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ORAL PRE-EXPOSURE PROPHYLAXIS

PUTTING A NEW CHOICE IN CONTEXT

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CONTENTS

BACKGROUND

The World Health Organization (WHO) anticipates releasing updated guidance on oral pre-exposure prophylaxis (PrEP), containing tenofovir (TDF), as an additional HIV prevention choice. The new guidance is likely to be significantly broader than previously and creates real opportunities to move forward with implementing PrEP as part of comprehensive HIV programmes.

This publication, produced collaboratively between UNAIDS, WHO and AVAC, is intended to complement WHO recommendations and support the optimal use of oral PrEP to protect individuals and contribute to ending the AIDS epidemic.

ESSENTIAL PRINCIPLES FOR ORAL PrEP

PrEP is effective

Pre-exposure prophylaxis (PrEP) is effective in preventing HIV transmission, and no significant difference has been found by sex, age or mode of sexual transmission. Oral PrEP has been evaluated in gay men and other men who have sex with men, transgender women, heterosexual men and women and people who inject drugs. In each of these contexts, the data are clear: PrEP works if taken correctly and consistently.

PrEP must fit within the broader HIV response

Ending the HIV epidemic requires synergy around the three zeros–zero new HIV infections, zero discrimination and zero AIDS-related deaths. Implementing PrEP should enhance HIV programmes, including testing and scaling up treatment, and its delivery must always form part of a combination prevention approach. PrEP complements other evidence-informed prevention approaches, including condom and empowerment programmes for sex workers, harm reduction for people who inject drugs and efforts to change the legal and social context that increases the risk of acquiring HIV for many people.

PrEP is a prevention choice

The decision to use PrEP rests with the individual. When presented with other HIV prevention options in a non-stigmatizing environment, individuals can choose the prevention strategy that is appropriate for them.

PrEP is not for everyone: it is for people at substantial risk of acquiring HIV

In deciding on who should be offered PrEP, needs and benefits (HIV prevention) should be balanced with harm (possible adverse events), costs and feasibility. People who are at substantial risk of acquiring HIV would achieve the greatest benefit from being able to access PrEP as an additional prevention choice.

PrEP: THE BASICS

PrEP is the use of antiretroviral medication by people who are HIV negative to prevent them from acquiring HIV. PrEP trials have taken place in Africa, Asia, Europe, North America and South America.

The trials to date have used TDF-based regimens–either TDF combined with emtricitabine (FTC) or TDF alone. The United States Food and Drug Administration announced its approval of daily oral TDF + FTC for PrEP in July 2012, and the United States Centers for Disease Control and Prevention have produced PrEP implementation guidelines for adults at higher risk of HIV exposure.[1]

Key conclusions from PrEP efficacy and effectiveness studies and demonstration projects

- Oral PrEP containing TDF can be highly protective for both men and women.
- Very low numbers of serious side effects have been seen in trials of TDF-based PrEP.
- Adherence and ongoing follow-up with regular HIV testing are essential. People who had high levels of adherence had high levels of protection. Lower adherence was associated with low or no protection.
- Where PrEP was proposed as a choice (in open-label extension and demonstration projects), people who would benefit most from PrEP used it most consistently.
- PrEP poses a risk of drug resistance if a person has undetected HIV when initiating or restarting PrEP. PrEP is only for people who are HIV–negative.
- The time elapsing before oral PrEP achieves high-level protection is five to seven days for anal sex and up to three weeks for vaginal sex.

PrEP AND TREATMENT WITHIN A COMPREHENSIVE HIV PROGRAMME

The UNAIDS Fast-Track[2] approach, the 90–90–90 target[3] and the prevention target of reducing the number of people acquiring HIV by 75% by 2020[4] all call for an expanded and accelerated scale-up of HIV treatment and combination prevention during the next five years. Using antiretroviral medicines for treatment and PrEP contributes synergistically to these targets and to the goal of zero discrimination.

1 Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014 clinical practice guideline. Atlanta: United States Centers for Disease Control and Prevention; 2014 (http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf, accessed 14 July 2015).

2 Fast-Track: ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014 (http://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf, accessed 14 July 2015).

3 By 2020, 90% of all people living with HIV will know their HIV status, 90% of all people who know their status will receive treatment and 90% of all people on treatment will have a suppressed viral load.

4 Understanding fast-track: accelerating action to end the AIDS epidemic by 2030. Geneva: UNAIDS; 2014 (http://www.unaids.org/sites/default/files/media_asset/201506_JC2743_Understanding_FastTrack_en.pdf, accessed 14 July 2015).

Common issues with antiretroviral medicines in a time of expanded treatment and prevention

- Safety: modern antiretroviral medicines used for prevention and treatment are very safe. Laboratory monitoring can minimize the risks of side-effects and drug resistance.
- Choice: use of prevention, treatment and all health services must be a personal choice, free of coercion. People need access to information to help them make informed choices.
- Access: people have a right to evidence-informed HIV prevention, treatment and services. Ability to pay should not determine someone's access to these services.
- Social barriers: discrimination is a major barrier to testing, treatment and prevention and exacerbates vulnerability to HIV. Interventions to address these barriers are needed along with advocacy for legal and structural change.
- Community role: community-based providers must play an increasing role in delivering prevention and treatment services, including PrEP. UNAIDS estimates that treatment provided in the community should increase from 5% today to 30% by 2020.[5]
- Testing: taking an HIV test is the entry point for any use of antiretroviral medicines. After testing, people are offered treatment and positive prevention (if HIV–positive) or prevention options, including PrEP (if HIV–negative). The availability of antiretroviral can enhance the uptake of testing.
- Prices: drug prices are a major factor in access, and lowering the cost of medicines is central to wider treatment and PrEP delivery. Drug prices have fallen dramatically over time, and there is the potential for further decreases.
- Delivery costs: new resources and efficiency can be found through integration with existing HIV budgets, technical support and service capacity along with appropriate task sharing.
- Support: many people benefit from social support in adhering to HIV treatment, PrEP and other health programmes. Social protection, including longer periods of schooling, may reduce the risk of acquiring HIV among young people, especially girls.

5 Fast-Track: ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014 (http://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf, accessed 14 July 2015).

THE NEED

The number of adults acquiring HIV is decreasing too slowly, and in some populations it is still rising. Additional prevention options are urgently required to respond to unmet prevention needs. PrEP is intended for people who are at substantial risk of HIV exposure and who do not always use condoms. This includes the people who lack the negotiating skills and power to insist on condom use as well as instances when condoms are exceptionally not available. PrEP can also be used specifically for safer conception.

Where there is no shared prevention decision-making, PrEP returns the control of the risk of acquiring HIV to the individual. PrEP is under personal control, it is invisible at the time of sex and the decision to take it is separate from the sex act.

As national programmes and funders focus on scaling up treatment to meet the 90–90–90 target, preventing people from becoming newly infected and reducing future treatment costs are also important. Testing and offering treatment to all individuals living with HIV will reduce the number of people acquiring HIV in the long term, but models and experience show that additional strategies are needed to contribute to ending the epidemic. UNAIDS modelling predicts that accelerating the scale-up of HIV prevention and treatment together will lead to significant economic benefits in low- and middle-income countries.[6]

HIV testing as the entry point for prevention and treatment

- HIV testing is being strengthened in accordance with the 90–90–90 target.
- Appropriate linkage depending on test results will ensure that that the investment in scaling up testing has the maximum public health benefit.
- People who test HIV–positive should be offered treatment.
- Testing HIV–negative provides the opportunity to discuss individual high- risk HIV behaviour and prevention options of which PrEP could be a part.
- Several research projects are investigating testing in populations with a high HIV incidence, linked to the choice of treatment or PrEP as appropriate. For serodiscordant couples, this includes the option of using PrEP as a bridge until viral suppression is achieved through the antiretroviral therapy of the partner living with HIV or for safer conception.

6 Fast-Track: ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014 (http://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf, accessed 14 July 2015).

DEMAND

Information about PrEP is spreading at different rates in different parts of the world. Three years have passed since the United States Food and Drug Administration approved PrEP, and PrEP is just starting to change HIV prevention for gay men and other men who have sex with men in the United States. Other parts of the world have much less information about PrEP although growing activism on PrEP is contributing to raising awareness. Increasing the awareness of and demand for PrEP for those at higher risk of acquiring HIV should be part of a broader effort to scale up HIV prevention and treatment for all populations.

COMBINATION PREVENTION

The precise components of effective combination prevention vary depending on population needs but can include male and female condoms with condom-compatible lubricant, comprehensive harm-reduction programmes, voluntary medical male circumcision, management of sexually transmitted infections, rights-based, peer-led behaviour counselling and viral suppression through treatment for people living with HIV. Since PrEP does not prevent other sexually transmitted infections and is not a contraceptive, its provision can be integrated with other sexual and reproductive health services.

BROADER CONSIDERATIONS

Will PrEP reduce other safer-sex behaviours?

No evidence has indicated this. Instead, evidence from trials suggests that PrEP can enable people to consider all their safer-sex strategies by addressing their fear and consequent denial of a higher risk of HIV.

Use of PrEP by women

Daily oral PrEP is the only currently available option that HIV-negative people can use discretely and not at the time of sex—characteristics that may make it especially important for women, including young women, adolescent girls and also those who are concerned about acquiring HIV in the context of a stable partnership.

PrEP AS PART OF A NATIONAL RESPONSE

Identifying where to begin phased introduction

The populations with the highest need for where PrEP can have the greatest impact can be given priority for initial implementation. Community ownership of HIV programmes is vital. All delivery of antiretroviral medicines should be discussed and designed cooperatively with potential users, their service providers, community leaders and programme planners, addressing barriers and strengthening enablers. Ensuring broad understanding that PrEP is a responsible and effective choice for protecting oneself and one's community is critical. The first PrEP roll-out programmes should be developed and monitored to gather information about community engagement, local identification of groups at substantial risk of HIV, adherence support, costing, efficient integration with other services and safety monitoring.

WHERE AND BY WHOM COULD PrEP BE DELIVERED? ELEMENTS OF A SUCCESSFUL PrEP PROGRAMME

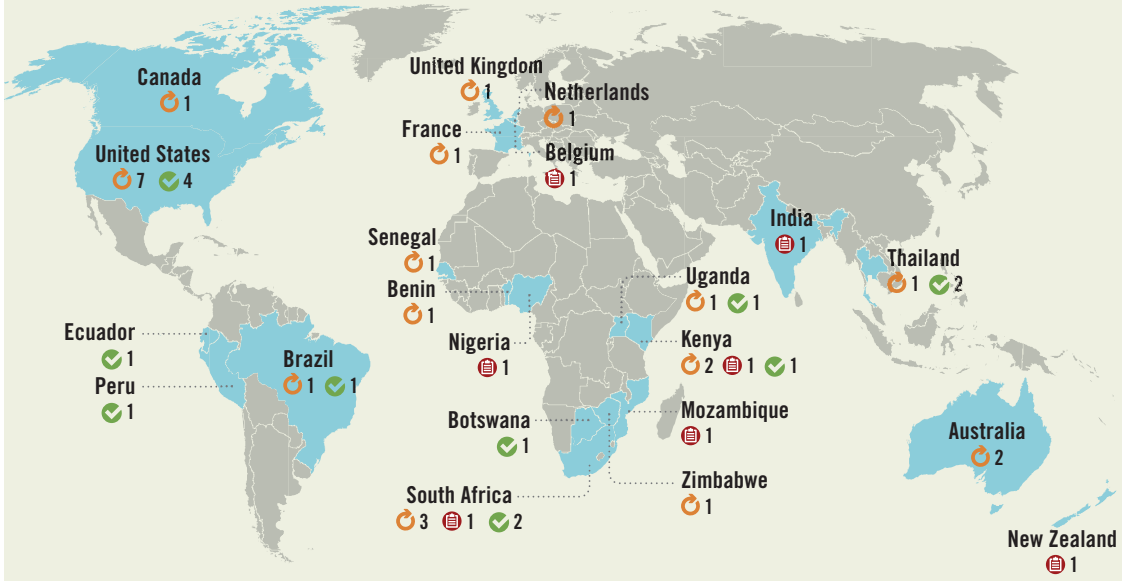
Services providing PrEP need to assure:

- Engagement and support from within the local communities.
- Guidance from the community to support access and adherence.
- Non-stigmatizing and user-friendly staff and environment.
- Integration with quality-assured HIV testing services.
- Trained PrEP prescribers.
- Other HIV prevention services, including condoms, lubricants and harm reduction.
- Support services for people taking PrEP.
- Linkage to HIV treatment for everyone who tests HIV positive.
- Appropriate laboratory facilities for safety monitoring, such as renal function.
- Confidential follow-up and regular HIV testing for monitoring and evaluation.

National engagement with PrEP and current recommendations as of July 2015

- In June 2012, the Southern African HIV Clinicians' Society issued guidance for the use of TDF + FTC as PrEP by gay men and other men who have sex with men, and as of July 2015 they are updating the guidance for other populations.
- In 2014, Kenya incorporated PrEP for key populations into its HIV Prevention Revolution Road Map.
- In 2015, Thailand and Brazil included PrEP in their national HIV programmes.
- The manufacturer of branded TDF + FTC has filed for regulatory approval as prevention in Australia, Brazil, France, South Africa and Thailand; these are still pending as of July 2015.
- The European Medicines Agency is updating its concept paper on the development of medicines to prevent HIV infection (as of July 2015).

Planned, Ongoing and Completed PrEP Evaluation Studies (June 2015)



KEY Ongoing Planned Completed

For the latest on these studies, visit *www.avac.org/prep/track-research.*

Data from demonstration projects and open-label extension studies are beginning to come in. So far, the findings suggest that people want and will take daily oral PrEP correctly outside of a clinical trial setting. Expanded and faster rollout is key.

COST CONSIDERATIONS

The generic fixed-dose TDF + FTC combination is available for US$ 78 per person per year and generic TDF for US$ 43 per person per year. Branded TDF + FTC costs from US$ 3800 to US$ 10 200 per person per year in high-income countries, and the lowest cost of branded TDF is US$ 91 per person per year.[7] HIV testing costs vary and are shared with increasing testing and treatment efforts.

PrEP can be a cost-effective addition, depending on how well it is integrated into comprehensive HIV programmes and given priority for people who are at highest HIV risk and want PrEP. Real-world costing data for PrEP programmes will become available as PrEP rolls out. These data will assist policy-makers in planning future resource allocation for PrEP as part of high-impact combination prevention and treatment programmes.

PrEP may also provide important benefits that are more difficult to cost. The wider effects of engaging with health-care services, including reproductive and sexual health services, can bring health care to previously marginalized populations.

PEPFAR country operational plans and concept notes and proposals for the Global Fund to Fight AIDS, Tuberculosis and Malaria are now considering PrEP pilot projects for HIV prevention. UNITAID recently announced that it would support new investment enabling the expanded use of PrEP. Private-sector programmes can and should also be explored, such as among employers of seasonal or transitory labour or truck drivers.

7 Global Price Reporting Mechanism [website]. Geneva: World Health Organization; 2015 (http://apps.who.int/hiv/amds/price/hdd, accessed 14 July 2015).

What next? Concrete steps in implementing PrEP

- Setting priorities.
  Based on reliable national and subnational data, identify potential early sites for implementing PrEP.
- Increasing demand.
  Provide information about PrEP and foster ownership to generate appropriate demand that will ultimately lead to uptake and adherence. Generating demand can also catalyse funding from international sources as well as national contributions secured via grants from the Global Fund to Fight AIDS, Tuberculosis and Malaria, existing prevention budgets and/or joint planning with the United States President's Emergency Plan for AIDS Relief (PEPFAR) and others.
- Tailoring prevention programmes with the population.
  The specific prevention combination proposed should respond to the needs and known risks of the priority population. Information from early PrEP implementation will inform further roll-out.
- Securing low-cost PrEP.
  This can be achieved through negotiations with the manufacturers or management of intellectual property rights[8] and securing a supply of generic PrEPs. Generic TDF and FTC + TDF are available in many markets, and patent protections for these agents will change in the next few years for many countries.
- Approving antiretroviral medicines as PrEP.
  Each country's medicines regulatory agency is responsible for authorizing the use of these antiretroviral medicines as prevention.
- Obtaining funding.
  Both donor assistance and domestic funding contributions can support early PrEP implementation and its integrated expansion into comprehensive HIV treatment and prevention programmes, based on the country's burden of disease and ability to pay.
- Exploring other funding options.
  Negotiations with existing health insurance systems on individual payment may also contribute.

8 For example, by using TRIPS flexibilities like parallel importation or a compulsory licence.

THE FUTURE BEYOND DAILY ORAL PrEP BASED ON TDF

Studies are underway to evaluate the safety and efficacy of alternative PrEP products based on antiretroviral medicines under way: both other active medicines (such as oral maraviroc) as well as other delivery systems, such a vaginal rings with dapivirine, long-acting injectables (cabotegravir and rilpivirine) and subcutaneous implants with TDF derivatives. Increasing choice among available antiretroviral drug prevention options can eventually contribute to improving access and adherence, but it is expected to take several years before they can be made widely available.

PrEP FAST FACTS

- Oral PrEP is an additional HIV prevention option for individuals at substantial risk of HIV exposure that will be effective as part of a comprehensive response to HIV.
- PrEP is safe and effective when used correctly and consistently.
- PrEP is not for everybody; it is not forever; and it does not replace condoms. Rather, PrEP is an additional option for ever that individuals at risk of HIV should be able to choose.
- PrEP can contribute to decreasing fear and stigma of HIV and to encouraging shared sexual decision-making.
- In situations of vulnerability and disempowerment, PrEP can return HIV prevention to individual control.
- People who use PrEP should take it every day and return to their health-care provider for repeat testing for HIV, safety monitoring, prescription refills and risk and adherence follow-up.
- Some people in clinical studies of PrEP had early side-effects such as an upset stomach or loss of appetite, but these were mild and usually went away in the first month. Some people also had a mild headache. No serious side-effects were observed.

THE ROLE OF UNAIDS

UNAIDS advocates for optimal scaling up of PrEP as an additional effective HIV prevention intervention.

Priority actions for UNAIDS in the next three years include:

- Increasing public demand by engaging civil society.
- Promoting the inclusion of PrEP in national HIV strategies and making the case for funding.
- Supporting countries in licensing the use of appropriate antiretroviral drugs for HIV prevention.
- Advocating for affordable PrEP and regulated generic manufacturing.
- Convening the required technical expertise for estimating cost and incidence.
- Working with national programmes to define eligibility for PrEP and to set priorities for PrEP appropriately.
- Promoting access and adherence to PrEP based on best practices.

THE ROLE OF WHO

WHO provides the normative global guidance on PrEP and is developing implementation guidelines for PrEP. WHO also provides technical support for developing, implementing and monitoring PrEP projects and programmes. WHO also supports the Global Fund to Fight AIDS, Tuberculosis and Malaria with technical advice on PrEP and how it can be included in national responses as part of combination prevention for people with a substantial risk of acquiring HIV.

ABOUT AVAC

AVAC is an international non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new and emerging HIV prevention options as part of a comprehensive response to the HIV and AIDS epidemic. AVAC is committed to:

- Advocating for policies and action that translate PrEP research into public health impact.
- Building a rapid-response civil society network advocating for evidence-informed policies.
- Improving research conduct and programme implementation.
- Providing tools for decision-making.
- Translating and sharing the latest information, including through the PrEP Watch web clearinghouse at www.prepwatch.org.

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