

PERSPECTIVES PAPER

The Use of Antiretroviral Therapy for the Prevention of New HIV infection in Populations at High Risk for HIV Sero-conversion in Nigeria

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Abstract

The last few years have witnessed a renewed commitment to HIV prevention. The evidence to support the use of antiretroviral therapy (ART) for prevention of new HIV infection in the form of Pre-exposure prophylaxis (PrEP) among men who have sex with men, transgender, people who inject drugs, heterosexual men and women and HIV-1 serodiscordant couples, or treatment as prevention (TasP) for serodiscordant couples have also grown. The need to explore the possible use of ART for HIV prevention in Nigeria has become imperative in view of its high HIV burden and the current slow pace of effort to achieve the universal target of reducing its HIV incidence by 50%. While PrEP and TasP are welcome addendum to the existing HIV prevention armamentarium, it is still important to conduct a demonstration project to identify strategies that can facilitate access to PrEP and TasP taking cognizance of the peculiar local challenges with respect to ART and HIV prevention commodity access. The country has therefore drawn a roadmap for itself on how to introduce ART for use for HIV prevention as either PrEP or TasP. This paper discusses the three year national roadmap that would enable the country generate the needed scientific evidence as well as extensive community support for use of ART for HIV prevention in Nigeria. This process includes the conduct of modeling and formative studies, and the implementation of a 24 months demonstration project. The outcome of the demonstration project would inform plans for the scale up of pre-exposure prophylaxis (PrEP) access for population(s) at high risk for HIV infection in Nigeria. (*Afr J Reprod Health* 2014; 18[3]: 127-134)

Keywords: Pre-exposure Prophylaxis, Nigeria, HIV, Prevention, Antiretroviral, Risk, treatment

Résumé

Les dernières années ont été marquées par un engagement renouvelé à la prévention du VIH. La preuve à l'appui de l'utilisation de la thérapie antirétrovirale (TAR) pour la prévention des nouvelles infections du VIH dans la forme de la prophylaxie de la pré-exposition (PPrE) chez les hommes qui ont des rapports sexuels avec des hommes, les transgenres, les personnes qui s'injectent des drogues, les hommes hétérosexuels et les femmes et les couples séro-discordants VIH-1, ou le traitement comme la prévention (TcP) pour les couples séro-discordants ont également augmenté. La nécessité d'étudier l'utilisation possible de la TAR pour la prévention du VIH au Nigeria est devenu impératif en vue de son fardeau du VIH qui est élevée et la lenteur actuelle des efforts pour atteindre l'objectif universel de réduire l'incidence du VIH de 50%. Alors que la PPrE et le TcP sont des bonnes addenda pour l'arsenal de la prévention du VIH existant, il est toujours important de mener un projet de démonstration pour identifier les stratégies susceptibles de faciliter l'accès à la PPrE et le TcP compte tenu de la connaissance des enjeux locaux particuliers à l'égard de la TAR et l'accès à la prévention de la marchandise du VIH. Le pays a ainsi élaboré une carte routière pour lui-même sur la façon d'introduire la TAR pour une utilisation pour la prévention du VIH soit la PPrE ou le TcP. Ce document traite de la carte routière nationale de trois ans qui permettra au pays de générer les preuves scientifiques nécessaires ainsi qu'un vaste soutien de la communauté pour l'utilisation de la thérapie antirétrovirale pour la prévention du VIH au Nigeria. Ce processus comprend la conduite de la modélisation et des études de formation, et la mise en œuvre d'un projet de démonstration de 24 mois. Le résultat du projet de la démonstration influence des plans pour la mise à l'échelle de la prophylaxie de la pré-exposition (PPrE) à l'accès pour la population ou les populations à risque élevé d'infection du VIH au Nigeria. (*Afr J Reprod Health* 2014; 18[3]: 127-134)

Mots clés: prophylaxie de la pré-exposition, Nigeria, VIH, prévention, antirétroviral, risques, traitement

Introduction

Global access to treatment for people living with HIV infection has improved significantly in the

past few years. However, during this same period, millions of people have newly become infected and known HIV prevention efforts have failed to stem the epidemic. Unless the influx of new

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infections is slowed, governments will be less able to provide care to those in need, and AIDS will continue to have a devastating effect on individuals, families, communities and nations.

Due in part to these concerns, as well as to the growing realization that AIDS is a long-term condition rather than a short-term emergency, the last few years have witnessed a renewed commitment to HIV prevention. This commitment has increasingly focused on developing new biomedical, behavioral and structural approaches to preventing HIV transmission and implementing proven approaches in combinations that are tailored to specific epidemiological and social contexts.

Over the past four years, five large-scale clinical trials designed to evaluate the use of ARVs for HIV prevention have provided strong evidence of effectiveness, and for the first time, the goal of ending AIDS epidemics in some locales and, in time, the world seems possible. Achieving this, however, depends on sufficient and sustained political will and the availability of resources. In one of these studies, the iPrEX trial, daily use of Truvada as pre-exposure prophylaxis

(PrEP) reduced sexual HIV acquisition by 44% in a population of gay men, other men who have sex with men (MSM) and transgender women who have sex with men—all of whom were at high risk of HIV¹. Also, the Partners PrEP study showed a 75% reduction in HIV incidence in heterosexual serodiscordant couples where the HIV-negative partner used PrEP²; and the TDF2 study showed a 62% reduction in HIV acquisition in heterosexuals³. The use of tenofovir for the prevention of HIV infection in people who inject drugs has been proven effective and showed a 49% reduction in HIV acquisition⁴. Table 1 provides an overview of the various trials that provide evidence for the use of antiretrovirals for the prevention of HIV infection.

Also, when early, continuous ARV treatment was used by HIV-positive sexual partners in serodiscordant relationships, HIV transmission reduces by 96%. This strategy is known as “treatment-as-prevention (TasP)”⁵. Prior evidence for the efficacy of ARV treatment for prevention of HIV infection was established by Donell et al⁶ where ART reduced HIV transmission in HIV serodiscordant couples by 92%.

Table 1: Human efficacy trials of use of oral Pre-exposure prophylaxis

Study name (location)	Population	No	PrEP Agent	Status
iPrEx ¹ (Brazil, Ecuador, Peru, South Africa, Thailand, US)	Men who have sex with men and transgender women	2,499	FTC/TDF	44% efficacy
Partners PrEP Study ² (Kenya, Uganda)	HIV serodiscordant couples	4,758	TDF, FTC/TDF	67% efficacy for TDF 75% efficacy for FTC/TDF
TDF2 Study ³ (Botswana)	Heterosexual men and women, ages 18–35	1,200	FTC/TDF	62% efficacy
Bangkok Tenofovir Study ⁴ (Thailand)	People who inject drugs	2,400	TDF	49% efficacy
FEM-PrEP ²⁵ (Kenya, South Africa, Tanzania)	Higher-risk women	1,950	FTC/TDF	Stopped for lack of efficacy April 2011
VOICE ²⁶ (South Africa, Uganda, Zimbabwe)	Women	5,021	TDF FTC/TDF	Oral TDF stopped for lack of efficacy September 2011 FTC/TDF showed no efficacy

PrEP and TasP are now among the most promising strategies for dramatically reducing the spread of HIV-1⁷. The effectiveness of TasP is based on the ability of ART to reduce the concentration of HIV-1 in plasma, and seminal and cervicovaginal⁸⁻¹¹ secretions to undetectable levels in the majority of patients within six months of initiation of therapy^{12,13}. Since the primary determinant of

HIV-1 transmission risk is the viral load (concentration of HIV-1) in plasma^{14,15}, reducing the viral load in both plasma and genital secretions (including semen) reduces the risk of HIV-1 transmission to sexual partners^{16,17}.

The efficacy of ART in preventing vertical transmission of HIV-1 has been well established. The provision of peri-partum zidovudine to

pregnant HIV positive women¹⁸, and the provision of post-natal ART to infants who are continuously exposed to HIV-1 through breast milk, is a globally accepted form of ARV-based PrEP¹⁹. Its success inspired the idea that antiretroviral prophylaxis could also be highly efficacious for preventing infection in the context of known and ongoing HIV-1 exposure²⁰. Multiple animal studies also provided evidence suggesting that ART could be used to prevent HIV-1 acquisition among those regularly exposed to the virus. Macaque SHIV challenge studies and humanized mouse HIV-1 challenge studies²¹ showed high levels of protection from daily oral dosing of tenofovir and Truvada. There is potential for greater protection from a Truvada, combination of FTC/TDF than with Tenofovir (TDF alone)^{22,23}. These data elated the HIV prevention field, and models now suggest that combining these strategies could dramatically reduce rates of HIV transmission before an HIV vaccine is discovered. A mathematical model by WHO showed the potential of ART to substantially reduce population-level HIV-1 incidence when administered through near-universal annual HIV-1 testing, linkage to care, and uptake of ART, regardless of CD4 count (together called the 'Test and Treat' or 'Test and Linkage to Care' concept)²⁴.

Within this cascade of positive trial results were two that did not demonstrate a benefit of daily use of ART as PrEP for HIV prevention among women. These were the FEM-PrEP and VOICE trials. In FEM-PrEP²⁵. The failure of Truvada to confer protection from HIV infection in these trials was linked to poor adherence to the use of study products which may be due to the low perception of risk for HIV infection despite the high HIV incidence²⁵⁻²⁷. The possibly of drug tolerability²⁸, and poor drug penetration into vaginal tissues²⁹ had also been allude to. Biological plausibility have also been suggested such as diminished protected effect of TDF-FTC in the presence of high viral load in the infecting partner as may occur in the acute phase of HIV infection²⁵; or the lack of efficacy of TDF-FTC is a high cytokine level²⁵.

The oral Tenofovir arm of the VOICE study also did not demonstrate a protective effect and

was subsequently stopped as futile³⁰. The arm of the VOICE trial studying the impact of daily oral Truvada was continued to completion. The results presented in early 2013 showed that daily oral Truvada was not effective due to poor adherence, since the drug was only detectable in less than a quarter of participants assigned to the treatment group²⁶.

The FEM-PrEP and VOICE studies suggest that the simple provision of PrEP to women is not sufficient to achieve effectiveness. Adherence during the period of use is critical and accurate assessment of the intervention's effectiveness is impossible if the drug is not taken as prescribed. In Africa, ART adherence has been excellent³¹ among individuals with advanced disease whose families are dedicated to supporting their treatment regimen. This day to day support enables people to overcome the severe structural and economic barriers to adherence that many experience. It tends to be sustained because families witness the dramatic functional improvement in the individual's health as a result of ART adherence. It is unclear whether HIV negative individuals (in the case of PrEP) and asymptomatic HIV positive people (in the case of TasP) and their families will share the same commitment to adherence when ART is prescribed to apparently healthy individuals who do not visibly benefit from it in the short term.

The need for use of PrEP and TasP in Nigeria

The impact of proven interventions might vary from place to place because the HIV epidemics have different features. In Nigeria, the HIV epidemic showed regional and population variability. While the 2010 ANC sentinel survey report shows that the national HIV prevalence is 4.1%, some states had HIV prevalence above 10.0% while others had prevalence below 2.0%. Also, while the national HIV prevalence was higher in urban (4.8%) than in rural (2.6%) areas, in some rural areas, the HIV prevalence as high as 21.3%³². Within the general community, variations were also observed. In the general population HIV prevalence is 3.4%³³. Specific population HIV prevalence ranged from 27.4% for non-brothel based female sex workers to 17.2% for men who

have sex with men (MSM) and 4.2% for people who inject drugs³⁴. Even within communities, the prevalence differs. For example, within the community of people who inject drugs, females are 7 to 33 times more likely to be HIV positive than males³⁵.

Because of the foreseeable challenges associated with PrEP use in the general population, its use will likely be limited to those in well-identified HIV high risk groups. A substantial fraction of new infections, for example, occur within stable serodiscordant marital or cohabiting relationships³⁶. A PrEP study called Partners in Prevention, for example, showed that in the absence of ART (either in the form of PrEP or TasP) but with continued access to HIV-1 testing with counseling before and after testing, individual and couples risk-reduction counseling, screening and treatment for sexually transmitted infections, free condoms with training and counseling, and referral for male circumcision and post exposure prophylaxis, the HIV incidence among serodiscordant couples was 1.99 per 100 person years³⁷. This is significantly higher than the rate of 1.15 per 100 person years found in the general population in one of the two countries involved with the Partner's PrEP study³⁸. In Nigeria, about 7.7% to 78.7% of HIV positive pregnant women who access antenatal care have HIV negative male sex partners. The highest HIV prevalence rates occurred among married couples in Southern Nigeria^{39,40}. Also, women were 11 times more likely to be the HIV positive partner than the HIV negative partner⁴¹.

When the rate of HIV serodiscordancy amongst couples is high, the risk of new HIV infections occurring is also high if concerted and appropriately targeted prevention efforts are not taken. The negative partners constitute a relatively small population (relative to the general population) at high risk of HIV infection. They can be targeted for prevention efforts through promotion of couples HIV-1 counseling and testing. Averting HIV-1 transmission is a clear advantage to the individuals in serodiscordant partnership, enough to serve as motivation for their sustained adherence to the intervention. Importantly, the HPTN 052 and Partners PrEP studies both demonstrated that TasP and PrEP can

be highly effective when used within HIV-1 serodiscordant sexual relationships.

In the context of a general HIV epidemic, women and girls are particularly vulnerable for a number of reasons, including the fact that the prevention tools currently available are not well suited to protect women from sexually-transmitted HIV. Male and female condoms, the most commonly promoted risk-reduction strategy, require that male partners elect or agree to use them, a condition that makes them useless during rape, sexual violence, and for women whose partners refuse to either use male condoms or permit the use of female condoms. In Nigeria, 58% of the PLHIV population are women⁴² and the prevalence of HIV infection among women increases with age. Only 3% of 15-19 year-old Nigerian females are HIV positive, but this increases to 5.7% among those 30-34 years old. Young women (between 20 and 24 years) are 2.4 times more likely to be living with HIV than their male peers (4.5% vs. 1.9%), largely because women are more vulnerable to infection and are likely to become infected earlier in life than men of the same age⁴³. Within the context of the Nigeria epidemic, women are considered vulnerable due to the large number of HIV positive persons (even if they, themselves, are monogamous), and due to their poor capacity to insist on consistent condom use. Male condoms are used by only 33.4% of women in Nigeria⁴⁴.

Epidemiological differences in the HIV epidemic across regions and within countries (including Nigeria) point to the need to design specific interventions tailored to the needs of groups of people or communities. Several large clinical trials currently underway or in the planning stages will test the efficacy of population-specific HIV prevention interventions. These should reveal which combination of prevention strategies best reduces HIV incidence in specific populations; an area of knowledge that is as necessary as knowing how protective these interventions are at the individual level. PrEP shows promise as a component of a combination HIV prevention package for populations and individuals most vulnerable and at-risk for HIV infection. In view of this, it is critical to explore the feasibility of using PrEP as part of a

combination prevention strategy to prevent new infections in populations most at risk for HIV infection in Nigeria.

One focal target is HIV sero-discordant couples. The high incidence rate of 1.2 per 100 person-years among serodiscordant couples even in a highly controlled trial environment where viral suppression for index partner was good⁴⁵, is an indication of the need to complement current HIV prevention package for serodiscordant couples in a country like Nigeria where the rate of serodiscordancy is high. For many of these couples, the consistent use of condoms may be challenging, especially within the context of a culture that promotes childbirth^{46,47}. Furthermore, about 29% of serodiscordant couples in the Partners PrEP studies had partners outside the conjugal relationship². These outside sexual relationship by the HIV uninfected partner increased as the years go by. Often sex is unprotected in these non-marital relationships⁴⁸.

Discussion

While there is every justification for targeting serodiscordant couples for the use of PrEP as part of their combination package for HIV prevention, there is also a need to explore public opinion about PrEP and its appropriateness for different target groups, including male and female sex workers, men who engage in sex with other men, and those women, girls and youths who engage in risky sexual behaviour.

The government of Nigeria has therefore designed a three phase research which will explore the feasibility of introducing PrEP as part of the HIV combination prevention strategy for serodiscordant couples. The first phase will explore the potential impact of the use of PrEP to reduce the risk for HIV infection among serodiscordant couples in Nigeria using a mathematical model. The second would be the conduct of an exploratory study to assess community interests and perceptions about the use of PrEP as part of Nigeria's HIV prevention armamentarium. It will also gather data on public opinion about which population(s) would be the most appropriate to involve in a PrEP demonstration study, and input on design and

implementation features that could best help to assure the success of a demonstration study on the use of PrEP as part of the HIV combination package for the target population(s). The outcome of the formative study would inform the design and implementation of a two year demonstration project which would help the country identify clearly, the appropriate service model(s) that would help ensure effective delivery of PrEP for the negative partner and TasP for the HIV positive partners in HIV-1 serodiscordant sexual relationships. Such a model should be able to avert new infections, be cost effective and scalable. Also, it should be able to identify mechanisms for effectively screening and identifying persons in acute infection so as to avoid PrEP initiation in these individuals. This is because it appears such individuals are more likely to select for resistant mutants²⁸.

The importance of the demonstration project cannot be overemphasized as these projects can simulate real live events for PrEP access. This is because strategies that work in clinical trials may not be effective or may not be optimally implemented in the real world⁴⁹. Proven and effective HIV control methods have not been scaled up significantly to achieve the needed impact in Nigeria. A demonstration project would help provide evidence that would help address challenges and barriers to PrEP access thereby providing evidence that can help facilitate rapid scale up of PrEP services in Nigeria. While there is interest in promoting wide access of PrEP to those at high risk of acquiring new infection, concerns about development of resistance to ARVs and the evolution of a drug resistant HIV pandemic is real⁵⁰ and efforts to mitigate the prospect for ARV resistance acquisition while on PrEP regimen needs to be looked into. Assessment and documentation of PrEP adherence is therefore essential as is the need for regular access to and uptake of HCT every three months, screening for STI and creatinine levels and regular risk reduction counselling²⁸. These make the roll-out of PrEP access programmes complicated: demonstration projects should however help to provide information on the ultimate design that can help address some if not all of these challenges²⁸.

The outcome of the project would also provide evidence for integrating PrEP into existing service delivery settings in the country in addition to learning how to provide community education about PrEP. It also would provide the opportunity to test and adapt the current U.S. Centers for Disease Control and Prevention clinical recommendations for prescription and use of PrEP⁵¹ for the Nigeria context. These findings would inform the review of the national HIV prevention and treatment plan in 2016 and help put to effective use ART for HIV control in Nigeria.

Conclusion

There is enough justification for the conduct of a PrEP and TasP demonstration project in Nigeria. With the high number of new infection (estimated as 220,394 in 2013), only 31.0% of eligible pregnant women having access to antiretroviral to reduce the risk of mother-to-child transmission in 2013, a mother to child HIV transmission rate of 27.3%, and only 19.8% of eligible adults and children receiving ART⁵², it is clear the HIV control programme in Nigeria faces huge challenges. Introduction of PrEP and TasP needs to be piloted taking cognizance of the local realities and identifying how the potential of these important additional HIV prevention tools can best be harness to enhance HIV prevention in the country.

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Contribution of Authors

MOF conceived the idea of the paper. JI and MOF collected the papers needed for the writing of the manuscript, were both engaged in the preparation of the manuscript and gave final consent to its publication.

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