MODULE 1

CLINICAL

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; performing appropriate testing before initiating someone on PrEP and while the person is taking PrEP; and how to follow up PrEP users and offer counselling on issues such as adherence.

Module 2: Community educators and advocates. For PrEP services to reach populations in an effective and acceptable way, community educators and advocates are needed to increase awareness about PrEP in their communities. This module provides up-to-date 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 addressing issues around 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 most effectively implemented in their own settings. It also contains a series of frequently asked questions about PrEP, with related answers.

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 under a pharmacist's supervision. It provides information on the medicines used in PrEP, including the optimal storage conditions. It also 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 are responsible for providing testing services at PrEP sites and associated laboratories. It offers guidance in selecting relevant testing services, including appropriate screening of individuals before PrEP is initiated and monitoring while they are taking PrEP. Information is provided on testing for HIV, creatinine, hepatitis B and C virus, pregnancy and sexually transmitted infections.

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.

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 clinical module

This module seeks to provide an overview of relevant information for clinicians, including physicians, nurses and clinical officers, who are providing PrEP in clinical settings. It describes important considerations when starting PrEP in an individual and monitoring PrEP use.

The following two-sided pocket card summarizes this module.

Example of a pocket card for PrEP providers

WHO CLINICAL PREP BASICS

Indications for PrEP (by history over the past 6 months):

HIV-negative AND
Sexual partner with HIV who is not virally supressed, OR
Sexually active in a high HIV incidence/prevalence population AND any of the following:
- Vaginal or anal sexual intercourse without condoms with more than one partner, OR
- A sexual partner with one or more HIV risk factors, OR
- A history of a sexually transmitted infection (STI) by lab testing or self-report or syndromic STI treatment, OR
- Use of post-exposure prophylaxis (PEP), OR
- Requesting PrEP.

Contraindications:
- HIV-positive
- Estimated creatinine clearance <60 ml/min
- Signs/symptoms of acute HIV infection, probable recent exposure to HIV
- Allergy or contraindication to any medicine in the PrEP regimen.

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Rx (example): TDF 300 mg + FTC 200 mg PO daily #90 tablets.

Counselling: Link tablet use with a daily routine.

Develop a plan for contraception or safer conception and for STI prevention.

Key effectiveness messages:
PrEP is highly effective for preventing HIV infection when used as prescribed.
PrEP does not prevent pregnancy or STIs.

Side-effects:
1 in 10 PrEP users may have side-effects such as nausea, abdominal cramps, headache; these are usually mild and resolve over the first month of taking PrEP.
1 in 200 may have creatinine elevation (typically reversible if stop PrEP).
1% average loss of bone mineral density; recovers after stopping PrEP.

Initial tests:
HIV test; suggest Cr, HBsAg, STIs screening (e.g. syphilis, gonorrhoea, chlamydia); consider HCV for MSM.
Every 3 months: HIV test, suggest check STIs, assess PrEP indications and use.
Every 6 months: Suggest Cr.'

#OfferPrEP

Special situations:
- Exposure to HIV in the past 72 hours: use PEP for 28 days, then start PrEP.
- Acute viral syndrome: consider re-testing in 1 month before PrEP initiation.
- Pregnancy and breastfeeding: PrEP can be offered and continued.
- If HBsAg *negative*: consider vaccination; if HBsAg *positive*: assess HBV treatment indications; consider risk of flare if PrEP stopped.
- Adolescents: may benefit from more frequent appointments e.g. monthly visits.

More information: http://who.int/hiv/pub/prep/prep-implementation-tool

Eligibility for PrEP

PrEP providers should educate and counsel potential PrEP users about the risks and benefits of PrEP and may conduct an individualized risk-benefit assessment to assess eligibility.

Eligibility criteria include:

- HIV-negative
- no suspicion of acute HIV infection
- substantial risk of HIV infection
- no contraindications to PrEP medicines (e.g. TDF/FTC)
- willingness to use PrEP as prescribed, including periodic HIV testing.

The sexual partner of someone with HIV who is not on suppressive ART

PrEP can protect the HIV-negative partner in a serodiscordant relationship when the HIV-positive partner is either not on antiretroviral therapy (ART) or has not yet achieved viral suppression.

ART that suppresses viral load is highly effective for preventing HIV transmission to others *(1)*. Still, PrEP may provide additional protection to serodiscordant couples in a number of situations:

1. ART may take up to six months to suppress viral load; in studies of serodiscordant couples, PrEP has provided a useful bridge to full viral suppression by the partner during that time *(2)*.
2. The HIV-negative partner has doubts about the effectiveness of the partner's treatment or has other partners besides the HIV-positive partner on treatment.
3. There have been gaps in the partner's treatment adherence or the couple is not communicating openly about treatment adherence and viral load test results.

In addition, any sign of intimate partner violence, controlling behaviour, or anger or fear in response to questions about HIV treatment may prompt a discussion about the risks and benefits of PrEP as a possible way to control the risk of HIV transmission. This would also be an opportunity to refer the person to prevention and treatment services for intimate partner violence.

Screening for "substantial risk of HIV infection"

PrEP should be considered for other people who are at substantial risk of acquiring HIV *(3)*. This could include someone in **a high HIV prevalence population or geographical location** who has had any of the following risk factors in the past six months:

- vaginal or anal sexual intercourse without a condom with more than one partner, OR
- a recent history (in the last six months) of a sexually transmitted infection (STI) by laboratory testing or self-report or syndromic STI treatment, OR
- has used post-exposure prophylaxis (PEP) for sexual exposure in the past six months.

Indicators of substantial risk of HIV infection vary depending on local HIV epidemiology and population group (see module on strategic planning).

Inconsistent use of condoms (male or female), including an intention to use condoms during sex with some occasional omissions or accidents, increases HIV risk *(4)*. Social desirability bias in reporting condom use may occur, so PrEP could be considered for people reporting any intercourse without a condom or concerns about their future use of condoms. For example, someone who reports a desire to stop using condoms may be already having sex without condoms.

Recently diagnosed STIs are often indicators of risk of sexual acquisition of HIV. The predictive value of STI indicators varies by region, the type of STI and a person's demographic characteristics. A new diagnosis of syphilis or genital herpes is a strong predictor of HIV risk among men who have sex with men in most settings and among heterosexual men and women in areas of high HIV prevalence. PrEP services should be prioritized; local epidemiology will be essential to guide decisions about when to offer PrEP and to which populations.

Requesting PrEP has been shown to be an indicator of substantial risk *(5–8)*. HIV incidence among people requesting PrEP has been higher than expected from observational studies in the same locality *(6–8)*. People at high risk of acquiring HIV infection who request PrEP tend to have greater PrEP uptake, adherence and retention. Clinicians should consider any request for PrEP seriously *(8)*, especially for individuals in settings where the local epidemiology indicates likely substantial HIV risk in their population group.

People who use and/or inject drugs are often at substantial HIV risk. WHO recommends a package of effective HIV services be provided for all people who inject drugs, including harm reduction (in particular opioid substitution therapy and needle syringe programmes). When these interventions are available, the risk of HIV transmission is significantly reduced. Providing these services should be a priority.

People who use and/or inject drugs may also be at risk of sexual transmission of HIV. In particular, this may be the case among people who use amphetamine type stimulants and engage in higher risk sexual practices (including among some subgroups of men who have sex with men in some settings). There may also be a link with sex work and not being empowered to use condoms consistently with all clients or with intimate partners.

Access to harm reduction remains the mainstay of HIV prevention for people who inject drugs. However, this population should not be excluded from PrEP services. PrEP can be considered for people who use drugs for whom harm reduction services – sterile injecting equipment and opioid substitution therapy – are not relevant, such as people using amphetamine type stimulants who are at substantial risk of HIV infection.

Practical screening questions

PrEP should be provided to individuals who want to use PrEP ***if local criteria for PrEP use are met.*** Easy and practical questions could be developed for screening individuals for PrEP. However, asking questions should not be seen as a way of rationing PrEP or excluding people from PrEP services. In PrEP demonstration projects and clinical services, people who asked for PrEP were likely to have made this choice based on a careful assessment of their own personal circumstances, risk and desire for additional HIV prevention.

Screening questions should be framed in terms of people's behaviour.

Screening questions can be used to introduce the consideration and offer of PrEP to people who are attending services but had not presented specifically to access PrEP. Preferably, screening questions should be framed in terms of people's behaviour rather than their sexual identity and should refer to a defined time period. It is important for PrEP providers to be sensitive, inclusive and non-judgemental, and support people who want and would benefit from PrEP rather than develop a screening process that would discourage PrEP use.

For example, some of the following questions could be used to identify individuals who may benefit from PrEP.

1. General screening questions. Any "yes" answer from a person presenting in a high HIV incidence setting should