

Will We End the HIV Epidemic?

**The Impact of HIV Treatment on HIV Prevention and
Implications for the 2010 Replenishment of the Global
Fund to Fight AIDS, TB and Malaria**



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**International
AIDS Society**

Stronger Together

The International AIDS Society (IAS) is the world's leading independent association of HIV professionals. Our vision is of a global movement of people working together to end the HIV epidemic, applying scientific evidence and best practice at every level of the HIV response. The IAS has three goals. We aim to:

- Increase knowledge and skills and foster creative solutions to challenges in the response to AIDS through dialogue and debate.
- Advocate for implementation of effective, evidence-based policies and programmes to enhance the global response to AIDS.
- Strengthen research capacity, identify research priorities across all disciplines and advocate to address them.¹

An end in sight?

Since the 2005 commitment by G8 leaders – and then all UN Member States – to work towards universal access to HIV treatment, prevention and care by 2010, many resource-limited countries have been highly successful in decreasing AIDS-related morbidity and mortality and slowing down the spread of HIV. The efforts to achieve this scale up have been driven by governments and civil society in these countries, with much of the resources provided by external partners, in particular the US PEPFAR² and the Global Fund to Fight AIDS, Tuberculosis (TB) and Malaria (the Global Fund). Since its inception in 2002, the investments made through the Global Fund are estimated to have saved 5 million lives, including through the provision of HIV treatment to 2.5 million people. The question now facing donors to the Global Fund is how many more lives they are prepared to save in the next three years – and whether they will make the bold investments required to make a real change to the future course of the HIV epidemic.

Since the Global Fund was created scientific knowledge has grown substantially. This knowledge, combined with implementation experience and wise investments, means that many low- and middle-income countries now have the human and technical infrastructure available to extend the lives of individuals with HIV and to make a dramatic reduction in HIV prevalence and incidence. Within the growing body of scientific knowledge there is exciting evidence emerging that shows that investments in HIV treatment will extend lives *and* also impact HIV prevention.

The Global Fund has established three funding scenarios which articulate the impact of different scales of investment on the course of the three diseases (AIDS, TB and malaria). While these scenarios are helpful, they give limited insights into the range of benefits of HIV treatment scale up, and have not yet calculated the substantial impact HIV treatment scale up could have on HIV prevention, and in turn the impact this could have on the future course of the epidemic. Increasingly, evidence demonstrates that investments in HIV treatment not only save and extend lives of individuals, but could also bring the epidemic to an end. In this paper we review the impact of HIV treatment on HIV prevention – and consider the consequences for the Global Fund Replenishment.

What is the impact of HIV treatment on HIV prevention?

Ever since effective HIV treatments have been scaled up there have been unhelpful debates suggesting a dichotomy between treatment and prevention. What is increasingly clear is that the links between HIV treatment and HIV prevention are more substantial and that creating a sharp division between treatment and prevention programmes is both inaccurate and counter-productive.

The initial commitment to universal access included a focus on treatment as a means to decrease AIDS-related morbidity and mortality along with a separate focus on prevention as a means to decrease rates of HIV transmission. Over the past five years it has become clear that the benefits of HIV treatment extend far beyond saving the lives of individuals with HIV: **antiretroviral therapy plays a key role in decreasing HIV transmission, and as a result the value of the original universal access commitment has dramatically increased.** Delivering HIV treatment to all who need it could cut new HIV infections by 30% within five years.³

Of course HIV treatment is by no means the only form of HIV prevention, and must be part of a combination prevention strategy that encompasses behavioural, structural, biomedical and community interventions. Yet, as critical funding decisions are being taken that will affect the capacity of countries to scale up programmes over the next three years, the full range of impacts of HIV treatment needs to be better understood. Scaling up to reach universal access not only directly benefits the individual patient; it is also emerging as one of the most effective *HIV prevention* tools available, and currently provides the best hope for reversing and ultimately defeating AIDS.

Scaling up treatment has also been shown to have multiple benefits to societies and health systems while extending life expectancy and retaining economically active individuals in the workforce. Recent evidence shows that antiretroviral therapy has:

- Reduced the burden of tuberculosis by 60% in people with HIV, and by 20% across the community as a whole in a South African study. Modelling shows it has the potential to do the same across nine countries with high HIV and TB burdens;^{4,5}
- Reduced mortality of uninfected children by 83% and orphan numbers by 93% in a Ugandan cohort when mothers with HIV receive treatment;⁶
- Reduced hospitalization by 75%-85% in South Africa, Uganda and Brazil, freeing up hospital beds and staff time to deal with other patients.⁷

Without sufficient treatment coverage, investments in HIV treatment and prevention will have only limited impact. Maximising coverage is the most sustainable response. By limiting new infections in the next five years, treatment costs that would otherwise continue to accrue for decades can be avoided.

The 2011-2013 Global Fund Replenishment period, as well as the upcoming 2010 MDG (Millennium Development Goals) Summit at the UN, provides donors and other partners with the first joint opportunity to act on this new evidence, by ensuring support for sufficient resources so that countries can take their AIDS programmes to scale – meeting the needs of those already infected with HIV and ultimately slowing and reversing the course of the epidemic.

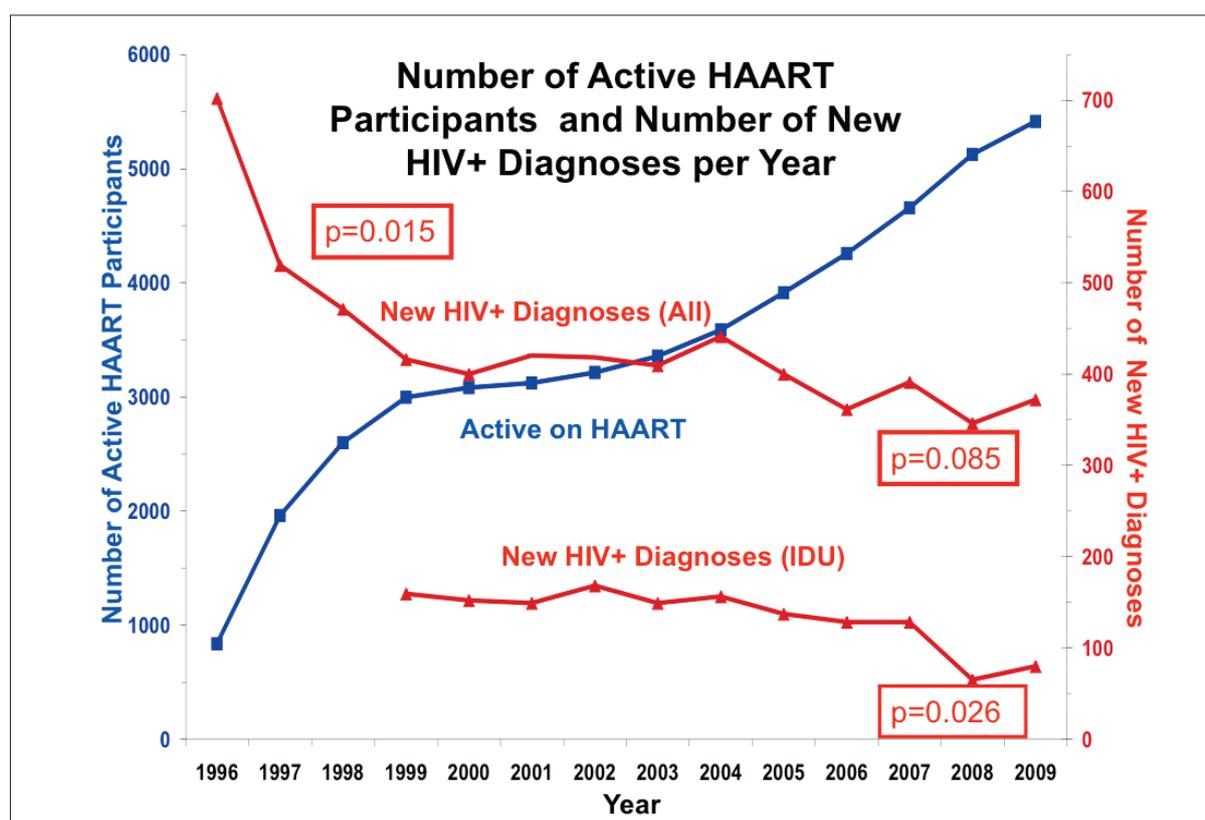
The emerging evidence

Interest in the use of treatment to prevent HIV transmission has grown in recent years as evidence of its potential impact has accumulated. The relationship between levels of the virus in a person's blood and the risk of HIV transmission was first established in people not receiving antiretroviral treatment. **The lower a person's viral load, the less likely they are to transmit HIV.**^{8,9} New evidence has now been generated to show that reducing virus levels with antiretroviral therapy similarly reduces the risk of HIV transmission in a variety of settings:

- **Antiretroviral therapy can virtually eliminate vertical transmission of HIV wherever it is fully implemented.**^{10,11} Already HIV treatment is having a direct effect on maternal and infant mortality in countries with a high burden of HIV. Vertical transmission of HIV could be virtually eliminated by 2015 if coverage is maximised using the most up-to-date treatment regimens. PEPFAR estimates that 340,000 children were born HIV-free between 2004 and 2009 due to the preventive effect of antiretroviral therapy.¹² As a result, scale-up of programmes to prevent mother-to-child transmission, including maternal treatment with three-drug combinations, has been recommended to eliminate vertical HIV transmission.¹³
- **Antiretroviral therapy reduces transmission of HIV in heterosexual couples by over 90%.** A systematic review of 14 studies reporting rates of HIV transmission in serodiscordant heterosexual couples in relation to viral load and antiretroviral treatment found no cases of transmission where viral load was undetectable (<400 copies/ml) on antiretroviral treatment, and a low overall risk of 0.46 transmissions per 100 person-years of follow-up from antiretroviral-treated patients.¹⁴ More recently, a study funded by the Bill & Melinda Gates Foundation evaluated 3,400 heterosexual HIV serodiscordant couples in seven African countries.¹⁵ All couples were appropriately counselled and given free condoms. Antiretroviral therapy was initiated when study participants met CD4 count eligibility criteria. Over the next one to three years, 103 new HIV infections were diagnosed. All but one HIV infection occurred within untreated couples, an estimated 92% reduction of HIV transmission by antiretroviral therapy. Further precise, quantitative evidence surrounding the effect of antiretroviral therapy on HIV transmission is expected to emerge from an ongoing randomized controlled trial of HIV treatment as prevention involving over 1,700 serodiscordant heterosexual couples currently underway under the auspices of the US National Institutes of Health (NIH).¹⁶
- **Antiretroviral therapy has been shown to reduce HIV transmission at the population level.** In Taiwan, the initial roll out of highly active antiretroviral therapy (HAART) was associated with a 53% reduction in new HIV positive diagnoses between 1997 and 2002.¹⁷ In British Columbia, Canada, new yearly HIV infections decreased by approximately 50% between 1996 and 1999, coinciding with the introduction of HAART (see chart below).¹⁸

In San Francisco a substantial increase in HIV testing and treatment between 2004 and 2008 was accompanied by a decline in new HIV diagnoses, a decrease in the average viral load in people living with HIV in San Francisco, and a decline in HIV incidence of around one-third in the same period.¹⁹ During this period the proportion of people diagnosed with HIV linked to care rose to 80%, and by 2008, 90% of these patients were receiving antiretroviral therapy.

Figure: Trends in HAART recipients and new HIV diagnoses in British Columbia, 1996–2009



Treatment was suppressing viral load to undetectable levels in 75% of these patients by 2008. As a result of all these factors the average viral load in the community fell significantly, by around one-third between 2005 and 2008.

- **Antiretroviral therapy has been shown to reduce HIV transmission among people who use injection drugs.**²⁰ Analysis of two prospective cohorts of people who use injection drugs in Vancouver has shown that the average viral load among HIV-infected drug users in the preceding six months was strongly associated with an individual's risk of HIV infection during the period 1996-2007, independent of unprotected sex and syringe sharing. Over the same period the use of antiretroviral therapy rose from 42.5% in 1996 to 69.6% in 2007 among cohort members. Across the province of British Columbia, HAART coverage increased steadily from approximately 2,500 to 5,000 patients between 2004 and 2009.²¹ This was associated with a decrease in the number of new HIV infections diagnosed, and a 50% decrease in new HIV infections diagnosed among people who use injection drugs. Taken together these results provide a strong rationale for the re-examination of the HIV prevention and treatment dichotomy, as well as the need for aggressive expansion of HAART among drug users with HIV.

This emerging evidence clearly indicates the urgent need to expand HIV treatment coverage in order not only to achieve a direct reduction in AIDS-related illness and death but also to achieve population-level prevention gains that could ultimately lead to the end of the epidemic. The upcoming Global Fund Replenishment cycle presents a critical opportunity for donors to act on this evidence, by providing the funding needed to support ambitious, quality programme scale up.

The potential of HIV treatment as prevention: what mathematical models show

Mathematical models have shown that antiretroviral therapy can have a dramatic impact on HIV transmission, with substantial cost savings. In 2006, Montaner et al published a basic model in which all people would be treated after one year of infection and would not transmit HIV while receiving treatment.²² The cost of treatment was assumed to be US\$365 a year. According to this model **global HIV prevalence would decline from 38 million in 2006 to less than 1 million in 2050, with an average annual treatment cost of US\$7 billion per year.** The overall cost would be US\$338 billion over 45 years.

Building on these findings, investigators based at the WHO published a model in 2008 using data from South Africa to examine the effects of a universal test and treat strategy in a generalised epidemic in comparison to the approach of treating all individuals at a CD4 count of 350.²³ This model assumed that all people would undergo annual testing and start treatment immediately, that antiretroviral therapy reduced the risk of HIV transmission by 99%, and that antiretroviral treatment and care cost US\$727 a year. No effect of other HIV prevention interventions was factored into the model. If the health system had the capacity to respond in the ways assumed in this model, the impact on the epidemic could be rapid and substantial. **The universal test and treat strategy is projected to reduce new infections by 95% within ten years and to reduce HIV prevalence to less than 1% within 50 years** – an outcome described as ‘elimination’.²⁴ Although initially the universal treatment strategy would cost South Africa three times more than treating everyone with a CD4 cell count below 350 cells/mm³ (US\$3.4 billion a year), the yearly cost would begin to fall after seven years, and by 22 years the approach would become less expensive than treating only those with CD4 counts below 350 cells/mm³ (approximately US\$1.8 billion).

Modelling by the Infectious Disease Epidemiology Group of Imperial College, London, also highlights the importance of the interaction between testing frequency, treatment initiation threshold and behaviour. Although this group’s model broadly confirms the main findings of Montaner et al and the WHO group, it also emphasises that the impact of HIV treatment scale up strategies are strongly dependent on the epidemiological context. In settings where there is more sexual mixing between individuals with high-risk behavioural patterns and those with lower risk patterns, the reduction in HIV incidence will tend to be lower.²⁵ This group also found that the most cost-efficient model for reduction of incidence might be to test 80% of the population every three to four years.

Modelling of future treatment costs in British Columbia has examined the potential impact of different levels of ART coverage within current medical guidelines on HIV incidence and drug costs in the province.²⁶ Expanding the number of eligible people receiving treatment by 50% would reduce new infections by 44% and save US\$21.5 million in treatment costs within five years. Based on these findings the province’s Ministry of Health has initiated a HAART Expansion program – known as Seek and Treat to Optimize prevention of HIV & AIDS – which aims to maximise the number of people with CD4 counts below 350²⁷ who are diagnosed and receiving antiretroviral treatment.

All these models agree that high rates of HAART coverage have the potential to reduce death rates and HIV transmission dramatically. Consequently **this strategy is potentially cost-averting.** Further, they also agree that failure to achieve sufficiently high coverage – or failure to test frequently enough – would lead to spiralling treatment costs without a long-term reduction in incidence.

HIV treatment as prevention: a price we can't afford not to pay

Two broad approaches to maximising the HIV prevention benefit of treatment have emerged. This has created some confusion, and potential misunderstandings. These approaches are not mutually exclusive but rather complementary:

- “Universal test and treat” (UTT) aims to test the entire population frequently, and to treat everyone with HIV.
- “Seek and Treat” aims to maximise the uptake of HIV testing and treatment within current medical guidelines.

The Seek and Treat approach can be best thought of as an immediate first step towards a UTT approach, where the resources are initially focussed on ensuring treatment access for those who need it most. The modelling by WHO suggests that treating everyone with a CD4 count below 350 – the current WHO recommendation – would reduce HIV incidence by around 30%, but would still result in a larger number of people ultimately on treatment and a higher annual treatment cost after ~20 years compared with a universal test and treat model.

However, modelling by Imperial College suggests that both the treatment threshold and the testing frequency have a strong influence on the long-term impact, and that for outcomes short of ‘elimination’, UTT is not necessarily the most cost-effective approach. As data accumulate in support of the UTT approach, the transition from Seek and Treat to UTT could be easily accommodated. Until then, Seek and Treat offers an immediate way forward, consistent with current medical guidelines, to improve and extend the lives of people with HIV, also aimed at decreasing HIV transmission as a realistic short term secondary gain.

While the use of HIV treatment as prevention is emerging as an exciting component of scaled up AIDS programmes, further research and clarification is needed. The reliability of projections developed from mathematical models is limited by the accuracy of the assumptions on which a model is built, and by the realities of implementation. Additional areas of uncertainty range from questions regarding the accuracy of mathematical models used in recent publications to questions regarding the acceptability and impact of massive scale up of HIV testing, and of long-term treatment in people where HIV treatment may not yet be medically indicated but is being prescribed to prevent HIV transmission. Many of these questions will be addressed by studies planned or underway.²⁸

Implications for the response to HIV

Maximising the HIV prevention impact of HIV treatment will require bold investments today in order to avert long-run costs over the next half century. Now is not the time to scale back commitments. The global economic crisis has hit the countries worst affected by AIDS hard, further weakening their ability to cope alone. Now is not the time to stand still. The stand-still option means millions of new HIV infections, as well as increased potential for substantial HIV resistance as treatment stock outs grow, and individuals are forced to interrupt their treatment. This will simply postpone – and likely increase – HIV treatment costs.

The Global Fund Replenishment process foresees three funding scenarios. Compared to the end of 2009 – where Global Fund resources support 2.5 million people on treatment and 345,000 HIV-positive women to receive PMTCT annually – each scenario proposes a progressively greater increase in coverage of services. With Scenario 1 (an investment of US\$13 billion over the three year period) by 2013 the Global Fund will support a total of 4.4 million people on HIV treatment – 20% of those in need – and 610,000 HIV-positive women would receive PMTCT each year. Scenario 2 (US\$17 billion) increases the proportion to just over a quarter (27% - 5.8 million people) of those in need of treatment; and 820,000 HIV-positive women will have the opportunity to prevent their children acquiring HIV.

It is only the most ambitious Scenario 3 – US\$20 billion – which could put the world on track to achieve universal access and the MDGs. This level of Global Fund resources would provide HIV treatment to over one third (34%) of those in need, and set the world on track to eliminate HIV transmission to babies by scaling up PMTCT to reach 76% of HIV-positive women. It is only at this (and higher) levels of investment that HIV treatment scale up could have the population impact that would realize the HIV prevention benefits of treatment. This ambitious scenario offers real hope of substantially reducing the rate of new infections.

As donors and other stakeholders meet in the Netherlands this month for the 3rd Global Fund Replenishment Meeting, the IAS recommends:

- That donors to the Global Fund make the bold investments required to meet Scenario 3. All evidence points in the same direction. While the precise benefit of HIV treatment for prevention remains to be quantified, scaling up treatment in line with current WHO guidance and consistent with the universal access commitment will result in substantially fewer new HIV infections.
- That donors continue to invest in the research required to expand knowledge of the impact of HIV treatment on prevention, the most effective ways to scale up programmes, to protect human rights, and to meet the needs of communities and individuals involved in programme scale up.
- That new WHO treatment guidelines – which expand the numbers eligible for HIV treatment and recommend newer, better tolerated drugs – are implemented in all countries without delay despite the fact that implementation will result in higher costs for national programmes. The emerging evidence on the HIV prevention benefit of treatment indicates that these guidelines have the potential to lead to huge financial savings over time. The donor community has a fiscal as well as a moral obligation to act on the emerging evidence, which shows how to scale up effective, comprehensive AIDS programmes and renew the drive for universal access.

Waiting five, ten or even fifteen years for further data on the impact of HIV treatment as prevention to accumulate will allow the burden of cost and suffering to escalate. The time for bold action, and ambitious investments, is now.

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