

**Kingdom of Cambodia
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Ministry of Health

**Concept-note on
HIV Pre-Exposure Prophylaxis (PrEP) Implementation
in Cambodia**

March 2019



National Center for HIV/AIDS, Dermatology and STD

Foreword

Cambodia is one of the only seven countries in the world which has achieved the HIV 90-90-90 targets in 2010, which is three years before the world's deadline¹. The Ministry of Health supports the implementation of the health sector strategic plan for HIV and STI for the period 2016-2020, and strategic priority interventions namely the test and treat, post-exposure prophylaxis (PEP), the partner notification tracing and testing (PNTT) and self-testing.

Participated by the Minister of Health of Cambodia in the 90-90-90 Targets Workshop in July 2017, in Paris, Cambodia's achievement on HIV and AIDS response was showcased, and the His Excellency Minister of Health stated in this special occasion that "We are proud of the expansion and coverage of life saving services that we have achieved. And we are committed to address the remaining challenges to sustain these results....".

Moving forwards to reach the 95-95-95 targets by 2025, and to move to virtual elimination, the Ministry of Health is specifically committed to support one key innovative approach to prevent HIV transmission amongst high risk populations, the PrEP that has already been implemented in most countries in the region.

The Ministry of Health strongly hopes that all concerned stakeholders will implement this PrEP concept note innovatively while contributing to a more efficient use of resources and achieving the goal of elimination of new HIV infections in Cambodia by 2030. (17)

Phnom Penh, 21 May 2019

Minister of Health

Prof. ENG HUOT
SECRETARY OF STATE

¹ UNAIDS Press release, 2017.

Acknowledgement

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My thanks also go to NCHADS' staff and all individuals from development partners for their contribution to the drafting of this document, especially thanks to the staff of Chhouk Sar Clinic and networks of high-risk populations who have also contributed to develop the concept note successfully.

Phnom Penh, 26.../April 2019



Dr. Ly Penh Sun
Director, NCHADS

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Abbreviations

3TC	Lamivudine (antiretroviral drug)
ARS	Acute Retroviral Syndrome
ART	Antiretroviral Treatment
ARV	Antiretroviral
B-IACM	Boosted-Integrated Active Case Management
CBO	Community-based Organization
EW	Entertainment Worker
FTC	Emtricitabine (antiretroviral drug)
GFR	Glomerular Filtration Rate
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
MSM	Men who have Sex with Men
NCHADS	National Center for HIV/AIDS, Dermatology and STD
PCR	Polymerase Chain Reaction
PEP	Post Exposure Prophylaxis
PLHIV	People Living with HIV
PrEP	Pre-exposure Prophylaxis
SOP	Standard Operational Procedure
STI	Sexually Transmitted Infection
TasP	Treatment as Prevention
TDF	Tenofovir Disoproxil Fumarate
TG	Transgender Women
TWG	Technical Working Group
UNAIDS	Joint United Nations for HIV/AIDS Program
USAID	United States Agency for International Development
WHO	World Health Organization

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List of contributors to the development of the concept note on PreP in Cambodia

Excellency Dr. Mean Chhivun	Advisor to the Minister of Health
Dr. Ly Penh Sun	Director, NCHADS
Dr. Lan Van Seng	Deputy Director, NCHADS
Dr. Ouk Vichea	Deputy Director, NCHADS
Dr. Samreth Sovannarith	Head of the Technical Bureau, NCHADS
Dr. Ngauv Bora	Deputy Head of Technical Bureau, NCHADS
Mr. Ung Polin	Program Officer, UNAIDS
Dr. Sok Bunna	Project Management Specialist HIV/AIDS, USAID
Dr. Robert Stanley	Senior HIV Technical Advisor, USAID
Dr. Steve Wignall	Director, FHI/360 Linkages
Dr. Frits van Griensven	Consultant, FHI360/Linkages
Ms. Seng Sopheap	Deputy Director, FHI360/Linkages
Dr. Chel Sarim	Program Specialist HIV/AIDS, FHI360/Linkages
Ms. Nith Sopha	FHI360/Linkages
Dr. Tea Phauly	Consultant
Mr. Im Chanry	Strategic Information Advisor, FHI360/Linkages

1. Introduction

1.1 Achievements

Cambodia is one of seven countries in the world which has achieved the 90-90-90 targets in 2010. HIV prevalence in the general adult population declined from an estimated 1.6% in 1998 to 0.6% in 2017². During the same year, Cambodia announced its intent to further control the HIV epidemic by achieving the UNAIDS 95-95-95 targets (95% of those infected know their status; 95% of those HIV+ enrolled in ART; 95% of those on treatment are virally suppressed at 12 months) and moving towards the elimination of new HIV infection by 2030. Through its boosted integrated active case management (BIACM) program, Cambodia has diagnosed approximately 85% of the estimated population of PLHIV, placed nearly all diagnosed PLHIV on ART, and has documented significant viral load suppression in PLHIV on ART.

1.2 Strategic priority interventions

Strategic priority interventions used so far to achieve 90-90-90 targets comprise increased access and uptake of HIV testing, including partner notification, tracing and testing (PNTT), decreased stigma and discrimination, robust B-IACM, HIV post-exposure prophylaxis and continued emphasis on 100% condom-use. To achieve 95-95-95 targets by 2025, the Royal Government of Cambodia is committed to support key innovations namely Test and Treat Strategy and HIV self-testing.

1.3 HIV epidemiology in key populations

While the above-mentioned strategic interventions are expected to further reduce and eventually control the spread of HIV in the general population, of concern is continued HIV transmission in a limited number of small high-risk key populations. Latest available key-population data show HIV prevalence is 3% among entertainment workers (EWs), 2% among men

² Estimation and projection, AEM 2017.

who have sex with men (MSM), 6% among transgender women (TG), and 15% among persons who inject drugs (PWID) (2-5).

Despite these high prevalence rates, consistent condom use among key population members remains low (69% in MSM during anal sex) (3), especially with non-commercial sexual partners (38% for TG) (6). In addition, structural barriers such as stigma and discrimination in the health care system and self-stigma continue to hamper easy access to HIV and STI testing, treatment and care services. Sexual partners of HIV-infected general population members with high, uncontrolled HIV viral load also remain at high risk for infection.

Entertainment venues for MSM and other men who have sex with men to socialize and meet sexual partners can be found in Phnom Penh and Siem Reap. Many MSM use online and hand-held social media providing a virtual space for them to find and meet sexual partners, sometimes in exchange for money, goods or favors (7). According to informal focus group discussions, practices such as sex-on-drugs parties with the help of stimulant and erectile dysfunction agents have been introduced and are gaining popularity in the MSM community of Phnom Penh. Elsewhere, such activities have been implicated in a surge of new HIV infections, often in outbreaks of phylogenetically associated chains of acute HIV infection (8, 9). Implementation of effective HIV prevention methods for high risk MSM, such as combination HIV prevention, including pre-exposure prophylaxis (PrEP), are essential to avoid the HIV outburst scenario seen elsewhere. The Treatment as Prevention (TasP) and PrEP have been implemented in some countries in the world and in Asia Pacific region.

1.4 Need for additional HIV prevention tools

The current health sector strategic plan for HIV and STI 2016-2020, articulates a more focused, targeted and prioritized responses for intensified HIV prevention programming among key and other populations at risk for infection. Combination HIV prevention, consisting of behavior change interventions, anti-retroviral (ARV) PrEP, and treatment-induced viral suppression (treatment as prevention), has been identified as essential approach to achieve epidemic control.

To expand access to the full range of combination prevention services, MoH endorses implementation of PrEP as an additional tool to reduce the spread of HIV in high-risk populations.

In the recent past, NCHADS and its partners have produced a series of successful concept notes, including operational guidance notes on reaching hard-to-reach sub-groups of key populations and peer-driven interventions for new HIV case detection. This current concept-note on HIV PrEP hopes to be another important step in the expansion of the prevention tool-box using PrEP to help achieve and maintain HIV epidemic control in Cambodia.

2. PrEP overview

2.1 World Health Organization recommendations

The World Health Organization (WHO) recommends the use of ARV PrEP containing Tenofovir Disoproxil Fumarate (TDF) alone or in combination with another nucleoside reverse transcriptase inhibitor (NRTI), such as Emtricitabine (FTC) or Lamivudine (3TC) as a scientifically proven, additional HIV prevention measure for people at substantial risk for HIV infection since 2012 (10,11,14, 17-20). The implementation is recommended as part of the combination of HIV prevention, which includes; 1) continues to emphasize behavioral modification (partner reduction), 2) condom use, 3) avoidance of penetrative sex and other risk behaviors (such as using or injecting drugs), 4) promotes regular HIV/STI testing, and 5) treatment and care. PrEP has been shown to be a highly efficient method to prevent sexually and parenterally acquired HIV infection when taken consistently. It has an excellent safety profile and has low risk for ARV drug resistance. Additional documents and guidelines on PrEP were produced by WHO, UNAIDS and US CDC in 2015-2018 to reinforce and expand its implementation.

2.2 Global and Asia-Pacific Regional PrEP Uptake and Practices

Many Western countries including the US, UK, France, Belgium and the Netherlands have embraced the WHO recommendations and have made PrEP available through insurance or self-pay. Australia, London, San Francisco and Washington DC have all shown that PrEP in

combination with early testing and treatment dramatically reduced new cases of HIV infection among high risk populations such as MSM and TG.

In the ASEAN region, with the exception of Singapore and Brunei (where HIV/ AIDS is not an issue), most countries have introduced PrEP as a new approach to prevent HIV transmission amongst high risk populations. Thailand, Lao PDR and Vietnam are moving to scale-up their PrEP programs. China, Malaysia and the Philippines are conducting or expanding PrEP demonstration projects. **Figure 1** shows countries in ASIA with current PrEP programming.

Figure 1: PrEP implementation in Asia

PrEP in Asia



3 Rationale

To end AIDS and eliminate new HIV infections by 2025 in Cambodia, more collective and intensified strategic efforts are necessary. The NCHADS-led Cambodian national HIV program has already achieved tremendous reductions in the number of new HIV infections. It has promoted

behavioral risk reduction, condom use and treatment as prevention through its test and treat strategy and early case detection via screening of individuals at high-risk.

PrEP offers a complementary bio-medical approach to prevent the acquisition of HIV infection and the consequent morbidity and mortality, human suffering, cost to society and stop onward transmission. For some, hopefully many, PrEP will be a positive attraction to come to clinics to access ARV and agree to HIV screening where in the past they may have avoided because of stigma associated with their risk behaviors or the possibility of being HIV infected.

In Cambodia, NCHADS plans to initially offer PrEP as a service for individuals at high risk for HIV infection attending Chhouk Sar Clinic and an ART clinic³ in Phnom Penh. EW, MSM and TG will be the primary target populations. A regimen of daily TDF+3TC (300/300mg) will be given. Recommended by WHO as an alternative to TDF/FTC (Truvada), this fixed-dose combination with either Nevirapine or Efavirenz, is already in use in Cambodia (10, 11). Following a one-year implementation period, close monitoring, and evaluation, the intent is to scale PrEP service to other public, private, and NGOs clinics in the country.

4. Objectives

The current concept note provides a summary and local adaptation of WHO, Australasian Society for HIV Medicine and US Centers for Disease Control HIV PrEP guidelines (10-20).

a) The objectives of this concept-note are to:

1. Support the prescription of locally approved and available co-formulations of TDF/3TC for PrEP;
2. Assist clinicians and health care workers in evaluating clients for HIV PrEP suitability and eligibility;

³ When making decision on the selection of a particular ART site, there is a need to ensure that such site has been frequently accessed by KPs.

3. Assist clinicians and health workers in counseling, initiating and monitoring clients on HIV PrEP.

b) The purpose of introducing PrEP is to reduce the spread of HIV infection among key-populations.

5. Implementing arrangements

5.1 Leadership, governance and coordination

PrEP implementation will be under the guidance of the National Technical Working Groups (TWG) for HIV Care and Treatment and for Prevention led by NCHADS. TWGs include community representation which will be crucial in assuring that there is awareness of this new addition to the prevention armamentarium and how it can be accessed.

The TWGs will play critical role in reviewing and commenting the PrEP standard operating procedures (SOPs) that will be developed and submitted to NCHADS who will in-turn submit it to Ministry of Health for approval. The TWGs will also have a role to monitor the implementation of the PrEP. Quarterly meeting will be organized for this purpose. With technical support of LINKAGES, the PrEP implementation team, composed of Chhouk Sar and ART Clinics staff, brokers and community representatives, will brief the TWGs on implementation progress.

5.2 PrEP eligibility criteria

5.2.1 Behavioral Risk Criteria

HIV-uninfected individuals of 18 years and older with substantial risk for HIV infection are eligible and will benefit most from PrEP. Common substantial risks include but are not limited to:

- Being an HIV uninfected sexual partner of a PLHIV who is not virally suppressed, or results of viral load testing are unknown (i.e., HIV discordant couples) and where condoms are not consistently used.

- Had condomless anal/vaginal/neovaginal sex in the past 6 months with more than one partner.
- History of any new sexually transmitted infection (STI) in the past 6 months.
- Used drugs for sexual pleasure during the past 6 months and there is condomless sex or inadequate access to sterile injecting equipment.
- Injected drugs in the past 6 months where injecting equipment shared or there is inadequate access to sterile injecting equipment.
- Received post-exposure prophylaxis (PEP) one or more times in the past 12 months.
- If the sexual partner of the person has one or more of the HIV risk factors listed above.

5.2.2 Clinical criteria

Even though PrEP has a good safety profile, there are several contra-indications for prescribing PrEP. Therefore, the following individuals may take PrEP:

- Must be HIV negative. So, someone being known to be HIV infected or suspected to be HIV infected or in the HIV window period where no HIV antibodies can be detected by 4th generation antibody tests cannot take PrEP. PCR, if available can reduce the window period to a few days but cannot eliminate it.
- Must be free of symptoms of acute retroviral syndrome (ARS).
- Must have good renal function (creatinine clearance (> 60 mL/mn)).
- Must be free of any ARV drug allergy (either to TDF or its companion drug 3TC).
- Must have enough body weight (>35 kg).
- Clients with chronic or acute hepatitis B infection may take PrEP but with caution under the guidance of an experienced physician. For someone on PrEP, he/she should be warned that stopping may cause suppressed HBV infection to flare.

PrEP has no or minimal drug interactions with commonly prescribed medicines nor significant side-effects and has proven to be safe in many randomized controlled trials. PrEP can be used safely by most people including:

- Pregnant or breastfeeding women.
- Women using hormonal drugs for contraception.
- Transgender persons on gender-affirmative hormone therapy.

5.3 Model for PrEP management

A graphic representation of the PrEP program overview is presented in **Figure 2** below.

5.3.1 Service delivery points of PrEP

5.3.1.1 Facility-based approach

Facility-based approach refers to PrEP service to be provided at a clinic where potential clients will come on the own to register, or could be referred by a broker. Initially, PrEP will be offered at Chhouk Sar Clinic which is a primary care clinic providing HIV and STI testing, counseling, treatment and care services. It is attended by a relatively large number of high-risk key population members. An ART clinic (to be selected amongst the four ODs in Phnom Penh) providing similar types of services to high-risk key populations will also be considered. Thirdly, the social health clinic could also be considered. NCHADS will provide overall guidance; CBOs will create demand and clinic staff will be responsible for the PrEP program enrollment and drug delivery. While most people will receive drugs free of charge⁴, paid⁵ option for those who can afford will be considered to ensure the sustainability of the program.

⁴ Criteria for paid option, the amount to be paid, as well as the management of income generated at the clinic level, will be discussed and decided.

⁵ For this initial period, PrEP will not be charged. But in the future, most probably this service will be charged to the clients.

5.3.1.2 Community-based approach

The community-based approach refers to the arrangement where outreach workers (brokers) will contact potential clients and encourage them to be on PrEP. Note that in this case only well-organized (capable) broker who are well linked to their peers will be selected. This approach intends to reach very high risk and hard to reach KPs who are unlikely to access the facility-based clinic for this purpose.

For instance, in the case of MSM group, the broker (PANPA) who manages 40 to 50 peers and their partners can play a critical role to provide PrEP information and counseling. The PANPA could be selected⁶, based on good relationship with their peers, to participate in the training on PrEP. They will perform the following key tasks: (i) behavioral risk assessment: as they know very well about sex behavior of their members, so they can fulfill the role of checking the behavioral risk criteria; and (ii) clinical assessment⁷: Community or peer initiated HIV testing and counseling (C/PICT) has been introduced since 2013. Some PANPA had participated in HIV counseling and testing using finger prick. These individuals could be trained on PrEP, perform clinical assessment and HIV testing of potential PrEP clients.

To ensure the clients' blood status of no HIV infection in the window period, the first HIV testing should be performed using a 4th generation⁸ HIV test at month zero and at month one. Knowing that there is no HIV tests can eliminate the window period, the HIV PrEP training package should include some knowledge on body weight (>35 Kgs), allergy fo PrEP ARV, and referral mechanism to ART facility.

5.3.2 Demand and awareness for clients

CBOs (outreach workers) will work closely with the MSM and TG communities to create awareness and demand of PrEP. Face-to-face contact, online programming and social media will

⁶ The same approach will be applied for EW, TG and PWID.

⁷ At the start the brokers may need coaching (in addition to the training) from a physician to do clinical evaluation; but later on he/she would be able to do on their own.

⁸ Another HIV test formula, using a 3rd generation test, was dropped as such test is no longer used.

be used to educate key population members about the availability of PrEP. They will stress the importance of combined protection of condom use with PrEP and adherence. The CBOs will also work with Chhouk Sar, ART Clinic or social health clinic to refer high-risk clients for PrEP and support adherence among those who choose to take it. The Strategic Behavior Change Communication team at NCHADS will use their social media channels to educate key populations about PrEP, its benefits and risks, importance of adherence and how to access it.

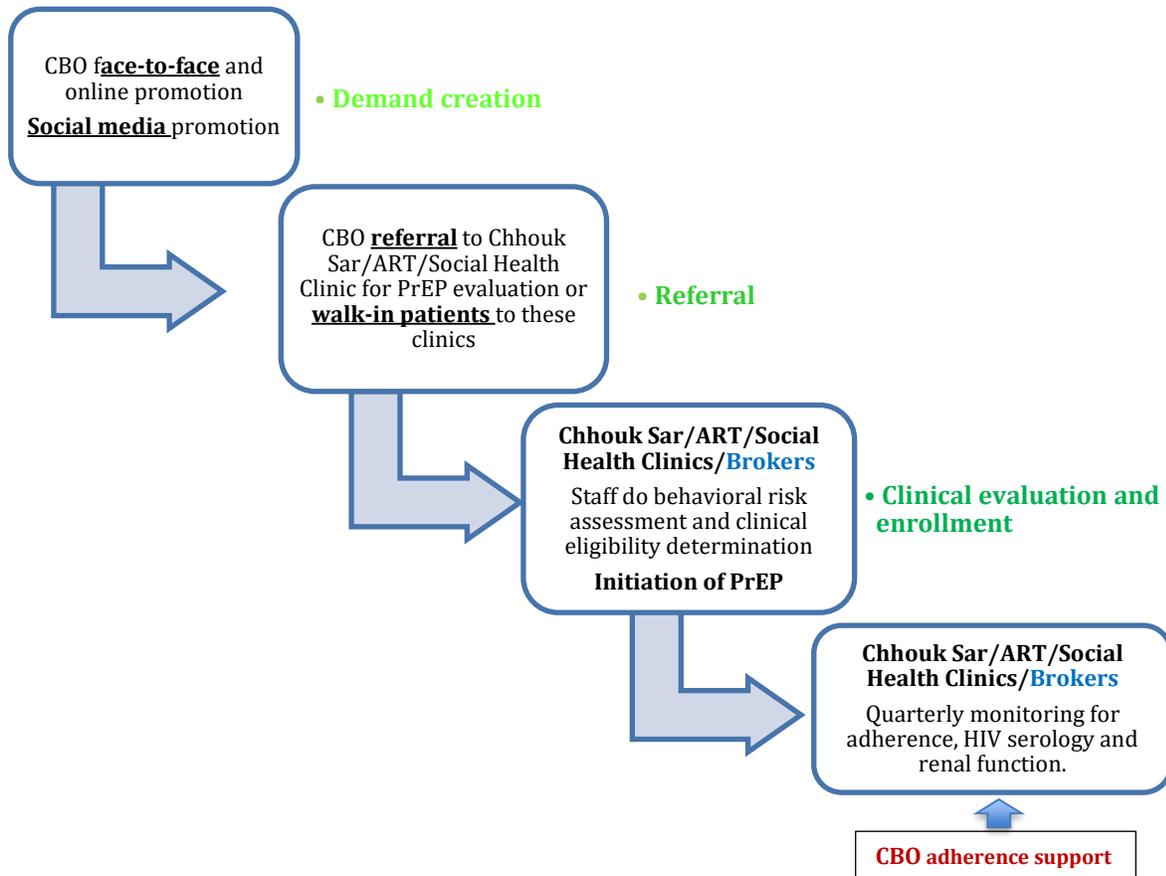
5.3.3 Identification of potential PrEP users

As highlighted above, potential PrEP users will be identified through two approaches:

- The first one, called facility-based, is cases that most potential users will come on their own (self-identified) to Chhouk Sar or ART clinic or Social Health Clinic requesting for registration and treatment. During counseling of first-time and repeat testers, those at high-risk will be educated and asked about their interest in taking PrEP; and they will be counseled regarding the benefits and risks of PrEP, and enrolled if eligible and committed to being adherent.
- The second one, called community-based, refers to those who will be contacted by brokers (EW's broker, MSM's broker or TG's broker) and asked to register and enrolled in the treatment. As above mentioned, clients will be counseled regarding the benefits and risks, and enrolled if eligible and committed to being adherent.

To this end, potential brokers (for EW, MSM, TG) in relevant location in Phnom Penh will be selected, trained and engaged in this initiative. A pharmacy might also be selected for those who do not want to go to the health facilities/clinics. NCHADS, with the support of FHI360, will be responsible for selecting and training of the brokers. For both options, free and paid services will be applied.

Figure 2: Diagram of PrEP Implementation



5.3.4 Prescription of PrEP

5.3.4.1 Clinical assessment

Prior to prescribing PrEP, medical history and a physical exam should be performed. Acute HIV infection should be suspected in persons with a recent high-risk exposure. Most common symptoms include fever, headache, coughing and malaise, whereas abnormalities are related to head, ears, nose and eyes, lymphadenopathy and tachycardia (12). Individuals presenting with symptoms or signs of acute HIV infection should not be started on PrEP until HIV infection has been excluded.

Also, those with known renal preconditions, especially renal function loss, should also be excluded. Therefore, all PrEP candidates should be evaluated for the presence of risk factors for renal disease, i.e., diabetes, hypertension, smoking, concurrent medication use or known history of renal impairment.

5.3.4.2 Counseling

Counseling for potential PrEP clients should focus on increasing awareness of PrEP as an additional HIV prevention method (i.e., should be applied in combination with other prevention methods including condom use, reduction in number of sexual partners), whether PrEP is the right prevention method given the risk behavior profile of the client and that PrEP provides optimal but not 100% protection from HIV infection. Pre-PrEP counseling should inform the client about the following topics:

- PrEP is highly effective when taken daily or on an event-driven basis. Effectiveness goes down if fewer doses are taken than recommended. If a dose is missed it should be taken the next day. Dose should never exceed 2 pills/day.
- Additional HIV prevention, e.g. condoms, should be used for the first 7 days. If using the daily regimen, at least seven days of PrEP intake are required to achieve protection from HIV infection through condomless receptive anal, vaginal intercourse and injection drug use.
- Additional HIV prevention measures should be taken during the period necessary to reach protective blood levels.
- Protection from HIV infection stops once PrEP is discontinued. PrEP should be continued for 28 days after the last possible HIV exposure.
- PrEP does not protect against STI and pregnancy. It should be advised to use PrEP in combination with condom use.
- Persons who inject drugs (PWIDs) should be educated about the single use of sterile injection equipment, avoidance of sharing of needles, syringes and other drug paraphernalia, and if possible, referred for opioid replacement therapy.
- PrEP can be taken with food or on an empty stomach. Linking PrEP intake with a daily routine (such as a meal) may improve adherence. PrEP can be taken with alcohol.

- PrEP drugs should be stored at room temperature, away from sunlight, heat, cold and moisture.
- PrEP drugs should not be shared or sold. Emphasize the risk of an alternative recipient being in the HIV window phase, having acute HIV infection, other contraindications and the risk of causing drug resistance.
- 90% of users experience no PrEP side-effects. Emphasize that most side-effects are usually mild and transient. Side effects may include gastrointestinal problems, dizziness and nausea and usually resolve within a few days (sometimes weeks) after starting PrEP.
- PrEP clients should come back to the clinic for laboratory evaluation (HIV/STI testing) and PrEP prescription refill every 3 months and check renal (kidney) function every 6 months.

5.3.4.3 Dosing, duration, follow-up and adherence to PrEP

Oral co-formulated TDF/3TC⁹ PrEP can be used daily for considerable time and is the preferred PrEP regimen in this concept note. PrEP can also be effective if taken daily for short periods of time or around single events of possible HIV exposure. This event-based strategy has been evaluated only for MSM. However, daily continuous PrEP use is believed to facilitate adherence because of its routine character and the unpredictability of HIV risk in many situations and persons. Dosing, duration, follow-up and adherence to PrEP, are recommended as follows:

- For daily PrEP dosing , oral co-formulated TDF/3TC¹⁰ should be taken daily and continuously during periods of high risk for HIV infection.
- For event-driven¹¹ PrEP dosing, the first dose (2 tablets) is taken 2 to 24 hours before the first sexual intercourse then one tablet daily for until 48 hours after the last sexual intercourse.
- Clinicians and health care workers (counselors) should help their clients deciding when to initiate and discontinue PrEP.

⁹ Myland company has already registered the two drugs, TDF and 3TC, necessary for PrEP implementation.

¹⁰ For now, there is a need to negotiate with GFATM on whether current drugs being used for ART treatment could be used to support PrEP and whether we could charge patients. In the future, there is a need to buy drugs necessary for PrEP.

¹¹ The event-driven dosing seems to be more preferred in many regions.

- The duration of PrEP use depends on whether HIV risk is episodic or continues over time.
- Initially, PrEP should be prescribed for one month. After the first month, then two months of pills and then on the next visit three months and repeated extensions of three months.
- PrEP users should be followed-up for laboratory, clinical and adherence monitoring at one month, followed by three-monthly.
- Adherence to PrEP should be addressed at every follow-up visit by self-report and pill-count where feasible.
- Those who are not adherent but are willing and eligible to continue PrEP should be given additional adherence counseling or referred to peer-based adherence support services.
- Those with persistent insufficient adherence (<4 pills per week) after counseling may compromise both PrEP efficacy and individual safety and should be taken off PrEP.
- When to stop PrEP: How you stop PrEP depends on which dosing you use.
 - Daily dosing: Continue daily PrEP for seven days after the last time you had sex.
 - On-demand dosing: If you had a recent risk, continue taking PrEP at your regular time for another 48 hours. This means taking two doses, one for each of the two days after your last risk. If in the future your circumstances change again, it is easy to restart PrEP.

If you stop PrEP and have a risk afterwards, contact your clinic in case post-exposure prophylaxis (PEP) might be needed. In the cases when PEP is used, it needs to be started as soon as possible.

5.3.4.4 Client monitoring

Pre-PrEP evaluation procedures, clinical follow-up and laboratory and adherence monitoring of PrEP clients are listed in **Table 1** below. After PrEP initiation, clients should return to the clinic for follow-up and laboratory monitoring every three months during the first year and every six months thereafter. In some cases, clinicians may want to see their clients after one month for HIV re-testing, assessment of early side-effects and adherence evaluation and to address any

questions or difficulties. A one-month clinic visit may also be considered for more controlled refill prescriptions following PrEP initiation.

Table 1: Pre-PrEP evaluation, clinical follow-up, laboratory and adherence monitoring of PrEP clients

Test/procedure	Visits				
	Month 0	Month 1 (optional visit)	Month 3	Every 3 months until month 12	Every 3 months thereafter
HIV serology	Y	Y	Y	Y	Y
Evaluation for ARS	Y	Y	Y	Y	Y
Medical history and physical exam	Y	Y	Y	Y	Y
Creatinine ¹² clearance	Y	N	Y	N	Every 6 months
HBV serology and management	Y	N	N	N	N
HCV serology	Y	N	N	N	Every 12 months
STI evaluation and management ²	Y	N	Y	Y	Y
Drug dispensing	Y	Y	Y	Y	Y
Adherence evaluation ³		Y	Y	Y	Y
Risk evaluation ⁴	Y	N	Y	Y	Y

ARS, acute retroviral syndrome; BMD, bone mineral density; HCV, hepatitis C virus; HBV, hepatitis B virus; PrEP, pre-exposure prophylaxis; STI, sexually transmitted infection

¹ Bone mineral density; ² Syphilis, N gonorrhoea, C trachomatis according to local guidelines – but not compulsory for PrEP; ³ If adherence is <4 pills per week, client should be referred for adherence support or PrEP should be terminated ⁴Between client and clinician/counselor observing PrEP stoppage rules (section 5.3.4.3)

5.3.5 Laboratory monitoring at baseline and follow-up

All clients with a sexual or drug use risk history indicating interest in PrEP need to undergo laboratory and clinical evaluation. Appropriate HIV and creatinine clearance testing are considered essential components of laboratory evaluation prior to and during PrEP administration because of their high potential for detrimental effects if left undetected or unaddressed, i.e., HIV drug resistance and disease and renal failure. A flow diagram for HIV and creatinine testing is presented in **Figure 3**. The rationale for different consecutive types of HIV

¹² Biomedic has been contacted and agreed to perform creatinine clearance test at a 20% reduced cost.

testing is based on the sequential emergence of HIV sero-markers following infection. Reactivity of HIV tests of different platforms is expressed in **Figure 4**.

5.3.5.1 HIV testing

All PrEP candidates need to undergo HIV testing and a negative result is required at time of evaluation. Dual combination ARV PrEP is insufficient to treat undiagnosed or acute HIV infection, and this under-treatment may lead to viral resistance. This HIV testing should be repeated every 3-6 months prior to reissuing or refilling prescriptions. A fourth generation HIV Ag/Ab test should be conducted within 7 days of first evaluation, and if non-reactive, clients should be told to start PrEP within the next 7 days. If a high-risk exposure (condomless sexual intercourse with a partner at high HIV infection risk or HIV infected or re-use of injection equipment among PWID) occurs during this period, clients may be started on PrEP immediately and closely monitored for HIV infection during the next 2-8 weeks with a fourth generation HIV test. If this test continues to be non-reactive, monitoring can be reverted to standard PrEP HIV testing.

Persons with indeterminate HIV test results should not be started on PrEP. They should be evaluated for early HIV infection and started on PrEP only when HIV infection is excluded.

5.3.5.2 Viral resistance

Overall, the risk of developing resistance as a result of HIV under-treatment among participants on PrEP is low. (21) Since most ARV resistance patterns result from poor ART adherence, there is a risk of breakthrough infection among PrEP users exposed to viral resistant HIV phenotypic strains. (22)

5.3.5.3 Hepatitis and STI testing

Ideally, clients should be tested for hepatitis B (HBV) and C (HCV) infection at baseline. Those with active or chronic HBV or HCV should be referred for specialist evaluation and treatment¹³.

¹³ This may not be possible due to the lack of the specialist.

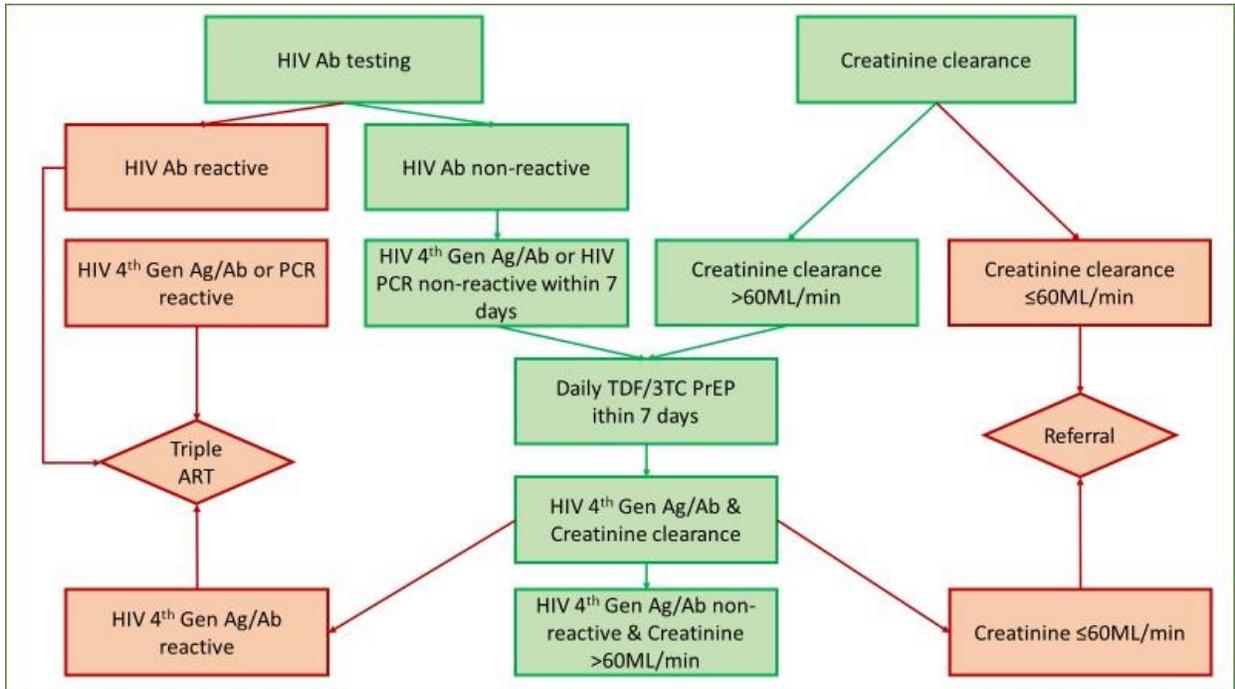
Individuals who test HbsAg and HbsAb non-reactive should be referred for HBV vaccination¹⁴. Daily PrEP can be given to clients with active HBV infection with a clear warning that stopping PrEP can cause a flare up of HBV. Screening and management of STI (syphilis, N gonorrhoea and C trachomatis) should occur according to local standard (simple lab or PCR).

5.3.5.4 Renal function testing

In general, ARV PrEP use has not been found significantly related to loss of renal function. However, some populations, such as those younger and older may be at higher risk for renal function while taking PrEP. Besides laboratory evaluation of renal function (estimated glomerular filtration rate [eGFR]) at baseline, individual's creatinine clearance should be measured every 3 to 6 months. Persons with an eGFR <60ml/min should not be prescribed or should be taken off PrEP. In case of discontinuation, usually renal function will return to normal within a few weeks. More intensive creatinine clearance monitoring may be warranted for those younger (<25 years) and those older (>45 years) or those with a baseline eGFR of <90/ml/min.

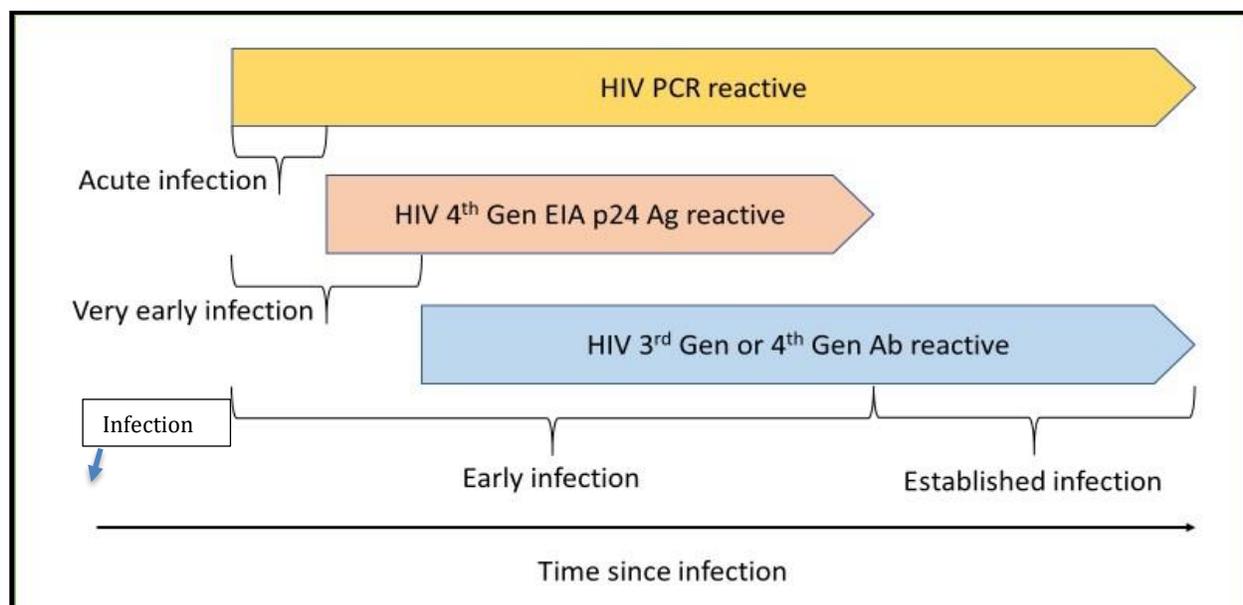
¹⁴ In case a patient needs a hepatitis B vaccination, that person will be referred to a private clinic where a charge will be made.

Figure 3: Flow diagram for HIV and creatinine clearance testing prior to and during PrEP administration



Second “HIV 4th generation Ab/Ag and creatinine clearance testing” would take place three months after PrEP initiation, and then the creatinine clearance testing would take place every six months thereafter. The HIV serology would take place every three months for the first year, and every three months thereafter with STI testing.

Figure 4: Sequential emergence of sero-markers and reactivity of HIV tests of different platforms over time



5.3.6 Logistic and supply management

Ultimately, PrEP and associated laboratory testing in Cambodia will be self-paid for those at the highest risk but for purposes of the initial phase, 120 slots for free PrEP (60 new users per month for two months) are reserved during the first year of the project. Since TDF/3TC is already available in country for HIV treatment through MoH channels, no new procurement process is needed, and used drugs can be replaced retroactively. Chhouk Sar clinic is providing public-funded ART (of which TDF/3TC is the core), hence no new supply chain or dispensing facilities need to be created. Similarly, HIV, HBV, HCV, syphilis, NG and CT testing are routinely performed at the clinic, and therefore no additional procurement or facilities are necessary. Creatinine testing will be performed by an outside specialist laboratory as it is not available at the public hospital.

6. Roles, responsibilities and training of staff involving in PrEP implementation

For PrEP to be implemented effectively and efficiently, relevant staff of Chhouk Sar or ART clinic and the brokers are expected to work together and perform essential tasks. These include (1) project manager, (2) project nurse/counselor and phlebotomist¹⁵ (if different from project nurse/counselor), (3) project physician, (4) laboratory technician(s), (5) cashier, (6) pharmacist and (8) data manager. Each of these individuals has their own roles and responsibilities to deliver. (See Annex for details)

NCHADS and relevant partners also need to develop a training manual necessary for this purpose. The training manual should also include clear indicators and tools necessary for monitoring of the PrEP implementation.

7. Monitoring and evaluation of PrEP implementation

Monitoring the implementation of HIV PrEP is essential to evaluate uptake, progress and success and to create evidence for decision making regarding the future of PrEP in Cambodia. Monitoring and evaluation are an ongoing process through which key indicators of success are collected and presented as counts, frequencies and tables by subgroup disaggregation. Regular data monitoring reports (e.g., weekly or monthly) provide information about the uptake of self-paid PrEP, retention and adherence, the number of HIV and STI cases detected and treated, side-effects and so on. A mid-term evaluation will be made at month 6 to assess progress made and re-direct the program as deemed necessary; and a more in depth evaluation will be made at month 12.

Several core monitoring and evaluation indicators are presented below (to be disaggregated by key population, age, sex, type of STI etc. as appropriate).

- Number of clients evaluated for PrEP use

¹⁵ This position might not be necessary if the project nurse/counselor is capable of vein injection and management.

- Number and percentage of clients initiated with PrEP
- Reasons for non-eligibility.
- Number of HIV infections detected and successfully linked to ARV treatment at first consultation and during follow-up
- Number of STI tests performed, detected and treated at first consultation and during follow-up
- Number and percentage of clients retained, dropped out, terminated or lost-to-follow-up over time
- Adherence self-reports and pill-counts
- Self-reported side-effects. Creatinine clearance follow-up.
- Proportion of clients with repeated HIV testing every 3 months
- Proportion of clients using condoms and at what usage rate
- Proportion of clients taking PrEP daily or as event-driven.
- There is a need to assess the future perspective vis-à-vis PrEP implementation, for which PrEP users, PrEP providers and related program staff will be interviewed.

8. Next steps

Next steps in the phased roll out of PrEP include:

- Submission of the PrEP concept note to the MOH
- Approval of the concept note by the MOH
- Assure supply of PrEP drugs, HIV and STI rapid tests, PCR for STIs, qualitative PCR to rule out early infection¹⁶ missed by rapid tests.
- Selection of a specific ART site convenient for KPs to access PrEP.
- Develop monitoring tools for TWGs to monitor the implementation.
- Training of Chhouk Sar and ART Clinics' staff on PrEP, risk assessments, eligibility criteria for PrEP, patient and program monitoring.
- Training of CBOs on PrEP and their role in demand creation and adherence support.

¹⁶ Currently, this may not be possible.

- Establish linkages between CBOs and Chhouk Sar, and ART clinic for PrEP referral and adherence support.
- Work with generic suppliers for import of TDF 3TC at affordable prices.
- In-depth interview to discuss patient and provider experiences and interest in event-driven PrEP.
- Program evaluation at six and twelve months of PrEP implementation.
- Develop an SOP for PrEP implementation at national scale after 12 month evaluation.

9. Annex

Below are key roles and responsibilities of each function as described under section 6.

9.1 Project manager

- Registers and records contact information of potential PrEP clients
- Conducts demographic eligibility screening
- Completes documents and send these to counselor
- Contacts, confirms and schedules PrEP clients for initiation and follow-up visits (using social media as appropriate)
- Oversees data recording and data entry.

9.2 Nurse/counselor/phlebotomist

- Explains PrEP use, eligibility and follow-up procedures and requirements, risks and benefits, importance of adherence, starting and stopping rules, alternatives to PrEP and costs of PrEP and related testing
- Answers client questions in this respect
- Conducts HIV risk eligibility screening
- Performs HIV and STI related counseling, including behavioral risk reduction and need for condom use while taking PrEP (including distribution of free condoms and water-based lubricant to clients)
- Performs a blood draw and collects other specimens as indicated
- Assures proper identification and transport of samples to the clinic laboratory
- Informs PrEP clients about results from HIV and other testing as delegated by the project physician
- Assures access to triple ARV therapy for clients testing HIV infected and makes referrals for specialist care for those with kidney dysfunction
- Re-evaluates HIV risk during follow-up
- Performs adherence counseling and pill counts
- Completes documents for review by the project physician
- Records relevant information on data forms.

9.3 Project physician

- Takes medical history and performs physical exam
- Evaluates client for the presence of STI and decides on treatment
- Examines client for presence of ARS
- Interprets results of laboratory testing
- Decides on final eligibility and continuation of PrEP
- Evaluates possible PrEP side-effects
- May request additional specimen collection and laboratory testing
- Writes PrEP prescriptions to be filled in the pharmacy
- Records relevant information on dedicated forms. Evaluate liver function in case of positive HBsAg and refer to specialist if needed

9.4 Laboratory technician

- Receives blood samples and other specimens for processing and testing
- Responsible for ordering and managing relevant test kits, other laboratory materials and specimen collection devices and related clinical supplies
- Performs HIV, HCV and syphilis serologic testing
- Prepares and aliquots specimens for transport and outside testing and receive results
- Assures good laboratory practice and safe collection and disposal of sharps and other hazardous materials and waste
- Completes designated forms to notify project physician and/or nurse counselor regarding results of testing
- Oversee data entry of laboratory results in the project data base.

9.5 Cashier

- Oversees appropriate billing of clients for PrEP medication and related testing
- Receives money from clients and provides invoices
- Responsible for daily balance between cash and invoices.

9.6 Pharmacist

- Fills prescriptions and keeps record of drugs dispensed
- Explains and reiterates drug usage rules to clients
- Guarantees continuous drug supply and prevents stock-outs
- Completes relevant forms for data entry and monitoring purposes.

9.7 Data manager

- Creates data record forms and oversees data entry
- Keeps source data information for monthly checking between sources and data base
- Performs daily back-up and cloud storage of data
- Produces weekly and monthly monitoring reports to evaluate project performance.

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