

The 10-year struggle to provide antiretroviral treatment to people with HIV in the developing world

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In March, 2006, the WHO took stock of the 3 by 5 initiative, which had been formally launched with UNAIDS 2 years earlier.¹ With 1·3 million people on antiretroviral treatment in developing countries by the end of 2005, the world had not reached the target of treating 3 million people living with HIV/AIDS. In terms of numbers, at least, some said that the campaign failed.

But the initiative did show that with the right vision and a determined effort by all relevant parties, development achievements that seem unthinkable are indeed possible. The apparent failure to achieve what was always an aspirational goal should not overshadow the fact that the progress on access to antiretroviral treatment might have no precedent in global public health. For no other life-threatening disease has the world moved from the first scientific breakthroughs to a commitment to achieve universal access to treatment in less than a decade.² But we should not forget that the number of new HIV infections still outpaces the expansion of access to treatment, and that progress remains slow in view of the millions still dying from AIDS every year.

The 16th International Conference on AIDS, taking place in Toronto in August, 2006, provides an occasion to consider some of the important milestones that have brought global treatment efforts to where they are today. This account discusses the milestones and political struggles involved in scaling up antiretroviral treatment in the developing world. They remind us of the enormous challenges and many frustrations that have had to be overcome on the path to greater treatment access, marked by a chronic scarcity of resources, capacity, foresight, and political will.

Vancouver 1996

At the 11th International AIDS Conference in Vancouver in 1996, researchers announced spectacular treatment results for HIV/AIDS patients. A cocktail of antiretroviral substances not only reduced viral load much more efficiently than any one drug, but also promised to prevent the development of resistance, which developed quickly in patients treated with single therapies. Leading researchers even postulated that such cocktails might be able to eliminate HIV from the body altogether.³

In rich countries, rapid uptake of antiretroviral treatment gave rise to the so-called Lazarus syndrome, with treatment almost miraculously restoring the health of many people terminally ill with AIDS. But at an average cost of up to US\$20 000 per person per year, large populations outside the industrialised world could not feasibly be put and kept on these drugs. Delivery of complex treatment regimens needed advanced health systems, and the cost exceeded by

several orders of magnitude the average overall health budgets of most developing countries.

These apparently insurmountable obstacles allowed the worldwide community to ignore the inequity between rich and poor countries with regard to treatment access. Treatment as an essential part of a comprehensive response to HIV/AIDS in developing countries was viewed as impossible, or even irresponsible. Indeed, the development community reacted with irritation when, in 1997, French President Jacques Chirac became the first major leader to highlight the issue. Speaking at the International Conference on STD/AIDS in Africa, Cote d'Ivoire, in December, 1997, Chirac stated that "We have no right to accept that there should now be two ways of fighting AIDS: treating sufferers in the developed countries, and simply preventing infection in the South... We must do all in our power to ensure that the benefit of the new treatments is extended to deprived populations in Africa and elsewhere in the world", and he called for the establishment of the International Therapeutic Solidarity Fund (ITSF).⁴ This signalled Chirac's genuine personal commitment to fighting AIDS, but the French could not fight the disease alone. In response to the French "solo", other international development partners instead consolidated their arguments as to why large-scale treatment access was impossible in poor nations.

The French have subsequently made important efforts to finance expanded access to medicines in poor countries, mainly through their large contributions to and unwavering support for The Global Fund to Fight AIDS, Tuberculosis and Malaria, and recently their initiation of the International Drug Purchasing Facility.

A precedent is set

In 1995, Peter Piot of UNAIDS initiated a dialogue with the pharmaceutical industry to work towards delivering antiretroviral therapies at affordable prices in poor nations. This was crucial not only because different companies produced different components of the drug cocktails, but also because anti-trust laws made discussion of pricing schemes between pharmaceutical companies impossible. As a consequence, the UNAIDS Drug Access Initiative was launched in December, 1997, and the first patients received drugs in Uganda and Cote d'Ivoire in early 1998, and in Chile later that year.

The Drug Access Initiative was a milestone towards the now well-accepted principle of differential pricing for medicines for developing countries at a time when there were few generic suppliers of antiretroviral drugs. At the outset, the price for a year of first-line antiretroviral treatment was US\$7200. As a consequence of the high

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Panel 1

"Our ultimate goal is to provide developing countries with proven strategies to improve care and increase access to the newest and most effective drugs. However, in order to assess and perfect the approaches we are trying, we must begin with small-scale pilot programmes, involving tough decisions to determine the limits of participation. But the alternative is to do nothing."

Peter Piot, February, 1998⁵

prices, the number of patients treated in the pilot initiative was modest: in the three countries combined around 4000 people received treatment by early 2000. But it was a start, as Piot noted (panel 1).

The Drug Access Initiative used various approaches to cover the cost of treatment. In Uganda, patients paid 100% of the cost of their treatment, with a high drop-out rate when patients ran out of funds. In Cote d'Ivoire, the intent of the government was to subsidise most of the cost of the drugs, but this did not guarantee sustained funding for the policy, with substantial interruptions in drug supply as a consequence. Additionally, establishing eligibility to enter the treatment programme and the level of co-payments needed a substantial investment. The resulting bureaucracy quickly became a bottleneck to drug access. In Chile, the government was able to cover the total cost of treatment, which was important for the programme's success (although improved access for all those in need was still required).

In 1999, when the Drug Access Initiative had been in operation for almost 2 years, awareness was growing that antiretroviral drugs could be sourced at a still lower price. In Uganda, one of the treatment centres started sourcing generic supplies from the Chemical, Industrial and Pharmaceutical Laboratories (CIPLA) in India, and the Drug Access Initiative in Cote d'Ivoire began sourcing zidovudine from Combino Pharm in Spain. The experience of the Brazilian AIDS control programme with local production of antiretrovirals at lower cost added to evidence of the efficacy of generic drugs. These experiences led the participants of the Drug Access Initiative to reconsider their procurement options.

Meanwhile WHO, under its new Director General, Gro Harlem Brundtland, had joined Piot in entering into a dialogue with the pharmaceutical companies to discuss a range of tensions between the companies and public-health needs worldwide. Between 1998 and 2000, Brundtland and Piot partly pressured, partly enticed the company leaders towards a much wider use of differential pricing for antiretrovirals. There was also international pressure to end the so-called treatment apartheid caused by high prices, and a growing threat of generic competition. The result was a proposal by the pharmaceutical industry to UNAIDS in March, 2000, to reduce treatment costs. In return, the UN would commit to mobilising support for the controlled use of their products and sustainable financing for them in developing countries.

The Accelerating Access Initiative was launched in May,

2000. This included the pharmaceutical companies and UNAIDS, WHO, the World Bank, UNICEF, and the UN Population Fund. As a consequence, the price of first-line treatment decreased to around \$1200 per year. This initiative stimulated the development of treatment access plans in 39 countries, all of which concluded individual pricing agreements with the companies. However, the roll-out of the initiative was slow and hindered by individual countries having to negotiate prices and conditions.

In September, 2000, Lieve Franssen, HIV/AIDS coordinator at the European Commission, called representatives from Act-Up and Médecins Sans Frontières, generic manufacturers such as CIPLA, and CEOs from the seven largest pharmaceutical companies to sit together with the leaders of WHO and UNAIDS and agree on a tiered price agreement for patented drugs for the treatment of HIV, tuberculosis, and malaria. At the meeting the CEOs expressed their willingness to launch such a scheme. At the same meeting CIPLA announced the availability of generic first-line antiretrovirals at US\$350 per patient per year.

With CIPLA increasingly influential in programmes led by non-government organisations and with its longstanding commitment to cost-effective pharmaceutical policies, WHO, with UNICEF, and supported by the World Bank, included antiretrovirals in a call for expressions of interest to manufacturers to supply HIV-related drugs to developing countries, and started a prequalification programme to assess drug quality. The prequalification of generic antiretrovirals by WHO, the creation of the Global Fund, and the Global Fund's decision to make generic antiretrovirals eligible for funding, with countries responsible for procurement using competitive mechanisms, all led to increasing market penetration of generic antiretrovirals and further price decreases from 2002 to the present day.

A breakthrough came in 2003 when fixed-dose combination therapies—reducing the number of pills per day from 10–15 to as few as two—gave generic drugs a competitive edge over their brand-name counterparts for reasons other than price. The cheapest regimen, a fixed dose combination of stavudine, lamivudine, and nevirapine, decreased in price from US\$350 annually in 2001 to \$168 in 2004, and was selling at between \$132 and \$148 in 2005.⁶ The price of combinations of zidovudine-lamivudine and efavirenz decreased more slowly and is currently around \$400. Second-line drugs remain even more expensive, with an average price of \$900 in least developed countries and \$1600 in middle-income countries in 2005.

Initiatives such as Piot's at UNAIDS, Brundtland's at WHO, and Franssen's at the European Commission provided the research-based pharmaceutical industry with ways to explore pricing models other than that of "small volume–large profit" previously applied to antiretrovirals; but a unique combination of generic competition and strong political, activist, and media pressure were crucial factors leading to the rapid reduction in prices. The

question remains, however, whether reductions could have been achieved earlier.

AIDS: more than a health issue

In 1998, for the 12th International AIDS Conference in Geneva, UNAIDS published country-specific estimates on HIV and AIDS prevalence and AIDS deaths for the first time, drawing worldwide attention to the devastating effect of the epidemic in the developing world.⁷ But persuading the development community of the threat posed by AIDS was still remarkably difficult. In the development field, AIDS was still seen as an issue for exotic public-health specialists. For example, during the discussions led by the United Nations Population Fund for the 5-year follow-up to the International Conference on Population and Development (known as ICPD+5) in June, 1999, there was a reluctance to include specific goals on HIV/AIDS. Only during the final phases of the negotiations were several worldwide HIV targets accepted⁸ as a result of pressure exerted by UNAIDS and major donors that were later considered in establishing the Millennium Development Goals. Although this acceptance represented a milestone, there was no mention of HIV treatment. When, in September, 2000, the landmark UN Millennium Declaration placed the response to AIDS and infectious disease among the priorities for development efforts over the next 15 years,⁹ it also contained no mention of HIV treatment.

In January, 2000, the United Nations Security Council took up a health issue for the first time. Speaking to the Council, US Vice President Al Gore stated that “for the nations of sub-Saharan Africa, AIDS is not just a humanitarian crisis. It is a security crisis—because it threatens not just individual citizens, but the very institutions that define and defend the character of a society.” Gore noted that “the first line of defence of this disease is prevention” but, without mentioning antiretrovirals, also called for the expansion of “basic care and treatment”, “affordable medicines”, and “treatment for opportunistic infections”.¹⁰ 6 months later, the Security Council passed Resolution 1308, which emphasised the threat to security posed by AIDS and drew attention to the need for treatment in the specific case of military personnel, “where appropriate”.¹¹

The human rights sphere has long contributed to knowledge about vulnerability of marginalised groups to HIV and the effect of stigma and discrimination on efforts to fight the epidemic. In 2001 and 2003, the former UN Human Rights Commission resolved that, in the HIV/AIDS epidemic, access to treatment is an essential component of full realisation of the right to health.^{12,13}

Durban

The 13th International AIDS Conference in Durban in July, 2000, the first to be held in Africa, focused the world's attention on the continent most seriously affected by the AIDS epidemic. Although Brazil had been a

pioneer in developing countries in providing treatment as early as 1996, and small-scale projects by non-government organisations—such as that of Partners in Health in Haiti—were showing promising results, Durban was where a worldwide movement for treatment access focusing on the needs of the world's poorest countries emerged as a major force.

Justice Edwin Cameron made a call to action in the inaugural Jonathan Mann Memorial Lecture. Speaking of the “shocking and monstrous iniquity” in poor countries' lack of access to treatment, Cameron told the 12000 delegates that “our over-riding and immediate concern should be to find ways to make accessible for the poor what is within reach of the affluent”. He presciently noted that “this Conference can be a turning point in the creation of an international impetus to secure equitable access to these drugs for all persons with AIDS in the world”.

While Cameron spoke, hundreds of members of the newly formed Treatment Action Campaign, many of them living with HIV/AIDS, marched on the conference centre demanding access to antiretroviral therapy. This event marked another milestone in a worldwide activist movement in which poor people from around the world began to assert their right to treatment.

Global commitment

In April, 2001, African leaders came together during the first African Summit on HIV/AIDS, Tuberculosis, and Other Infectious Diseases in Abuja, Nigeria. In his opening address, the UN Secretary General, Kofi Annan, proposed the creation of a Global Fund, dedicated to the battle against HIV/AIDS and other infectious diseases. He requested that “this Fund must be structured in such a way as to ensure that it responds to the needs of the affected countries and people.” Among five priorities for action, he concluded that “...we must put care and treatment within everyone's reach”.¹⁴

The first UN General Assembly Special Session on AIDS was scheduled for June, 2001. Before this event, leading scientists produced an estimate of how much an effective response to HIV/AIDS would cost.¹⁵ The study modelled scale-up of a set of proven interventions and attached a price tag of about US\$10 billion per year. The paper helped to inspire political debate before and after the session by providing a sense of what might be possible. Among the possible targets for scale-up was the assumption that 3 million people could be reached with antiretroviral treatments by 2005 in developing countries.

UN Member States committed to scaling up a comprehensive response involving prevention, treatment, care, and support, and endorsed the creation of a global health fund. The Declaration of Commitment was the first internationally agreed, time-bound set of goals, based on agreed indicators of progress. These included specific targets for prevention as “the mainstay of the response”. On treatment, Member States committed to “make every

Panel 2

"Does anyone deserve to be sentenced to certain death because she or he cannot access care that costs less than US\$2 a day? Is anyone's life worth so little? Should any family become destitute as a result? Should children be orphaned? The answers must be no, no, no and no! Yet this is what is happening. Every day."

Dr Brundtland, July, 2002¹⁹

effort to provide progressively and in a sustainable manner, the highest attainable standard of treatment for HIV/AIDS, including the prevention and treatment of opportunistic infections, and effective use of quality-controlled anti-retroviral therapy in a careful and monitored manner to improve adherence and effectiveness and reduce the risk of developing resistance".¹⁶ Although the Declaration represented a substantial increase in worldwide commitment, its cautious language on treatment and absence of a specific target still indicated concerns about the feasibility of expanding access.

In late 2001 and early 2002, a number of factors converged to increase the momentum for treatment access. In 2001, Dr Brundtland decided to re-establish a separate HIV/AIDS department at WHO. WHO took the first steps in developing guidance on a public-health approach including simplified treatment regimens and clinical monitoring. The first edition of the WHO treatment guidelines for resource-limited settings¹⁷ was published in March, 2002 (including the first mention by WHO of the 3 by 5 target). These guidelines included simplified schemes for treatment and clinical diagnosis, including reduced laboratory support. These approaches would facilitate wider access to large populations in need of treatment in the poorest countries, and recognise that the general health benefits for these populations would dramatically outweigh the risk of failure to detect, and to correct for, adverse reactions and treatment failure.

In April, 2002, WHO took the important step of adding ten antiretroviral drugs to its List of Essential Medicines, pointedly noting that "cost was not a factor in determining suitability of the drugs for the list".¹⁸ Both the list of essential drugs including antiretrovirals and the WHO treatment guidelines are well-accepted standards today. However, we can easily forget how bold and controversial these steps were at the time. For example, the US National Institutes of Health (NIH) had provided a grant to WHO to produce the simplified treatment guidelines. When NIH did not want to fully subscribe to the approach proposed, WHO took the unprecedented step of returning the funds to NIH.

Panel 3

"AIDS can be prevented. Antiretroviral drugs can extend life for many years. And the cost of those drugs has dropped from \$12 000 a year to under \$300 a year—which places a tremendous possibility within our grasp. Ladies and gentlemen, seldom has history offered a greater opportunity to do so much for so many"

George W Bush, January, 2003

The Board of the Global Fund Board to Fight AIDS, Tuberculosis and Malaria held its inaugural meeting in January, 2002. The prospect of substantial new resources for countries' AIDS programmes, together with the preparedness of drug companies to further reduce prices, held enormous promise. At the 14th International AIDS Conference in Barcelona in July, 2002, International AIDS Society President Joep Lange told delegates that "if we can get cold Coca Cola and beer to every remote corner of Africa, it should not be impossible to do the same with drugs". Activists interrupted a speech by US Secretary of Health Tommy Thompson to demand "Where's the 10 billion?" After Thompson's disrupted speech, Dr Brundtland addressed several goals for the health sector which would frame WHO's work on HIV/AIDS (panel 2), stating that "we are aiming for 3 million people worldwide to be able to access ARVs by 2005". Activists then called on WHO to back its rhetoric with a concrete plan for reaching the target of three million people on treatment.

Events during the AIDS Conference, and the evidence presented that antiretroviral treatment is possible in some of the poorest areas of the world,^{20,21} led the Dutch Government to organise a meeting of like-minded donors in October, 2002. The donors came together with UNAIDS and WHO in The Hague, Netherlands, to discuss whether and how they should support treatment access in developing countries. Much of the discussion still focused on why treatment scale-up was not possible—or was dangerous—rather than on how to overcome the obstacles. The Canadian International Development Agency, for example, brought a draft of its new worldwide HIV/AIDS strategy to the meeting, which contained no reference to antiretroviral treatment at all.

An alliance was formed of sympathetic organisations, agencies, and governments (including those of Thailand, Brazil, Uganda, USA, and UK), to be known later as the International HIV/AIDS Treatment Access Coalition (ITAC). ITAC was officially launched as a worldwide partnership platform for treatment access by Dr Brundtland in December, 2002,²² but because of the reluctance of some key donors in the coalition, the ITAC launch document omitted the specific target of 3 million on treatment by 2005. The much broader target of universal access—the successor target to 3 by 5 today—seemed more acceptable at that time and was included in the document instead (though without reference to a specific date).

In January, 2003, the WHO Executive Board nominated Dr Lee Jong-wook to succeed Dr Brundtland. At about the same time, President George W Bush announced that the US government would contribute US\$15 billion to the worldwide AIDS response over the next 5 years, with treatment forming a major component of the initiative and explicit targets "to support treatment for 2 million HIV-infected people, to prevent 7 million new HIV infections and to support care for 10 million people infected and affected by HIV/AIDS, including orphans

and vulnerable children" (panel 3).²³ Whether and how WHO should further advance the treatment agenda therefore loomed as an important challenge for Dr Lee.

That Dr Lee unequivocally embraced the treatment agenda is now part of his legacy. In his inaugural speech to the 56th World Health Assembly in May, 2003, he declared that "I will ensure that WHO provides leadership toward the bold '3 by 5' target: three million people in developing countries on antiretroviral treatment by 2005". The Assembly went on to pass a resolution endorsing the Global Health Sector Strategy for HIV/AIDS, a 2-year old initiative of Dr Brundtland. The delegation of the Canadian government, whose draft strategy only months earlier had failed to mention treatment, proposed an amendment to the resolution specifically mentioning the 3 by 5 target. The Canadian government later became the single most important donor for the 3 by 5 initiative.

In September, 2003, Richard Feachem, Executive Director of the Global Fund, and Piot joined Lee at the follow-up meeting to the UN General Assembly Special Session in New York to declare the gap between those who do and do not have access to treatment a "global health emergency".²⁴ By December, WHO had launched its plan for achieving 3 by 5 and UNAIDS allocated additional resources for its support.²⁵

Although generally welcomed by activists, the WHO plan met with a less than enthusiastic response. This was in part because of the perception that, in its eagerness to raise its profile, WHO had failed to build a consensus, implicitly placing much of the responsibility for achieving the target on its own shoulders. While WHO could only support the implementation efforts of its Member States, time was lost in disputes over ownership and the feasibility of achieving the target, rather than the action needed. Nearly a year passed between the launch of the WHO plan and the resources and personnel becoming available to fully implement it.

Despite these problems, 3 by 5 gave early impetus to securing resources for treatment. Round 4 of the Global Fund launched in January, 2004, receiving considerable technical input from WHO and other partners, became the unofficial treatment round. It led to a near-doubling of the number of people who would be put on treatment through Global Fund-supported programmes. Funds made available through PEPFAR have also supported substantial scale-up of treatment programmes. Despite the collective failure to achieve 3 by 5 there is little doubt that, without the initiative, the numbers of people on treatment would not have tripled in just 2 years, or increased eight-fold in Africa. In 2005, WHO calculated that 250 000 to 300 000 lives had been saved in 2 years as a result of improved access to treatment.

Towards universal access

The impatience that has driven the campaign for access to treatment has been its strongest engine, but has also obscured the momentous scale and speed of the change

we have witnessed over the past decade. Wider and more equitable access to treatment has given hope and renewed energy to what seemed a hopeless fight just a few years ago. As Piot said at the UN General Assembly's High-Level Meeting on AIDS in May this year, "More has been achieved in the last five years of this epidemic than in the first twenty".

However, along with that hope and energy has come a loss of attention to prevention, resulting in an increase in new infections in many rich countries. The reason is obvious: there has been no activist movement for prevention similar to that for treatment.

But treatment alone will not stop the epidemic: the more than 4 million new infections every year far outnumber any projections of the number of people who can be put on treatment. Thus the epidemic will continue to grow.

The global response to HIV/AIDS has been hampered by the apparent need to choose between prevention and treatment. In fact, this choice has often served as a way to extend the debate itself instead of taking action. Only when we truly overcome this false dichotomy will we be able to finally turn the epidemic around. Only when we begin to appreciate fully how treatment access can help to overcome ignorance and stigma, and only when we include and mobilise affected communities for prevention as well as for treatment will we be able to mount the sustained and effective response we need.

As Salomon and his colleagues have noted, "prevention makes treatment affordable, and treatment can make prevention more effective."²⁶ There are some encouraging signs. In June, 2005, the Board of UNAIDS approved the first global prevention policy after much debate, highlighting the intrinsic links between prevention and treatment. Treatment Action Campaign in South Africa has now taken on prevention in a robust manner, organising marches to demand AIDS education and access to condoms in schools earlier this year. The Swedish government has hosted a meeting to stimulate more effective constituency building for prevention with various AIDS and other activists. However, if we are to realise the goal of universal access to comprehensive prevention programmes, treatment, care, and support by 2010, as agreed by UN Member States at the recent meeting to chart progress against the 2001 Declaration of Commitment,²⁷ the dialogue on these issues must become more serious, and the 16th International AIDS Conference in Toronto is the right place for it. This meeting needs treatment activists from around the world to talk about how they can mobilise their constituencies to avoid further spread of the virus, and the medical community to articulate better how it can offer prevention to those who seek treatment, care, and support. And leaders at global, country, and community levels must become serious about the concrete steps needed to make real the sometimes vague commitments made in the UN General Assembly Special Session and the various UN resolutions.

The recent goal of universal access is accompanied by a commitment “to support and strengthen existing financial mechanisms, including the Global Fund to Fight AIDS, Tuberculosis and Malaria, as well as relevant United Nations organizations, through provision of funds in a sustained manner while continuing to develop innovative sources of financing, as well as pursuing other efforts, aimed at generating additional funds” to fill the resource gap of more than \$10 billion every year.²⁷ Without additional resources, we risk losing the extraordinary momentum that has built over the past decade.

We might never have the perfect plan to stop AIDS. As Justice Edwin Cameron has said: “It is unlikely that in our lifetimes we will attain perfection” in our response to this epidemic. But only by replacing the dichotomy between treatment and prevention will we truly harness their interdependence, and only if we live up to the political and financial commitments made over the past decade will we come anywhere near the perfection of ending the AIDS epidemic.

Conflict of interest statement

B Schwartländer is the Director for Performance Evaluation and Policy at the Global Fund to Fight AIDS, Tuberculosis and Malaria. He has previously served as the Director of the HIV Department in WHO and the Director of Strategic Information and Evaluation at UNAIDS with responsibilities in Global Policies on HIV and AIDS. I Grubb is the Policy Analyst, HIV Department, WHO. J Perriens has been the responsible officer for the Drug Access Initiative and the Accelerated Access Initiative at UNAIDS and the Director for Treatment and Care in the HIV Department of WHO with responsibilities for global policies on treatment.

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References

- WHO/UNAIDS. Progress on global access to HIV antiretroviral therapy: a report on “3by5” and beyond. Geneva, Switzerland: WHO, 2006.
- G8 Gleneagles Summit. In 2005 G8 leaders endorsed the goal of “provide as close as possible to universal access to treatment for AIDS by 2010”. Gleneagles, Scotland: G8, 2005. <http://www.g8.gov.uk/servlet/Front?pagename=OpenMarket/Xcelerate/ShowPage&cc=Page&cid=1119518698846> (accessed July 12, 2006).
- Perelson AS, Essunger P, Cao Y, et al. Decay characteristics of HIV-1-infected compartments during combination therapy. *Nature* 1997; 387: 188–91.
- Chirac J. Address to conference delegates. 10th International Conference on STD/AIDS in Africa; Abidjan, Cote d'Ivoire; Dec 10–17, 1997.
- Mwaura P. AIDS drugs plan starts in Uganda and Côte d'Ivoire. <http://www.un.org/ecosocdev/geninfo/afrec/vol11no3/aidsbox.htm> (accessed July 12, 2006).
- WHO Global Price Reporting Mechanism: Prices paid for antiretroviral drugs by low and middle income countries in 2005—a summary report by the Global Price Reporting Mechanism on Antiretroviral Drugs. Geneva, Switzerland: WHO, 2006; <http://www.who.int/hiv/amds/gprm/en/> (accessed July 12, 2006).
- UNAIDS. Report on the global HIV/AIDS epidemic. Geneva, Switzerland: UNAIDS, 1998.
- UN General Assembly. Key actions for the further implementation of the programme of action of the International Conference on Population and Development. New York, USA: United Nations, 1999. http://www.unfpa.org/upload/lib_pub_file/561_filename_icpd5-key-04reprint_eng.pdf (accessed July 12, 2006).
- UN General Assembly. United Nations millennium declaration. New York, USA: United Nations, 2000. <http://www.un.org/millennium/declaration/ares552e.pdf> (accessed July 12, 2006).
- Vice President Al Gore. Statement in the Security Council, New York, USA: United Nations, 2000. http://www.usunnewyork.usmission.gov/00_002.htm (accessed July 12, 2006).
- Security Council. Resolution 1308 (2000): on the responsibility of the Security Council in the maintenance of international peace and security: HIV/AIDS and international peacekeeping operations. New York, USA: United Nations, 2000. <http://www.un.org/docs/scres/2000/sc2000.htm> (accessed July 12, 2006).
- High Commission on Human Rights. Resolution 2001/5: the protection of human rights in the context of human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS). Geneva, Switzerland: UN High Commission on Human Rights, 2001. [http://www.unhcr.ch/Huridocda/Huridoca.nsf/\(Symbol\)/E.CN.4.RES.2001.51.En?Opendocument](http://www.unhcr.ch/Huridocda/Huridoca.nsf/(Symbol)/E.CN.4.RES.2001.51.En?Opendocument) (accessed July 12, 2006).
- High Commission on Human Rights. Resolution 2003/29: access to medication in the context of pandemics such as HIV/AIDS, tuberculosis and malaria. Geneva, Switzerland: UN High Commission on Human Rights; 2003. [http://www.unhcr.ch/Huridocda/Huridoca.nsf/\(Symbol\)/E.CN.4.RES.2003.29.En?Opendocument](http://www.unhcr.ch/Huridocda/Huridoca.nsf/(Symbol)/E.CN.4.RES.2003.29.En?Opendocument) (accessed July 12, 2006).
- UN Secretary General. Secretary General proposes Global Fund for Fight against HIV/AIDS and other infectious diseases. New York, USA: United Nations, 2001. <http://www.un.org/News/Press/docs/2001/SGSM7779R1.doc.htm> (accessed July 12, 2006).
- Schwartländer B, Stover J, Walker N, et al. Resource needs for HIV/AIDS. *Science* 2001; 292: 2434–36.
- United Nations General Assembly. Declaration of Commitment on HIV/AIDS: “Global Crisis—Global Action”. <http://www.un.org/ga/aids/coverage/FinalDeclarationHIVAIDS.html> (accessed July 12, 2006).
- WHO. Scaling up antiretroviral therapy in resource-limited settings: guidelines for a public health approach (1st edn). Geneva, Switzerland: WHO, 2002.
- WHO. Report of the WHO Expert Committee, 2002 (including the 12th Model List of Essential Medicines). Geneva, Switzerland: WHO. WHO 2002:EB111/28, Technical Report series. No 914.
- WHO. Speeches of the Director General. Geneva, Switzerland: WHO, 2002. http://www.who.int/director-general/speeches/2002/english/20020709_InternationalCollaborationScalingUptheRRResponsetoAIDS.html (accessed July 12, 2006).
- Farmer P, Léandre F, Mukherjee J, Gupta R, Tarter L, Kim JY. Community-based treatment of advanced HIV disease: introducing DOT-HAART (directly observed therapy with highly active antiretroviral therapy). *Bull World Health Organ* 2001; 79: 1145–51.
- WHO. Antiretroviral therapy in primary health care: experience of the Khayelitsha programme in South Africa. Case study. Médecins sans Frontières South Africa, Department of Public Health at the University of Cape Town, and the Provincial Administration of the Western Cape, South Africa. Geneva, Switzerland: WHO, 2003.
- International HIV/AIDS Treatment Access Coalition. A commitment to action for expanded access to HIV/AIDS treatment. Geneva, Switzerland: WHO, 2002. WHO/HIV/2002.24.
- US Department of State. The Presidents Emergency Plan for AIDS Relief, 5 year strategy. Washington DC, USA: US Department of State, 2005. <http://www.usaid.gov/cgi-bin/goodbye?url=http://www.state.gov/documents/organization/48746.pdf> (accessed July 12, 2006).
- WHO. World Health Organization says failure to deliver AIDS medicines is a global health emergency. <http://www.who.int/mediacentre/news/releases/2003/pr67/en/index.html> (accessed July 12, 2006).
- WHO. The WHO strategy: treating 3 million by 2005—making it happen. Geneva, Switzerland: WHO, 2003.
- Salomon JA, Hogan DR, Stover J, et al. Integrating HIV prevention and treatment: from slogans to impact. *PLoS Med* 2005; 2: e16.
- United Nations General Assembly. High-level meeting on AIDS uniting the world against AIDS (Political Declaration, Para 20). New York, USA: United Nations, 2006. <http://www.un.org/ga/aidsmeeting2006/> (accessed July 12, 2006).