely on donors to keep a fraction of their population healthy while the rest go with hardly any care. [Emphasis added.] (http://www.cgdev.org/content/general/detail/1423520)

Although Secretary Clinton says that PEPFAR will serve as the cornerstone, a cornerstone is a small part of a building and it is likely that PEPFAR will be a small part of the entire U.S. health assistance edifice. Moreover, the reference to "keeping a fraction of the population healthy" is a clear reference to support for AIDS treatment. She is pointing to the need to rebalance health sector aid away from too narrow a focus on increasing the numbers of AIDS patients who benefit from ART support and in favor of health interventions that strengthen recipient countries' ability to provide all types of health care for their entire populations.

The expression "rather than" unfortunately suggests that the United States is considering reneging on the implicit lifetime entitlement it has already granted to the 2.4 million people now on U.S.-funded AIDS treatment. I doubt that Secretary Clinton meant to wave that red flag, given that such a decision would contradict the objectives just announced by PEPFAR on December 1, 2009, not only to respect that entitlement but also to add another 1.6 million people to the U.S.-supported treatment rolls by the year 2014. However, even adding 1.6 million people to treatment rolls over five years is a considerable deceleration from the rate of 1 million new patients per year that PEPFAR attained in 2008.

D. The reduction in the cost of treating one AIDS patient

Effective AIDS treatment began in 1993 with the introduction of zidovudine or AZT, the first drug that could slow HIV reproduction. But treatment with an antiviral drug and drugs for the attendant opportunistic illnesses cost as much as $100,000 per year and was only available in rich countries (Scitovsky, A. A. and Over, A. Mead, 1988). Furthermore, it soon became apparent that treatment with the single antiviral would help a patient for only a limited number of years before the virus developed resistance to that drug and would again spread within the body with fatal results[12]. In response medical researchers developed the concept of "combination therapy" or "triple-drug-therapy," which greatly slowed the development of drug resistance in the individual patient. However, these more effective combination therapy regimes were also more complex for the doctors and patients, and more expensive as well. By 1997 the cost of triple-drug ART averaged $20,000 per patient year, with only occasional lower-price deals available for a few middle-income countries like Thailand and Brazil that bargained sufficiently forcefully with the drug firms (Ainsworth et al, 1997). That was the year when President Chirac proposed extending ART to all, an objective that seemed quixotic because of both the cost per patient and the numbers in need.

Since that time, AIDS treatment has improved remarkably in quality while the cost per patient-year has continued to fall. In the late 1990s and the early 2000s, quality improvements stemmed from scientific breakthroughs in understanding the biology of the virus and better health service delivery systems for ART. Greater availability in turn resulted from Indian pharmaceutical firms entering into the production and distribution of generic versions of branded ART drugs—a trend that the multinational firms holding the patents for those drugs and the U.S. government at first vigorously opposed. Pressure by AIDS advocates and a coalition of nongovernmental organizations led by the Clinton Foundation helped the WHO promote the use of these generic drugs. However, in 2004, the newly created PEPFAR program insisted on buying only branded versions, a policy that reduced the cost-effectiveness of U.S.-supported ART and threatened to impede the

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[12] Because monotherapy with AZT and imperfect adherence slow, but do not completely suppress, viral reproduction, a descendent of the original virus eventually appears that by chance is resistant to that drug and then is able to reproduce, crowding out the other genetic variants and leading to treatment failure in that patient. Drug resistance is an example of Darwinian selection operating at "warp" speed within the body of a single patient.

attainment of PEPFAR's ambitious treatment objectives. Tension between the Bush Administration's support of the intellectual property rights of U.S. ART patent holders and the PEPFAR goal of expanding the availability of ART came to a head in 2005, with PEPFAR switching to the generics the following year.

The result of these various pressures on drug prices has been dramatic reductions in the annual cost of drugs required for ART. Indeed, as Figure 8 shows, by 2008, the annual cost to low- and middle-income countries of a patient-year of ART typically had fallen to about half of its 2004-2005 level. While the upper-middle-income countries continue to pay higher prices for the same drug combinations, the gap between the prices paid has been narrowing.[13]

Should we expect treatment costs to fall further in the years ahead? One way to estimate this is to start from the unit prices for ART and build up the per patient cost by adding on the cost of the associated health care delivery—what is known as a "bottom-up" approach (see Table 1). We find that for first-line ART, when inpatient days and outpatient visits are added to the price of the drugs, the "average variable cost" of treatment (a cost that we assume is constant for any given country, but varies over countries by income level) ranges from $169 for low-income countries to $333 for upper-middle-income countries Patients who fail first-line therapy and get access to second-line therapy will generate an average variable cost ranging from $1,024 to $2,288—in other words, second-line therapy continues to be almost ten times as expensive as first-line therapy in a low-income country. Now we just need to calculate the large costs of setting up a new program and expanding it to scale up to ever larger patient loads—that is, the "average *fixed* costs"—to arrive at the total cost per patient, or the "average *total* costs."

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[13] When a country is unaware of prices paid for a drug by other countries, its negotiators are in a weak position relative to the representatives of pharmaceutical manufacturers or suppliers and therefore may agree to pay a higher price than the seller would be willing to accept. The advent of the WHO's Global Price Reporting Mechanism, supported by the Price Reporting Mechanism at the Global Fund for AIDS, Tuberculosis and Malaria, has improved the availability of price information and therefore may have directly contributed to the price reductions that it reports in Figure 8.
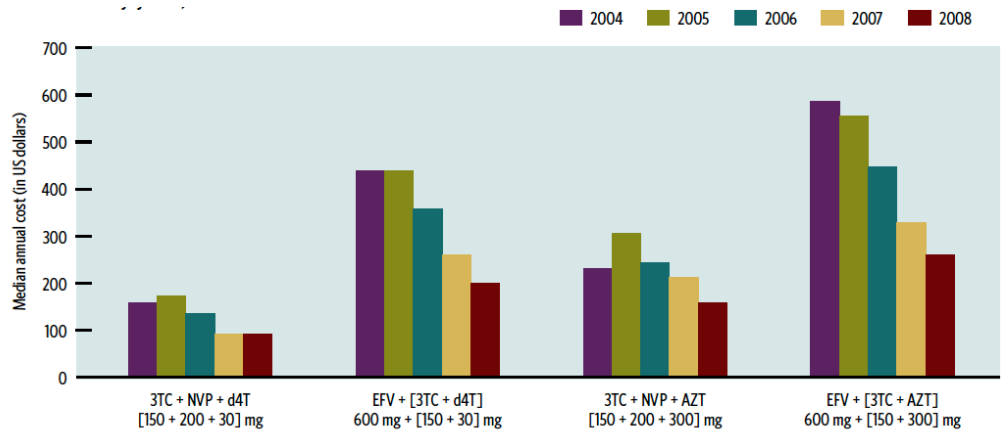
Panel a) Low-income countries (GNI per capita of US$ 935 or less).
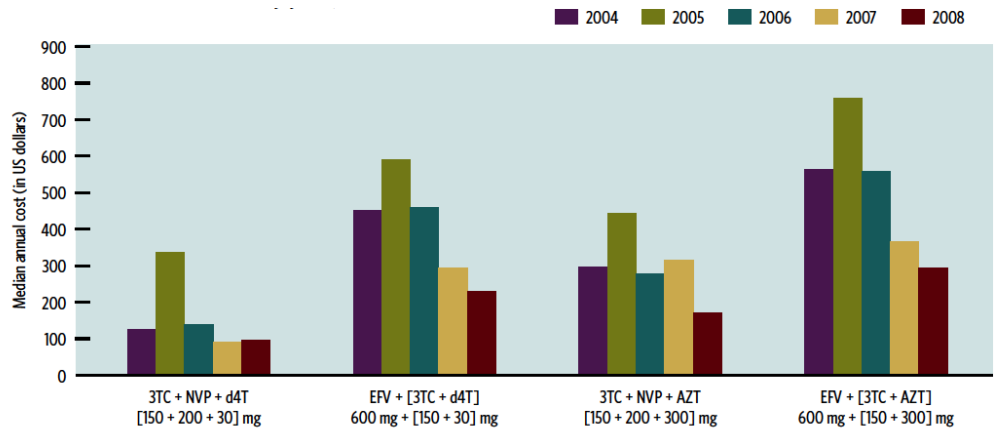
Panel b) Lower middle-income countries (GNI per capita between US$ 936 and US$ 3705)
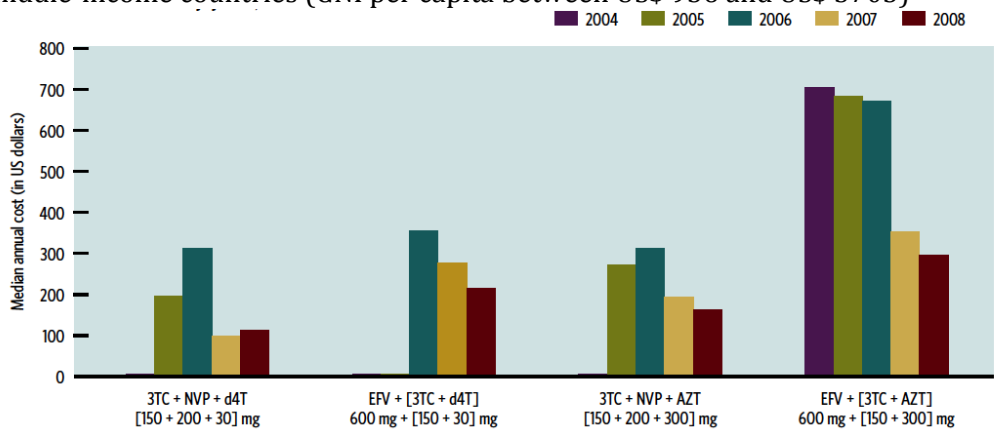
Panel c) Upper-middle-income countries (GNI per capita between US$ 3,706 and US$ 11,455).

Figure 8. The price of the cocktail
In recent years, the cost of ART for the developing world has dropped sharply
Source: (UNAIDS, 2009)
Note: Each panel shows the trend over time for each of the four most widely used first-line triple-drug combinations within
at a given income level. The combination on the left, which includes lamivudine (3TC), nevirapine (NVP) and stavudine (d
used by 45 percent of all patients in the 36 countries that responded to WHO's survey. Moving to the right, the other three
combinations were used by 11, 17 and 18 percent respectively, (UNAIDS, 2009)

Table 1. Combining the "bottom-up" and the "top-down" approaches
Trying to get a handle on average total costs for AIDS treatment
(Average annual cost per enrolled patient and cost components of ART for countries enrolling 3,000 patients at three different income levels, 2007

	Annual cost components	Low income country ($460 per capita)	Lower-middle income country ($2,000 per capita)	Upper-middle income country ($5,430 per capita)
a.	First line drugs	$148	$209	$234
b.	Second line drugs	$1,003	$1,629	$2,189
c.	Inpatient days (2.0)	$16.30	$39.36	$71.77
d.	Outpatient visits (9.6)	$4.96	$13.79	$27.61
e.	Average variable cost: first line (Rows a + c + d)	$169	$262	$333
f.	Average variable cost: second line (Rows b + c + d)	$1,024	$1,682	$2,288
g.	Average fixed cost (assuming 25,000 patients)	$127	$573	$1,357
h.	Average total cost (1st line) (Rows e + g)	$296	$835	$1,690
i.	Average total cost (2nd line) (Rows f + g)	$1,151	$2,255	$3,645

Notes: Average inpatient and outpatient days per AIDS patient (rows c and d) are from Stover (personal communication). Average total cost of first-line therapy (row h) is estimated by the author from data on total expenditure on ART, total patients on ART and gross national income per person (UNAIDS, 2008b). Figure 10 displays the fitted relationship and shows graphically the derivation of average total cost at three levels of national income per person. Row g is computed as row h minus row e. Then row i is computed as row f plus row g.
Sources: Costs of first and second line drugs are interpolated to the specified income level from the WHO/UNAIDS Universal Access Progress Report 2009, (UNAIDS, 2009).

Unfortunately, data on average fixed costs for ART treatment in developing countries is severely lacking. So we need to take another approach—the "top-down" approach—to first get a handle on average total costs. Drawing on UNAIDS estimates of aggregate treatment expenditures and total patients enrolled for 57 countries for at least one of the years 2005 through 2007, we find that a typical country was spending about $1,000 per patient-year of treatment, with enormous variation above and below this number (See Annex A.). In addition, we learn that the total cost per patient is somewhat smaller for larger programs. From the average total costs, we can now subtract the average variable costs to arrive at the average fixed costs. The problem, however, is that we only have average total costs for a few years for 57 countries. The way around this is to derive a statistical relationship between average total cost and two key country characteristics—income per capita and total enrolled patients—and then use that relationship to estimate the average total cost for every country now and into the future.

So what is the bottom line? Overall, we see relatively stable average total costs for AIDS treatment going

forward. The big question is what that will mean for countries' fiscal burdens.

III. The future fiscal burden of treatment

Only a few years ago the WHO championed the idea that the world should strive to provide "universal access" to AIDS treatment for all who needed it, and they still reference this goal in the title of recent reports on AIDS treatment (World Health Organization et al., 2007; World Health Organization, 2009b)[14]. What would "universal access" cost and how plausible is it as an objective?

A. The future cost of AIDS treatment at constant unit costs

International donor subsidies to the cost of AIDS treatment in poor countries are already large—in 2007, all donors together spent an estimated total of $5 billion on AIDS, of which about half was spent on treatment (Ravishankar, Nirmala, Gubbins, Paul, Cooley, Rebecca J., Leach-Kemon, Katherine, Michaud, Catherine M., Jamison, Dean T., and Murray, Christopher J. L., 2009). What would happen if the world opts for universal treatment—that is, 80 percent of those in need receive treatment when they reach the WHO's new criterion for treatment (a CD4 count of 350 cells per milliliter)? And let us assume that these patients receive treatment at constant unit costs per patient-year, and that the number of new infections drop at about 5 percent per year? As Figure 9 shows, by the year 2030, the number of people on treatment will increase more than ten-fold to about 46 million, and the costs will rise about 17 times to $67 billion (constant 2009 dollars) a year.[15]

To gauge the magnitude of this sum, note first that it does not include any expenditure on other objectives of HIV/AIDS policy, such as HIV prevention and care for those orphaned or widowed by the disease. It is almost three times the total value of all U.S. foreign assistance in 2007, which was about $26 billion, including aid to Afghanistan, Egypt, and Israel (Radelet et al, 2009). And it is almost two-thirds the total amount of foreign assistance by all donors in 2007, which was $103.5 billion (http://www.oecd.org/dataoecd/17/39/44285701.gif).

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[14] The International AIDS Society stated in 2009 that Universal Access is defined as treatment for 80 percent of those in need. UNAIDS allows each country to define its own "universal" access targets. The most modest definition is that of Mozambique, which for 2010 defined "universal" to mean 45 percent.

[15] With these numbers the unmet need for ART will decline rapidly as will the "funding gap" defined as what it would cost to provide treatment for the other 20% of those who need care. (Command specification for this run: aidsproj using aidscgd2008.dta, uptake(.8) cd4(350) takeoff(2010) horizon(2030) strtyr(2007) trgtyr(2020) scale(0) world)

Moreover, if total foreign assistance continues to grow at about 3 percent per year in real terms (more than the rate of growth of the rich countries' GDP) and only half of the $67 billion must be funded by donors (as suggested by Figure 7) , reaching universal access under these assumptions would require that $33 billion of $180 billion in foreign assistance, or about 18 percent of the total, be spent on AIDS treatment.

Under these assumptions, this prodigious expenditure of more than three quarters of a trillion dollars on AIDS treatment over the next 20 years would indeed achieve the AIDS transition— because by the year 2032, the total number of new infections worldwide would fall from the current level of more than 2 million per year to about 715,000 per year, which would be slightly less than the number of deaths from AIDS that year. As a result, the number of people living with AIDS and the number on AIDS treatment would begin a slow decline but would remain above 40 million until the year 2050 and beyond (Figure 9, panel a). Expenditures would continue to rise for another decade, finally peaking in 2042 at $74 billion before they also begin to decline (Figure 9, panel b). In the absence of dramatic improvements in first-line therapy, by the year 2050 almost half of the patients will have failed their first-line regimen and moved on to second-line drugs, or to even more expensive alternatives, consuming almost two-thirds of total treatment expenses.

AIDS treatment: Numbers, costs & entitlement
Total for all countries
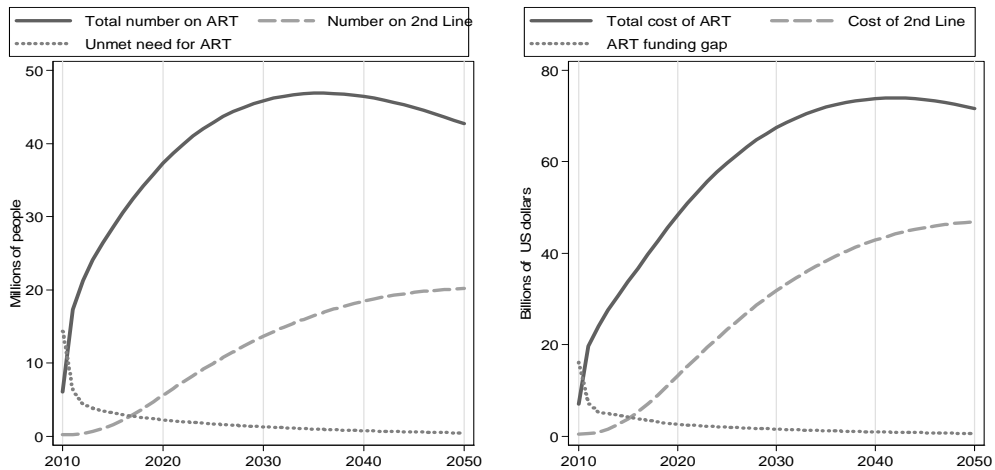
Adjusting at 80.0 % of unmet need each year

adrate1 = 0.084, adrate2 = 0.040, bdrate = 0.040, erate = 0.243, ndrate = 0.100, incmult = 0.950

Figure 9. Ballooning numbers and costs with universal access
Projections of numbers on treatment, total costs of treatment if uptake is 80 percent of unmet need each year, unit costs are constant, and the rate of new infections declines at 5 % per year, 2010-2050.

AIDS treatment: Numbers, costs & entitlement
Total for all countries
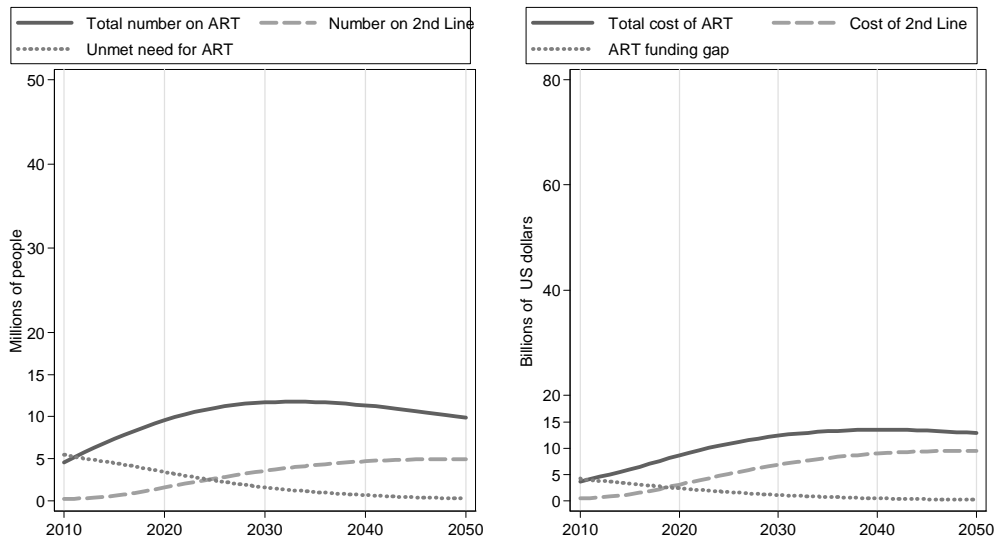
Adjusting at 15.0 % of unmet need each year

adrate1 = 0.133, adrate2 = 0.040, bdrate = 0.040, erate = 0.094, ndrate = 0.325, incmult = 0.850

Figure 10. Effective HIV prevention can contribute to an affordable outcome
Projections of numbers on treatment, total costs of treatment if unit costs decline with scale, uptake is 15%, and the rate of new infections declines at 15 % per year, 2010-2050.   Source: Authors' calculations.)

Our goal is to present a vision of a faster AIDS transition, one that would sustain current AIDS entitlements and add to the treatment rolls while remaining affordable. Let us begin by changing just four assumptions. Suppose that the modest economies of scale estimated above to have occurred in the last few years continue to be enjoyed over the next decades, so that unit costs decline continually at 1.4 percent for every 10 percent increase in the number of patients under treatment. Suppose further that HIV prevention becomes much more effective, so that the decline in new cases occurs at 15 percent per year instead of 5 percent per year. And suppose that the uptake percentage in each country will remain about the same as the uptake that has been achieved the last three years, with about 15 percent of those in need being added to treatment rolls each year, but in this case at an average CD4 count at ART initiation of 130 (consistent with recent experience).

Now we see that the numbers on treatment come down by three-quarters and peak in 2033 (Figure 10 panel a). Although 15 percent of those needing treatment receive it each year, the total number on treatment eventually declines as the result of the natural life cycle of those on treatment, and the reduced number of new HIV infections peaks at 12 million because of the declining incidence of new infections starting now. Total costs in 2030 are $12.4 billion instead of $67 billion, for a reduction of more than 80 percent (Figure 10 panel b). Under this scenario, the number of new infections drops below the number of deaths by 2011, only two years from now.[16] The AIDS transition is within reach.

B. Possible "game-changing" shocks to future treatment costs

1. Change in recruitment threshold

On November 30, 2009, the WHO released revised guidelines recommending that patients begin treatment when their CD4 count reaches 350 rather than waiting until it drops to 200 (World Health Organization, 2009a). But there is an ongoing debate regarding whether poor countries should adopt the new AIDS treatment

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[16] Other assumptions for Figure 9 and 10 include: Median CD4 count at recruitment is unchanged at 130, second line therapy coverage reaches 95 percent by the year 2020, the elasticity of average fixed cost with respect to scale is -0.146. The command line for this scenario:
aidsproj using aidscgd2008.dta, uptake(0.15) takeoff(2010) horizon(2050) incmult(0.85) strtyr(2007) trgtyr(2020) world

guidelines or continue to prioritize recruitment at the 200 level. The existence of a health benefit is one side of the story, and a recent study provides convincing evidence that in resource-rich settings there are definite health advantages to the average person with HIV beginning ART at 350 (When to start Consortium and Jonathan Sterne, 2009). The other side of the story, however, is the cost of earlier treatment initiation—which will go up because of the longer period of drug taking. But how much costs will rise hinges on whether, and by long the patient's age of death is postponed. For policymakers, two key questions arise. How large will the cost increase be compared to the increased benefit? And when there are insufficient resources to cover the costs of all who need treatment at more advanced stages of the disease, how should policymakers trade the use of resources for healthier people against the recruitment of a larger percentage of sicker people?

The dilemma for PEPFAR

To better understand the tradeoff involved in moving to an earlier CD4 count, consider the situation from the point of view of the PEPFAR program. On December 1, 2009, the White House announced a new five-year strategy for PEPFAR that aims to increase the number of patients PEPFAR directly supports on ART from the current 2.4 million to at least 4 million by 2014. PEPFAR managers can meet this goal in two ways that cost about the same: recruit earlier (that is, start HIV infected people on treatment before they are very sick as counseled by the new WHO guidelines); or expand access (that is, direct the drugs to people who have been infected longer and are therefore sicker. The second choice seems the most humane and equitable: give drugs to the patients who need it most. However, because the prognosis of these patients is generally less good than that of people more recently infected, recruiting patients earlier in their illness actually averts more deaths.

We can visualize PEPFAR's dilemma in Figure 11, which plots various contours to show the tradeoff between the annual rate of uptake of new patients (on the vertical axis) and the starting CD4 count at ART initiation (on the horizontal axis). The two points indicated with arrows are two ways that PEPFAR and its partners could reach PEPFAR's 2014 target of 4 million patients on ART. The shaded line that shows the combinations of uptake and average CD4 of recruitment that would reach 4 million is almost exactly overlaid by a dashed line that is a cost contour that shows all the combinations that cost the same total 5-year budget. It turns out that reaching the 4 million mark will require a 5-year budget of $11 billion at any of these combinations.

We know that if enrollment remains at the current level of 2.4 million, the number of averted deaths by 2014 will be an estimated 7.1 million less the number of deaths to occur if 4 million patients are enrolled. With a policy that favors access but maintains recruitment at a CD 4 = 130, that number of deaths will be about 5.6 million (indicated by the steep gray line), while with a policy favoring early recruitment (a higher CD4 count), total deaths drop to 4.9 million (the steep black line).
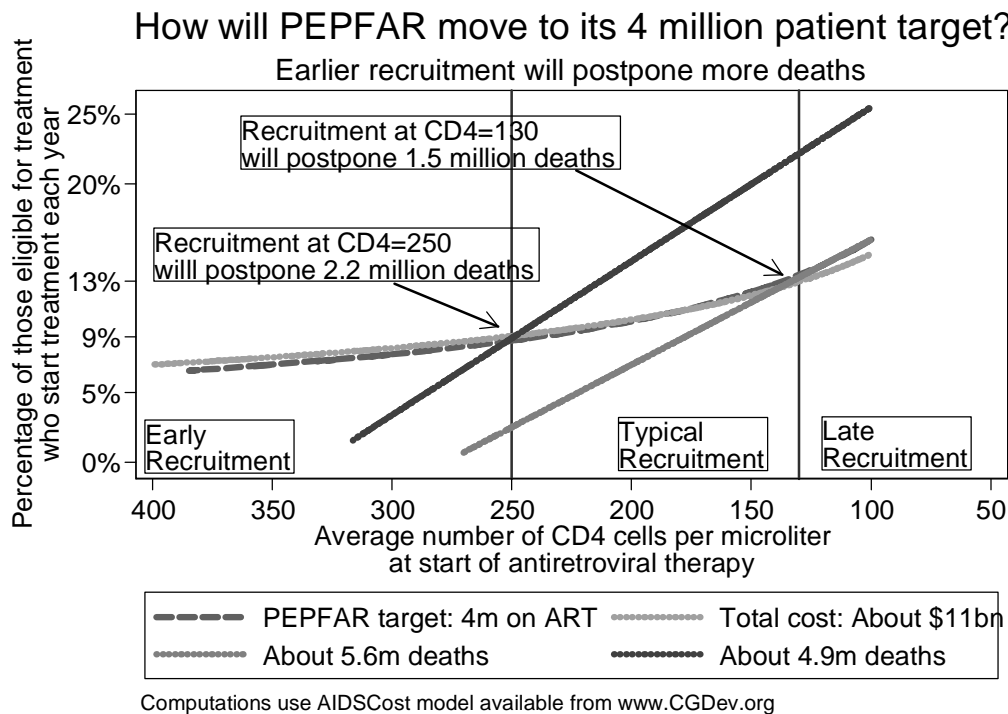
How will PEPFAR move to its 4 million patient target?
Earlier recruitment will postpone more deaths

Recruitment at CD4=130 will postpone 1.5 million deaths

Recruitment at CD4=250 willl postpone 2.2 million deaths

Early Recruitment

Typical Recruitment

Late Recruitment

y-axis: Percentage of those eligible for treatment who start treatment each year — 25%, 20%, 13%, 9%, 5%, 0%

x-axis: Average number of CD4 cells per microliter at start of antiretroviral therapy — 400, 350, 300, 250, 200, 150, 100, 50

Legend:
- - - - PEPFAR target: 4m on ART
········· Total cost: About $11bn
········· About 5.6m deaths
●●●●●●● About 4.9m deaths

Computations use AIDSCost model available from www.CGDev.org

Figure 11. PEPFAR's conundrum
Earlier recruitment will postpone more deaths but fail to take in some of the sickest patients
(Tradeoff between greater access and improved effectiveness in AIDS treatment)
(Source: Author's estimates as described in Annexes B and C) A previous version of this analysis appeared on the CGD health blog at: http://blogs.cgdev.org/globalhealth/2009/12/how-will-pepfar-reach-4-million-aids-patients-on-treatment-by-2014-expanded-access-or-earlier-recruitment-millions-of-years-of-life-hang-in-the-balance.php*)*

So what are PEPFAR's options? Both the line representing 5.6 million total deaths and the line representing 4.9 million deaths intersect with the line showing the 4 million patient PEPFAR target and, in about the same locations, with the line showing the $11 billion budget. This means that PEPFAR and its partners could use the same budgetary resources and meet the same goal for patients on treatment in either way. Continuing annual uptake of new patients at 13 percent of those in need while holding constant the starting CD4 at 130 would

mean expanding the current practice of identifying AIDS patients when they are sick, typically by testing

people who have sought health care for their opportunistic illnesses. Deaths during this period would be reduced

from 7.1 million to 5.6 million for a saving of 1.5 million.

A policy favoring early recruitment would adopt a passive approach to recruiting sick people from health

centers and instead recruit much more aggressively through programs that test and counsel healthy people. To

maintain the same overall treatment budget and target 2014 enrollment, uptake would be cut from 13 percent to

9 percent. If the average starting CD4 count can be increased to 250, the 23 PEPFAR countries modeled here

will experience about 4.9 million deaths through 2014, or about 700,000 fewer AIDS deaths than would be the

case with the expanded access policy. Thus, if the objective were to use the 4 million patient enrollment target

and the associated budget to postpone as many deaths as possible beyond 2014, PEPFAR and its partners should

favor the lower access with early recruitment policy over higher access with continued late recruitment. In

terms of postponed deaths, early recruitment would be the more cost-effective policy.

However, this cost-effectiveness comparison is not sufficient to propose a blanket PEPFAR policy of preferring

early recruitment over increased access. To begin with, in comparison to the ideal of universal access, even an

improved annual uptake rate of 13 percent denies treatment each year to 87 percent of those who are eligible for

it. While other sources of financing in these countries, including the Global Fund for AIDS, Tuberculosis and

Malaria, national governments, domestic and international NGOs, and the patients themselves might together

directly support another one or two million patients, perhaps increasing the uptake rate from 18 to 30 or even 40

percent, this would still leave many patients unserved. Furthermore, the choice to allocate resources to earlier

recruitment rather than increased access implies prioritizing relatively healthy HIV positive patients for

treatment over those with low CD4 counts who are in more desperate straits. These considerations are likely to

convince many policy makers to prioritize access over early recruitment, regardless of the increased number of

deaths.

These are tough choices with no easy answers, not unlike battlefield triage. While PEPFAR may have a view

about which point on the 4 million patient contour to aim for, I believe it would be unethical for any donor to

impose the choice of any given point on this contour on other governments. The difficulty of this choice, and of choices along other tradeoff envelopes, underlines the importance of another theme of PEPFAR's new strategy – "partnership" in decision-making with the host country.

2. Change in the costs of drugs

In the past decade substantial savings on drug costs have been achieved through increased competition from generic versions and bulk procurement agreements with the manufacturers of branded drugs. The Clinton Foundation has taken the lead in the negotiations that have achieved the price reductions of branded drugs. Given the foundation's role in achieving these historic price reductions, it is noteworthy that its Chief Executive Officer makes no mention of the possibility that branded drugs might become significantly cheaper owing to further such negotiations in a recent article he coauthors proposing ways to "bridge the resource gap" in AIDS treatment (Soni and Gupta, 2009). Instead the authors point to pressures that might tend to raise the cost per patient of first-line drugs, such as the move to replace a drug called stavudine, which costs $80 per patient year, with a drug with fewer side effects called Tenofovir, which costs $200 per patient year.

Furthermore, as Indian pharmaceutical firms are increasingly constrained by India's participation in the TRIPS agreement, they may compete less aggressively in the markets that supply poor countries with these drugs. If this occurs, either the market share of less expensive Indian generics might fall or their average prices may cease decreasing or even rise. Innovations in the design of drug procurement mechanisms such as WHO's recently developed "Global Price Reporting Mechanism" and the DFID-Funded META Project may help to reduce the prices of drugs on transactions between poor countries and major donors. However, the opportunity for achieving dramatic additional price reductions on first-line drugs may be limited in the future

As for second-line drugs, UNAIDS recently reported that few patients in low- or middle-income countries are currently receiving second-line treatment with public resources. Data from WHO's Global Price Reporting Mechanism shows that the percentage of publicly funded patients receiving second-line therapy has actually declined from 4 percent in 2006 to 3 percent in 2007 and most recently to two percent in 2008. This information, however, conflicts with data from WHO's 2008 survey (see Annex Box A). The survey says that

while only 0.2 percent of South Asian patients and 2.7 percent of Sub-Saharan African patients are on second-line therapy, 8.7 percent of Thai patients and 30 percent of Latin American patients receive this much more expensive treatment. Furthermore, as Soni and Gupta point out, the proportion of people needing more expensive "second-line" drugs increases over time[17].

The bottom line is that while the cost per patient year of second-line drugs may continue to fall in the future, as it has in the past few years, the pressures to slow or reverse first-line drug price reductions apply with equal force to second-line drugs. Thus, for future projections, we assume that first-line and second-line drug prices will remain constant.

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[17] The calculations in this book second-line coverage is assumed to increase gradually from its current level, assumed to be the regional average given by WHO, to 95 percent coverage by the year 2020.

3. Increased task shifting to reduce clinic costs

Delegation of routine AIDS treatment tasks previously performed by the physician to mid-level health care

personnel can potentially improve efficiency and lower costs, without sacrificing quality. The United States has
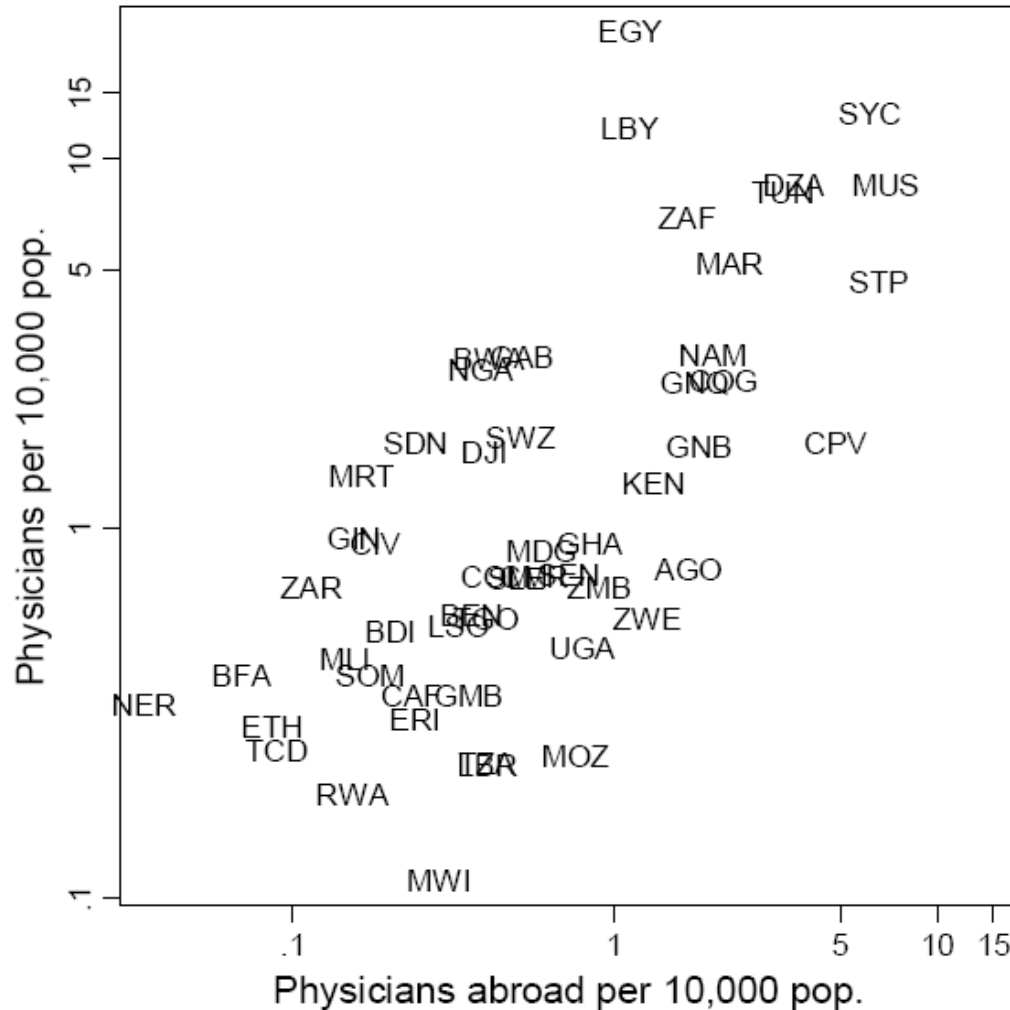
Figure 12. Keeping doctors
More doctors abroad go hand-in-hand with more doctors at home.
 (Source: (Clemens, 2007))

experimented with delegation in ambulatory medical care for decades, with a particular push immediately after

the Vietnam War (Golladay et al., 1976). But there are limits to this strategy when the mid-level personnel are

insufficient in numbers or lack the training to take on ART tasks.

Some have attributed the lack of health care personnel in poor countries to the brain drain, but others argue—as

illustrated in Figure 12—that an increase in the number of physicians from a given country who work abroad

goes hand-in-hand with an increase in the number working at home. Take the case of Zambia, which has arguably the worst AIDS epidemic in the world and can be located in the middle of the scatter plot (abbreviated "ZMB"). According to Soni and Gupta, the Zambian government has analyzed its health manpower shortage and concluded that in to address its physician shortage at home, it must increase enrollment in its health manpower training institutions, which means increasing their capacity and attracting more students. As my colleague Michael Clemens has pointed out (Clemens, 2007), a country is not likely to attract the most qualified students to its expanded health training program if it attempts to limit mobility after graduation. By increasing its production of physicians and nurses, and accepting that a proportion of them will emigrate, Zambia hopes to emulate other countries with strong health manpower programs like South Africa (ZAF), Mauritius (MUS), and Tunisia (TUN)—in the process moving itself to the northeast part of Figure 12.

Another constraint on task delegation is the scale of a medical practice. If the number of patients is too small and each requires at least an occasional minute of the doctor's time, the most economical staff design is that of the solo practitioner. As the number of patients expands, opportunities emerge for health personnel to specialize and for physicians to delegate an increasing share of their work. Indeed specialization and delegation are two ways in which economies of scale can be realized. The obverse of this advantage is that doctors who serve small populations of AIDS patients may have difficulty taking full advantage of mid-level health workers owing to diseconomies of small scale.

4. Rising costs of approaching full coverage

When discussions of scaling-up AIDS treatment take place, it is frequently assumed that there will be perpetually increasing returns to scale in the form of ever lower unit costs of treatment. Recently, however, experts in the medical community have joined economists in warning that the advances in treatment so far obtained have been the "low-hanging fruit"—meaning that costs could even go up.

One reason that unit costs of treatment might rise dramatically would be the effort to extend treatment into smaller population centers. If there are indeed important reductions in unit cost obtainable from increasing the number of patients served from a small to medium number, the converse would also be true: there will be

diseconomies in building and operating the small-scale AIDS treatment centers that will be required to extend coverage outside the major urban centers of the developing world. The other major possible source of diseconomies of scale-up could be driven by the effort to assure treatment access and adherence among those who are less educated, poorer, or less motivated than the patients who have so far come forward. The contribution of these socioeconomic determinants to treatment access and success is not yet well understood.

IV. The rationing dilemma: Who gets a seat in the lifeboat?[18]

When the rate of expansion of free treatment begins to slow, as it will begin to do by 2010, patients needing treatment, their families and friends, health care providers, and patients already benefiting from treatment will all become acutely aware of the mechanisms that each country and each ART provider adopts to ration care. Whether inadvertently or by government intention, prices will increasingly be used to ration AIDS treatment. As a result, the mix of new patients accepted in ART programs will shift increasingly toward the upper regions of each society's income and wealth distribution. At the lower end of those who can afford treatment, paying for ART will impoverish patients and their families.

It is difficult to estimate the potential impact on poverty in a developing country of any given prevalence of AIDS treatment, but we can get a sense of the problem by examining the impact of catastrophic health expenditures on household expenditure per capita over a period of one year. We will take the case of Bangladesh, even though the data precedes the AIDS epidemic (and Bangladesh has been largely spared so far). Unfortunately a similar analysis of catastrophic health expenditures is not yet available for an African country.

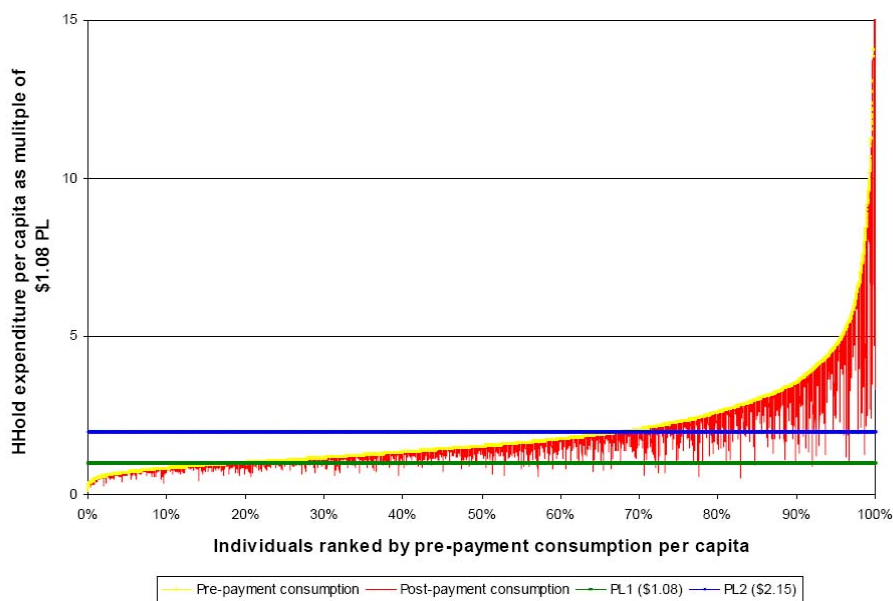[18] This section draws on (Over,AM, 2009).

Figure 13. On the precipice of poverty
Out-of-pocket health expenses can push individuals and families into poverty
(Impact of health expenditure on household net consumption patterns in Bangladesh)
(Source: (Van Doorslaer,E et al., 2007b)
Note: **Vertical lines represent reductions in household expenditure per capita caused by health spending.**
Lines that drop below the poverty lines represent individuals pushed into poverty in 2000.)

The Bangladesh case is illustrated in Figure 13. The vertical axis measures the household's expenditure per

member per day in multiples of the poverty line of $1.08 per day. A second horizontal line is constructed at

another less-strict poverty line of $2.15 per day. The upward sloping curve displays the cumulative distribution

of household expenditure in Bangladesh before health outlays are made. And the downward pointed "paint drips"

from the curved shape of the cumulative expenditure distribution show the effect of subtracting out-of-pocket

health expenditure from total expenditure (most likely for acute, rather than chronic, illnesses).

What can we learn from Figure 13? We can see that if health expenditures are excluded, about 20 percent of the

Bangladeshi population lived in households where daily consumption was less than $1.08 per day and about 70

percent lived in households below $2.15 per day. But if we "correct" the traditional measure of household

wellbeing to include the health outlays, the result is dramatic for some households—indeed, bringing net

consumption per household member below one of the poverty lines. And health expenditure large enough to

reduce a family to penury can be fairly classified as "catastrophic." Note that even households that would

otherwise have been in the top decline of household expenditure were reduced to poverty by one of the two measures once health expenditure was netted out of their annual consumption[19].

Although Figure 13 dramatically depicts the problem of catastrophic health expenditures, it unavoidably overstates the prevalence of the problem—vertical "paint-drips" to be visible take up too much space, making it look as if virtually all households suffer substantial reductions in well-being from health expenditure. So we need to take another approach to get a better grip on prevalence. For that, we construct a table that gives the percentage of individuals whose household expenditure net of health care costs is in fact below the poverty line. We draw on data from four South Asian countries (Van Doorslaer et al (2004).

As Table 2shows, in India, this re-definition of poverty would push an additional 20.6 million below the higher poverty line and 37.4 million people below the lower one, increasing the proportion of Indians suffering from the most extreme form of poverty by 12 percent. In Bangladesh, Nepal, and Sri Lanka, health expenditure increases the number of those below the lower poverty line by 17, 6, and 8 percent respectively. Although these increases in measured poverty are smaller than might be inferred from Figure 13, they are still substantial.

Moreover, many who seek private sector treatment for AIDS are likely to be pushed below the poverty line. Suppose that an individual spends approximately $365 a year out-of-pocket on AIDS treatment, which is enough to cover the full cost of first-line triple-drug therapy at generic prices plus doctor visits and some laboratory tests. In a four-person household, this would add $0.25 per member to daily health expenditure. From Figure 13 we can see that households at about the 40th percentile of Bangladesh's expenditure distribution, which had no other health expenditure, would be pushed down below the lower poverty line by a single AIDS

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[19] The situation is actually a bit more complex. Since people have insurance and precautionary saving, some out-of-pocket payments are pre-financed and therefore should not be seen as immiserating. This pre-financed proportion should instead be subtracted from both gross and net consumption. In Figure 13, this would have the effect of shifting an individual "paint-drip" to the left and also making it shorter. If the slope of the cumulative expenditure curve is sufficiently flat (that is, less than 45 degrees) such a shift could move an individual who appears to be immiserated by health care expenditures to a position from which health expenditure no longer pushes him/her below the poverty line. See Van Doorslaer, Wagstaff and coauthors for an in-depth discussion (Van Doorslaer et al, 1993; Van Doorslaer,E et al., 2007a; Wagstaff et al., 1989; Wagstaff, 2002).

patient, to be on a par with households at the 20th percentile. Two AIDS patients in a household would severely impoverish a household that had previously been at the 45th percentile of the expenditure distribution.

What would be the result of the impact of out-of-pocket AIDS treatment expenditure on poverty in India? Suppose that the distributions of overall expenditure and health expenditure for the poorest 40 percent of India's population are similar to those of the lowest 40 percent of the Bangladeshi population. Further suppose that all of the estimated 500,000 to 1,600,000 people who are estimated to be living with AIDS in India are in households that would otherwise be above the $1.08 poverty line, but not above the 40th percentile of the Indian income distribution. Because there were between 300 million and 500 million Indians living under the $1.08 poverty line in 2000, AIDS would increase the number of strictly poor by less than 0.5 percent. In so doing, it would increase the percentage of the population below the stricter poverty line by about 3 percent, from about 35 percent to 38 percent.

Table 2 Getting a better fix on AIDS prevalence
Out-of-pocket payments for health care could push South Asian countries into poverty

| | Poverty line of $1·08 per day | | | | | Poverty line of $2·15 per day | | | | |
| | Change in poverty head count | | | | | Change in poverty head count | | | | |
	Prepayment head count*	Postpayment head count	Percentage point change	Number of individuals	Percentage change	Prepayment head count	Postpayment head count	Percentage point change	Number of individuals	Percentage change
Bangladesh	22·5%	26·3%	3·8%	4,940,585	16·8%	73·0%	76·5%	3·6%	4,653,875	4·9%
India	31·1%	34·8%	3·7%	37,358,760	11·9%	80·3%	82·4%	2·1%	20,638,361	2·6%
Nepal	39·3%	41·6%	2·2%	515,933	5·7%	80·4%	81·7%	1·3%	290,280	1·6%
Sri Lanka	3·8%	4·1%	0·3%	60,116	8·3%	39·1%	40·8%	1·7%	325,783	4·3%
Uganda	51.5%					75.6%				
Kenya	19.7%					39.9%				

Source:(Over,AM, 2009; Van Doorslaer et al, 1993; Van Doorslaer et al., 2006; Van Doorslaer, Eddy, O'donnell, O., Rannan-Eliya, R. P., Somanathan, A., Adhikari, S. R., Garg, C. C., Harbianto, D., Herrin, A. N., Huq, M. N., Ibragimova, S., Karan, A., Lee, T. J., Leung, G. M., Lu, J. F., Ng, C. W., Pande, B. R., Racelis, R., Tao, S., Tin, K., Tisayaticom, K., Trisnantoro, L., Vasavid, C., and Zhao, Y., 2007b).

A final caveat , however, is that this analysis does not take into account the fact that AIDS treatment must continue for the rest of the patient's life—in other words, it is more like a chronic illness than an acute illness. A household might recover its economic status after a single catastrophic expenditure depresses net expenditure for a single year. But that same household would need more robust coping strategies to deal with a stream of

catastrophic expenditures over several years. To analyze chronic disease, one would need a graph like Figure 13 that would be constructed for wealth (or "permanent income") instead of expenditure. .And to push this analysis further, it would be necessary to have information on the distribution of HIV infections across the income or expenditure distributions for the most severely affected countries in Africa and Asia, as well as the poverty and health expenditure data depicted in Figure 13 and Table 2. While a poverty head count can be estimated for any country with a household expenditure survey, until recently there has been no population-based information available on the distribution of HIV infection by socioeconomic class in almost any country in the world.[20]

Using this new data, it will be possible to predict the impact of any given rate of uptake of free ART and any ART rationing rule on poverty. Such calculations drive home the equity issues raised by out-of-pocket expenditures for AIDS treatment and may enable estimates of the impact on out-of-pocket ART expenditure and poverty of any public sector decision regarding the uptake of patients on publicly financed ART. Besides delineating the social impact of any rationing decision, this type of analysis highlights the importance of *preventing* HIV, especially among the poor, who can least afford to pay even transport fees to access treatment.

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[20] An early challenge to the assumption that HIV prevalence would be higher among the poor or uneducated is presented in (Ainsworth et al, 1997). The incorporation of blood tests into general purpose national surveys have shown that the highest HIV prevalence levels are often at mid or even at the highest levels of socioeconomic status in African countries (Barnighausen et al., 2007; Montana et al., 2008).

V. Spillover effects of AIDS treatment: beneficial and perverse

A. Evidence of macroeconomic benefits of AIDS treatment

Public sector support of ART for AIDS patients could benefit the economy as a whole for several reasons.

- To the extent that ART extends the productive life of AIDS patients, it enables households, communities, and employers to receive greater returns on previous investments in the patients' education and on the job training. This effect has the potential not only to improve productivity but also to encourage private investment in human capital.

- Publicly financed AIDS treatment constitutes a fiscal stimulus that—given sufficient flexibility in the supply of domestic factor inputs such as health personnel—can expand employment and stimulate economic growth. In severely affected countries where AIDS treatment is extended to a large fraction of the adult population, this stimulus and the consequent multiplier effect on growth could be substantial.

- Government-sponsored ART removes a potential obstacle to foreign direct investment that generates employment, acting as a kind of employment subsidy. In comparison to an alternative in which the government asked employers to subsidize ART for all employees in need, a publicly financed ART program could stimulate foreign investment and thus boost economic growth.

- If the alternative to public sector financing of ART delivery is private financing and delivery of ART with much lower adherence rates, public sector ART financing may be preventing or slowing the domestic and international spread of drug-resistant strains of HIV. Although only applicable if public sector ART financing assures high adherence, this consideration could be the most important for the longer-run welfare of individual countries and for global public health.

B. Effects of AIDS treatment on other health care

For a long time, a source of heated debate has been whether AIDS treatment helps or hurts health systems—a topic on which the empirical data is sparse. There are anecdotal reports of AIDS treatment creating a two-tier health system, with resources drawn out of the second "lower" tier of general primary and secondary care into the "upper" tier of AIDS treatment. But there are also photographs from Rwanda, for example, that show the dramatic improvement in the physical condition of a health center after it has been remodeled with AIDS treatment money. A major problem in addressing this question is to know what would have happened in these health care facilities if AIDS treatment had not been introduced ((Price et al.) (2007)). In other words, in the absence of PEPFAR, would the Rwandan health centers have been strengthened anyway by donor money as many of them have been in the past?

While the "before/after" photographs of a Rwandan health center show dramatically what has happened there because of AIDS money, these same photos could plausibly be reversed to tell the story of how past health center improvements have been followed by lack of maintenance and then decay. So the question is whether the instances of strengthening that we see in Rwanda and elsewhere are only temporary and will be followed by decay as has happened in the past. Furthermore, does the focus on AIDS treatment financing increase or decrease the risk of future decay?

The good news is that this whole debate is fast becoming moot. In 2009, the Obama administration announced the Global Health Initiative, which integrates the PEPFAR program within an effort to strengthen developing country health systems more generally, and with efforts at the Global Fund for AIDS, Tuberculosis and Malaria to fund health system strengthening. In the future, AIDS programs will be judged at least in part by their contributions to health system functioning. The challenge will be how to measure whether the health systems are indeed becoming stronger. .

C. *Effects of AIDS treatment on HIV prevention: good and bad*

Uptake: stimulate the demand for testing

Treatment availability unquestionably stimulates the demand for HIV testing, which in turn stimulates the demand for AIDS treatment among those who find themselves to be HIV positive. This seemingly virtuous circle assures that the "unmet need" for treatment, which is estimated by epidemiological models, will increasingly express a political demand and, for those with purchasing power, an economic demand for treatment. This is one of the important dynamics of AIDS treatment that supports higher spending.

Disinhibition: reduce the incentive to avoid infection

A separate question, however, is whether HIV testing affects sexual and injection drug user risk behavior, and if so, is it positively or negatively. The answer it turns out is nuanced, depending upon the sex, the age, the education, the number of previous times the individual has been tested, and, especially the HIV test result.

To begin with, we are unsure whether there has been any reduction in risk behavior as a result of a fear of AIDS and of learning about ways to protect oneself. Data from ante-natal clinics in some African countries shows a decline in the prevalence of HIV among young women, but in at least one country, Kenya, a recent household survey of HIV prevalence shows an increase in prevalence.

One way that Africans may have adjusted their behavior to protect themselves against AIDS is to marry earlier. But given that the trend away from extremely early marriage by African girls has been heralded as a mark of socioeconomic development with important spillover benefits for children, it would be unfortunate if young women were responding to the AIDS threat by seeking "safe haven" in earlier marriage (Anne Case, "The impact of HIV on marriage patterns in sub-Saharan Africa", workshop presentation, Amsterdam, 2009). This would especially be problematic if, as some contend, marriage were to actually increase the risk of HIV infection. Thus, a previously unnoticed benefit of effective treatment could be to reassure young women about staying single longer and thereby encourage a healthy postponement of marriage into the twenties. .

Biological: enhance prevention efforts

Because effective AIDS treatment reduces the number of virus cells in the blood stream to undetectable levels, it has long been argued that AI DS treatment might itself constitute an effective HIV prevention tool. Randomized controlled trials are underway in the United States in both Washington, DC, and the Bronx that should yield more information on the efficacy of this approach. Unfortunately as suggested by the analysis in an accompanying essay, the impact of a "test-and-treat" strategy—that is, annually testing the entire population, and for those who test positive, beginning treatment immediately—on affordability will make the approach infeasible in the near term.

VI.   Assuring HIV prevention through better treatment

As we move forward into an AIDs transition the need is to identify ways that AIDS treatment can leverage increasingly effective HIV prevention. By marshalling the available incentives and finding new ones, there is hope that treatment can make an improved contribution to the creation of the fiscal space that treatment itself will require.

A. Performance based funding for AIDS treatment

 A relatively new policy instrument for the health sector is the application of performance based incentives (PBIs) to increase the productivity or improve the quality of health care. We can define these incentives as "the transfer of money or material goods conditional on taking a measurable action or achieving a predetermined performance target" (Eichler et al, 2009), p. 6). They include "incentives on both the demand and the supply sides, at both individual and collective levels, [which operate at] the interface between provider and patient" (ibid.). But they exclude from their purview, "the conditional payments that donor agencies offer to national [or sub-national] governments" (ibid.).[21] Typical PBIs include conditional cash transfers, transportation subsidies, food support, and financial rewards to providers for results (or penalties for poor performance).

One country that has experimented with performance based financing (PBF) for health care delivery for many years is Rwanda (ibid., pp. 189ff). In 2006, when it began to scale-up PBF to its entire health care delivery system, Rwanda decided to design the scale-up to permit rigorous evaluation of the PBF approach, which had been under way since 2002. To do so, the government allocated PBF to 79 of 165 facilities and withheld the reward system from 86 facilities. The assignment was partly random and partly based on matching criteria, so that the facilities with PBF would be as similar as possible to those without it. During the period from 2006 to 2008, AIDS treatment was also being scaled up in Rwanda in the same facilities. To ensure that the provision of

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[21] For a fuller discussion of performance-based incentives, see Essay 2.

this additional complex service not confound the evaluation, Rwanda balanced the AIDS treatment rollout between the groups with PBF rewards and those without.

How did the PBFs work? Preliminary results show that health personnel exposed to the PBIs were more productive than personnel who were not (Gertler et al, 2009). [22] Furthermore, the health personnel with better training and knowledge responded more to the incentives. These results held for all facilities, including those with integrated HIV/AIDS diagnosis and treatment services. Even so, a word of caution The results suggest that while the mere presence of AIDS services actually increased child preventive care, the presence of AIDS services combined with a PBF incentive system more than offset this beneficial effect. Thus, care must be taken to adjust the relative strength of the incentives across different types of services if the intention is not to reduce other services.

In addition, other studies show that PBF systems can improve patient return for test results (Chaisson et al, 1996) (Thornton, 2005) and improve patient adherence to ART (for example by providing transportation vouchers) (Sorensen et al., 2007). By deploying these types of PBI systems, governments can hope to out-source to the private sector key HIV prevention and treatment services.

Yet another type of PBI—aimed at improving incentives for successful AIDS treatment—would be to out-source to patients the monitoring of providers. This could substitute for, and perhaps improve upon, a portion of the expensive and logistically challenging monitoring that would otherwise be performed by a central authority. How would it work? Treatment resources would be allocated to accredited groups of ART patients instead of to health care providers or facilities[23]. Patient groups would receive be training in advocacy and charged with assuring, to the best of their ability, the exact adherence of each group member—and CD4 counts would be monitored. Among the groups in a given geographic region, those that succeed in sustaining and improving the

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[22] Gertler et al., "Paying Health Care Providers for Performance: Evidence from Rwanda," Presentation to the Economics Reference Group, January, 2009. http://www.heard.org.za/research/economics-reference-group/fifth-meeting , Accessed April 25, 2010.
[23] This idea was first suggested in a study of the economics of AIDS treatment in Thailand. The example given was of an affinity group of AIDS patients that not only supported its members to assure they understood the providers' instructions but also carried them out. (Revenga et al, 2006)

clinical indicators for existing members would be the first to receive the allocation of a new treatment "slot" when one is available. Furthermore, a given group of patients would also be able to move its treatment budget from one group of providers to another. By giving the ART clients more bargaining power vis-à-vis the health care providers than any one of them would have alone, such an approach would inject into the subsidized transaction between patient and health care provider an element of market discipline.

B. Cash-on-Delivery for AIDS treatment

One type of PBI that we believe would make a huge difference in the AIDS battle would be "cash-on-delivery" (COD), which applies incentives to the top levels of governmental organization, such as the state, the province, or the nation—a recognition that top-level leadership on this issue has been lacking[24] . The COD approach aims to help donors facilitate longer-term commitments to sustained effort on a particular objective by establishing a reward mechanism that provides payments for the achievement of specific objectives, payments that governments can use to motivate actors and their constituencies at every level. It is quite explicitly a reward or a prize that the country or state has won because of its achievement of a challenging, worthwhile, internationally recognized social objective. For example, Barder and Birdsall (Barder and Birdsall 2006) suggest that a payment of $100 per child be made to the recipient government for every additional child enrolled above those that were enrolled at the beginning of the period.

Application of the COD approach to the provision of ART for AIDS patients has much in common with its application to education. In both cases, a COD program contract would need to recognize and reward both "enrollment" and "persistence" in the program. For students, "enrollment" means school enrollment, while "persistence" means the regularity of school attendance leading to grade completion. In AIDS treatment, the education concept of "enrollment" can be compared to the medical concept of "treatment initiation," while "persistence" can be interpreted as successful adherence to medication. A COD program for AIDS treatment would reward improvements in both treatment initiation and adherence to medication according to a pre-agreed payout function.

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[24] For a more on cash-on-delivery, particularly for prevention, see Essay 2.

Furthermore, in both education and AIDS treatment, "enrollment" of an individual is much more valuable to that person if it occurs at the appropriate time in the individual's life. The student who waits too long to start school forever loses the opportunity to maximize the benefits of schooling. Similarly an AIDS patient who waits too long to start treatment has a worse prognosis than a patient who begins treatment promptly on attaining ART eligibility.[25] Thus an appropriate payout function should reward timely initiation of treatment, without excessively penalizing unavoidably tardy initiation. Given these structural similarities between primary education and AIDS treatment, lessons learned in either of these areas might be applicable to the other. Transferable lessons might include the nature of a feasible reward structure and the best systems for auditing results.

The COD approach to funding AIDS treatment has several advantages over current funding approaches. First, with a properly structured reward or "payout" rule, COD can reward all dimensions of treatment success, not just the total number enrolled in treatment. A treatment program that accepts many people, but fails to sustain each one is unacceptable.[26] This imbalance can be addressed by designing the payout function so that it rewards a patient's surviving an additional month at a higher rate than it rewards a month of treatment for a new patient. By rewarding the program for survival, the program will automatically reward adherence, quality of care, and early recruitment. By also rewarding the total number enrolled in treatment, the COD program will encourage an AIDS program to reach out to ever larger numbers, including the poor.

One essential ingredient for the success of a COD program for AIDS treatment will be establishing, at the time the COD agreement is signed, a mutually agreed method for measuring the results against which the program will pay rewards. Donor and recipient must agree not only on which results to reward but also on how to

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[25] According to WHO, eligibility for treatment is determined largely by the patient's "CD4 count". While a person who is HIV negative has a normal CD4 cont between 800 and 1,000 CD4 cells per milliliter of blood, an HIV positive person's count eventually falls towards zero. Many countries have adopted a WHO recommendation to declare a patient eligible for treatment when their CD4 count drops below 200. Patients who wait longer, have lower CD4 counts and thus weaker immune systems which open the door to opportunistic illnesses.

[26] See Over (2008 WP144) (Over,M, 2009) and Institute of Medicine (Institute of Medicine, 2007) for suggestions that the U.S. PEPFAR program has focused excessively on increasing the number of patients on treatment regardless of their success at remaining on treatment.

measure those results, who will do the measurement, and who will audit them. The difficulty of this measurement problem is directly related to the number of patients under treatment.

This difficulty can be illustrated by looking at the success of treatment in 125 countries, all of which have different numbers of those in need (from less than 5,000 to over 60,000) and those receiving ART (from less than 5,000 to over 60,000). The reality is that 57 of these countries need to keep track of fewer than 5,000 patients—a much more manageable task than keeping track of all the students who would be the subject of a COD education program in any country. Another 50 countries currently treat, or need to treat, between 10,000 and 60,000 patients. These countries will find measurement more challenging, but with assistance in the construction and maintenance of a strong patient data management system, they should be able to provide results data on all their patients. Only for the 20 or 30 countries with the largest AIDS treatment rolls and the weakest patient data management systems might it be necessary to use a representative survey of patients rather than complete data on all of them.

After seven years of enhanced effort on AIDS treatment the international community has achieved much but the AIDS treatment challenge seems only to be growing. By adopting the perspective of the "AIDS transition," the community of donors and recipients can align the incentives of all parties to assure that treatment uptake continues and that expanding uptake contributes in measureable ways to slowing HIV transmission. Joint success in these efforts will in turn open up fiscal space to continue treatment for decades to come.

Annex A. Alternative approaches to estimating the average cost of antiretroviral treatment

While there have been many studies of the cost of HIV prevention activities, the cross-country determinants of the cost of antiretroviral therapy have not yet been estimated[27]. In theory, we would expect that average costs in a country would increase with its level of wealth and decrease with the number of patients it treats (due to economies of scale). Beyond these two factors, we would hope that the individual facilities providing ART services and the country at large would improve their efficiency over time. It might also be the case that the availability of donor support for ART would reduce incentives to economize and therefore inflate costs.

In the absence of a cross-country sample of facility cost data, we can look for the influence of these potential determinants of cost by analyzing the expenditures on antiretroviral therapy that individual countries reported to UNAIDS as part of their UNGASS-mandated reporting requirements. Figure demonstrates that a countries national income and the total number of patients treated do indeed explain about a third of observed variation in average costs. A country whose per capita income is 10 percent higher will on average spend about 8.5 percent more per patient-year. For example, the average expenditure per patient in 2007 of a country with 25,000 patients under treatment would be $296 dollars if the

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[27] On the costs of HIV prevention activities, see (Guinness et al., 2005; Guinness et al., 2007; Kumaranayake and Watts, 2000; Marseille et al., 2007). For antiretroviral therapy, individual cost studies have been done, but unfortunately no one has yet published data on a large enough range of study sites to permit estimation of economies of scale (Cleary et al., 2006; Leisegang et al., 2009; Nachega et al., 2010; Over et al., 2006; Over et al., 2007). Although the 2008 PEPFAR authorization bill mandates that the US Administration provide to Congress "by September 30, 2009" studies which estimate the unit cost of ART, at the time of writing the administration has not yet complied with this mandate. See the discussion of the implication of the mandate here: http://blogs.cgdev.org/globalhealth/2008/08/pepfar-reauthorization-iv-targ.php

Average reported expenditure on ART
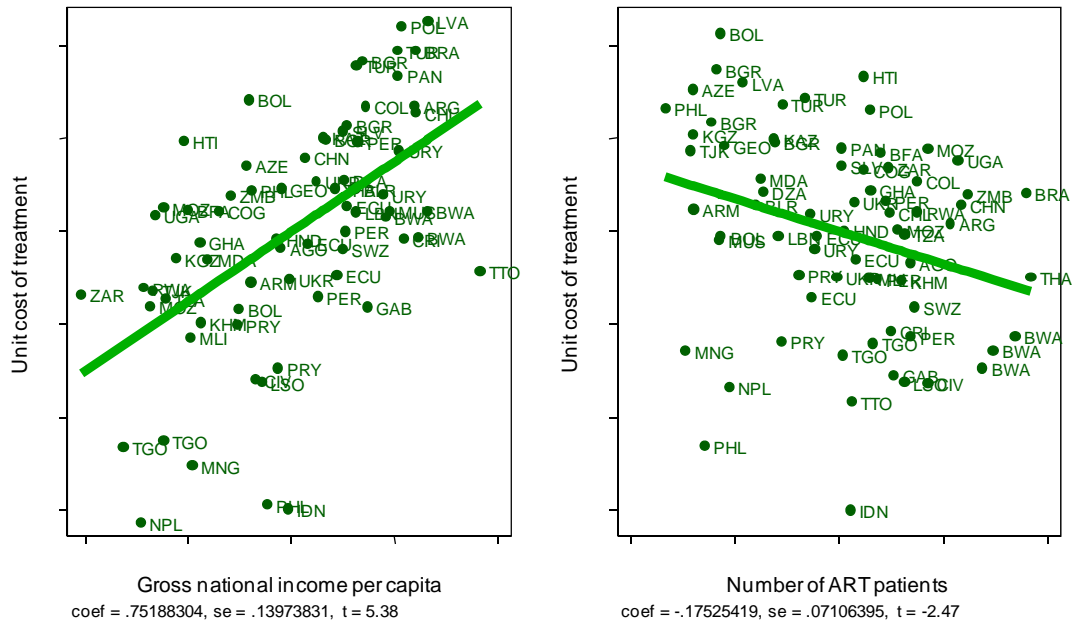increases with national income
and declines with number of ART patients

Figure 14. **Average cost of treatment rise with national income and fall with number of ART patients**
Notes: These two scatter plots display the partial effects of gross national income per capita and of total ART patients, holding the constant the other variable and a dummy variable for the year. The three letter codes are the World Bank country codes.
Source: Author's calculations based on data from Annex 2 of (UNAIDS, 2008a).

country's per capita income were $460, $835 if the country's per capita income were $2,000 and $1,690 if the country's per capita income were $5,430[28]. We also learn that the number of enrolled patients matters. A country with a 10 percent larger patient enrollment benefits from about a 1.5 percent reduction in average cost per patient. Thus, the upper-middle-income country with an income per capita of $5,430 would spend $1,690 per patient-year when treating 25,000 patients, but only about $1,500 per patient-year if it doubles its treatment rolls to 50,000 patients.

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[28] This is the source of the figures in row h of Box A, Table 1

Estimated economies of scale in AIDS treatment at three income levels c. 2007
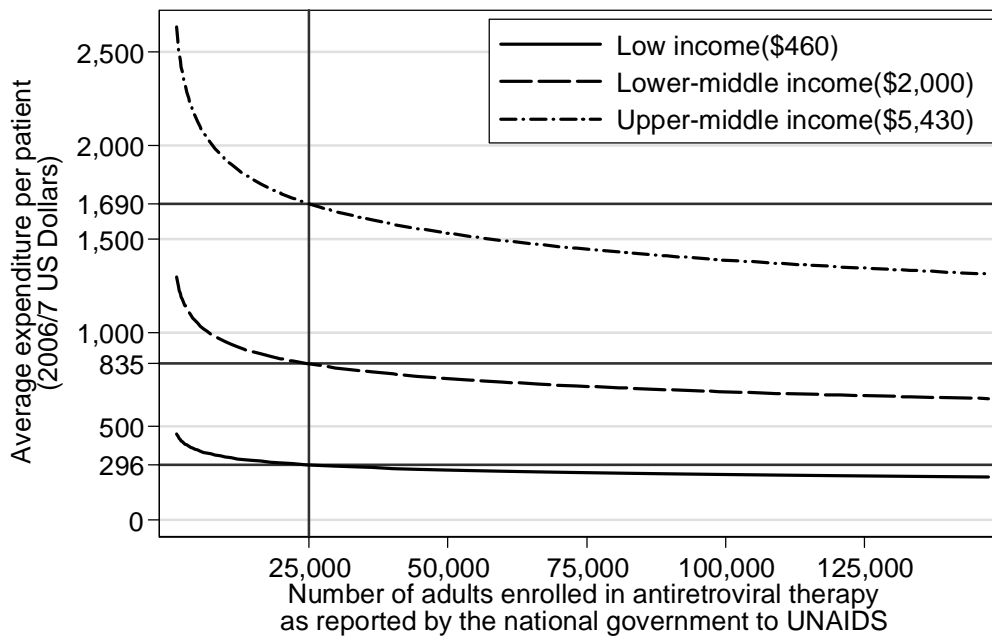

Figure 15. More income and more patients is better
Average expenditure depends on per capita income and on size of the treatment program
Note: These curves display the fitted values from a log-linear regression of the total expenditure per patient data in on the logarithms of the variables gross national income per capita and the number of patients receiving treatment. .

(Source: Author's construction from econometric estimate of average expenditure function)

In addition, we discover that there are other factors besides per capita income and number of enrolled patients that have influenced the 86 percent drop in costs in nominal terms between 2005 and 2007. Given that the drug component decreased by only about 50 percent, the rest of the reduction must have occurred either in the quantity of health services used per patient or in the average fixed cost per patient. The most likely explanation is that 2005 saw large investments in capacity without commensurate increases in the number of patients, which then occurred the following two years

We can now pull all this data together to project future costs. First, we assume that reductions from lower drug prices and lower average fixed costs have stabilized,[29] but we allow future average cost reductions owing to economies of scale from the increased numbers of enrolled patients[30]. Conversely, if countries scale down their treatment programs, either because of successful prevention or fiscal constraints, the cost reductions from scaling up will be reversed and the average cost per treated patient will consequently rise by about 1.5 percent for every 10 percent reduction in treatment numbers. Second, we assume a pronounced positive correlation between a country's income per capita and all components of the unit cost of delivering ART. Indeed, we have seen that countries with higher incomes pay as much as double for exactly the same three therapeutic molecules. And we have found the elasticity of per patient expenditure on ART is about 0.71, suggesting that a country with 10 percent higher income per capita will spend about 7 percent more per patient—meaning that there could be an upward pressure on unit costs going forward.

So what is the bottom line? Overall, we see relatively stable average total costs for AIDS treatment going forward. The big question is what that will mean for countries 'fiscal burdens.

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[29] For a fuller discussion of future drug prices, see page 33.
[30] In the attempt to achieve treatment coverage close to 100 %, average costs would be likely to rise due to the requirement that treatment facilities be located in small communities, where the small numbers of patients would prevent economies of scale. Since such high treatment coverage rates are unlikely to be financed, partly for exactly this reason, the models in this book do not incorporate these eventual scale diseconomies. See Over, Lundberg and Bautista (forthcoming).

Annex Box A. Estimating the average ART expenditure per enrolled patient from the top down

In order to estimate the average cost to treat patients with antiretroviral therapy in all countries in the world in future years, we have merged data from two UNAIDS reports, one on financing AIDS programs and one on the total number of people on treatment. For the years 2005 through 2007 a total of 57 countries submitted AIDS financing and AIDS treatment data for the same year at least once. Some did so several times, giving us a total of 73 observations. The following table gives summary statistics on these 73 observations.

Table 1. Summary data on expenditures on and enrollment in antiretroviral therapy in 73 countries reporting both for 2005-2007

Year	Number of countries reporting both expenditure and enrollment	Average number of adults enrolled in antiretroviral therapy	Average total reported expenditure on antiretroviral therapy (US Dollars)	Average gross national income per capita in current US dollars	Average expenditure per patient on antiretroviral therapy
2005	13	13,859	$12,833,769	$2,486	$2,755
2006	40	16,923	$18,654,850	$2,598	$1,788
2007	20	16,720	$12,582,000	$3,377	$2,069
Total	73	47,501	$44,070,619	NA	NA
Overalll average	NA	16,321	$15,954,425	$2,791	$2,037

Sources: UNAIDS (2008) UNAIDS/WHO (2009)

Note: NA= Not applicable

The estimated regression equation representing the average expenditure function is given by:

Log(Expenditure per enrollee) =
Constant + Income Elasticity * (GNI per capita) + Scale Elasticity * Log(Number of enrollees)
+ Change from 2005 * (Dummy = 1 for year = 2006 or 2007)
+ Change to 2007 * (Dummy = 1 for year = 2007) + Disturbance term

Table 2. Estimated coefficients of the average expenditure function for antiretroviral treatment, 2005-2007

Independent variable (coefficient meaning)	(1) coefficient	(1) t-statistic	(2) coefficient	(2) t-statistic
Log of GNI per capita (coefficient is the income elasticity)	0.690***	4.860	0.706***	4.840
Log of number receiving AIDS treatment (coefficient is the scale elasticity)	-0.138**	-1.999	-0.142**	-2.028
Dummy variable =1 for years 2006 and 2007 (coefficient gives percentage change since 2005)	-0.863**	-2.221	-0.801**	-1.961
Dummy variable =1 for year 2007 (coefficient gives percentage change from 2006 to 2007)			-0.186	-0.520
Constant	3.311**	2.533	3.224**	2.433
Number of observations	73		73	
R^2	0.350		0.353	
F(3,69) or (4,68)	12.407		9.275	
Smear coefficient	1.766		1.757	
note: t-statistics are the ratios of the coefficients to their standard errors. Asterisks indicate standard levels of statistical significance according to the following convention: *** p<0.01, ** p<0.05, * p<0.1				

Equation (2) tests the hypothesis that average expenditure reductions from 2006 to 2007 were statistically significant and finds that they were not. In order to assure the lowest cost projections consistent with the data, we nevertheless use equation (2) for projecting the logarithm of future average costs We then convert from logarithms back to currency units and multiply these projected values by the estimated "smear coefficient" of 1.757 in order to project average rather than median cost per enrollee (Duan, 1983).

[1] Estimating an average cost function on a small number of observations and then applying the results to project current and future average costs for countries and years outside the sample requires heroic assumptions. The advantage of this approach is that, in contrast to other less quantitative approaches, the assumptions are explicit. We assume that the 57 countries are representative of all the countries with public sector programs delivering ART. Since the distribution of all three variables in our analysis, expenditure, number enrolled in treatment, and gross national income (GNI) per capita are skewed with long right-hand tails, we assume that the logarithms of these variables will better reveal the shape of any underlying average cost curve. (That is, we assume that disturbance term in a regression linear in logarithms will be normally distributed.) And perhaps most important, we assume that the degree of efficiency displayed over the years 2005 through 2007 will continue to characterize these countries into the future.

Annex B. A meta-analysis of the health benefits of early initiation of antiretroviral therapy

The purpose of this annex is to present our methods for estimating the benefits of earlier recruitment to ART.

We base our approach on a systematic comparison of published data on the survival of patients who start early to those who start late, as illustrated in Figure 16. We see that without treatment, an HIV infected person has a probability of death approaching certainty as the CD4 count approaches zero. However, treatment does reduce mortality dramatically for those who are able to adhere to the treatment regime and are retained by the treatment program. We also see that for those who start treatment when their CD4 count is 400 or above, estimated mortality is about 0.04 (about 4 percent). This percentage rises to 10 percent for a starting CD4 count of 50, and then rapidly rises toward 100 percent as the CD4 level approaches zero. This percentage rises to 10 percent for a starting CD4 count of 50, and then rapidly rises toward 100 percent as the CD4 level approaches zero. Moreover, every 10 percent decline in CD4 at ART initiation is associated with a 3.0 percent rise in first year.[31]

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[31] The fitted trend line is linear in logarithms. The slope of a function that is linear in logarithms is referred to by economists as an "elasticity" and has the virtue of being unit-free. It gives the percentage change of the dependent variable associated with a one percent change of the independent variable. Here the estimated elasticity is -0.30.
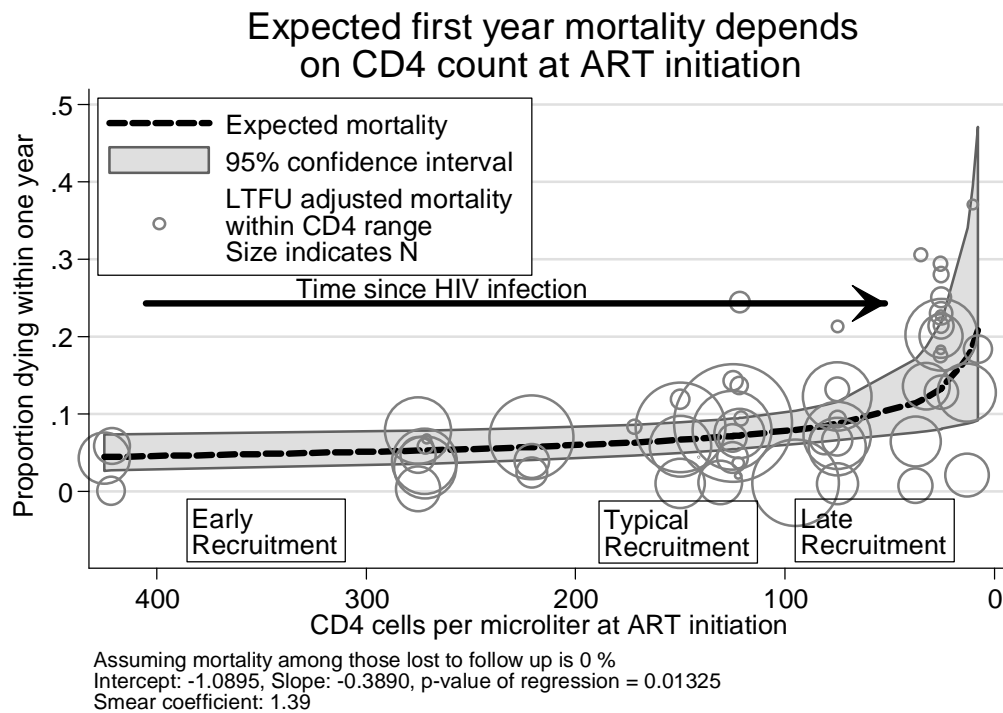
Figure 16. Living longer
The sooner ART begins, the lower the expected first-year mortality
(Estimated association between CD4 count per microliter at ART initiation and first year mortality, without adjustment for loss to follow-up)
(Source: Fox, McCarthy, Over, forthcoming)

The problem is that this approach to estimating the benefits of earlier ART initiation is subject to at least two

sources of bias. First, the mortality of those who dropped out of treatment programs and could not be traced is

not included in these estimates and is likely to be higher than for those who continued treatment. Researchers

who have attempted to trace those who have stopped attending their treatment sessions have learned the fate of

fewer than half of them. One recent review of these studies (Brinkhof et al., 2009) found that about 40 percent

of the lost to follow-up (LTFU) who were successfully traced had died within the year, and it seems likely that

the mortality rate among the untraced was even higher. This omission is likely to underestimate the mortality of

those on ART, especially at low CD4 counts. Second, the mortality of those with less severe symptoms at any

stage in their disease might be excluded from this data because they did not seek care—an omission that is

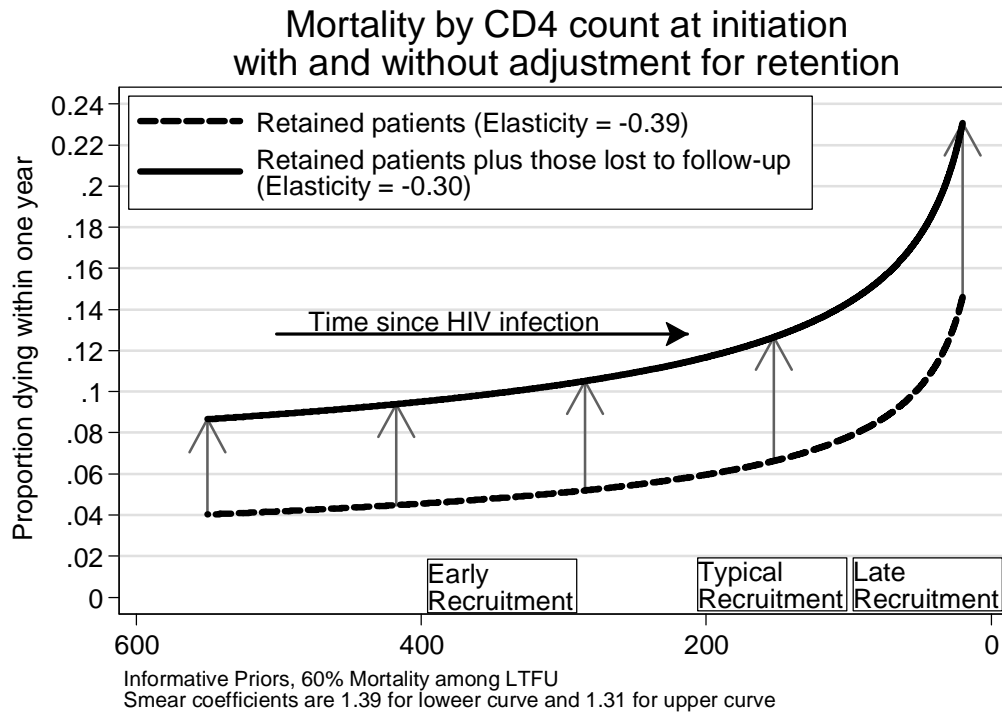likely to overestimate the mortality of those on ART, especially at high CD4 counts.

Mortality by CD4 count at initiation with and without adjustment for retention

Figure 17. Retention matters
First-year mortality after beginning ART is about twice as high if mortality among those lost to follow-up is taken into account
(Source: Author's calculations based on Fox, McCarthy, Over, forthcoming)

We attempt to correct for these two biases in three steps. First, we estimate the mortality of the LTFU and use it

to adjust upward the curve from Figure 16 as shown in 17.[32] Now we see that first-year mortality after ART

initiation is not as low we had thought, a strong vote for the need to stick with the program.

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[32] Our method for estimating mortality among the (LTFU) is to choose the value of that mortality that maximizes the goodness-of-fit of the log-linear regression of mortality on CD4 at initiation. The best fitting value is 60 percent mortality among those lost-to-follow-up that yields the upper of the two mortality curves(Fox, McCarthy & Over, forthcoming). By assigning the LTFU mortality to those who start ART, we are implicitly assuming that this attrition from treatment programs will remain constant across the various scenarios under consideration. However, with appropriate additional management effort and patient adherence support, both of which are costly, LTFU and its associated mortality could both be reduced.

Second, we use the latest estimates from historical cohorts who did not have access to treatment to anchor mortality at the highest CD4 counts (eART-linc, 2008). Figure 18 shows this by overlaying the adjusted mortality estimates of those on ART from **Error! Reference source not found.** on the relationship between mortality and CD4 count at initiation for those not on ART derived from the historical cohorts (eART-linc, 2008). The intersection of the two lines at a CD4 count of about 350 is implausible because it would imply that starting ART at a CD4 count above 350 would increase the patient's risk of death. Instead this intersection can be interpreted as confirming that the estimates in the literature of the mortality of those on ART are unrealistically high for patients who started with high CD4 counts.
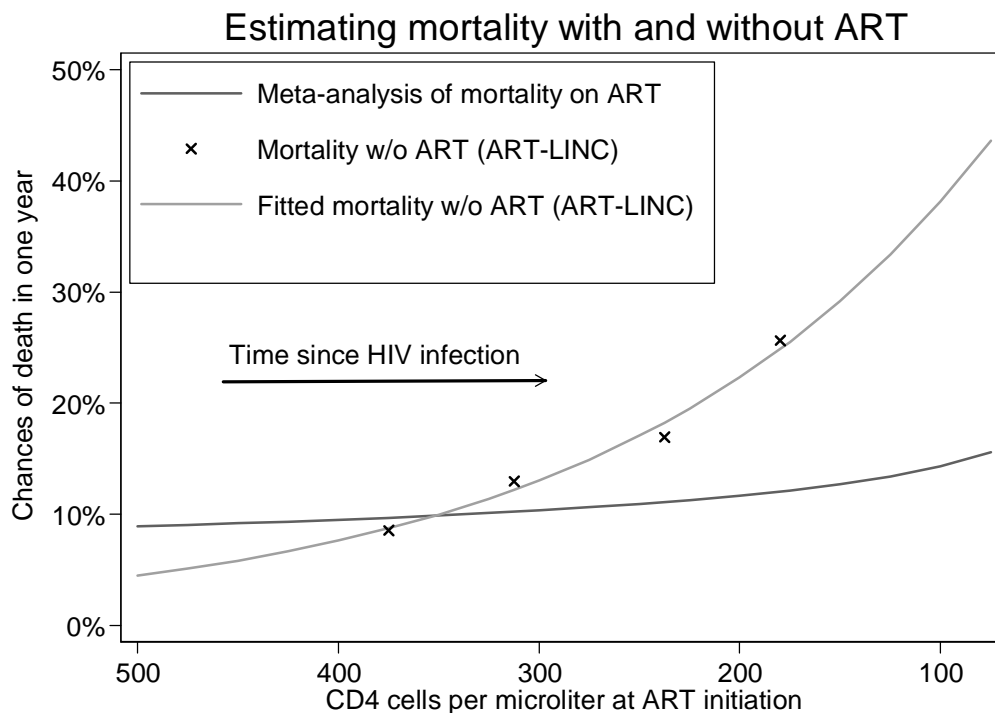

Figure 18. At high CD4 counts mortality estimates from the eART-Linc data are smaller than from patients who actually entered therapy at these high CD4 levels
(Mortality profiles of those with and without ART in poor countries)
(Sources: Author's construction based on (eART-linc, 2008) and Figure 17**)**
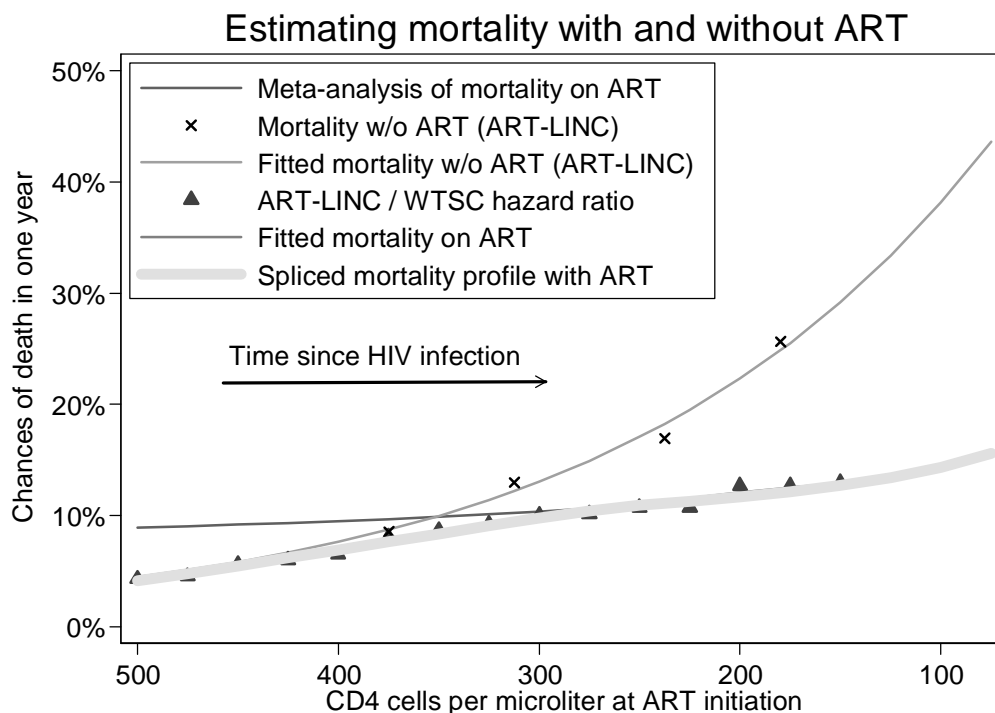
Estimating mortality with and without ART

Figure 19. The most plausible mortality profile at all CD4 counts must be assembled by splicing the minimum mortality at high CD4 conts from ART-Linc with the minimum mortality levels from the metaanalysis of patients in treatment
(Estimated first-year mortality with and without ART)
(Source: Author's construction)

Third, we use the latest estimates of the hazard from incrementally postponing ART to splice together the two

estimates from poor countries. One approach to estimating the benefits of ART by CD4 count would be to

reconcile the two sources of information by assuming there are no treatment benefits above CD4 = 350. This

would amount to the assumption that first-year mortality on ART is the minimum of the two curves in Figure 18.

However, this hypothesis is inconsistent with the latest information from rich countries from the When to Start

Consortium (WTSC) (When to start Consortium and Jonathan Sterne, 2009) on the benefits of early initiation.

An approach which recognizes the potential mortality reduction even in poor countries of earlier treatment

initiation is to use the WTSC estimates of the incremental hazard from ART postponement to infer the reduced

mortality risk at high CD4 counts while relying on the meta-analysis for estimates of mortality at low CD4

counts. This approach is implemented in Figure 19.[33] The health benefits of ART estimated in this report are

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[33] Dividing the no-ART hazard rates from the curve fitted to the ART-LINC study data by the WTSC hazard
ratios generates the triangle points in Figure 19. The graphs shows that these triangles converge to the adjusted
Footnote continued on next page

derived from the difference between estimated no-ART mortality shown in the figure as the narrow line labeled

"Fitted mortality w/o ART" and the estimated mortality on ART shown in the figure as the wide line labeled

"Spliced mortality profile with ART."

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no-ART mortality at low CD4 counts, thus tying together all three data sources (eART-linc, 2008; When to start Consortium and Jonathan Sterne, 2009) (Fox, McCarthy and Over, forthcoming) and supporting the assumption that the rich country hazard ratios can plausibly be applied to the poor country no-ART hazard rates.

Annex C. A model for projecting future AIDS treatment costs

The model used to project the costs of AIDS includes both a compartment-based difference equation of the spread of the epidemic and a simple model of the unit cost of treating a patient. The figure here presents the structure of the epidemiological model. The model is available for download from www.CGDev.org and the code is open source. Because the model runs using the Stata statistical software, a copy of that program is necessary to execute the model.
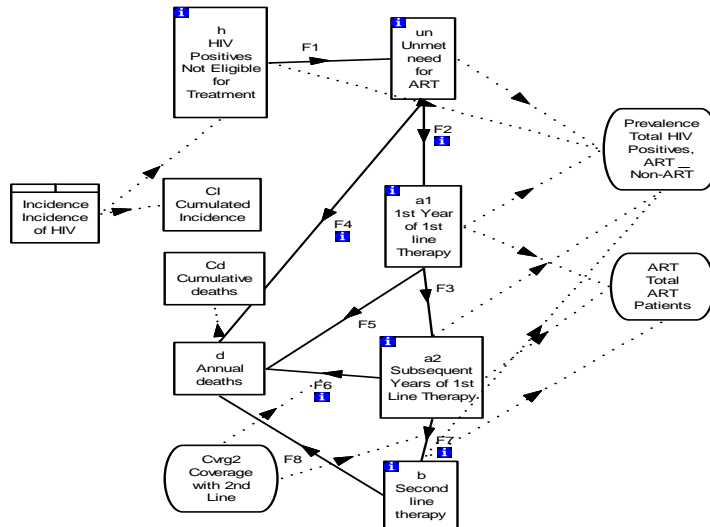

Figure 14. Flow diagram for predicting the future growth of AIDS treatment costs (Source: Author's construction)[34]

To use the model, one can select values of any of the parameters listed in the following table. Or one can leave the parameters unspecified to run the model with the default values listed in the table. The only parameter that does not have a default value is the "uptake" parameter, which specifies the user's assumption regarding the proportion of unmet need for treatment that will be added to treatment rolls each year in each country. The user may select any individual value between zero and 1.0, which is then used to model uptake in every country in the simulation. Alternatively, the user can specify the parameter as "uptake" that directs the program to use the idiosyncratic, country-specific uptake rates that are embodied in the cross-country data. A reference manual and user's guide for this software is available at www.CGDev.org . The software itself can be found and installed on your Stata machine by typing the phrase "findit AIDSCost" without the quotes, but respecting the capitalization, at the Stata command prompt.

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[34] See (White, 2007) for discussion of appropriate parameter values for the model and the Spectrum projection model for an alternative modeling platform: http://www.futuresinstitute.org/. On cost assumptions, see ((Bollinger, Stover, and UNAIDS) (2007)).

Table 2. Parameters used in the AIDSCost computer program for projecting the cost of AIDS treatment with default values.

	Name	Default Value
Scale-up of 1st line modeled as constant proportion, sigma, of unmet need, where sigma is constant across all countries and equal to:	*sigma*	No default here
Ratio that HIV incidence is of last year's incidence	*incmult*	0.95
First year of projections (projection takeoff)	*takeoff*	2008
Last year of projections (projection horizon)	*horizon*	2020
2nd line ART to start in year	*strtyr*	2007
2nd line ART to reach target in year	*trgtyr*	2020
Starting coverage rate for 2nd line ART[35]	*strtcov2*	
Target coverage rate for 2nd line ART	*trgtcov2*	0.95
The median CD4 count at ART initiation is: this choice of the CD4 initiation parameter and the user-chosen value, if there is one, which overrides that default. In each row, only the right-most value is used in the subsequent projections.	*cd4*	130
Proportion of HIV+ newly eligible for ART	*erate*	0.094
ART Death Rate during first year on 1st line	*adrate1*	0.133
ART Death Rate during subsequent years on 1st line	*adrate2*	0.04
ART Death Rate of AIDS patients on 2nd line	*bdrate*	0.04
Non-ART Death Rate of AIDS patients	*ndrate*	0.325
Cost computations based on following parameters		
Lower bound for 1st-line drug costs[36]	*rxc1lb*	$88
Upper bound for 1st-line drug costs	*rxc1ub*	$261
Lower bound for 2nd-line drug costs	*rxc2lb*	$819
Upper bound for 2nd-line drug costs	*rxc2ub*	$2,634
Number of bed-days per year per patient	*hsbedn*	1.56
Number of out-patient visits per patient	*hsvstn*	9.5
Average fixed non-drug cost at ART=1000	*nonrxcaf*	$750
Elasticity of average fixed cost w.r.t. ART	*scale*	-0.142

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[35] The model embodies the assumption that, for those people who fail first-line ART, access to second-line ART expands along a logistic curve from about 5 percent of all patients needing it now to 95 percent of all patients needing it in 2016.

[36] Drug costs are assumed to vary across countries with the 2006 GDP per capita of the country according to the patterns observed by WHO in that year and then to remain constant in any given country over time.

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