MODULE 4

LEADERS

WHO IMPLEMENTATION TOOL FOR PRE-EXPOSURE PROPHYLAXIS (PrEP) OF HIV INFECTION

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World Health Organization

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Introduction

Following the WHO recommendation in September 2015 that "oral pre-exposure prophylaxis (PrEP) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches", partners in countries expressed the need for practical advice on how to consider the introduction of PrEP and start implementation. In response, WHO has developed this series of modules to support the implementation of PrEP among a range of populations in different settings.

Although there is growing acknowledgement of PrEP's potential as an additional HIV prevention option and countries are beginning to consider how PrEP might be most effectively implemented, there has been limited experience with providing PrEP outside research and demonstration projects in low- and middle-income countries. Consequently, there is often uncertainty around many implementation issues. The modules in this tool provide initial suggestions for the introduction and implementation of PrEP based on currently available evidence and experience. However, it is recognized that this evidence may evolve following wider PrEP use; therefore, it is likely that this tool will require regular updating.

PrEP should not replace or compete with effective and well-established HIV prevention interventions, such as comprehensive condom programming for sex workers and men who have sex with men and harm reduction for people who inject drugs. Many people who could benefit most from PrEP belong to key population groups that may face legal and social barriers to accessing health services. This needs to be considered when developing PrEP services. Although the public health approach underpins the WHO guidance on PrEP, the decision to use PrEP should always be made by the individual concerned.

Target audience and scope of tool

This PrEP tool contains modules for a range of stakeholders to support them in the consideration, planning, introduction and implementation of oral PrEP. The modules can be used on their own or in combination. In addition, there is a module for individuals interested in or already taking PrEP. (See Summary of modules below.)

This tool is the product of collaboration between many experts, community organizations and networks, implementers, researchers and partners from all regions. The information presented is aligned with WHO's 2016 consolidated guidelines on the use of antiretroviral drugs for HIV treatment and prevention.

All modules make reference to the evidence-based 2015 WHO recommendation on PrEP. They do not make any new recommendations on PrEP, focusing instead on suggested implementation approaches.

Guiding principles

It is important to adopt a public health, human rights and people-centred approach when offering PrEP to those at substantial risk of HIV. Similar to other HIV prevention and treatment interventions, a human rights-based approach gives priority to issues concerning universal health coverage, gender equality and health-related rights including accessibility, availability, acceptability and quality of PrEP services.

SUMMARY OF MODULES

Module 1: Clinical. This module is for clinicians, including physicians, nurses and clinical officers. It gives an overview of how to provide PrEP safely and effectively, including: screening for substantial risk of HIV; testing for HIV before initiating someone on PrEP and how to follow up PrEP users and offer counselling on adherence.

Module 2: Community educators and advocates. Community educators and advocates are needed to increase awareness about PrEP in their communities. This module provides information on PrEP that should be considered in community-led activities that aim to increase knowledge about PrEP and generate demand and access.

Module 3: Counsellors. This module is for staff who counsel people as they consider PrEP or start taking PrEP and support them in coping with side-effects and adherence strategies. Those who counsel PrEP users may be lay, peer or professional counsellors and healthcare workers, including nurses, clinical officers and doctors.

Module 4: Leaders. This module aims to inform and update leaders and decision-makers about PrEP. It provides information on the benefits and limitations of PrEP so that they can consider how PrEP could be effectively implemented in their own settings. It also contains a series of frequently asked questions about PrEP.

Module 5: Monitoring and evaluation. This module is for people responsible for monitoring PrEP programmes at the national and site levels. It provides information on how to monitor PrEP for safety and effectiveness, suggesting core and additional indicators for site-level, national and global reporting.

Module 6: Pharmacists. This module is for pharmacists and people working in pharmacies. It provides information on the medicines used in PrEP, including on storage conditions. It gives suggestions for how pharmacists and pharmacy staff can monitor PrEP adherence and support PrEP users to take their medication regularly.

Module 7: Regulatory officials. This module is for national authorities in charge of authorizing the manufacturing, importation, marketing and/or control of antiretroviral medicines used for HIV prevention. It provides information on the safety and efficacy of PrEP medicines.

Module 8: Site planning. This module is for people involved in organizing PrEP services at specific sites. It outlines the steps to be taken in planning a PrEP service and gives suggestions for personnel, infrastructure and commodities that could be considered when implementing PrEP.

Module 9: Strategic planning. As WHO recommends offering PrEP to people at substantial HIV risk, this module offers public health guidance for policy-makers on how to prioritize services, in order to reach those who could benefit most from PrEP, and in which settings PrEP services could be most cost-effective.

Module 10: Testing providers. This module is for people who provide testing services at PrEP sites and laboratories. It offers guidance in selecting testing services, including screening of individuals before PrEP is initiated and monitoring while they are taking PrEP. Information is provided on HIV testing, creatinine, HBV and HCV, pregnancy and STIs.

Module 11: PrEP users. This module provides information for people who are interested in taking PrEP to reduce their risk of acquiring HIV and people who are already taking PrEP – to support them in their choice and use of PrEP. This module gives ideas for countries and organizations implementing PrEP to help them develop their own tools.

Module 12: Adolescents and young adults. This module is for people who are interested in providing PrEP services to older adolescents and young adults who are at substantial risk for HIV. It provides information on: factors that influence HIV susceptibility among young people; clinical considerations for safety and continuation on PrEP; ways to improve access and service utilization; and inclusive monitoring approaches to improve the recording and reporting of data on young people.

ANNEXES

Review of evidence. A wide range of evidence including the following two systematic reviews informed the 2015 WHO recommendation on PrEP for people at substantial risk of HIV infection: (i) Fonner VA et al. *Oral tenofovir-based HIV pre-exposure prophylaxis (PrEP) for all populations: a systematic review and meta-analysis of effectiveness, safety, behavioural and reproductive health outcomes*; (ii) Koechlin FM et al. *Values and preferences on the use of oral pre-exposure prophylaxis (PrEP) for HIV prevention among multiple populations: a systematic review of the literature*.

Annotated Internet resources. This list highlights some of the web-based resources on PrEP currently available together with the stakeholder groups they are catering to. WHO will continue to provide updates on new resources.

The leaders module

- HIV transmission continues
- New approaches to combination HIV prevention are needed

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- PrEP is a promising new intervention for people at substantial risk for HIV
- PrEP has been widely studied

→

- PrEP is highly effective and safe
- PrEP can be cost-effective

This module addresses leaders and decision-makers involved in making public policy on health, including ministers of health, ministers of finance and community advocates whose opinions and voices are essential to increase the focus on, funding for and delivery of effective HIV programmes.

United Nations 90 – 90 – 90 targets

- By 2020, 90% of all people living with HIV will know their HIV status.
- By 2020, 90% of all people with diagnosed HIV infection will receive sustained ART.

Prevention and treatment can be synergistic; both are needed to meet the United Nations fast-track 90 – 90 – 90 targets for ending the AIDS epidemic *(1)*. The World Health Organization (WHO) recommends supporting and strengthening prevention alongside treatment. (See the WHO *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV*.[1]) Effective implementation of these recommendations, along with other existing prevention approaches, requires political and policy action at all levels.

In 2016, WHO also released the *Global health sector strategy on HIV 2016–2021*, which calls for rapid acceleration of the global HIV response over the coming few years followed by sustained action through to 2030 and beyond. This can only be achieved through renewed political commitment, additional resources, and technical and programmatic innovations *(2)*. The strategy promotes a people-centred approach grounded in principles of human rights and health equity.

WHO strongly recommends offering **antiretroviral therapy (ART)** to all individuals diagnosed as HIV-positive regardless of the duration of infection or the severity of their disease *(3)*. This *Treat all* approach can save more lives, prevent both horizontal and vertical transmission, and reduce the spread of tuberculosis, which often occurs among people living with HIV who are not receiving ART *(4–6)*.

WHO also recommends the use of **pre-exposure prophylaxis (PrEP)** for people at substantial risk of acquiring HIV *(3)*. PrEP is the daily use of tenofovir (TDF) or a combination of tenofovir and emtricitabine (FTC) (also known as Truvada®) to prevent people who do not have HIV from acquiring it. These antiretroviral medicines used for PrEP have been shown to be safe and effective in preventing HIV infection when taken as prescribed.

People at substantial risk of acquiring HIV, who might benefit from using PrEP, include:

"I know condoms protect me from getting HIV and STI infection but I would like to have PrEP as I could control it by myself and it kills the fear of getting AIDS."

Sex worker
Sonagachi brothel, India

- people in serodiscordant couples (that is, when one person has HIV and the other person does not) until the person with HIV is fully virally supressed on ART;
- people from key populations in many settings (such as sex workers, men who have sex with men, people who inject drugs and transgender people);
- young women in places with a high HIV incidence in southern and eastern Africa.

1 Available at http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/.

WHO recommendations

- **Antiretroviral therapy (ART)** should be initiated in all children, adolescents and adults living with HIV at any CD4 cell count.
- **Pre-exposure prophylaxis (PrEP)** containing an antiretroviral drug called tenofovir should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches.

Implementing PrEP involves more than just ensuring the supply of medicines. PrEP programmes also involve regular testing for HIV, screening for other sexually transmitted infections (STIs) and adherence support, and linking to treatment any people who receive a reactive result when they are tested for HIV before starting PrEP or who seroconvert (that is, who test HIV-positive for the first time while using PrEP).

PrEP is as an additional HIV prevention choice. It should not replace or undermine other effective and well-established HIV prevention interventions.

PrEP is intended as an additional prevention choice. Its implementation should not replace or undermine other effective and well-established HIV prevention interventions, such as condom programming and harm reduction for people who inject drugs. PrEP should be offered as part of a comprehensive testing, prevention and treatment service.

The goal of this module, together with the other modules in this WHO *PrEP implementation tool* is to build on the WHO PrEP recommendations and help to ensure that PrEP is offered appropriately and for maximum benefit.

HIV epidemic continues to devastate

Despite progress against HIV, more than 2 million people still acquire HIV every year *(7)*. Each person with HIV requires lifelong ART to stay healthy and alive and to prevent further transmission. In 2016, 18 million people in the world were on ART. This figure equates to half of the 36.7 million people with HIV now eligible for ART following the new WHO *Treat all* recommendation.

The HIV epidemic has had a devastating impact on humanity, disrupting families, contributing to unemployment, undermining productivity and interrupting schooling. In addition, it contributes to social marginalization and to stigma and discrimination against many vulnerable populations, including sex workers, men who have sex with men, people who inject drugs, transgender people and migrants.

Policies can help prevent HIV

Policy change can make a crucial difference in efforts to end the AIDS epidemic. Policy can assure that the national response to HIV broadens the reach of HIV treatment and includes PrEP within the context of a comprehensive prevention approach. Where people with HIV or at high risk of acquiring HIV are criminalized or discriminated against, reviewing and revising policies and laws as needed is important to establish the equitable access to services that is essential for an effective HIV response.

Policy change may be necessary at many levels, including making HIV prevention and treatment a national priority; revising policies on who can provide services (including task sharing so that nurses or other appropriate providers can deliver ART and PrEP services); introducing regulatory policies that allow antiretroviral drugs to be used for prevention; and improving procurement processes to ensure a consistent supply of medicines and laboratory reagents at affordable prices.

"'How can you afford to implement this new intervention?' I always reply, 'How can we afford not to?' Once you answer this question you will find the way to make it happen. However, we must ensure that the PrEP offer is part of a comprehensive approach to prevention."

Dr. Aaron Motsoaledi

Minister of Health, South Africa

Research shows that PrEP works when taken regularly

More than 10 rigorous clinical trials have shown that PrEP prevents HIV acquisition.

Unlike many other interventions, there is substantial evidence from research trials supporting the efficacy of PrEP. More than 10 clinical trials, with participants from a total of 18 countries, have shown that, used for PrEP, antiretroviral drugs containing TDF, or a combination of TDF and FTC, effectively prevent HIV acquisition. In these trials, the risk of acquiring HIV decreased by more than 90% when participants used PrEP consistently. The trials involved both men and women in populations that carry a disproportionate burden of the HIV epidemic. The results of the trials have been published or presented at major meetings *(8–17)*.

Medicines used for PrEP are safe for all populations

The medicines used for HIV treatment and PrEP have a good safety profile. Side-effects are not common; moreover, they are typically mild and resolve in the first few weeks of use.

Risk of drug resistance is uncommon, occurring in approximately one in every 1000 PrEP users in clinical trials, almost exclusively among people who already had acute, undetected HIV infection when they started PrEP. Therefore, testing people for HIV before they start PrEP is essential to avoid drug resistance. Offering PrEP reduces the number of new HIV infections, each of which would require lifelong ART with substantial ongoing risk of drug resistance. Thus, PrEP is expected to decrease the public health burden of HIV drug resistance.

PrEP appears to be safe during pregnancy and breastfeeding. The risk of HIV acquisition during pregnancy and breastfeeding and the accompanying increased risk of mother to child HIV transmission far outweigh any potential risk of fetal or infant exposure to TDF used for PrEP. Furthermore, PrEP can be an additional tool to help serodiscordant couples conceive safely.

Specific policies needed to expand HIV treatment and PrEP

Political leadership is needed to ensure that medicines regulatory authorities and public health officials review evidence for offering immediate ART to all people with HIV and offering PrEP to people who do not have HIV but face substantial risk of acquiring it.

Policies may need adaptation so that people who do not have HIV can use HIV treatment drugs for prevention.

Political leadership is also necessary to commit the resources required for effective implementation of these policies.

Regulatory policy and approval

Several countries already include PrEP in their national HIV strategies. In other countries, policies may need to be expanded or adapted to permit the use of HIV treatment medicines for prevention by people who do not have HIV. For example, in most countries post-exposure prophylaxis (PEP) is widely accepted for use in HIV prevention after needle stick injury among healthcare workers or after sexual assault or other sexual exposure. The antiretroviral drugs used for PEP can be prescribed off-label based on expert medical opinion and without government regulatory approval. A similar approach could be considered for PrEP, particularly as a way to make PrEP available quickly without waiting for a lengthy regulatory process. Some countries, however, have sought, or are seeking, the formal approval of medicines regulatory authorities for the use of TDF/FTC for prevention. As of June 2017, TDF/FTC has been approved for PrEP in more than 15 countries and is under consideration in many more.

Procurement and supply chain

Since the medicines for PrEP and PEP are already used to treat HIV infection, they are currently available in most countries. Coordinated procurement and distribution systems are vital to ensure cost-effectiveness and prevent gaps in the supply of these medicines, which could lead to treatment failure, HIV transmission and drug resistance. Negotiations at the international and national levels will be important to ensure that medicines and laboratory supplies are purchased at the lowest available prices.

PrEP is becoming more available

Although PrEP is still not widely available in most countries and the number of people on PrEP is still low, its use is increasing in some parts of the world. For example, there have been an estimated 100 000 PrEP users in the United States since 2012, when the regulatory authorities in that country approved the use of TDF/FTC for PrEP. Plans to scale up use of PrEP are being carried out in an increasing number of countries in all regions.

PrEP can be cost-effective

Ultimately, HIV treatment and PrEP save money.

Expanded HIV treatment and PrEP require resources for salaries, training, medicines and laboratory testing. Ultimately, however, investing in these services may save money. Treatment prevents complications of HIV infection, which are expensive to treat and in some instances, such as tuberculosis, can be transmitted to others.

PrEP will also save costs because:

- PrEP prevents new HIV infections among its users, thereby averting the costs of lifelong ART.
- As PrEP also prevents onward transmission to others, additional cases of HIV infection will be averted, further avoiding the need for HIV treatment.
- Since people who would benefit from PrEP are those at greatest risk of infection, the impact-for-cost ratio of PrEP will be relatively high compared with other prevention approaches.
- PrEP is not a lifelong treatment; rather, it is used during specific periods of risk, therefore, costs are incurred on an *ad hoc* basis only.

"New York is leading the fight against AIDS, and this program will ensure individuals with the greatest risk of exposure can receive the support they need to stay healthy. […] Expanding PrEP assistance is a critically important step toward eradicating the AIDS epidemic in this state."

Andrew Cuomo

Governor of New York, USA

In many countries, the medicines used for HIV treatment and PrEP are now available in generic form at low cost. As of 2016, the average unsubsidized price paid by low- and middle-income countries for the medicines used for PrEP is approximately US$ 32.24 for TDF alone and US$ 55.10 for TDF/FTC per person treated per year *(18)*.

PrEP offers many social benefits

PrEP has mobilized people in the struggle for better health.

PrEP can strengthen global HIV treatment initiatives by decreasing the number of people who require lifelong treatment. It may also increase HIV testing by motivating people at higher risk of infection to test for HIV. This could result in increased and earlier diagnosis of people with HIV and their linkage to treatment. In addition, PrEP can provide another prevention option for people at ongoing HIV risk, particularly where other prevention choices may be difficult to use consistently or when people are unable to insist on condom use – for example, women who consider their partners to be at high risk of HIV although they have not been tested, or women whose partners are infected and not virally supressed on ART.

PrEP services are likely to attract people at higher HIV risk, who may also have other health and social needs. Therefore, PrEP access can serve as the gateway to additional social and health services, such as prevention and treatment of other STIs, contraceptive services, and counselling and social support.

"Maintenant que la PrEP a montré qu'elle fonctionne, il me semble que l'extension de l'accès à la PrEP n'est pas seulement une affaire de politique de santé publique, mais un droit humain impératif." ["Now that PrEP has been shown to work, access to PrEP is not only a public health policy matter, but an imperative human right."]

Francoise Barre-Sinoussi

Research director at the INSERM, France

PrEP can decrease HIV stigma by broadening the social responsibility for preventing HIV infection. It also offers a new option for serodiscordant couples, especially in the context of safer conception. PrEP has started to reinvigorate HIV prevention and to mobilize communities and people at ongoing HIV risk to call for more prevention choices.

HIV treatment, PrEP and PEP are important services that can have significant benefits in reducing HIV-related illnesses and deaths and preventing new HIV infections. Putting these services at the centre of national HIV plans can foster broad-based support in communities and countries.

Conclusion

Although implementing PrEP poses challenges in planning, managing and funding combination HIV prevention, it also offers new opportunities for accelerating the global HIV response. Realizing the promise of PrEP will require governments, funders, civil society and other stakeholders to join forces to systematically address important issues such as the licensing of antiretroviral medicines for PrEP use, setting priorities for locations and populations for implementation, making services user-friendly and ensuring adherence.

Supplementary information

Questions and answers on PrEP

What is PrEP?

PrEP stands for pre-exposure prophylaxis. It is the use of antiretroviral drugs by people who do not have HIV infection in order to prevent them from acquiring HIV. By definition it is a chemoprophylaxis.

PrEP tends to denote oral PrEP, which involves taking tablets orally. Other forms of PrEP are currently under investigation, including the use of a long-acting injectable and a vaginal ring.

Why do we need another option to prevent HIV?

Rates of new HIV infections globally have not fallen significantly over the past five years and continue to be high in some parts of the world and among some populations. Therefore, additional prevention choices are needed, such as PrEP, which can have benefits both for individual and public health. PrEP is being considered by many countries as an additional prevention choice for people at substantial risk of acquiring HIV – as part of combination HIV prevention programmes.

What is the evidence supporting the effectiveness of PrEP?

Most research on PrEP has focused on two antiretroviral drug regimens: TDF alone and TDF in combination with FTC. Based on high-quality evidence, the use of PrEP by any person at substantial risk of acquiring HIV infection is strongly recommended.

Twelve trials on the effectiveness of oral PrEP (TDF alone or TDF/FTC) have been conducted. These trials were held among a variety of populations, including serodiscordant couples, heterosexual men, heterosexual women, men who have sex with men, people who inject drugs, and transgender people. These trials took place in Africa, Asia, Europe, Latin America and the United States. Implementation projects, often referred to as demonstration projects, are underway in many countries to examine how PrEP can be offered in the frame of existing health services.

Is PrEP recommended by WHO?

Yes. In September 2015, WHO issued a strong recommendation supporting the implementation of PrEP for HIV prevention for people at substantial HIV risk. This recommendation is based on high-quality evidence obtained through a systematic review and meta-analysis of clinical research findings on PrEP. This systematic review conducted by WHO considered data from 15 randomized controlled trials and three observational studies and demonstration projects. Seven of the randomized controlled trials were double-blind placebo-controlled trials.

What does WHO actually recommend?

WHO recommends that people at **substantial risk of HIV** should be offered PrEP. In 2014, WHO recommended offering PrEP to men who have sex with men. On the basis of further evidence of the effectiveness and acceptability of PrEP, in September 2015 WHO broadened the recommendation to include all population groups at substantial risk of HIV infection.

Offering PrEP should be a priority for populations with an HIV incidence of approximately three per 100 person-years or higher. PrEP should be considered as an additional prevention choice in a comprehensive package of services, for various people and in various settings, and that also includes HIV testing, counselling, male and female condoms, lubricants, antiretroviral treatment for partners with HIV infection, voluntary medical male circumcision and harm reduction interventions for people who use drugs.

Who is PrEP for?

PrEP is for all people at substantial risk of HIV infection. PrEP can be particularly beneficial for people who are unable to use other HIV prevention methods, for example people who struggle using condoms or have barriers to condom use.

PrEP has sometimes been erroneously viewed as an option solely for men who have sex with men. Even though a majority of PrEP users globally are men who have sex with men, PrEP is also effective in women and other men. Thus, current

implementation efforts are also focusing on offering PrEP to women at substantial risk for HIV, including sex workers in some countries – particularly in sub-Saharan Africa, transgender women in most regions, and adolescent girls and young women in high incident settings in southern and eastern Africa. Among serodiscordant couples, the HIV-negative partner may benefit from taking PrEP when the partner with HIV infection is not virally suppressed on ART. PrEP may also be considered for women who would like to become pregnant when they have a partner with HIV who is not virally supressed on ART or who has not been tested but is at high risk of HIV.

PrEP is not suitable for everyone; moreover, it is not intended for lifelong use.

Which medicines can be used for PrEP?

Most of the evidence that PrEP is efficacious comes from clinical trials that have investigated TDF/FTC. One key trial, the Partners PrEP trial, showed that TDF alone and TDF/FTC had similar efficacy in reducing transmission of HIV in serodiscordant heterosexual couples. From a regulatory approval perspective, most countries that have approved PrEP have given authorization for a fixed-dose combination of TDF/FTC. In the future, there may be other medicines and formulations for PrEP.

Is PrEP always effective in preventing HIV infection?

PrEP provides very high levels of protection when used consistently. Clinical trials to date have shown that, when PrEP is taken properly, it can provide very high levels of protection from HIV infection (>90% reduction in HIV risk).

However, when the medicines are not taken as directed, PrEP effectiveness may be significantly lower. PrEP demonstration projects have shown that the majority of people, including people at substantial HIV risk, can adhere to PrEP consistently. However, adherence will benefit from regular encouragement and support at the individual level to address challenges in regular pill-taking.

Does PrEP protect against any other STIs?

PrEP prevents HIV infection when used consistently; however, its protection is limited to HIV. PrEP does not protect against STIs such as viral hepatitis infection, syphilis, gonorrhoea or chlamydia, nor does it offer women any protection against unintended pregnancy.

Is PrEP safe?

PrEP has an excellent safety profile. Across 10 randomized controlled trials, rates of adverse events did not differ between PrEP and placebo arms. TDF-containing PrEP may have an impact on the kidneys. Therefore, renal function needs to be examined prior to initiating a person on PrEP and monitored during PrEP use.

TDF is also recommended by WHO to treat hepatitis B virus (HBV) infection. PrEP containing TDF can be used safely in people with HBV. Not all people with evidence of chronic HBV infection require treatment (see the WHO *Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection*)*(19)*. If HBV treatment is indicated, daily oral PrEP containing TDF can be used for treatment of HBV and HIV prevention concurrently. If PrEP is stopped, consideration should be given to continuing another active HBV treatment (if indicated) to avoid the risk of virological and clinical flares.

Can PrEP be used during pregnancy and breastfeeding?

All data reviewed by WHO show that PrEP is safe during pregnancy and breastfeeding. The antiretroviral drugs used for PrEP – TDF alone or TDF/FTC – are frequently used for HIV treatment in combination with other antiretroviral drugs. In 2016, WHO conducted a systematic review that specifically examined the safety of PrEP. The main conclusion of that review was that there does not appear to be a safety-related rationale for disallowing or discontinuing PrEP during pregnancy and breastfeeding for HIV-negative women who are at continuing risk of HIV acquisition.

What package of prevention services should be provided along with PrEP?

HIV testing is needed before a person is initiated or restarted on PrEP. Re-testing is also needed to ensure there is no HIV breakthrough infection.

Condoms should be offered to all PrEP users. Condoms are the mainstay of HIV prevention among sex workers, who should be empowered to demand the use of condoms with clients. Clean injection equipment and opioid substitution therapy are the mainstay of HIV prevention among people who inject drugs, and should be made available. The reproductive desires of all PrEP users should be assessed and contraception provided whenever requested.

People at substantial risk for HIV infection are also at risk for other STIs, therefore, testing and treatment of STIs or syndromic management should be available. Counselling should be client-centred and interactive and include the formulation of individualized plans for protection from HIV and other STIs as well as the attainment of reproductive goals. Hepatitis B vaccination should be provided if the vaccine is available. ART is recommended for people who test HIV-positive. Sexual partners who are HIV-positive should be offered HIV treatment.

Will PrEP cause people to stop using condoms or have more sexual partners?

Condom use has been studied in-depth in the clinical trials that have established PrEP effectiveness. No evidence was reported of a decrease in condom use or an increase in the number of sexual partners after people started using PrEP.

It is important to recognize that while some people use condoms consistently, many – if not most – do not. Condoms are used less frequently if pregnancy is desired or is not a concern, or if there is a wish for greater intimacy. Periods of substantial HIV risk are often characterized by little or no condom use or frequent changes in sexual partners. PrEP may be valuable during such periods, when sexual exposure to HIV is already high.

Does PrEP cause HIV drug resistance?

The risk of HIV drug resistance is low during PrEP use, occurring in approximately one in 1000 PrEP users in clinical trials. The occurrence of drug resistance in those trials was almost exclusively among people who had acute undetected HIV infection when they started PrEP.

What are the costs associated with PrEP uptake – both in high uptake and lower uptake scenarios?

The costs of PrEP are lower than treatment costs, partly because the medicines used for PrEP are less expensive than full combination therapy used to treat HIV infection. Furthermore, while PrEP is used during periods of risk, treatment of HIV is a lifelong intervention. Furthermore, treated HIV infection is sometimes associated with medical conditions that require costly treatment, for example cardiovascular disease and certain types of cancer.

A large portion of the cost of PrEP is the price of the medicines, which is as low as US$ 32.24 per person per year for TDF and US$ 55.10 per person per year for FTC/TDF in many countries.

Are there other PrEP medicines being investigated?

Topical and longer-acting PrEP medicines and formulations are being investigated, which could provide more choice and improve long-term adherence. These include slow-release dapivirine in vaginal rings, long-acting cabotegravir injections and subcutaneous implants with TDF derivatives. If they prove to be effective, they may also be tested in combination with contraception.

Where is PrEP being implemented?

Many countries are considering adopting the WHO recommendation for oral PrEP and are looking at how to balance the introduction of PrEP with other prevention options and the critical need to offer HIV treatment to all people with HIV.

PrEP is being distributed in the context of clinical trial research, pilot projects and larger-scale demonstration projects.

PrEP is also available informally in most countries from Internet sources. In addition, PrEP is often available formally through private healthcare providers. The country with the largest number of PrEP users is currently the United States, where clinical guidance for PrEP was first issued in 2011 and regulatory approval of TDF/FTC was given by the Food and

Drug Administration in 2012. Since then, over 100 000 people have been prescribed PrEP. In Europe, France was the first country to approve the use of TDF/FTC for PrEP and offer it under its social healthcare system. Norway and Scotland are also now offering PrEP under their national health systems.

In Africa, there are many countries that are beginning to implement PrEP, particularly in regions where HIV incidence remains high (for example, eastern and southern Africa). Currently, South Africa and Kenya have the most ambitious plans for the roll out of PrEP. PrEP programmes for adolescent girls, young women and sex workers are being considered in several high burden countries, including as part of the PEPFAR DREAMS programme.

In the Asian-Pacific region, Australia is implementing PrEP – with an estimated 10 000 PrEP users enrolled in a number of PrEP demonstration projects. TDF/FTC has regulatory approval in Australia, although it is not currently being reimbursed by health authorities.

Several countries In Latin America participated in the first large multi-country PrEP clinical trial called iPrEx. Brazil has plans to implement PrEP throughout the country under its public health system. Other countries in the region are looking to implement PrEP among populations at high risk of HIV infection, particularly men who have sex with men and transgender persons.

Do you need regulatory approval for PrEP?

Each country's medicines regulatory agency is responsible for authorizing the use of antiretroviral drugs for HIV prevention. Some countries may decide to make PrEP available off-label, while other countries may elect to have an indication for PrEP. In order to have an indication for PrEP, the manufacturer has to file a dossier with the national medicines regulatory agency.

To date, more than 15 countries have provided medicine manufacturers with marketing authorization (regulatory approval) for the use of TDF/FTC as PrEP. Approval is pending in at least a further 10 countries.

Further reading

Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. Geneva: World Health Organization; 2015 (http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/).

Consolidated guidelines on the use of antiretroviral therapy: a public health approach. Geneva: World Health Organization; 2016 (http://www.who.int/hiv/pub/arv/arv-2016/en/).

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