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Ending AIDS: chimera or reality?

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The worldwide response to the epidemic of HIV ranks among the greatest scientific and public health achievements (1). In 1981 the Centres for Disease Control reported five deaths from what is now called HIV/AIDS. By 1983 the virus had been identified at the *Institut Pasteur*, two years later the genome of the virus had been fully sequenced, after another two years the first ELISA test for HIV had been licensed and in 1987 AZT, the first anti-retroviral drug, was approved by the Food and Drug Administration (USA). Drug development proceeded apace and by 1996 triple therapy was available at the cost of $10,000/yr. By 2006 the cost of first line therapy in developing countries had fallen to about $100/yr. A range of drugs is now available to treat HIV allowing infected people to live a normal life while remaining non-infectious to others with minimal side effects and resistance.

The key to controlling the epidemic has been the roll-out of anti-retroviral treatment (ART) which can reduce a person's viral load by 100 times within one month and by 10,000 times within one year (2). In 1996 (3) the International AIDS Society (IAS) recommended treatment for everyone with a $CD4^+$ cell count below 500/μL and in 2000 (4) included those with a viral load greater than 30k/mL with some flexibility at lower viral loads if the $CD4^+$ cell count was greater than 500/μL. Also in the year 2000 the Department of Health and Human Services (USA) (5) recommended treatment for everyone whose $CD4^+$ cell count was below 500/μL. In contrast to these ambitious recommendations, the World Health Organization (WHO) took a more cautious approach (6). With some *caveats* concerning clinical staging and AIDS related opportunistic infections, the WHO recommended starting treatment at $CD4^+$ cell counts below 200/μL in 2002, considering treatment below 350/μL in 2003, starting treatment below 350/μL in 2009, below 500/μL in 2013 and irrespective of $CD4^+$ cell count only in 2015. Waiting until an infected person's immune system was severely compromised before starting treatment resulted in low access to treatment and millions of avoidable infections, illnesses and deaths (7).

Building on the President's Emergency for AIDS Relief (PEPFAR), started by President George W. Bush (8), and with support from international donors and national governments, about 20 million people of the roughly 40 million living with HIV are now on life-saving ART (9) significantly reducing the incidence of new infections in many of the worst affected countries (10, 11). Trials of voluntary medical male circumcision (12) and pre-exposure prophylaxis (13) showed their potential for preventing transmission (14, 15) and mathematical models have demonstrated the feasibility of ending AIDS (16, 17).

However, a recent article in *Science* (18) suggests that the ambitious campaign to end AIDS by 2030 is off-track, that funding for efforts to slow the spread of HIV by treating all infected people has flat-lined, that some countries cannot or will not mount aggressive responses, that we will not meet the prevention goal and there is a prevention crisis. Others have warned against an increasing complacency in the response (19), and some have argued that the combination of drug resistance, demographic shifts and dwindling funds means that the world is at a critical juncture, forcing a collective reappraisal of strategies used to treat people and prevent the spread of the virus (20).

Prospects of epidemic control

We do not share the sense of pessimism around the HIV response and ending AIDS(16, 21, 22). Using trends in the rate of new HIV infections in eastern and southern Africa we have assessed the current state of the epidemic and the prospects for controlling it in many of the worst affected countries of eastern and southern Africa (11). If we let an incidence of 1 per 1,000 adults represent a *control threshold* then this has been reached, or will probably be reached, by 2020 in eastern Africa and is reachable by 2020 in those southern African countries that do not have particularly strong social and economic ties to South Africa if they continue to scale up their treatment programmes. In South Africa and its immediate neighbours Lesotho, Mozambique and Swaziland, the epidemic was particularly severe, and these countries are unlikely to reach the control threshold by 2020 but with sufficient political will and commitment to 'treatment for all' could do so by 2030 (11).

By 2005 Ethiopia had reached the control threshold, and Rwanda was not far behind. In Kenya and Uganda there was a period of stasis between 2000 and 2005, but in both countries, the incidence declined as ART was rolled out and they are on track to reach the control threshold by 2020. In Tanzania

the incidence of HIV has been in a steady decline since the year 2000, and they are also on track to reach the control threshold by 2020.

The epidemic of HIV has been greater in southern Africa than in eastern Africa, and all countries in this region are some way off reaching the control threshold. Botswana has a very effective HIV control programme and should reach the control threshold by 2020. Malawi has had a severe epidemic and is one of the poorest countries in the world, but their HIV programme has been a model for other countries in the region (23), and they are on track to reach the control threshold by 2020. In Namibia and Zambia there has been a slow, steady decline and they will have to scale up treatment more aggressively if they are to reach the control threshold by 2020. In Zimbabwe, the incidence has been falling steadily since the early 1990s (24) and continues to do so.

The situation in South Africa and the countries' most dependent on it is comparatively worse. Lesotho, which depends strongly on South Africa, had a very severe epidemic, primarily as a result of the migrant labour sent to work in the mines in South Africa (25, 26), and has had a high incidence for the last ten years. However, the incidence is falling, and Lesotho could reach the control threshold by 2025 if they aggressively scale up treatment. The epidemic of HIV in Mozambique started later and was less severe than in the rest of southern Africa, but the incidence has been in decline for the last ten years, and they too could reach the control threshold by 2025 if they aggressively scale up treatment. South Africa has had the biggest epidemic in the world and the country is still some way from the control threshold, but the decline in incidence has been steady. Swaziland had a very severe epidemic but the rapid scale up of ART suggests that they too could meet the control threshold by about 2025.

There are two important *caveats*. First, reaching the control threshold still leaves up to about 20 thousand new infections a year in eastern and southern Africa.(27) As the lesson of polio reminds us finding and treating the last 0.1% of the population that is infected each year, many of whom will be in marginalized and vulnerable populations, and making sure that they are on ART will remain a challenge and demand more focused and imaginative approaches to case finding, treatment and prevention. Additionally, ending HIV will depend on maintaining the roughly 40 million people currently infected with HIV on treatment for the next 30 to 40 years, when they will die of natural causes not related to HIV, unless and until a cure can be developed. Even assuming a modest cost of, say, US$ 100 per person per year for ART treatment and support, this corresponds to a continuing financial commitment of US$ 4 Bn per year, but this is substantially less than the approximately US$ 40 Bn per year currently committed to HIV and AIDS. What matters now is that we finish what we started and plan the response with care and commitment.

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