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HIV infection remains a major problem for the world. Globally, there were over 35 million HIV-positive people in 2012, with 1.6 million people dying from the infection. South Africa has the highest number of HIV infections in the world: 6.3 million in 2013. Of these, 360,000 were children under 15, and 59% of the infected adults were women. About 200,000 people died of AIDS (the end-stage of HIV infection) and there were about 2.4 million under-18s orphaned due to HIV.

Effective treatment is possible, but maintaining current levels of prevention and treatment activities would mean that there would be significantly more sufferers by 2030. However, scaling up of interventions would put the epidemic into permanent, long-term decline. Taking into account future gains in income and economic productivity plus savings in healthcare spending, scaling up efforts globally could give benefits worth 15 times the investment by 2030.

There are two recommended targets to strengthen the fight against AIDS, and both are highly relevant to South Africa.

The first target is to increase the number of people treated with anti-retroviral therapy (ART), concentrating at first on those who are sickest (having the weakest immune systems). The normal measure of immune system strength is the CD4-cell count, and the aim is to treat 90% of people with CD4 count below 350 cells/µL (cells per microliter) with ART, before extending treatment to people with higher CD4 counts.

South Africa is currently implementing the most recent WHO (World Health Organization) guidelines on AIDS, which recommends extending ART to people with a cell count below 500 cells/µL. But coverage of those with weaker immune systems is still only about 61% and there is a strong case for concentrating on these patients first. The improvement to their health is greater and, since these individuals are significantly more infectious, treatment would help prevent further transmission.

Achieving 90% coverage of the target group of patients would give health benefits worth nine Rand for each Rand spent. This does not take account of economic benefits, which would make this treatment even more cost-effective.

A second target is to expand circumcision to include 90% of HIV-uninfected men. This has two main benefits, the first being to reduce HIV infection of men through heterosexual intercourse by 60%. After some delay, this also reduces rates of infection among women. One of the big advantages of circumcision is that it is a relatively cheap intervention which lasts a lifetime, unlike ART which means taking medicine for life.

Currently, fewer than a third of South African men are circumcised. However, over two thirds of uncircumcised men are willing to accept circumcision if it protects from HIV infection and other sexually transmitted infections. About the same proportion of mothers and fathers are also willing to circumcise their sons for the same reason.

Because the costs of circumcision are lower than extending ART, every Rand spent would pay back 24 Rand, not including indirect economic benefits. Extending ART would cost an additional $11 billion, while scaling up
circumcision would cost only $356 million. But both targets are very important and worthwhile. As for any large-scale public health program, there are significant challenges to implementation, but the results would certainly make this justified.
Key messages:

- A modeling exercise commissioned by the Joint United Nations Programme on HIV/AIDS (UNAIDS) found that if the current coverage levels of HIV prevention and treatment activities are maintained, the prevalence of HIV globally will be significantly higher in 2030 than it is currently (i.e., the HIV epidemic will again be on the rise).
- The modeling also found that if countries achieved UNAIDS’ ambitious new coverage targets for existing HIV prevention and treatment programs, new HIV infections and AIDS-related deaths will have decreased by 90% by 2030 compared to 2010.
- UNAIDS estimates that the benefits of investing in a scale-up of HIV prevention and treatment programs will have surpassed the investment costs by 15 times by 2030.
- We recommend increasing the coverage of male circumcision among HIV-uninfected men as the most cost-beneficial goal for South Africa to address the HIV epidemic in the period 2015 to 2030. Achieving this target would avert 685,000 HIV infections in South Africa by 2030, and 2.2 million HIV infections by 2050.
- Circumcision is a relatively cheap one-off intervention that lasts for life. In fact, the estimated cost of achieving 90% circumcision coverage among HIV-uninfected men in South Africa, and maintaining this coverage level until 2030, is only an additional $325 million (3.9 billion Rand).
- We also recommend increasing the coverage of HIV medicines (antiretroviral therapy or ‘ARVs’) first among those with the weakest immune system (CD4-cell count <350 cells/μL) before increasing coverage among healthier HIV patients.
Introduction

Thirty years after the human immunodeficiency virus (HIV) was first identified, the HIV epidemic continues to cause large-scale human suffering and economic losses. In 2012, an estimated 35.5 million people were living with HIV and 1.6 million people died of HIV/AIDS (UNAIDS, 2013); and, as of 2012, 17.8 million children lost one or both parents due to HIV (UNICEF, 2014). Economically, HIV is projected to continue to slow economic growth in sub-Saharan Africa, the region with the highest HIV burden, for many years to come (UNAIDS, 2005; Vasilakis, 2012). South Africa is one of the countries most heavily affected by the HIV epidemic in the world being one of the five so-called hyperendemic countries (i.e., countries with an adult HIV prevalence greater than 15%). According to the latest statistics by the Joint United Nations Programme on HIV/AIDS (UNAIDS) (UNAIDS, 2014a), 6.3 million people were living with HIV in South Africa in 2013, making South Africa the country with the largest number of HIV-infected people in the world. Of these, 5.9 million were adults aged 15 years and older and 360,000 were children younger than 15 years. More than half (59%) of HIV-infected adults in South Africa are women. Approximately 200,000 people died of AIDS, the end-stage of HIV infection, in South Africa in 2013 and the country has approximately 2.4 million orphans younger than 18 years due to HIV (UNAIDS, 2014a).

Goals for HIV for the post-2015 development agenda

The Copenhagen Consensus Center’s Post-2015 Consensus effort includes two analyses that focused on HIV/AIDS, one by a team at the Harvard T.H. Chan School of Public Health (Geldsetzer, Bloom, Humair, & Baernighausen, 2015) and one by a team at UNAIDS (Ghys & Izazola-Licea, 2015). Ghys and Izazola-Licea at UNAIDS point out that recent modeling commissioned by the organization has shown that if the current coverage levels of HIV prevention and treatment activities are maintained, the prevalence of HIV will have risen by 2030. On the other hand, if the coverage levels of existing HIV prevention and treatment efforts and of new interventions, such as pre-exposure prophylaxis, are scaled up, the HIV epidemic will have undergone a permanent and long-term decline. From an economic perspective, this results in the important conclusion that investing in HIV prevention and treatment efforts now will save costs in the future. In fact, Ghys and Izazola-Licea point out that preliminary analyses are showing that if gains in income and economic productivity, and in savings from medical care spending, are taken into account, the benefits of investing in a scale-up of HIV prevention and treatment targets surpass the investment costs by 15 times by 2030. UNAIDS’ recommended goals and coverage targets can be found in Table 1 on page 4 of Ghys and Izazola-Licea’s Viewpoint Paper at http://www.copenhagenconsensus.com/sites/default/files/health_hiv_aids_viewpoint_-_ghys_izazola_0.pdf.

Both the Harvard and UNAIDS team agree that there should be a focus of resources and efforts for HIV prevention and treatment on those countries that are most heavily affected by the HIV epidemic. Ghys and Izazola-Licea, however, also point out that there is a need for global solidarity in the fight against HIV whereby countries are responsible for financing their HIV response according to their gross domestic product (GDP). Thus, low-income countries are likely to require significant funding from international sources for their national HIV response while upper middle-income countries, such as South Africa, should increasingly ‘wean off’ international funding for HIV.

In addition, both the Harvard and the UNAIDS team recommend that coverage of male medical circumcision should be increased in HIV high prevalence countries, including South Africa. In particular,
Geldsetzer et al. propose two goals to address the HIV epidemic in high prevalence countries, such as South Africa, for the period 2015 to 2030:

Goal 1: Focus on increasing coverage with HIV medicines (antiretroviral therapy or ‘ART’) first on the sickest (i.e., those with the weakest immune system) before increasing coverage amongst healthier HIV-infected people. The CD4-cell count is a measure commonly used to measure the strength of an HIV-infected person’s immune system. Thus, this goal specifies to achieve ART coverage of at least 90% among HIV-infected adults with a CD4 count <350 cells/μL before expanding the HIV treatment scale-up to people with higher CD4 counts.

Goal 2: Attain male circumcision coverage of at least 90% among HIV-uninfected adult men.

What is the rationale for Goal 1 (increasing coverage of ART)?

Since the advent of antiretroviral drugs, the World Health Organization (WHO) has gradually increased its recommended threshold for starting patients on antiretroviral therapy (ART) to include increasingly healthy patients. WHO treatment thresholds are based on the CD4 count, a cell count that decreases in concentration with deteriorating immune system function. In 2006, the WHO issued a recommendation that patients with a CD4 count <200 cells/μL should be started on ART (WHO, 2006). In 2010, this threshold was increased to <350 cells/μL (WHO, 2010) before it was further increased to <500 cells/μL in 2013 (WHO, 2013). South Africa is currently in the process of implementing the WHO 2013 guidelines. These increases, while not without controversy, were based on evidence that earlier ART benefits patients’ health. In 2011, a clinical trial, hailed as a game changer in the HIV field, provided evidence for even earlier initiation of ART. It showed that providing ART early in the course of the disease reduces the chance of an infected person passing HIV to an uninfected partner by 96% (Cohen et al., 2011). Similarly, at the population level, researchers at the Wellcome Trust funded Africa Center for Health and Population Studies found that increasing ART coverage in the general community in rural KwaZulu-Natal is associated with a reduced risk of HIV acquisition (Tanser et al., 2013), strengthening evidence that led to calls for using HIV treatment as prevention. Currently, several large ongoing trials aim to establish the effect of providing ART to all HIV patients regardless of CD4 count, i.e. treatment as prevention, when implemented at the population level in sub-Saharan Africa (Essex, DeGruttola, Lebelonyane, & Habibi, 2013; Havlir & Kamya, 2013; Hayes et al., 2014; Iwuji et al., 2013; Stop AIDS Now!, 2014), including one trial in KwaZulu-Natal (Iwuji et al., 2013).

In an utopian scenario of unlimited resources, few would dispute that all HIV-infected individuals should be offered treatment regardless of the strength of their immune system given the current evidence base for providing treatment early in the course of the infection. However, in the real world where financial and human resources are limited, countries in sub-Saharan Africa, including South Africa, are still far from reaching universal treatment coverage among those with lower CD4 counts. As of 2012, only an estimated 61% of all HIV-infected individuals with a CD4 count <350 cells/μL and 34% of those with a CD4 count <500 cells/μL were receiving ART in sub-Saharan Africa (UNAIDS, 2013), in part because only about half (48%) of those infected with HIV know their status (UNAIDS, 2014b). Compared with providing ART only to those with a CD4 count <350 cells/μL, treatment as prevention would roughly double the number of treatment-eligible patients in hyperendemic countries (UNAIDS, 2013, 2014b). Given that antiretroviral medications are expensive, treatment as prevention would undoubtedly require very large additional financial investments. Using a discount rate of 3%, an estimate indicated that implementing treatment as prevention in South Africa would have costed an additional US$11.8 billion in 2009 over the following 12 years as compared with maintaining the current coverage level of ART (Bärnighausen, Bloom, and Humair, 2012a). This raises a fundamental question about resource
allocation in hyperendemic countries: Should treatment as prevention be implemented immediately, or should resources be targeted first at the unfinished agenda of achieving universal coverage among those most in need of treatment before offering ART to those with stronger immune systems? We recommend the latter approach for two main reasons.

The first reason is that providing ART to an individual with a weak immune system is, on average, more cost effective than offering treatment to a patient with a stronger immune system because the weaker a patient’s immune system is, the more dramatic is their health status improvement with ART. Additionally, the preventive effect of ART is higher among those with a weaker immune system because, with the exception of a very early acute infection stage lasting one to four months, patients with CD4 <200 cells/μL (i.e., a very weak immune system) are significantly more infectious than those with a stronger immune system (Hollingsworth, Anderson, and Fraser, 2008). Thus, by providing ART to those with a weaker immune system (CD4<350 cells/μL) before gradually offering it to healthier HIV-infected patients, South Africa would get the ‘biggest bang for the buck’ before the country incrementally rolls out ART to all those who need it.

The second reason for a gradual rollout of ART from sickest to healthiest patients is that implementing treatment as prevention immediately may lead to a “crowding-out” effect whereby healthier patients may prevent sicker ones from receiving treatment (Bärnighausen, Bloom, and Humair, 2014; Bärnighausen, Humair, and Bloom, 2012b). Such a crowding-out effect arises when human (e.g., nurses and physicians), financial, or physical resources (e.g., the number and location of healthcare facilities) are insufficient to provide ART to all eligible HIV-infected people. In this case, providing ART to a somewhat healthy patient may imply that a less healthy patient cannot receive the life-saving treatment. Several mechanisms can generate crowding-out effects. Sicker patients are physically weaker and are therefore, on average, less able to travel to the next HIV clinic and wait, often for hours, to be seen by a health worker than their healthier peers. Similarly, patients in more advanced stages of HIV disease are less likely to be employed than patients in earlier stages of the disease. They may therefore be less able to afford the out-of-pocket expenditures associated with treatment, such as for transport. Crowding-out effects are not only highly undesirable based on cost-effectiveness reasoning but also based on ethical grounds; they would violate most conceptions of fairness in access to health care. Offering ART to people in earlier stages of HIV disease only when all, or nearly all, people in more advanced disease stages are receiving treatment will prevent crowding-out effects.

What is the rationale for Goal 2 (increasing coverage of circumcision)?

If effectively implemented, male medical circumcision is plausibly a highly cost-beneficial intervention to address the HIV epidemic for several reasons. First, circumcision has been shown to be effective in preventing new HIV infections: three large clinical trials conducted in South Africa, Kenya, and Uganda have shown that circumcision reduces HIV infection by men through heterosexual intercourse by 60% (Auvert et al., 2005; Bailey et al., 2007; Gray et al., 2007). Second, while circumcision targets men, after some delay, rates of infection in women also reduce substantially as fewer of their sexual partners are infected. Third, circumcision is a one-off intervention that lasts for life (in contrast to, e.g., antiretroviral drugs that have to be administered continuously). Fourth, the implementation costs of circumcision will be comparatively low as the procedure does not require expensive equipment or medications and does not necessarily require a physician or surgeon (WHO, 2008). Fifth, great potential exists for scaling up circumcision in hyperendemic countries and sub-Saharan Africa as a whole. In 2007, the WHO and UNAIDS selected 13 African countries to scale up circumcision to 80% of HIV-uninfected men between
the ages of 15 and 49 years by 2016. These countries collectively only reached 28% of this target by the end of 2013, with only Nyanza province in Kenya (85% of target reached) achieving more than 50% of the target (WHO, 2014). South Africa, which is one of these priority countries, only reached 31.8% of this target. Yet, the level of acceptability of circumcision is encouraging with a review finding that a median of 65% of uncircumcised men in sub-Saharan Africa are willing to be circumcised (Westercamp and Bailey, 2007). The acceptability of circumcision is also high in South Africa where Lagarde et al. found that, in the Westonaria district, 73% of uncircumcised men were willing to be circumcised if it protects from sexually transmitted infections (STIs) and HIV. In addition, 47% of respondents thought that women preferred circumcised men and 71% of non-circumcised fathers, 82% of circumcised fathers and 70% of mothers were willing to circumcise their sons if it protects from STIs and HIV (Lagarde, Dirk, Puren, Reathe, & Bertran, 2003). Similarly, two further studies found that 51% of uncircumcised men in KwaZulu-Natal and 59% of uncircumcised men in a South African township were willing to be circumcised (Rain-Taljaard et al., 2003; Scott, Weiss, & Viljoen, 2005).

The costs and benefits of achieving each goal

We designed a mathematical model to calculate the cost-benefit of each of these goals for South Africa. Both Goal 1 (90% ART coverage among those with a weak immune system) and Goal 2 (90% circumcision coverage) were cost-beneficial, meaning that the benefits in dollars or Rand are higher than the costs. The benefit in dollars is calculated by attaching a money value to each life year that is gained. For the purposes of this analysis, we used $3,000 or $5,000 per life year gained, which is a commonly used “value of life” in the field of health economics. In addition, of course, there are economic benefits to reducing HIV disease. For example, Bor et al. have found that patients in rural KwaZulu-Natal who were on HIV treatment (ART) had nearly full recovery of employment as compared to their employment status three to five years before they started treatment (Bor, Tanser, Newell, & Bärnighausen, 2012). We did not take these “indirect” economic benefits into account in our analysis; if we had done so, the results would have shown an even higher benefit of the interventions.

If South Africa was to achieve 90% ART coverage among those with the weakest immune system, the estimated benefit would be nine Rand for every Rand spent. The benefit-to-cost ratio is considerably higher for achieving 90% circumcision coverage, for which the benefit by 2030 is 24 Rand for every Rand spent. It is important to bear in mind that the benefits of achieving each goal increase, and the costs decrease, over time as the course of the HIV epidemic is altered favorably by these interventions in the long-term. Indeed, achieving the circumcision coverage would avert approximately 685,000 HIV infections by 2030 and 2.2 million HIV infections by 2050. Similarly, achieving the circumcision target would prevent 31,000 AIDS-related deaths by 2030 and 71,000 AIDS-deaths by 2050.

The main reason for the higher ‘bang for the buck’ of the circumcision target is that circumcision is a relatively cheap one-off procedure, while ART is a continuous healthcare service, which entails expensive long-term medications. Compared with maintaining current coverage levels of ART and circumcision, the additional cost of scaling up circumcision is only about US$356 million, while the additional cost of scaling up ART is US$11 billion, which is roughly double the cost of maintaining the current coverage levels of ART and circumcision in South Africa. Increasing the circumcision coverage, however, would only require an additional 3% investment. However, scaling up ART for those with the

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1 This is the median value of the four benefit-to-cost ratios calculated using $1000 and $5000 per disability-adjusted life year, and discount rates of 3% and 5%.
weakest immune systems (CD4-cell count <350 cells/μL) is also a highly cost-beneficial intervention and, in our view, an important goal for HIV and AIDS for South Africa for the period 2015 to 2030.

However, both of our goals, as is the case with any large-scale public health program, face significant implementation challenges. To successfully increase ART coverage, we recommend extensive facility- and community-based HIV testing programs and the scale up of innovative measures to improve retention across the entire HIV care cascade. To increase coverage of circumcision, the South African government should increase funding for both circumcision programs and demand creation. Simultaneously, national circumcision programs should focus on service efficiency through streamlining clinical procedures and task shifting to lower healthcare cadres without significantly compromising on quality of care.
References


