

## Trends in AIDS deaths, new infections and ART coverage in the top 30 countries with the highest AIDS mortality burden for 1990-2013

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Antiretroviral therapy (ART) prevents disease progression including tuberculosis (TB), mortality and HIV transmission and studies suggest that expanded access to treatment in some settings could lead to the eventual elimination of HIV. From 1995 to 2013, ART averted an estimated 7.6 million AIDS-related deaths globally, including 4.8 million deaths in sub-Saharan Africa (1,2). After the discovery of triple drug treatment for HIV in 1996 it became increasingly clear that earlier diagnosis and treatment is essential to prevent immune degradation and HIV transmission. Recognizing the benefits of earlier ART, the World Health Organization (WHO) issued HIV treatment guidelines in 2002, 2006, 2010 and 2013 that recommended progressively earlier ART initiation. In 2013 the recommendations were initiation of ART at CD4 count  $\leq 500$  cells/mm<sup>3</sup> for adults and adolescents. Additionally, they included “test and treat” criteria irrespective of CD4 count for pregnant women, HIV-positive partners in serodiscordant couples, children younger than five tuberculosis (TB) or hepatitis B coinfection (3). In 2015 the TEMPRANO and START trials confirmed observational data that suggested that waiting for a lower CD4 cell count increases the risk of adverse events including illness, death and transmission (4,5). WHO recently announced that it would issue guidelines that recommended initiating treatment irrespective of CD4 cell count later in 2015. Although access to treatment reached 15 million people by March 2015, we clearly need to reconsider business as usual to ensure access to life-saving treatment for the estimated 22 million people living with HIV not receiving ART (2).

Treatment has already had a major impact and in this short report we assess expanded HIV treatment for the prevention of AIDS-related deaths. We analyzed the available UNAIDS data in *AIDSinfo* (6,7), to describe AIDS-related deaths, ART coverage and new HIV infections in 30 countries with the highest AIDS mortality burden and compared it with data from eight high-income countries. For illustrative purposes, we also explored the potential impact of reaching international treatment expansion targets in South Africa and Nigeria - two countries with the largest HIV epidemics, but with different trends of AIDS-related deaths over time - through the examination of four treatment expansion

scenarios. The complete methods for our analyses are described elsewhere, including references to evidence cited here (8).

### *AIDS deaths in the top 30 countries*

Thirty countries accounted for 1.3 (87%) of estimated AIDS deaths in 2013. Sub-Saharan Africa and Asia and the Pacific are the regions with the highest numbers of AIDS-related deaths. Eight countries (Nigeria, South Africa, India, Mozambique, Tanzania, Zimbabwe, Uganda and Kenya) accounted for 58% of the global AIDS-related deaths in 2013. A table including the estimated deaths per 1000 people living with HIV for top 30 countries with the highest burden of estimated AIDS deaths in 2013 can be found in the original article (8). Of the 30 countries, Central African Republic (91 per 1000 people living with HIV), South Sudan (82 per 1000), Côte d'Ivoire (75 per 1000), Cameroon (72 per 1000) and Chad (71 per 1000) had the highest death rates. The largest number of estimated AIDS-related deaths in 2013 was in Nigeria and South Africa; the death rate was 65 and 31 per 1000 people living with HIV, respectively. A comparison of death rates for selected high-, low- and middle-income countries demonstrates significant higher death rates in South Africa (31 per 1000) and Nigeria (65 per 1000) when compared with countries in North America and Europe (~ 5-20 per 1000). A figure with the trends in estimated death rate per 1000 people living with HIV from 2011-2013 can be found in the original article (8). Between 2001 and 2013 the estimated annual death rate in Botswana decreased by 76% and approximates the rate for the United States. A number of countries achieved an “AIDS death to treatment tipping point” ratio of less than 1 whereby more people are put on ART than those estimated to be dying in a given year (Angola, Haiti, India, Malawi, Mozambique, Myanmar, Namibia, Tanzania, Uganda, South Africa, Zambia, and Zimbabwe).

### *AIDS-related deaths, new HIV infections and ART coverage in Nigeria and South Africa*

Nigeria and South Africa account for 27% of the global HIV burden and have the highest AIDS-related death burden. In 2013, new HIV infections in South Africa

and Nigeria were 340,000 and 220,000; the number of AIDS deaths were 200,000 and 210,000, respectively. There has been a significant decline in AIDS deaths in South Africa when compared with Nigeria. ART scale-up has progressed more slowly in Nigeria, especially between 2010 and 2013. In 2013, 42% of the people living with HIV were on ART in South Africa, compared to ART coverage of 20% in Nigeria. Between 1990 and 2013, ART has averted nearly 1 million and 0.4 million AIDS-related deaths in South Africa and Nigeria, respectively. A projection of estimated deaths in the *Current ART Coverage Scenario* suggests that maintaining the current levels of ART coverage through 2020 would avert 1.3 and 0.5 million deaths between 2014 and 2020 for South Africa and Nigeria, respectively, compared to the *No ART Scenario*. Compared to the *Current ART Coverage Scenario*, increasing ART coverage to reach the UN 90-90-90 Target (i.e. *90-90-90 Scenario*) would avert an estimated 2.2 million and 1.2 million deaths for South Africa and Nigeria, respectively.

#### *Re-thinking our current approach to preventing AIDS-related mortality*

The global community has made considerable progress in addressing this unprecedented epidemic. The estimated number of annual AIDS-related deaths has decreased 38% from 2.4 million in 2005 to 1.5 million in 2013. This reflects the decline in annual new HIV infections, which peaked at 3.7 million nearly a decade earlier (7). The decline also reflects the ART prevention impact on illness, death, transmission and costs; indeed, evidence is accumulating that people who access ART early in the course of HIV infection may live a near-normal lifespan. ART has other benefits including reducing the individual risk of developing TB by 65%, improving employment for individuals and preventing significant societal and health sector costs. Globally, access to treatment has expanded from thousands of people in 2000 to 15 million reported on ART in March 2015 (2). Although these gains are impressive, our analyses found very high death rates in many settings, low ART coverage, and significantly high rates of AIDS-related deaths. These findings are grounds for serious concern and for re-thinking our current approach to preventing AIDS-related mortality.

Each of the estimated 35 million people living with HIV will eventually need treatment for their own health, and the time from infection to ART eligibility is a matter of months to a few years. Access to ART is included in mortality estimates as it has a direct impact on an

individual's risk of death. Therefore, it is no surprise that where one lives often has a significant impact on your risk of death and life expectancy. We found significant variations in the regional burden of AIDS-related deaths, with sub-Saharan Africa and Asia and the Pacific encompassing 90% of the global HIV mortality burden. Eight countries, including only one outside of sub-Saharan Africa (India), account for over 50% of global AIDS-related deaths. Additionally, the top two countries account for 27% of global mortality. Our estimates illustrate the unacceptably high annual AIDS-related death rate in many geographic settings and the growing divide between those with and those without earlier access to life-saving ART. In some lower income countries, people living with HIV have 10 to 20 times higher death rates than those living in some higher income countries. Indeed, the stark differences in annual death rates between higher income countries in North America and Western Europe and lower income countries raise important ethical, equity and human rights issues. This is not only a "North-South" phenomenon—this disparity in annual risk of death also exists between some of the heavily burdened countries in low- and middle-income categories.

Treatment as part of the overall prevention solution to the HIV epidemic is critical. To turn the tide on the HIV epidemic and reduce the total number of people living with HIV, new HIV infections need to be prevented through improved access to a continuum of HIV services including ART. For successful HIV elimination, new infections reflecting the basic reproductive number ( $R_0$ ), or transmissions from a person living with HIV within their lifetime, will need to be below 1 and less than the annual number of people accessing treatment. In sub-Saharan African HIV epidemics the median value of  $R_0$  is 4.6 and in all but 5 countries  $R_0$  is less than 6.3. If the recently proposed UN 90-90-90 Target is achieved, this should reach elimination ( $R_0 < 1$ ) in 70% of all countries in sub-Saharan Africa and will reduce  $R_0$  to less than 2 in the remaining 12 countries, making elimination easy to achieve by other high-impact prevention methods. Our results highlight that an accelerated response including ART to decrease both mortality and transmission is needed to "turn off the tap" and move towards ending the epidemic.

Assuming a life expectancy of 10 years after HIV infection without ART, the estimated annual death rate would be about 100 people per 1000 living with HIV. Our examination of the two countries with the largest number of annual AIDS-related deaths highlights both

the marked geographic differences between our response and the grave implications of chronically inadequate ART coverage. South Africa has set ambitious targets (9), invested considerable resources, and has improved access to HIV testing and treatment for people living with HIV to reach nearly 42% ART coverage in 2013. In this setting of rapidly expanded access, the estimated number of AIDS-related deaths and new HIV infections are sharply declining. However, this is contrasted by the estimations for Nigeria, which suggest that while ART coverage is increasing slowly and remains below 20% and new infections are declining, the number of AIDS-related deaths is increasing. We project that South Africa and Nigeria could avert millions of deaths through the expansion of ART access, however, the number of deaths averted will directly depend on whether people living with HIV have earlier access to ART.

Nigeria and South Africa are not alone in their efforts to expand access to ART to avert illness, death and transmission. For example, although Botswana is heavily impacted by HIV and has one of the highest burdens of HIV globally with the 2003 HIV prevalence among women attending antenatal clinics estimated at 40%; in 2004 the prevalence was estimated at 28% in adult women and 20% in adult men. However, through the rapid expansion of access to HIV testing and ART, Botswana has reduced its estimated AIDS-related death rate nearly 75% to levels commensurate with the United States. Mortality rates among people living with HIV will be higher in countries that recommend that people defer treatment until they are severely immune-compromised below a CD4 count of  $<350$  cells/mm<sup>3</sup> and/or they present in clinic with an AIDS-defining illness(es). Reported and published national ART initiation guidelines for the 30 high-burden countries illustrate that although Brazil and Thailand recommend ART initiation irrespective of CD4 count, only 14 countries representing 49% of the global HIV burden have adopted the WHO 2013 ART initiation criteria (8,10).

Our study has a number of limitations including the paucity of data on AIDS mortality. However, our results are directionally consistent with recent estimate studies and show similar trends in AIDS deaths (11, 12). The strong relationship between ART coverage and the prevention of AIDS-related mortality is both logical and scientifically sound. Improving data collection regarding ART coverage for key populations would improve our ability to estimate progress towards

reducing the impact of HIV on incidence, prevalence and mortality.

The global response to the HIV epidemic has been remarkable and has averted millions of premature deaths. However, despite these impressive gains, our study illustrates the continuing significant negative impact of HIV. It also highlights the missed public health opportunity to expand access to earlier HIV testing and ART to avert millions of premature AIDS deaths and reduce new HIV infections, particularly in low- and middle-income countries.

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