

Antiretrovirals for the World: Needs and Challenges

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“Lack of access to antiretroviral therapy is a global health emergency. To deliver antiretroviral treatment to the millions who need it, we must change the way we think and change the way we act.”

JONG-WOOK LEE, DIRECTOR-GENERAL, WORLD HEALTH ORGANIZATION

AT THE XIII INTERNATIONAL AIDS CONFERENCE, HELD IN 2002 IN Barcelona, the World Health Organization (WHO) challenged the global HIV/AIDS community to expand access to care and treatment to at least half of those in immediate need—to put antiretroviral therapy into the hands of three million people in resource-limited settings by the end of 2005. On World AIDS Day 2003, WHO released a detailed and concrete plan to achieve this ambitious goal. The “3 by 5 Initiative,” as it has come to be known, has been heralded as the first big step towards universal access to AIDS care and treatment.

Dr. Alice Pau, who has spent part of the last year working in South Africa, returned to PRN in March to discuss some of her experiences and to provide an overview of the 3 by 5 Initiative and the strategies in place to support it. “Some people claim that it’s too late to be implementing a program like this, that we should have acted earlier,” Dr. Pau said in her introductory remarks. “However, it’s not as late as it would be if we were not acting at this point.”

I. The Global Impact of HIV/AIDS

EACH YEAR, WHO AND UNAIDS PUBLISH UPDATED DESCRIPTIONS OF THE global AIDS epidemic. The estimates are nothing less than harrowing. In 2003, HIV/AIDS is thought to have claimed three million lives and was spread to an additional five million people, bringing the global total to 40 million people living with HIV/AIDS (UNAIDS/WHO, 2003).

According to the 2003 UNAIDS/WHO report, HIV prevalence has remained relatively steady—generally at high levels—for the past several years across much of sub-Saharan Africa. This is due to the fact that high levels of new HIV infections are persisting and are now matched by high levels of AIDS mortality. In this region of the world, the hardest hit by the HIV/AIDS epidemic, between 25 and 28.2 million adults and children are living with HIV/AIDS and between 3 and 3.4 million were newly infected with the virus in 2003. This translates into a staggering average adult prevalence of 7.5% to 8.5%, with more than 25% of young adults in some countries currently living with HIV/AIDS.

Of equal concern are emerging epidemics in Eastern Europe and Central Asia, in Eastern Asia and the Pacific Islands, and in South and Southeast Asia. In Eastern Europe and Central Asia, between 1.2 and 1.8 million people are currently living with HIV/AIDS, with new diagnoses being documented in 180,000 to 280,000 people in 2003. In East Asia and the Pacific, the prevalence of HIV/AIDS has been estimated to be between 700,000 and 1.3 million people. And in South and Southeast Asia, prevalence estimates are between 4.6 and 8.2 million people.

Beyond the incidence and prevalence rates are the social and economic consequences of the HIV/AIDS pandemic. “HIV infection clearly

TABLE 1. Expectation of Life at Birth With and Without AIDS for Groups of Affected Countries in Major Areas and for the Most Affected Countries, 1999–2000, 2000–2005, and 2010–2015

Country group or country	1995–2000		2000–2005		2010–2015	
	With AIDS	w/o AIDS	With AIDS	w/o AIDS	With AIDS	w/o AIDS
All 45 Countries	56.9	59.8	57.5	61.7	60.4	65.2
35 countries in Africa	48.3	54.8	48.2	57.1	52.4	61.2
4 countries in Asia	62.2	62.8	64.0	64.9	67.7	68.9
6 countries in Latin America and the Caribbean	66.1	66.9	67.2	68.2	69.5	70.7
9 countries with prevalence of 14% or more	49.3	61.5	45.3	63.6	47.5	67.1
The most affected countries:						
Botswana	44.4	67.6	36.1	69.7	43.0	73.0
South Africa	56.7	63.3	47.4	65.8	42.0	69.6
Swaziland	50.8	60.2	38.1	62.7	39.2	67.2
Zimbabwe	42.9	66.5	42.9	68.5	50.2	71.4

Source: United Nations Population Division

means an increase in life lost,” Dr. Pau commented. “It also weakens government, decreases the workforce and productivity, and contributes to economic collapse.” Additionally, unchecked HIV infection contributes to increasing crime rates, increasing poverty and starvation, increasing stigmatization and discrimination, and the destruction of families and entire communities.

Dr. Pau reviewed nationwide life-expectancy estimates published in *World Population Prospects: The 2000 Revision*, researched, written, and published by the Department of Economic and Social Affairs of the United Nations (United Nations, 2001). As in previous *Revisions*, the impact of HIV/AIDS has been explicitly incorporated in projecting the population of highly affected countries. In the *2000 Revision*, 45 countries are in that category and include 35 countries in sub-Saharan Africa, four countries in Asia, and six countries in Latin America. In the 35 highly affected countries of Africa, life expectancy at birth is estimated at 48.3 years in 1995 to 2000, 6.5 years less than it would have been in the absence of AIDS (see Table 1). By 2015, the population of these 35 African countries is projected to be 84 million, 10% less than it would have been without AIDS. The demographic impact of AIDS is even more dramatic in the nine African countries with the highest HIV prevalence (>14%), which include Botswana, Kenya, Lesotho, Malawi, Namibia, South Africa, Swaziland, Zambia and Zimbabwe. In 1995 to 2000, average life expectancy in those countries was 49.3 years instead of the 61.5 years it would have been in the absence of AIDS, a reduction of 12 years. By 2005 to 2010, the United Nations projects the average life expectancy at birth in these countries to decrease to 45 years instead of rising to 65 years as projected in the absence of the disease.

Fortunately, the global response has expanded significantly in the past two to three years. Spending (domestic and external) on HIV/AIDS programs in developing countries continues to increase. Numerous organizations, working to coordinate HIV prevention and clinical care services, are now in operation and several countries have begun extending antiretroviral and other AIDS-related medications to some of their citizens. But the fact is, the expansion of resources is still no match for the raging epidemic.

Drawing upon estimates from the World Health Organization (WHO), Dr. Pau pointed out that greater than 95% of people living with HIV/AIDS live in developing countries and that six million people are in immediate need of antiretroviral therapy. Approximately 400,000 (6.7%) of them are currently receiving antiretroviral therapy, with one-third of them in Brazil, where low-cost generic antiretrovirals are the mainstay option. “Based on these projections,” Dr. Pau explained, “WHO calls for antiretroviral treatment reaching three million people by the year 2005. This is WHO’s 3 by 5 Initiative.”

Antiretroviral Distribution: Does it Work?

A NUMBER OF PILOT PROGRAMS, AIMED AT SECURING ACCESS TO ANTIRETROVIRAL therapy, have been initiated in a handful of developing countries. One program reviewed by Dr. Pau is the UNAIDS and Uganda Ministry of Health HIV Drug Access Initiative, one of the first pilot antiretroviral programs in Africa. “This is not a national program that provides drugs free-of-charge to individuals,” Dr. Pau explained. “They are actually asking the individuals to pay for their own medications and their own laboratory testing. So you can imagine that this is a select group of individuals, with decent incomes, who can afford the price of their own health care.”

In a paper published by Dr. Paul Weidle and his colleagues with the U.S. Centers for Disease Control and Prevention, clinical and laboratory information for 476 Ugandan patients receiving HIV care between

August 1998 and July 2000 was analyzed (Weidle, 2002). Of the 476 patients evaluated, 399 were started on antiretroviral therapy at some point during these two years; 204 (51%) were receiving triple-drug therapy, 189 (47%) were receiving dual-nucleoside reverse transcriptase inhibitor (NRTI) therapy, and six (2%) were receiving NRTI monotherapy. Prior to initiating therapy, the median CD4+ count was 73 cells/mm³ and the median viral load was approximately 200,000 copies/mL.

Eighty-eight percent of the patients self-reported adherence to the regimens prescribed. “The most common reason for poor adherence,” Dr. Pau said, “was financial in nature. Thirty-three percent of the patients who self-reported poor adherence spoke of financial difficulties that prevented continued access to the prescribed drugs.”

The probability of remaining alive and in care was 63% at six months and 49% at one year. Unsurprisingly, patients receiving triple-drug therapy had greater virological responses than those receiving dual-NRTI therapy or monotherapy. In contrast, survival rates after one year were similar among patients receiving triple-drug therapy or dual-NRTI therapy, in those with CD4+ counts above 50 cells/mm³ prior to initiating therapy. Among patients who initiated therapy with CD4+ counts below 50 cells/mm³, however, triple-drug therapy was associated with significantly higher survival rates than dual-NRTI therapy at one year. “This is really the first study we’ve seen demonstrating a survival benefit among HIV-positive individuals in developing countries receiving antiretroviral therapy,” she concluded.

II. Setting the Tone: WHO Antiretroviral Treatment Guidelines

WITH EFFORTS CURRENTLY UNDER WAY TO SCALE-UP ACCESS TO FREE OR low-cost antiretrovirals in the developing world, WHO and UNAIDS have also focused on developing guidelines intended to support and facilitate the safest and most efficient use of these medications. This effort is recognized in the form of *Scaling Up Antiretroviral Therapy in Resource-Limited Settings: Treatment Guidelines for a Public Health Approach*, official antiretroviral treatment guidelines published by WHO, first in 2001 and revised in December 2003 (WHO, 2003). Among the key tenets of these guidelines are recommendations to standardize and simplify antiretroviral regimens, to support the efficient implementation of treatment programs in resource-limited settings, and to ensure that these programs balance evidence-based medicine with limited resources, in order to avoid the use of substandard treatment protocols.

When To Start?

THE WHO GUIDELINES ARE WRITTEN TO REFLECT THE LIMITED ACCESS TO laboratory testing found in most resource-limited settings. CD4+ cell counts, for example, are unavailable to the vast majority of the six million people thought to need antiretroviral therapy immediately. Similarly, viral load testing is out of the question in many settings—even if the money were available, the laboratory facilities are not. Recognizing the urgency of the need for treatment, WHO recommends adapting treatment protocols to the setting. In capital cities, for example, CD4+ cell counts might be used to determine when treatment should be started. In rural areas, where health centers may lack electricity, running water, and all but the most rudimentary testing, clinical staging alone would be more appropriate.

TABLE 2. Recommendations for Initiating Antiretroviral Therapy in Adults and Adolescents with Documented HIV Infection

WHO Stage	CD4+ count (cells/mm ³)	Total Lymphocyte Count (TLC)
IV	Any	Any
III	Consider if <350 cells/mm ³	If CD4 not available, regardless of TLC
II	<200 cells/mm ³	If CD4 not available, TLC <1,200
I	<200 cells/mm ³	TLC not to be used in decision

Source: World Health Organization (WHO). *Scaling up antiretroviral therapy in resource-limited settings: Treatment guidelines for a public health approach*. WHO: December 2003. Accessed at: http://www.who.int/3by5/publications/documents/arv_guidelines/en/

In settings where laboratory testing is unavailable, WHO guidelines suggest that all patients with clinical stage IV disease—AIDS—should receive antiretroviral therapy (see Table 2). For settings with some access to laboratory facilities, total lymphocyte count (TLC) may be used to guide therapeutic decisions. Where CD4+ cell counts are available, WHO’s antiretroviral therapy eligibility includes: all patients with CD4+ counts < 200 cells/mm³ regardless of WHO stage; patients with both CD4+ counts < 350 cells/mm³ and WHO stage II or III; and all patients with

WHO stage IV, regardless of the CD4+ cell count. Viral load testing is not considered a prerequisite for decisions about treatment initiation.

Which Antiretrovirals to Use?

WHO GUIDELINES STRESS THAT INDIVIDUAL COUNTRIES USE A “PUBLIC health approach” to facilitate the scale-up of antiretroviral therapy. This means that antiretroviral treatment programs should be standardized as much as possible. In particular, WHO recommends that countries select a single first-line and a limited number of second-line regimens for large scale use, while at the same time recognizing that individuals who cannot tolerate or fail the first- and second-line regimens would be referred for individualized care by specialized physicians (where available).

As well as the standard considerations of potency, durability, side effects, pill counts, and cost, decisions about which antiretroviral drug regimens to use in resource-limited settings must take additional factors into account. In regions where access to effective family planning is limited, and where most women present for prenatal care in the third trimester, regimens must be safe to use during pregnancy. Because the prevalence of HIV/TB coinfection is extremely high, planners must select at least one antiretroviral drug regimen that can be used during TB treatment. Because the majority of patients lack access to refrigeration, agents such as ritonavir and liquid stavudine—known to lose potency if not kept in cold storage—are out of the question for many.

Taking these considerations into account, WHO currently lists two non-nucleoside reverse transcriptase inhibitor (NNRTI)-based combi-

TABLE 3. First-Line Antiretroviral Regimes in Adults and Adolescents and Characteristics That Can Influence Choice

Antiretroviral Regimen	Major Potential Toxicities	Usage in Women (of Childbearing Age or Pregnant)	Usage in TB Coinfection	Fixed-Dose Combination (FDC) Available?	Laboratory Monitoring Requirements	Price for Least-Developed Countries, June 2003 (US\$/Year)
Stavudine (d4T) Lamivudine (3TC) Nevirapine (NVP)	d4T-related neuropathy, pancreatitis, and lipoatrophy; NVP-related hepatotoxicity and severe rash	Yes	Yes, in rifampicin-free continuation phase of TB treatment.	Yes	No	281-358
Zidovudine (ZDV) Lamivudine (3TC) Nevirapine (NVP)	ZDV-related GI intolerance, anemia, and neutropenia; NVP-related hepatotoxicity and severe rash	Yes	Use with caution in rifampicin-based regimens	Yes	Yes	383-418
Stavudine (d4T) Lamivudine (3TC) Efavirenz (EFV)	d4T-related neuropathy, pancreatitis and lipoatrophy; EFV-related CNS toxicity and potential teratogenicity	No	Yes, but EFV should not be given to pregnant women or women of childbearing potential, unless effective contraception can be assured	No. EFV not available as part of FDC; however partial FDC available for d4T/3TC	No	350-1086
Zidovudine (ZDV) Lamivudine (3TC) Efavirenz (EFV)	ZDV-related GI intolerance, anemia, and neutropenia; EFV-related CNS toxicity and potential teratogenicity	No	Yes, but EFV should not be given to pregnant women or women of childbearing potential, unless effective contraception can be assured	No. EFV not available as part of FDC; however, partial FDC available for ZDV/3TC	Yes	611-986

Source: World Health Organization (WHO). *Scaling up antiretroviral therapy in resource-limited settings: Treatment guidelines for a public health approach*. WHO: December 2003. Accessed at: http://www.who.int/3by5/publications/documents/arv_guidelines/en/

nations as the preferred first-line treatment regimens. The regimens listed are: 1) nevirapine and lamivudine with either stavudine or zidovudine; or 2) efavirenz and lamivudine with either stavudine or zidovudine. As highlighted by Dr. Pau, these regimens are recommended based on a variety of factors. “There is efficacy data concluding that they are effective and they are less costly, do not need refrigeration, and easy to administer,” she explained. “And with efavirenz, there is less drug-drug interaction when rifampin is being used to treat tuberculosis. Some of these regimens are also available in fixed-dose combinations.”

The recommended first-line antiretroviral regimens and the factors that can influence choice are reviewed in Table 3.

There are also some notable disadvantages and concerns associated with NNRTI-based regimens in resource-poor countries. First and foremost, NNRTIs are not active against HIV-2 and group O HIV-1 strains. NNRTI resistance is also a concern, with increasing frequencies of NNRTI resistance being observed in females receiving single-dose nevirapine to help prevent vertical transmission of the virus to their babies. With efavirenz there is the potential for teratogenicity, which is a significant concern in light of the fact that women of child-bearing potential comprise 50% of the HIV-infected population in many developing countries. Another concern is that the WHO guidelines do not currently recommend routine laboratory monitoring of transaminases in patients receiving nevirapine-based regimens. What’s more, if therapy is initiated with a fixed-dose combination that contains full-dose nevirapine—as opposed to standard dose-escalation practices—there may be an increased risk of nevirapine toxicities.

Protease inhibitor (PI)-based regimens are currently reserved as second-line treatment options. However, they should be considered as a first-line option in some situations; for example, in areas where the prevalence of NNRTI resistance exceeds 5% to 10%, for viral types that are not likely to respond to NNRTIs (e.g., HIV-1 or HIV-1 group O), or there is intolerance to NNRTIs. Countries are free to determine which PIs to include in their antiretroviral treatment programs, and may include: lopinavir/ritonavir, nelfinavir, and/or ritonavir-boosted indinavir or saquinavir.

The most obvious advantage of PI-based regimens is their proven efficacy. But there are a number of disadvantages including their high costs (no generic versions of PIs are available), high pill burden, food and water requirements, significant drug interactions, need for refrigeration (at least for some PIs), no fixed-dose combinations with NNRTIs, and gastrointestinal intolerance (especially problematic in populations with a high incidence of diarrhea and malnutrition).

III. The 3 by 5 Initiative

THE WHO AND UNAIDS 3 BY 5 INITIATIVE IS A PLAN TO PROVIDE antiretroviral therapy to three million people with HIV/AIDS in developing countries by the end of 2005. For this initiative to be achievable, it will require concerted, sustained action by many partners. To chart the direction and to show what WHO/UNAIDS themselves will be doing to accelerate action, WHO/UNAIDS has developed an initial strategic framework. This strategic framework for scaling up of antiretroviral therapy contains 14 key strategic elements. These elements fall into five categories—the pillars of the 3 by 5 Initiative. These are: 1) global leadership, strong partnership and advocacy; 2) urgent, sustained country support; 3) simplified, standardized tools for delivering antiretroviral therapy; 4) effective, reliable supply of medicines and diagnostics; and 5) rapidly identifying and reapplying new knowledge and successes.

Hurdles and Challenges: Governmental and Financial Support

“IN ORDER FOR US TO TREAT THREE MILLION HIV-POSITIVE PATIENTS in developing nations by 2005, there are going to be a number of hurdles and challenges,” Dr. Pau admitted. “These challenges are not insurmountable, but they can be quite difficult.”

One challenge discussed by Dr. Pau is the need for consistent governmental support. Importantly, access to antiretroviral treatment should not be used as a political agenda in developing countries, and for treatment programs to work, they will require support from all levels of government. Consistent financial support, from government and non-government institutions, is also a necessity. “Antiretroviral cost is only a small component of the overall cost of care,” Dr. Pau pointed out. “Securing financial support is integral to developing long-term plans. What’s needed is secure funding sources, including from local government, UNAIDS, the World Bank, Global Funds, and non-government organizations. Financial support is very much needed to continue training health-care providers.” There are also financial needs to improve the overall health-care infrastructure, including better-equipped medical facilities—in both urban and remote sites—with improved laboratory and diagnostic capabilities.

Hurdles and Challenges: Drug Procurement

DRUG PROCUREMENT IS ANOTHER CHALLENGE. WHILE THE COST OF antiretroviral therapy is the most obvious barrier, other procurement issues may also be problematic. As noted, a secure cold chain is required for some agents. Pharmacy facilities may need to be upgraded, and technical assistance with drug forecasting, stocking, and management may also be necessary in some settings.

A major question facing many leaders involved in antiretroviral treatment programs in developing nations is whether to use generic or trade-name products. “How reliable are these supplies?” Dr. Pau asked. “What are the quality control measures of the manufacturer? What about the product equivalence and bioequivalence?”

Fortunately, some comparative data are available. In a study conducted by Dr. Scott Penzak and his colleagues at the National Institutes of Health, the contents of nevirapine in four generic formulations and Viramune-brand nevirapine were evaluated (Penzak, 2003). Nevimune, India-based Cipla’s generic alternative, contained 197.8 mg of nevirapine. Nevirez, produced by India-based Aurobindo Pharma, contained 205.5 mg nevirapine. Triomune 40—Cipla’s fixed-dose combination containing single doses of nevirapine, stavudine (40 mg), and lamivudine (150 mg)—contained 191.4 mg nevirapine, whereas Triomune 30 (using 30 mg of stavudine) contained 194.2 mg nevirapine. A single 200 mg tablet of Viramune-brand nevirapine contained 196.6 mg of the drug. “The five drugs were within the criteria to be considered as chemically equivalent,” Dr. Pau added. “What we don’t know at this point is if they are bioequivalent. Whether they have the same degree of absorption and have the same pharmacokinetics when given to patients.” More equivalency studies will be done with other generic products to be marketed by different manufacturers from various countries.

WHO has taken on the challenge of prequalifying generic antiretroviral agents. Using the agency’s accepted expertise, WHO has inspected the production facilities, manufacturing procedures, and bioequivalence data to develop a list of prequalified antiretroviral agents. As of December, several generic formulations, including fixed-dose combination products, were prequalified by WHO.

Other challenges facing secure drug acquisition and maintenance in-

clude the upswing in reports from various countries with respect to counterfeit drugs. Reports of drug diversion and theft are also increasing, often in association with the black-market sale of antiretroviral drugs.

An example of what can go wrong when drug acquisition and maintenance is not solidified can be found in a recent Nigerian imbroglio. In 2002, the Nigerian government agreed to provide 14,000 patients with generic antiretrovirals for less than \$8.30 a month. However, additional funds were not allocated in time to replenish the depleting stock and the country ran out of antiretrovirals in early 2004. “Some patients were forced to stop treatment,” Dr. Pau said. “Some centers gave out expired drugs and some centers with valid stock took bribery from patients to give out the drugs.”

Hurdles and Challenges: Patient Factors

HIV-INFECTED INDIVIDUALS LIVING IN DEVELOPING COUNTRIES FACE many hurdles that can limit access to HIV care and treatment. Poverty itself translates into lack of funds for basic necessities. It also tends to mean malnutrition and starvation; food supplementation may be part of a treatment strategy. Those living in poverty generally have little or no access to care and often lack basic transportation to medical facilities.

Poor living conditions are another mitigating factor. Many homes suffer from poor sanitation, with lack of clean water and evidence of sewage. Many homes are without electricity and, in a large number of developing countries, extreme heat can pose a significant challenge.

Personal and community belief systems can also hinder access to antiretroviral therapy and much-needed medical care. Many patients in developing countries use traditional and complementary medicines, seeking care from traditional healers rather than the formal medical system. “They use many different types of complementary medicines and herbal medicine,” Dr. Pau explained. “There’s a distrust of Western medicine. However, these practices will continue and efforts should be made to engage traditional healers in HIV care and to initiate research into the safety, effectiveness, and possible drug interactions associated with traditional medicines.”

Comorbidities also need to be considered. Coinfections with tuberculosis, malaria, hepatitis B, and parasites are not uncommon and can have a significant effect on antiretroviral treatment efficacy and safety if not properly addressed. High rates of anemia have been documented in various populations.

Antiretroviral Use in Developing Countries: Special Considerations

THERE ARE ADDITIONAL CONSIDERATIONS THAT NEED TO BE RECOGNIZED in developing and implementing antiretroviral treatment programs. Dr. Pau explained that culturally acceptable educational materials must be developed and made available to HIV-positive individuals, their partners, and their caregivers. “Many of the individual patients in the United States and other Western countries go to the internet and read about the antiretroviral agents,” she said. “They know more about these drugs than we do. But now we are going to be educating communities that know nothing about HIV, not to mention not knowing anything about why they have to take these antiretroviral drugs.” In this respect, there is a need for adherence counseling and it may be necessary to assess living conditions—such as drug storage needs and dietary conditions—prior to prescribing and dispensing therapy. “Some patients do not want to keep the drugs out in the open or in a place where people can see them. In turn, they hide them in a place that could be quite hot and damage the

medications.” Additionally, some antiretroviral treatment programs may want to consider treating all family members with the same antiretroviral regimen and schedule. There also needs to be equal access for men, women, and children, and programs should continue HIV prevention and vertical transmission prevention efforts.

There are also a number of educational needs among health-care providers and community workers. Adherence counseling is vital. Health-care providers and community workers also need to know how to effectively monitor antiretroviral therapy efficacy, recognize side effects and how best to manage them, understand potential drug interactions, and have the know-how and necessary tools to diagnose and treat AIDS-related opportunistic complications.

The 3 by 5 Initiative: Is It an Achievable Goal?

DOES DR. PAU BELIEVE THAT WHO/UNAIDS’S 3 BY 5 INITIATIVE IS AN achievable goal? “I guess I’m not that optimistic,” she demurred. “I don’t think it will be quite achievable. However, it has acted as a catalyst in terms of increasing funding as well as improving the overall infrastructure of the health-care system.” She also noted that developing countries must continue prioritizing their needs and the resources they can use for HIV care. Wealthier nations, along with non-government organizations, must continue their financial support and the pharmaceutical industry must sustain its commitment to developing nations, not only by offering drugs at lower prices, but also in continuing the development of easier-to-use agents—including better storage requirements—and fixed-dose combinations (see Capsules on page 2).

The potential benefits of increased access to antiretroviral therapy and health-care are notable to say the least. More widespread availability of these drugs can improve longevity of those living with HIV/AIDS and thus increase the “productive generation.” It may also contribute to public health, in terms of reducing the risk of HIV transmission. And looking at the larger picture, the successful implementation of these programs may improve the overall medical infrastructure for other diseases, increase literacy and education, and potentially improve the economy of the countries most affected. “We may fall short of the intended goal,” Dr. Pau said, “but we’re already seeing incredible improvements.” 

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