

# Massive Benefits of Antiretroviral Therapy in Africa

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(See the major article by April et al on pages 491–9.)

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One of the most positive, life-affirming, and transformational public health efforts in modern history is the US President's Emergency Plan for AIDS Relief (PEPFAR) [1–4]. This bilateral program (which involves the United States and individual partner nations) has had an unprecedented \$44.3 billion appropriated from the US Congress from fiscal year 2004 through fiscal year 2012 (as of 31 March 2013), including over \$7 billion to its multilateral partner, the Global Fund to Fight AIDS, Tuberculosis and Malaria [5]. Additional funds have been provided by other donor nations, typically through the Global Fund, and by national governments of low- and middle-income countries. These resources have gone toward the global effort to prevent human immunodeficiency virus (HIV) infection and to offer lifesaving antiretroviral therapy (ART)-based care to HIV-infected persons [6]. With its many partners, PEPFAR has directly supported >6 million persons, most in sub-Saharan Africa, among the >10 million persons estimated to have begun ART as of 2013. Since South African legal rulings and the

change in government in 2009, the Government of South Africa has been an enthusiastic partner—with its people and with the global community—making up for lost time in the effort to address the epidemic and cooperate with its neighbors in southern Africa [7–9]. No nation has a higher number of infected persons than South Africa, and the southern African nations have the highest prevalence of HIV infection in the world, ranging to over half of the adult population in certain venues and age groups [10]. The Government of South Africa, with support from PEPFAR and the Global Fund, has supported the Herculean efforts of health workers, activists, and patients to reverse the immense levels of HIV-related morbidity and mortality that filled its cemeteries and devastated societies and their economies [11].

In this issue of the *Journal*, investigators from the United States, South Africa, France, and Côte d'Ivoire describe use of the Cost-Effectiveness of Preventing AIDS Complications–International mathematical model (CEPAC) to estimate the lifetime per capita survival benefits of ART in South Africa, using data-driven assumptions and robust simulations [12, 13]. It was estimated that ART could extend the life spans of South Africans with HIV infection from 9.3 to 10.2 life-years, across the 8 simulated cohorts. The assumptions were based on real-world programmatic information, not theoretical benefits of more-idealized programs. April et al estimated the total

population lifetime survival benefit for all persons starting ART during 2004–2011 to be 21.7 million life-years, of which 2.8 million life-years (12.7%) had already been realized by the end of 2012. The authors' models include well-considered sensitivity analyses that suggest plausible “high-low” variability in their estimates. Estimates of infections averted because of lower infectiousness of HIV-infected persons with ART-induced viral load declines were not attempted by April et al, but their consideration could reflect still additional benefits of ART in preventing infections due to lower viral load and obviating the need for future ART in those protected persons [14–18].

The magnitude of the benefit of South African ART-based programs is astounding. Despite the political decisions made by a prior South African government to retard ART scale-up, South Africa's aggregate benefits from ART from 2004 to 2011 (8 years) are commensurate with the considerable benefits reported previously for the United States from 1989 to 2003 (15 years) [19, 20]. The South African burden of HIV disease is >5 times higher than that in the United States (5.6 million vs 1.1 million infected persons in 2012), although the US population is >6 times higher than that in South Africa (314 million vs 51 million in 2012). Hence, increasing coverage will increase South African years of life gained even further, a projection presented by April et al [12]. The authors estimate that benefits could improve to 28.0

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million life-years saved by 2030 if both improved linkage to care and universal second-line ART are provided.

There are myriad imponderables regarding future incidence rates. Will the incidence of HIV infection increase with new generations of sexually active persons who might not perceive HIV infection to be as serious as prior generations did? Or will evolving community norms for sexual behavior result in a declining incidence, as noted in Uganda and Thailand in the 1990s? Will HIV incidence decrease with the scaling up of combination prevention programs that are likely to have prevention benefits, such as medical male circumcision and treatment expansion at higher CD4<sup>+</sup> cell counts? Or will the incidence rise if donor nations start to scale back their donations for HIV drugs, programs, and laboratories?

Despite relatively low HIV testing and ART coverage, ecological associations from KwaZulu-Natal suggest that even modest coverage may reduce community-level transmission risks [21]. We do not know why most of southern Africa has experienced a decline in the incidence of HIV infection in recent years, but such changes would considerably modify the findings for 2012–2030 yielded by the CEPAC in the study by April et al.

More progress can be made by detecting infections earlier after onset, by expanding treatment coverage, and by increasing levels of treatment adherence. This optimism should be tempered with a historical perspective, to avoid past mistakes. During 1999–2008, South African government leadership had a both a president and a minister of health who doubted openly that HIV caused AIDS or that antiretroviral drugs were needed. In fact, the minister of health recommended nutritional interventions, including beetroot, garlic, lemons, beer, and African potatoes, in lieu of pharmacological interventions as “treatment” for immunodeficiency. The president, in turn, placed prominent HIV denialists, who supported him in justifying the denial of HIV testing services or ART-based care, on South Africa’s Presidential AIDS

Advisory Panel in 2002. Years of delay ensued, inhibiting support for program expansion for universal HIV testing, for prevention of mother-to-child transmission in antenatal clinics, for care of adults and children living with HIV, and for the prevention benefits that would have accrued to sexual partners of persons who could have been treated and had their virus load suppressed [22]. With successful legal challenges, a revolt within the president’s own cabinet, and protests from health providers, HIV activists, and even powerful labor union forces, presidential opposition was overcome, and ART was expanded in South Africa. The government in power since 2009 is led by a president and cabinet ministers who solidly support medical and public health interventions to reduce the incidence, morbidity, and mortality of HIV infection, using modern tools. Progress has been impressive, but we must remember how easy it is for political leaders to either block or boost progress.

The grim period of South African HIV-related antiscience reminds us of other periods in the often heroic but occasionally notorious history of the HIV/AIDS epidemic, a history still being made. On the notorious side are the dysfunctional policies of all too many national governments. Blood bank officials from the United States and France, among other countries, refused to implement logical screening strategies to protect the blood supply in the early 1980s. The US government did not fund needle/syringe exchange programs (NSP) until 2009 but then reinstated the ban on such funds in fiscal year 2012 via the Consolidated Appropriations Act of 2012 (HR 2055) [23]. Several nations in Eastern Europe and Central Asia, including Russia, have ongoing bans on both NSP and opiate substitution therapy, with a consequent rampant incidence of HIV infection among persons who inject drugs. In other countries (eg, Pakistan), no NSP bans are in place, but governments are ineffectual in deploying programs. The criminalization of vulnerable persons in such key populations (eg, men who have sex with men, sex workers, and persons who

inject drugs) leads to denial of lifesaving HIV prevention and care services in countries across the world, such as Uganda and Afghanistan. Another example involves health bureaucracy–associated delays in approving and implementing essential task-shifting activities that could involve health paraprofessionals and community workers in the fight against HIV/AIDS.

There is much talk of transition to local control of HIV programs. South Africa has already made huge progress in this regard. South Africans and global HIV/AIDS policymakers and donors can see how many life-years have been gained by investment in ART-related efforts [12]. Estimates of the numbers of orphans averted and infections prevented can follow. The global community has invested more into HIV prevention, control, and treatment than for any other single disease. The investment is paying off.

A final note concerns the issue of sustainability. Some nations (eg, South Africa and Botswana) will do better than others (eg, Zambia and Mozambique) in taking on the bulk of management responsibility for HIV services [24–26]. The history of infection control is riddled with examples in which progress was followed by premature withdrawal of global resources and subsequent rebounds in disease incidence. PEPFAR continues to face daunting challenges in areas such as scale-up, particularly in the care of orphans, destitute widows, and/or children living with HIV; loss to follow-up; HIV-tuberculosis program integration; and gender-power dynamics [27–32]. Implementation science research [33] can help determine why some programs struggle [34], why some succeed [35], and how to transform struggling programs into successful ones [36–38]. As the US Congress seeks to cut expenditures to balance budgets, we hope that the bipartisanship that has characterized the Bush and Obama presidential administrations from the inception of PEPFAR in 2004, to this writing in 2013, will continue to bolster this essential investment for the future of the African continent [39].

## Notes

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