



## Message from Toronto — Deliver AIDS Treatment and Prevention

Robert Steinbrook, M.D.

The clear message from the XVI International AIDS Conference in Toronto in August was that the growth of the pandemic continues to outpace the broad and expanding efforts to control it.

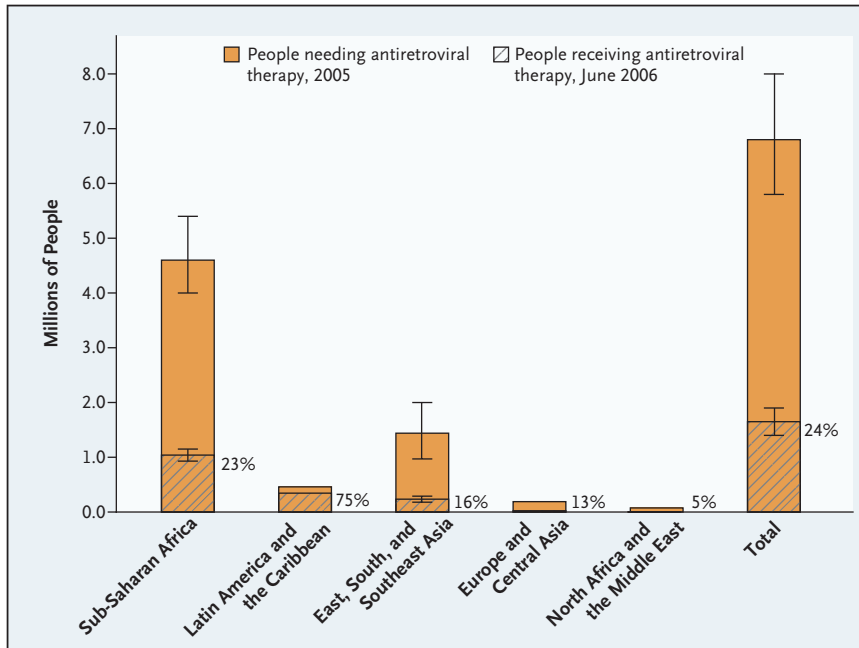
The conference had 26,057 participants, a record number. The meeting's theme — “time to deliver” — suggested both ongoing urgency and frustration at the pace of the response. The World Health Organization (WHO) never came close to its goal of providing antiretroviral medications to 3 million people by the end of 2005. In June 2006, an estimated 1.65 million people in low- and middle-income countries were receiving antiretroviral therapy, including about a million in sub-Saharan Africa (see bar graph) and between 60,000 and 100,000 children. In some countries, therapy is provided to more than 25% of those in need (see

line graph), and coverage is improving in many countries, but not in all — for example, coverage in Uganda decreased from 51% in December 2005 to 35% in June 2006. Although the number of people being treated in Uganda has grown, the estimated number who require treatment has increased even faster.

Since highly active antiretroviral therapy became available a decade ago, the treatment of HIV infection has been streamlined — for example, from 10 pills daily taken in three doses with food restrictions to as little as 1 pill once a day. Many presentations at the conference showed that treating HIV is feasible in all coun-

tries. The best price for a first-line regimen of generic antiretroviral drugs in low-income countries is now about \$130 a year for adults (down from \$285 in April 2004) and less than \$200 a year for children. However, the average cost of first-line regimens remains considerably higher, and second-line regimens may cost \$1,500 or more per year.

In 2005, there were an estimated 4.1 million people newly infected with HIV and 2.8 million AIDS-related deaths.<sup>1</sup> The vast majority of the estimated 38.6 million people living with HIV do not know that they are infected, and stigma and discrimination related to HIV remain major issues throughout the world. Financing for AIDS programs in low- and middle-income countries is estimated at \$8.9 billion in 2006, but the estimated need is \$14.9 billion, and in 2008, it will be



**Estimated Numbers of HIV-Infected People Who Need Antiretroviral Therapy and Numbers Receiving the Therapy, According to Region.**

Data are from the WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS). For some regions, the range of estimates is indicated by I bars.

\$22.1 billion.<sup>1</sup> In his address to the conference, Bill Gates — who was one of the stars of the event, along with his wife Melinda and former president Bill Clinton — observed that although the number of people receiving antiretroviral drugs has been increasing by about 450,000 per year, about 10 people become infected for each person who begins treatment. Even with optimistic assumptions about continued decreases in treatment costs, Gates argued, “the harsh mathematics of this epidemic proves that prevention is essential to expanding treatment.”

In many countries, the provision of HIV treatment — and medical care in general — is compromised by profound shortages of skilled health workers and dysfunctional and inefficient health care systems. Frustrated by low salaries and poor working

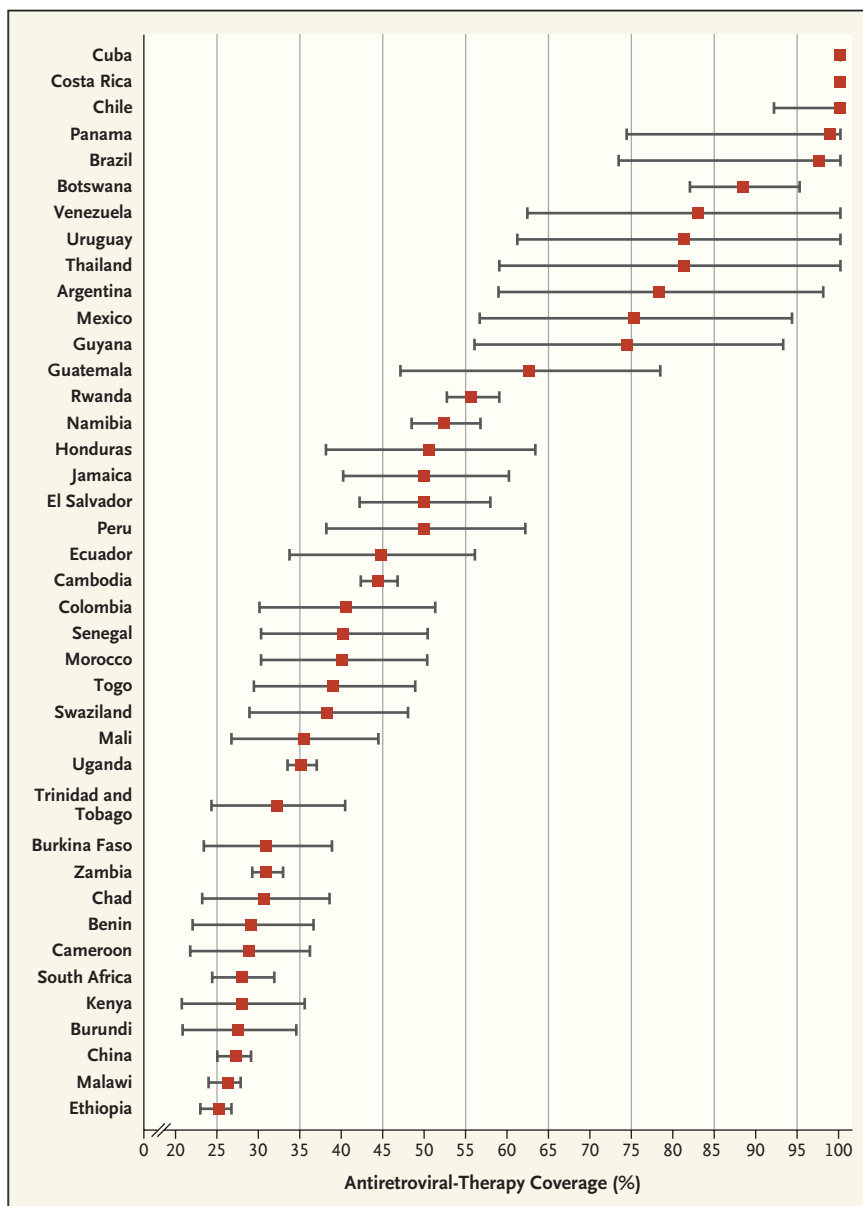
conditions, physicians and nurses leave their countries. Anders Nordström, the acting director-general of the WHO, told the conference that “no improvement in financing or medical products can make a lasting difference to people’s lives until the crisis in the health workforce is solved.” The organization’s new goal is universal access to HIV–AIDS prevention, treatment, care, and support by 2010. It advocates that countries that are “implementing a public health approach to scale-up” provide “free access at the point of service delivery to basic HIV services, including consultation fees, HIV testing and antiretroviral therapy.”<sup>2</sup>

Definitive prevention and control of AIDS require a safe and effective vaccine. But no successful vaccine is on the horizon. In her address, Françoise Barré-

Sinoussi of the Institut Pasteur in Paris described the history of HIV vaccines as “dreams and nightmares.” Unfortunately, less than one fifth of people who are considered to be at high risk for infection currently have access to effective prevention methods, such as HIV testing for adults (0.6%); education, the provision of clean needles and syringes, and drug treatment for injection-drug users (4%); condoms (9%); and programs to interrupt mother-to-child transmission (9%).<sup>1,3</sup> There is enormous room for improvement. For example, mother-to-child transmission of HIV could nearly be eliminated throughout the world with the use of antiretroviral drugs, alternatives to breast-feeding, and cesarean delivery, as it has been in many high-income countries.

Many new approaches to prevention are being evaluated, often in large controlled trials.<sup>3</sup> These include cervical barriers, such as the diaphragm; therapy to suppress herpes simplex virus type 2, the primary cause of genital herpes, which is a risk factor for acquiring and transmitting HIV; and microbicides that could be applied to the vagina or rectum. Microbicial products that are being explored might deliver antiretroviral medications through a ring placed inside the vagina — a technology that would be convenient to use and could release drugs for many days.

Several new approaches are controversial: male circumcision, pre-exposure prophylaxis with antiretroviral drugs, and expanded treatment of infected persons not only for their own health but also to prevent HIV transmission. A recent trial in South Africa showed



Low- and Middle-Income Countries with More Than 25% Coverage for Antiretroviral Therapy, June 2006.

Data are from the WHO and UNAIDS. Bars show ranges of estimates. European countries and countries with fewer than 1000 persons receiving treatment are not shown.

that male circumcision substantially reduced the risk of HIV infection.<sup>4</sup> Additional trials are ongoing in Kenya and Uganda. Circumcision, however, requires surgery and raises cultural and personal issues. At present, there are insufficient data and no in-

ternational recommendations to promote circumcision for the prevention of HIV infection.

Pre-exposure prophylaxis is based on the hypothesis that daily administration of antiretroviral medications to uninfected persons who are at high risk will

prevent infection. The medications in clinical trials are tenofovir and a combination pill containing tenofovir and emtricitabine; results could be available in 2007 or 2008. There is concern about the safety of this method, the potential for selection of resistant viruses, and the wisdom and acceptability of initiating long-term antiretroviral treatment in healthy people.

In his address, Julio Montaner of the University of British Columbia advocated expanded access to highly active antiretroviral therapy to render infected persons less infectious, thereby reducing the rate of HIV transmission.<sup>5</sup> This approach is untested, and treatment of all infected persons may not be feasible or ethically acceptable. Moreover, the new approaches, despite their promise, do not eliminate the potential for HIV transmission and could encourage people who are at risk for infection to continue to engage in high-risk behaviors.

In HIV-prevention trials, researchers are obliged to minimize the potential harms to subjects, most notably the risk of HIV infection. However, if fewer subjects become infected, larger and longer studies will be needed. A consensus is also emerging that providing antiretroviral therapy to subjects who acquire HIV infection during the course of a study “is an indispensable part of the agreement between trial sponsors and trial participants.”<sup>3</sup> There is disagreement, however, about the obligation to people whose infection is detected when they are screened for eligibility, as well as about who should assume the long-term financial costs and manage the complexity of treatment — trial sponsors, the

country where the trial is conducted, an international fund, or someone else. Although trial participants are unlikely to need treatment until years after they become infected, they will eventually need it for life.

AIDS prevention and treatment are inextricably linked; it is not possible to deliver one without the other. By August 2008, when the XVII International AIDS Conference is held in Mexico City, it

will be clear whether the world is continuing to lose ground to the AIDS pandemic or finally getting ahead of it.

**An interview with Mark Wainberg, cochair of the XVI International AIDS Conference, can be heard at [www.nejm.org](http://www.nejm.org).**

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## Global Health — The Gates–Buffett Effect

Susan Okie, M.D.

Standing before a giant AIDS ribbon, Bill and Melinda Gates greeted some 26,000 researchers and public health workers on the opening night of last month's conference hosted by the International AIDS Society in Toronto. Bill Gates's voice echoed through the stadium as he assured the conference delegates, "Melinda and I have made stopping AIDS the top priority of our foundation." The Gateses spoke in turn, revealing both their passion and their clear-eyed intellectual engagement. Bill Gates talked of the new optimism he senses in Africa with the increased availability of antiretroviral drugs, but he warned that without increased prevention efforts, the provision of long-term treatment for infected persons is "simply unsustainable." Melinda Gates spoke of the stigmas that limit efforts to control AIDS, noting that government officials in many countries refuse to accompany them when they meet with sex workers. The philanthropists promised to increase their foundation's fund-

ing for research on new prevention tools for women and called for expanded access to proven measures such as condoms, clean needles, and HIV testing. The demonstrators who had heckled previous speakers were silent; the Gateses were interrupted only by cheers.

In a world with many celebrities but few heroes, Bill Gates has attained heroic status by committing much of his enormous fortune to the advancement of global equity. He and his wife have targeted the causes of health disparities between rich and poor, and their foundation has become a driving force in international aid and in research on AIDS and other diseases. In June, the Bill and Melinda Gates Foundation's likely impact on global health was amplified when Warren Buffett, the world's second-richest man, announced plans to give most of his fortune to the foundation established by the richest one.

Buffett's gift, worth about \$37 billion, will double the foundation's endowment from \$29 bil-

lion to approximately \$60 billion, making it by far the world's largest charitable foundation. The gift will also increase the foundation's annual giving from \$1.36 billion last year to about \$3 billion, or approximately \$1 per year for every person in the poorer half of the world's population. By comparison, the World Bank estimates that total health-related aid to developing countries in 2004 (from governments, international organizations, and private sources) was about \$12.7 billion (see graph).

If Gates donates more of his own fortune and if the value of Buffett's donated Berkshire Hathaway stock rises, the Gates Foundation's annual giving will increase further. Yet the projected cost of solving major health problems in the developing world is far higher than even the most optimistic projections for giving by Gates. In 2000, the United Nations adopted Millennium Development Goals to be achieved by 2015; they included substantially reducing child and maternal mortality, reversing the spread of