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The Evolving HIV/AIDS Response And The Urgent Tasks Ahead

A timeline of events from 1981 on, leading up to the financial and other challenges of the present.

by **Stefano M. Bertozzi, Tyler E. Martz, and Peter Piot**

ABSTRACT: AIDS continues to outpace the science, financing, prevention, and treatment efforts of the past quarter-century. There have been different epochs along the evolutionary timeline of the global AIDS response, from the discovery of HIV to the threat posed by the current economic crisis. This timeline serves as a reference to how we have arrived where we are today, in the hope that understanding our past will help us set the course for a more efficient and effective future response. [Health Aff (Millwood). 2009;28(6);1578–90]

SINCE AIDS WAS IDENTIFIED IN 1981, epidemiology, science, financing, and programmatic response have all experienced periods of rapid change. Much beyond AIDS has been affected.¹ Here we present an annotated timeline that charts AIDS from its discovery up to the current global economic downturn and its possible impact on the response. The focus is not so much on understanding the past, but on learning from past successes and failures to inform future planning.

Discovery (1981–1985)

The world was taken by surprise when doctors reported a new disease among homosexual men in the United States in 1981. It would take two years before scientists isolated the virus responsible for AIDS and another two years before an antibody test was available to diagnose infection. This period of scientific discovery created optimism that science would outpace the spread of infection. In April 1984, Margaret Heckler, the U.S. secretary of health and human services under President Ronald Reagan, confidently stated that a vaccine would likely be available within two years after the isolation of the virus, now known as HIV. The

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“By four years after its discovery, AIDS had been identified in every region of the world.”

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world would soon have its “magic bullet.”

During these initial years of the pandemic, there was a rapid increase in the number of AIDS cases reported among men who have sex with men, as well as recognition of the presence of the virus in central and eastern Africa. However, the cases in Africa appeared to have a different pattern of transmission from those occurring in the United States and Europe. In Africa, most cases were reported among heterosexuals with no history of injecting drug use or blood transfusion,^{2,3} thus increasing the list of possible routes of transmission.

By four years after its discovery, AIDS had been identified in every region of the world. Recognized routes of transmission included blood transfusion; sexual intercourse; and from mother to child during pregnancy, birth, or breastfeeding. The most rapid increases in infections were observed among men having sex with men, hemophiliacs, and injecting drug users.

As the number of AIDS cases continued to rise, so did the number of organizations committed to supporting those with HIV. The movement was largely a local effort, with a rise in organizations such as the AIDS Project Los Angeles and Gay Men's Health Crisis in New York. International efforts were also slowly coming together. By 1983 the World Health Organization (WHO) started global HIV surveillance and held its first meeting on AIDS, and in 1985 the first international AIDS conference took place in Atlanta, Georgia.

This period of discovery was characterized by hope and optimism. The public health community believed that people would change their risk behaviors once they understood the modes of transmission. There was confidence in the power of science and belief that a vaccine, the most effective of prevention tools, would soon be available. The focus was on the virus, less so on the people it affected.

An Emerging Global Response (1986–1994)

The recognition soon grew that the virus was spreading around the world. Median HIV prevalence among pregnant women in Kampala, Uganda, was above 11 percent by 1986.⁴ This suggested massive spread in the general population. The global community mobilized slowly to address the epidemic.

In 1987 the WHO launched its Special Programme on AIDS, later renamed the Global Programme on AIDS. This effort formed the largest disease-specific program within the WHO and had a budget of more than US\$92 million by 1989.⁵ The program played a catalytic role in helping countries around the world develop “National AIDS Programs” and plans, and in providing key staff for many of the programs in low-income countries.

The U.S. Food and Drug Administration (FDA) approved zidovudine (AZT) in

1987. This was the first drug available to treat HIV, rather than the opportunistic infections and cancers that HIV causes. It was extremely expensive, initially marketed at approximately \$10,000 for a year's supply.⁶ It also had major toxicity and a survival benefit of less than ten months.⁷ These factors combined meant that there were no serious discussions about making it available in developing countries.

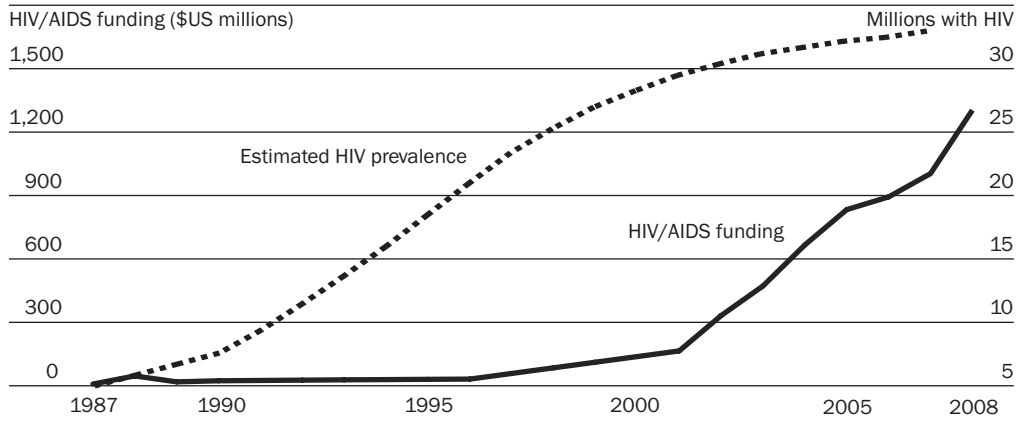
Advances in prevention science were more disappointing. By the end of 1994, the two years Margaret Heckler predicted it would take to have a vaccine ready for testing had come and gone five times over. Because HIV is not an especially hardy virus, there was also great optimism that it would be easy to identify a non-toxic chemical that could be used in the vagina to prevent sexual transmission. The first clinical microbicide efficacy trial was started in 1992.⁸ Unfortunately, the seemingly easy goal of developing an effective microbicide also proved elusive.

Surprisingly, in retrospect, the global scientific community did not respond to these setbacks in biomedical prevention science as it might have: by redoubling its efforts to improve its understanding of behavioral prevention. Science continued to be almost exclusively focused on biomedicine, especially as measured by the proportion of research funding. Prevention programs continued to act in concert with the belief that if one explained how the disease was transmitted and provided condoms and clean needles, people's self-interest would motivate behavior change. The dramatic success of the prevention response by the gay community in the United States helped convince people that effective behavioral prevention was feasible with available tools. Thus, international assistance for AIDS, dominated by the WHO and the United States during this time, focused extensively on promotion of condom use (the first condom social marketing programs were launched in 1986) and voluntary testing and counseling. However, even by 1994 it was clear that knowledge and access to tools were not enough.

The emerging global response accelerated rapidly. Governments mobilized throughout the world, and there were sizable increases in funding, especially for programs in developing countries. However, by mid-1994, funding had stagnated. Even though the WHO reported a cumulative total of 985,119 cases of AIDS and estimated that the actual number could be as high as four million,⁹ funding was no longer keeping pace with the epidemic (Exhibit 1).

Stagnation (1995–1998)

To improve the coordination of the HIV/AIDS response among United Nations agencies—amid concerns that this would not occur with Hiroshi Nakajima as WHO director general—the member states in 1996 formed a new organization dedicated solely to AIDS: the Joint United Nations Programme on AIDS (UNAIDS).¹⁰ The transition from the former Global Programme on AIDS to UNAIDS was anything but smooth. Funding levels achieved under the old program were not sustained, while the scope of work under the responsibility of UNAIDS grew. The global response lost momentum. The global epidemic accelerated.

EXHIBIT 1**Estimated Global Prevalence Of HIV Infection And Global Funding For HIV/AIDS, 1987–2007**

SOURCE: UNAIDS. 2008 report on the global AIDS epidemic. Geneva (Switzerland): UNAIDS; 2009 Aug.

NOTES: HIV/AIDS funding (solid line) relates to the left-hand y axis. Estimated HIV prevalence (dotted line) relates to the right-hand y axis.

Despite the political and financial turmoil, these four years saw the most important scientific advances since the discovery of the virus. At the very end of 1994, the publication of results from the ACTG 076 trial on prevention of mother-to-child transmission had shown that AZT could reduce such transmission by two-thirds.¹¹ The publication of results from the Mwanza treatment study in 1995 provided convincing evidence that treating sexually transmitted infections could slow HIV transmission.¹² These developments were the first important advances in biomedical prevention since the advent of a test to screen blood for transfusion (1985). They also identified the first prevention interventions that did not require changing sexual or drug-use behavior. After these advances, treatment of sexually transmitted infections and programs to prevent mother-to-child transmission became cornerstones of prevention programs—even though coverage rates for the latter remained at very low levels in most countries until recently. Perhaps in part because of these advances, investment in behavioral prevention research continued at a low level. Investment in structural prevention research, aimed at modifying the drivers of risk behavior, remained virtually nonexistent.

In 1996, at the International AIDS Conference in Vancouver, the AIDS world received electrifying news. Triple therapy, or the combination of three antiretroviral medicines, significantly increased survival.¹³ Although this breakthrough transformed HIV from an invariably fatal infection to one resembling a chronic disease, it also exacerbated the difference between people with HIV in high-income countries and those in the rest of the world. The extremely high costs of the drugs rendered them unavailable for some 90 percent of the world's HIV-infected people. Over the following years, as it became clear that these drugs were transforming

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lives, outrage at this injustice slowly grew. Pharmaceutical manufacturers did not price-discriminate to maximize their sales and profit in each country, but rather maintained relatively constant global prices out of fear that offering lower prices in developing countries might jeopardize their high-income-country markets. The activist community, the traditional public health and development communities, and religious groups—especially in the United States—helped lay the groundwork for the end of stagnation and the reinvigoration of a global response.

One defining event was the founding of the Treatment Action Campaign in South Africa in 1998 by Zackie Achmat and other people with HIV, who literally fought for their survival. This campaign was important because at this time, AIDS activists in Western countries were not yet engaged with their colleagues in the developing world. On the other side of the southern Atlantic, the Brazilian government started offering free antiretroviral therapy to its citizens, while producing generic versions of antiretroviral drugs in the country to reduce their price.

Sadly, during these years of relative stagnation in the global response, the epidemic grew the most. UNAIDS reported that at the end of 1997 there were 30.6 million people living with HIV; 2.3 million people had died from AIDS that year alone. The total number of AIDS deaths since the beginning of the epidemic had reached 11.7 million.¹⁴ The global epidemic was growing rapidly; even in South Africa, the African continent’s wealthiest country, HIV incidence reached levels far beyond those that Uganda had reached ten years earlier.

Consolidation And A Change In The Game (1999–2003)

As demand for a strengthened global response grew, UNAIDS came into its own. It successfully transitioned from being an underfunded substitute for the AIDS programs in the WHO and the United Nations Development Program to an organization living up to its mandate to coordinate the responses of the UN system. Not only did UNAIDS as an organization begin to expand, but also many cosponsoring agencies developed their own programs. Most notably, the WHO became engaged in care and treatment; the United Nations Children’s Fund, in the cause of vulnerable children; and the United Nations Population Fund, in sexual and reproductive health. The World Bank started its Multicountry AIDS Program in Africa in 2000. The Millennium Development Goals (MDGs) outlined in September 2000 included a goal for combating HIV/AIDS.

The year 2001 was the tipping point for the global response, with the collective breaking of the silence on AIDS by African leaders. At a special summit of the Organization of African Unity hosted by President Olusegun Obasanjo in Abuja, Nigeria, UN Secretary-General Kofi Annan launched his call for a “war chest” for

AIDS. This was followed by the UN General Assembly Special Session on AIDS in June 2001. The signed commitment by countries produced during the special session explicitly stated their dedication to achieving the MDG goal dedicated to slowing and reversing the spread of HIV by 2015. They also pledged to contribute \$7 billion for AIDS by 2005—a goal that, in defiance of the norm, was in fact achieved. In 2002 the Global Fund to Fight AIDS, Tuberculosis, and Malaria was launched to mobilize new funding for the three diseases.

Meanwhile, antiretroviral drug prices dropped by more than 90 percent as a result of a confluence of events: (1) UNAIDS/WHO negotiations with pharmaceutical manufacturers; (2) treatment activism; (3) the Accelerating Access Initiative of five UN agencies with five pharmaceutical companies; and (4) the appearance of Indian generic manufacturers of the drugs. As prices decreased and drug development continued, the number of antiretroviral drugs available to treat HIV disease increased to twenty-four by the end of 2003.¹⁵

The consolidation of the response demonstrated that global consensus could be achieved, that significant funding could be mobilized, and that real progress could be made. But it remained to be seen if the scale of the response could reach the levels needed.

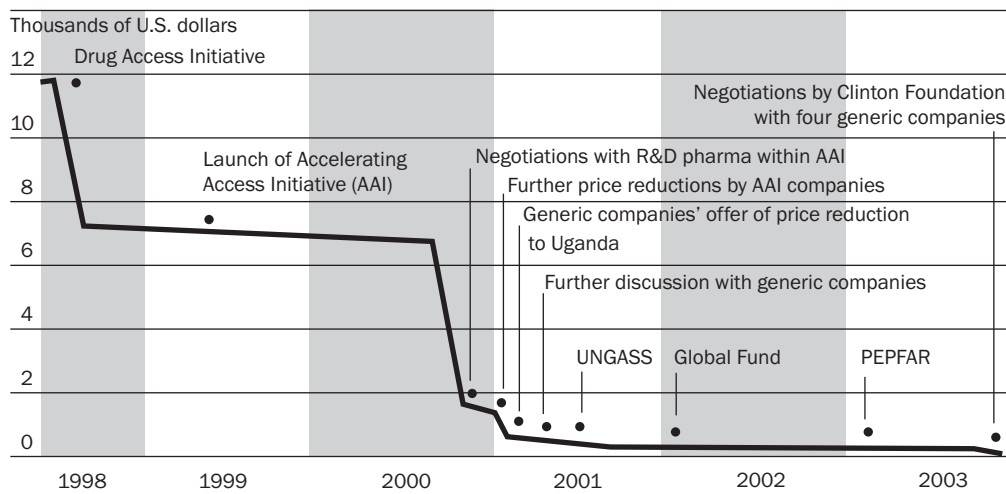
Treatment Scale-Up (2003–2006)

As the decade reached its midpoint, the combination of political momentum, affordable drug therapy, and the explosive epidemic in southern Africa called the international community into action.

President George W. Bush, in his State of the Union address in 2003, requested US\$15 billion for AIDS over a five-year period. His President's Emergency Plan for AIDS Relief (PEPFAR) was arguably the first time in which resource levels even remotely began to match the magnitude of the problem. The U.S. Congress committed the US\$15 billion to the goals of preventing seven million infections, providing two million people with antiretroviral drug therapy, and providing care to ten million people affected by HIV/AIDS.¹⁶

Additionally, former President Bill Clinton, through his foundation, negotiated further drastic price reductions for drugs at the end of 2003. These negotiations lowered the price of antiretroviral therapy to \$140 per year per person,¹⁷ which was 75 percent less than the price of brand-name drugs and 50 percent less than available generics. Uganda offers a very good example of how price negotiations over the years drastically reduced the costs of a year's supply of therapy (Exhibit 2). With proven feasibility and effectiveness of therapy in high and low-income settings, lower prices made treatment a more realistic possibility for all HIV-infected people and unleashed a powerful movement.

The further reduction of costs gave way to unprecedented goal setting and funding availability for the global HIV/AIDS response. World AIDS Day 2003 saw the launch of the UNAIDS/WHO 3 by 5 Initiative, dedicated to placing three mil-

EXHIBIT 2**Prices Of First-Line Antiretroviral Regimen In Uganda, U.S. Dollars Per Year, July 1998–October 2003**

SOURCE: Knight L. UNAIDS: the first ten years [Internet]. Geneva (Switzerland): UNAIDS; 2008 May [cited 2009 Sep 25]. Available from: http://data.unaids.org/pub/Report/2008/JC1579_First_10_years_en.pdf

NOTES: UNGASS is UN General Assembly Special Session. PEPFAR is (U.S.) President's Emergency Plan for AIDS Relief.

lion people in low- and middle-income countries on treatment by the end of 2005.¹⁸ Treatment was now the major focus of the global response.

The advances in treatment availability pushed prevention down on the priority scale in general, but this period was also one of changes in priorities within prevention. The U.S. PEPFAR-led response adopted the “ABC” prevention approach (abstinence, be faithful, and correct and consistent condom use). Frustration over the lack of large-scale success of existing behavioral approaches continued to increase. Arguments for abstinence-based prevention gained ground, despite the lack of evidence of effectiveness.¹⁹

Even as understanding continued to grow about the virus and its pathogenesis, vaccine development stalled. Microbicide trials did not demonstrate the protection hoped for; worse still, some products even increased the risk for HIV in women, as reported earlier from Kenya.^{20, 21} HIV continued its spread across the globe, with 3.4–6.2 million new infections occurring worldwide every year. In 2006 UNAIDS reported for the first time that there were as many women as men living with HIV and that in sub-Saharan Africa, women accounted for more than 60 percent of people with HIV.²²

Treatment scale-up transformed how HIV infection affected much of the world. HIV was now a disease that could be managed by drugs, thus improving and prolonging the quality of life of people with HIV in the very countries experiencing the epidemic's most brutal toll.

Prevention Rises Again (2007–2009)

The reduction in antiretroviral drug prices, the increase in international financing, and the initiation of hundreds of thousands of individuals on treatment underscored the enormous costs of *not* preventing HIV.

Despite the scale-up of treatment to 1.3 million people worldwide, 4.1 million people in total were infected in 2005.²² At the International AIDS Conference in Toronto in 2006, UNAIDS announced that for every person newly put on antiretroviral treatment, there were three new HIV infections. Bill Gates and others stressed the need to invigorate HIV prevention. Kevin De Cock, then the director of the WHO Department of HIV/AIDS, warned in his conference plenary that “we cannot treat our way out” of the epidemic.

Awareness that not all countries would experience the high prevalence rates and accelerated epidemics seen in southern Africa also affected the reshaping of prevention efforts. Generalized, all-inclusive messaging that reached everyone, everywhere, gave way to more focused, population-specific prevention messages.

Prevention science, too, saw advances. Recent studies show progress in microbicide development.^{23, 24} Male circumcision has also been shown to dramatically decrease HIV acquisition among circumcised men,^{25–27} leading some to call it the “surgical vaccine.” The period also saw the initiation of several clinical trials of pre-exposure prophylaxis with antiretroviral drugs.^{28, 29} Although the expectations are high that pre-exposure prophylaxis can be effective, there is far less optimism about its feasibility for large populations. Most recently, the results from the RV 144 vaccine trial in Thailand have shown for the first time that a vaccine can prevent HIV transmission—a result sure to revitalize the search for a highly effective vaccine.³⁰

This period was, and remains, a time of readjustment. At the end of 2007, there were thirty-three million people living with HIV, more than three million people on treatment, and 2.7 million new infections that year alone.³¹ AIDS continues to outpace the science, financing, prevention, and treatment efforts of the past quarter-century.

Financial Crisis: Adapting For The Future

We cannot yet know whether the current financial crisis will lead to backsliding in donor and national commitments to funding HIV/AIDS, but it is impossible to believe that it will not slow the rate of growth. Making serious progress against universal access targets would require accelerating funding, as the number of people who need to be maintained on treatment consumes an ever larger proportion of current expenditures. Whether there will be less money for AIDS, or just less than had been expected, demand for funds will outstrip funding for the first time since 2001. Expectations of continually improving access to services, especially treatment, will not be met, with predictable, justifiable outcries from people with HIV

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and program managers alike.

The global economic downturn, while slowing the growth of the HIV response, may provide an opportunity to improve the efficiency and quality of programs. The global community should continue to raise the level of spending for HIV/AIDS programs. But in the interim, all actors in the community—from the largest donor to the manager of a small community-based organization—will need to shift focus from ensuring that funds for HIV/AIDS are implemented, to trying to maximize the health gains for affected populations with the money that is currently available to spend.

What does this shift of focus imply for policymakers? It requires holding programs at all levels accountable in new ways:

■ **Strategy.** Generic responses to heterogeneous problems waste money. Policymakers need to understand that not all HIV/AIDS epidemics are the same, in that they are not driven by the same underlying causes. So although treatment needs may be similar from place to place—an antiretroviral drug that works in sub-Saharan Africa is also going to work in Eastern Europe—that isn’t true for prevention. The primary driver of the epidemic in the Ukraine—injecting drug use—is entirely unlike the main driver in Botswana, which is sexual contact between men and women. Efficient and effective prevention programs must be highly customized to the context—something that is only possible if you “know your epidemic.” Programs must anticipate where infections in a country are expected to occur (at what ages, in which cities, affecting which populations), so that they can focus on ensuring that interventions are focused on preventing those particular infections. Earmarks that require prevention funds to be used for specific interventions have handicapped program managers’ ability to tailor programs to their local epidemic, unnecessarily wasting resources. Local program managers need more flexibility than such earmarks permit.

■ **Time frame.** An emergency response is appropriate for an earthquake, but wasteful and ineffective for an epidemic that has been with us for more than twenty-five years. Policymakers grapple with this because every day thousands of people die of AIDS, making the epidemic simultaneously a daily emergency and a struggle that can be successful only in the long-term. A more effective, more efficient response will look different from previous efforts in several ways:

(1) Massive prevention programs, such as those supported by PEPFAR, the Global Fund, and the World Bank, must generate rigorous evidence of their impact (or lack thereof) so that every subsequent generation of prevention programs can be more effective than the last.

(2) Interventions designed to change fundamental social and structural drivers

of transmission can take years to produce their beneficial effects. Examples are overcoming gender inequity, which leaves women vulnerable to HIV infection, or police violence against men who have sex with men, which drives them underground and thus beyond the reach of prevention programs. Policymakers must be willing to put these interventions in place and wait, possibly a decade or more, for the results.

(3) Cadres of new employees must be educated to run programs and provide services across the board. This means new doctors, new nurses, new managers, and new technicians, among others. The current strategy of providing only short-term training to existing staff or relying on high-cost expatriates is not sustainable. This requires a planning horizon that is longer than five years.

(4) If policymakers are serious about efficiently expanding access to high-quality services to many more people, they must be willing to invest in strengthening the physical and managerial capacity of the local systems that deliver these services. Relying on international nongovernmental organizations and consulting firms as stand-ins for strong local systems is neither sustainable nor efficient over the medium to long term.

(5) Too many of today's management indicators create incentives to focus on short-term outcomes. For example, PEPFAR's focus on reporting the number of people receiving treatment creates incentives to get people on treatment, rather than ensuring that they have the support they need to be able to adhere to treatment and reap its potential benefits. A longer-term approach would focus on how much we are extending the lives of people with HIV—not just putting them on treatment, but helping them stay on it. Similarly, in prevention, the goal is not to provide the maximum number of prevention messages, but rather to prevent the maximum number of infections. If all we count is the former, then we create incentives to provide a lot of services for the people who are easiest to reach, rather than for those who need services the most.

■ **Management.** When funding is increasing rapidly, managers focus on rapidly scaling up implementation rather than maximizing efficiency—even in the private sector.³² Now that funding is scarce, policymakers need to ensure that programs are getting maximum value for money, at all levels.

(1) International assistance needs to channel funds through the most efficient mechanism. For example, U.S.-supported programs may be efficiently supported through PEPFAR if they require a lot of U.S.-based technical assistance; programs that don't will be more efficiently supported through the Global Fund.

(2) Program managers in most countries don't have an adequate picture of the coverage and quality of their HIV interventions, especially in the field of prevention. Policymakers need to insist upon modern management practices with functioning management information systems. Otherwise, it is impossible to know if even the best-laid plans are being implemented as intended.

(3) Finally, efficiency must be managed right down to the point at which the

services reach the client. Programs must track the cost and quantity of services produced at the level of the production units. This includes community-based organizations doing community outreach, nongovernmental organizations providing voluntary counseling and testing services, and clinics providing antiretroviral therapy, among others. Without this information, poorly run clinics don't even know that they are poorly run, and they certainly don't have the opportunity to learn from those that are well run.

TO BE ABLE TO CALL THE NEXT ERA of the global AIDS response “overcoming HIV,” policymakers must learn from history and recognize that not even an effective vaccine would be a magic bullet that would eliminate AIDS. Thus, they have to support combination prevention that is integrated with care—such as programs in high-prevalence countries that simultaneously seek to change harmful social norms (such as compensated sex between adolescent girls and older men); promote the use of and access to condoms and clean needles; rapidly scale up circumcision for infants and adults; ensure that prevention education is done with and for people with HIV; and protect the human rights of those most vulnerable. They must insist that prevention responses are adapted to each country's epidemic, making sure that those most at risk are protected first. They should fund large-scale programs only if they include impact and program evaluations to better understand what works and why. And they must find new patience—the patience needed to shift from a search for short-term fixes to investing in the long-term struggle, whether they be donors, national leaders, or leaders in civil society. Having the patience and purpose to undertake this major shift in focus is our only real hope for success.

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NOTES

1. Merson MH, O'Malley J, Serwadda D, Apisuk C. The history and challenge of HIV prevention. *Lancet*. 2008;377(9637):475–88.
2. Van de Perre P, Rouvroy D, Lepage P, Bogaerts J, Kestelyn P, Kayihigi J, et al. Acquired immunodeficiency syndrome in Rwanda. *Lancet*. 1984;2(8394):62–5.
3. Piot P, Quinn TC, Taelman H, Feinsod FM, Minlangu KB, Wobin O, et al. Acquired immunodeficiency syndrome in a heterosexual population in Zaire. *Lancet*. 1984;2(8394):65–9.
4. United States Agency for International Development. What happened in Uganda? Declining HIV prevalence, behavior change, and the national response. Hogel JA, editor. Washington (DC): USAID; 2002 Sep.
5. World Health Organization Global Programme on AIDS. Progress report number 5 [Internet]. Geneva (Switzerland): WHO; 1989 May [cited 2009 Sep 22]. Available from: http://whqlibdoc.who.int/HQ/1989/WHO_GPA_DIR_89.4.pdf
6. Protest over AZT price led to the arrest of 19. *New York Times*. 2009 Feb 9.
7. Lemp GF, Payne SF, Neal DP, Rutherford GW. The effect of zidovudine (AZT) on survival of AIDS patients in San Francisco. Paper presented at: Fifth International Conference on AIDS; 1989 Jun 4–9; Montreal, Quebec. Abstract no. W.B.P.354 [cited 2009 Sep 22]. Available from: <http://gateway.nlm.nih.gov/MeetingAbstracts/ma?f=102177987.html>
8. Kreiss J, Ngugi E, Holmes K, Ndinya-Achola J, Waiyaki P, Roberts PL, et al. Efficacy of nonoxynol 9 contraceptive sponge use in preventing heterosexual acquisition of HIV in nairobi prostitutes. *JAMA*. 1992;268(4):477–82.
9. World Health Organization Global Programme on AIDS. The HIV/AIDS pandemic: 1994 overview [Internet]. Geneva (Switzerland): WHO; 1994 [cited 2009 Sep 30]. Available from: http://whqlibdoc.who.int/hq/1994/WHO_GPA_TCO_SEF_94.4.pdf
10. Knight L. UNAIDS. The first ten years [Internet]. Geneva (Switzerland): UNAIDS; 2008 May [cited 2009 Sep 25]. Available from: http://data.unaids.org/pub/Report/2008/JC1579_First_10_years_en.pdf
11. Connor E, Sperling R, Gelber R, Kiseley P, Scott G, O'Sullivan MJ, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med*. 1994;331(18):1173–80.
12. Grosskurth H, Mosha F, Todd J, Mwijarubi E, Klokke A, Senkoro K, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet*. 1995;346(8974):530–6.
13. Markowitz M, Cao Y, Hurley A, O'Donovan R, Peterkin J, Anderson B, et al. Triple therapy with AZT and 3TC in combination with nelfinavir mesylate in 12 antiretroviral-naïve subjects chronically infected with HIV-1. Paper presented at: 11th International Conference on AIDS; 1996 Jul 7–12; Vancouver, British Columbia. Abstract no. LBB.B.6031.
14. UNAIDS. Report on the global HIV/AIDS epidemic 1998 [Internet]. Geneva (Switzerland): UNAIDS; 1998 Jun [cited 2009 Sep 22]. Available from: http://data.unaids.org/pub/Report/1998/19981125_global_epidemic_report_en.pdf
15. U.S. Food and Drug Administration. Antiretroviral drugs used in the treatment of HIV infection [Internet]. Rockville (MD): FDA; 2009 May 20 [cited 2009 Sep 22]. Available from: <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSActivities/ucml18915.htm>
16. President's Emergency Plan for AIDS Relief [Internet]. Washington (DC): PEPFAR; [cited 2009 Sep 22]. Available from: <http://www.pepfar.gov/about/index.htm>
17. UNAIDS [Internet]. Geneva (Switzerland): UNAIDS. Press statement, UNAIDS APPLAUDS Clinton Foundation's agreement with pharmaceutical companies to cut prices of AIDS drugs; 2003 Oct 23 [cited 2009 Sep 22]. Available from: http://data.unaids.org/Media/Press-Statements01/clinton_ps_23Oct03_en.pdf
18. World Health Organization. The 3 by 5 initiative [Internet]. Geneva (Switzerland): WHO/UNAIDS; c2009 [cited 2009 Sep 22]. Available from: <http://www.who.int/3by5>
19. Underhill K, Montgomery P, Operario D. Sexual abstinence only programmes to prevent HIV infection in high income countries: systematic review. *BMJ*. 2007;335(7613):248.
20. Roddy RE, Zekeng L, Ryan KA, Tamoufe U, Weir SS, Wong EL. A controlled trial of nonoxynol 9 film to reduce male-to-female transmission of sexually transmitted diseases. *N Engl J Med*. 1998;339(8):504–10.

21. Van Damme L, Ramjee G, Alary M, Vuylsteke B, Chandeying V, Rees H, et al. Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. *Lancet*. 2002;360(9338):971-7.
22. UNAIDS. 2006 report on the global AIDS epidemic. Geneva (Switzerland): UNAIDS; 2006 May.
23. Dobard C, Parikh U, Sharma S, Cong ME, Smith J, Garcia-Lerma G, et al. Complete protection against repeated vaginal simian HIV exposure in macaques by a topical gel containing tenofovir alone or with emtricitabine. Paper presented at: 16th Conference on Retroviruses and Opportunistic Infections; Montreal, Quebec; 2009 Feb 8-11. Abstract no. 46.
24. Karim SA, Coletti A, Richardson B, Ramjee G, Hoffman I, Chirenje M, et al. Safety and effectiveness of vaginal microbicides BufferGel and 0.5% PRO 2000/5 gel for the prevention of HIV infection in women: results of the HPTN 035 trial. Paper presented at: 16th Conference on Retroviruses and Opportunistic Infections; Montreal, Quebec; 2009 Feb 8-11. Abstract no. 48LB.
25. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet*. 2007;369(9562):643-56.
26. Gray RH, Kigozi G, Serwadda D, Makumbi F, Wataya S, Nalugoda F, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet*. 2007;369(9562):657-66.
27. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 trial. *PLoS Med*. 2005;2(11):e298.
28. A pilot study of pre-exposure prophylaxis (PrEP) to evaluate safety, acceptability, and adherence in at-risk populations in Uganda, Africa [Internet]. Study no. NCT00931346. Bethesda (MD): National Institutes of Health; [updated 2009 Sep 2] [cited 2009 Sep 22]. Available from: <http://clinicaltrials.gov/ct2/show/NCT00931346>
29. Botswana TDF/FTC oral HIV prophylaxis trial [Internet]. Study no. NCT00448669. Bethesda (MD): National Institutes of Health; [updated 2007 Apr 2] [cited 2009 Sep 22] Available from: <http://clinicaltrials.gov/ct2/show/NCT00448669?term=Botswana&rank=1>
30. U.S. Military HIV Research Program [Internet]. Washington (DC): MHRP; c2009. Press release, HIV vaccine study first to show some effectiveness in preventing HIV; 2009 Sep 24 [cited 2009 Oct 5]. Available from: <https://www01.hjfi.org/apps/internet/hivnewscenter.nsf/phase3pressrelease>
31. UNAIDS. 2008 report on the global AIDS epidemic. Geneva (Switzerland): UNAIDS; 2008 Aug.
32. Nasar S. U.S. output per worker is growing. *New York Times*. 1992 Nov 27.