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Pre-exposure prophylaxis and antiretroviral therapy for HIV prevention in South Africa – which is the best use of resources?

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HIV in RSA still a major concern - more interventions for HIV control available

An estimated 1.6 million new HIV infections occurred in 2012 in sub-Saharan Africa (1), highlighting the need for continued investments in HIV treatment and prevention efforts. With an HIV prevalence of about 18%, South Africa (RSA) remains a particularly affected country, despite sustained investments in HIV control programs such as expansion of antiretroviral therapy (ART). In recent years, scientific innovations in HIV control have expanded the range of available interventions – male circumcision, topical microbicides, oral pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP) have all sparked significant interest due to their potential effectiveness (ART reduces HIV transmission by up to 96%, PrEP by more than 60%) and versatility (circumcision is effective without additional actions required from the person, PrEP is meant for use by uninfected individuals, ART is given to infected individuals). While all these options are potentially available, resources remain limited and choosing which interventions to implement at scale is a difficult task, given the complex nature of disease transmission, the impact of behaviour in epidemic dynamics (number of partners, rates of condom use, adherence to treatment/prevention regimens), and the different costs of these programs.

The effects of scaling up ART and PrEP in RSA, alone and in combination

Our recent paper in BMC medicine (2) analyzes the effects of scaling up PrEP and ART for HIV prevention in South Africa, to help decision makers understand how these interventions would work if considered independently or in combination.

PrEP is an HIV prevention intervention in which an uninfected individual takes an oral fixed dose combination of tenofovir disoproxil fumarate and emtricitabine daily. Clinical trials have demonstrated that PrEP can reduce the chance of acquiring HIV by 63% to 73%, in both heterosexuals (3,4) and men who have sex with men (5). Some concerns, however, were raised in two different trials in African women, where study arms were terminated for lack

of effectiveness, most likely attributed to low adherence to the recommended regimens (6,7).

ART is given to infected individuals, and it has significant health benefits in terms of both quality and length of life – if adherent to medication, infected individuals can live relatively healthy lives. ART also reduces the viral load of the infected person, reducing the likelihood they will transmit the disease via a risky sexual contact. In 2011, the HPTN052 clinical trial quantified the additional prevention benefit of ART, showing that HIV transmission is reduced by up to 96% (8). Recently, the World Health Organization has recommended that HIV infected individuals start treatment earlier in the course of the disease (before CD4 cell count, a marker of HIV progression, falls below 350 cells/ μ L), to reap as many of the health and prevention benefits of ART as possible (9). As of 2013, South African guidelines support ART initiation only for those in later disease stages (CD4 count below 350 cells/ μ L), and it is unclear when implementation of earlier access will happen (10).

A mathematical model to project the HIV evolution in RSA under various scenarios for intervention scale up

In our research, we developed a mathematical model of the HIV epidemic in South Africa, based on epidemic characteristics available from scientific literature. We used our model to measure the impact of scaling up PrEP, alone or in conjunction with ART scale up. For ART, we considered a policy that allows only those with advanced disease to be eligible for treatment (current guidelines), and a broader policy that allows any individual diagnosed with HIV to start treatment immediately (universal treatment). For PrEP, we considered broad use in the general population, to get a quantitative measure of the maximum impact such a program could have, and also more narrow use in individuals at higher risk of acquiring HIV due to lower condom use and higher number of partners (focused PrEP). The latter may be a more feasible program to implement given the practical challenges of reaching a large number of healthy people and getting them to take a daily medication. We also considered various combinations of these programs, to evaluate the results that could be obtained by scaling them up in

parallel. To compare the different combinations, we looked at the infections that could be averted over 20 years, as well as the quality adjusted life years that could be gained (a measure of both how much longer individuals live, and how much better). We also evaluated the costs of the programs, to understand how to best use the limited resources available for HIV control.

Scaling up ART to all infected individuals should be a priority in South Africa

We found that if only one program can be implemented, then universal ART (“test and treat”) is the most effective, and could avert up to 4 million new infections over 20 years. In comparison, scaling up ART by the current guidelines averted only half as many infections. Offering PrEP broadly averted 3.4 million infections, followed closely by focused PrEP with 3.1 million. Hence, most of the benefits can be obtained by accurately targeting PrEP to a small proportion of the adult population (about 10%) who is at higher risk of HIV acquisition. The combinations of PrEP and ART averted more infections than implementing each program alone, but the total benefits were less than the sum of both, since we cannot avert the same infection twice (for example, by offering PrEP to the uninfected partner and ART to the infected partner in a serodiscordant couple only one infection is averted).

Perhaps the most relevant part of our findings are the relative costs and benefits of the programs we considered, when compared to simply continuing with the current HIV control policies in place in South Africa. If high risk individuals can be reliably identified and recruited into a PrEP program, then focused PrEP can be a cost saving intervention, meaning that we would spend less money over 20 years than if we simply continue with the current policies. If, however, such a program is not feasible in practice (for example, if it is too difficult to identify and retain high risk individuals in the focused PrEP program), then ART is the preferred alternative. For the most efficient use of funds, we would prioritize scaling up ART as much as possible, and only after that we would consider offering PrEP on a broader scale. When comparing universal ART with guidelines ART, we found that offering ART more broadly has better returns on investment, since the additional costs of scale up are offset by the benefits of having more infected individuals on treatment, which reduces a large proportion of the new HIV infections they could be causing. These results hold even when looking over shorter timeframes (10 years). Our work supports the

importance of continued HIV control efforts in South Africa, and provides insights into the prioritization of scaling up ART and PrEP, given the limited resources available.

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