衞生防護中心
Centre for Health Protection

Scientific Committee on AIDS and STI

Guidance on the use of HIV Pre-exposure Prophylaxis (PrEP) in Hong Kong

Preamble

With the emergence of science and international initiatives on HIV pre-exposure prophylaxis (PrEP), the Scientific Committee on AIDS and STI developed an interim statement[1] on PrEP in December 2016. The statement delineated interim principles of PrEP practice for selected people at high and ongoing risk of HIV infection, as an additional measure for individual protection against HIV.

2. There has been increasing knowledge overseas as well as important progress on the experiences of PrEP utilisation in the local context. This document primarily serves to provide updated guidance on PrEP use with different regimens, and the clinical monitoring and counselling required to maximise its effectiveness when used.

Principles of practice for PrEP

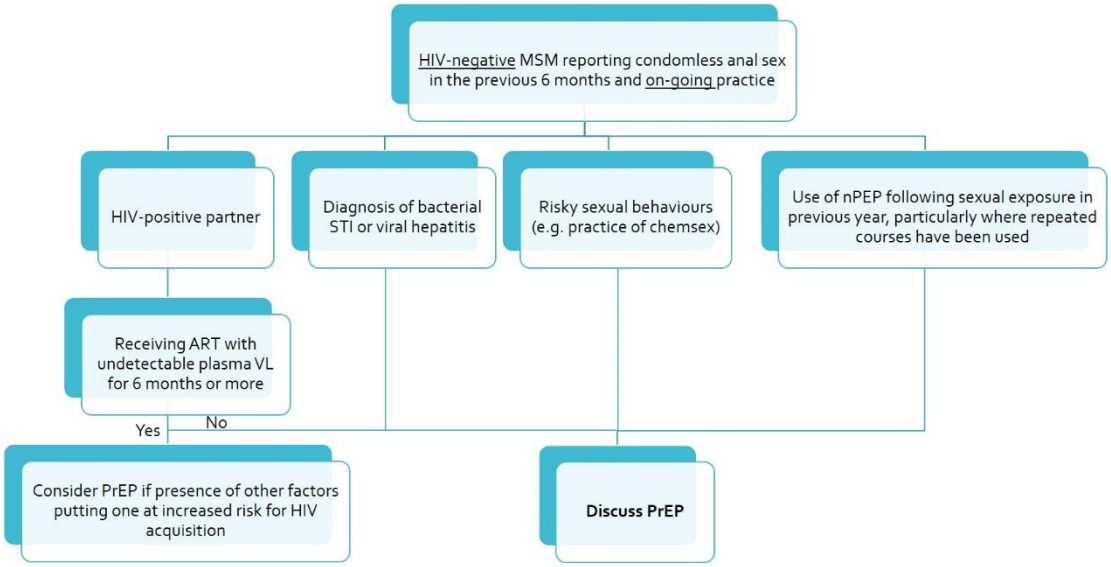
I. PrEP should be considered as part of HIV combination prevention in individuals with elevated ongoing risks for HIV acquisition

3. The level of risk for HIV acquisition should be determined on a case-by-case basis with reference to the local epidemiology. In Hong Kong, the HIV epidemic currently concentrates in certain population at risk. Sexual transmission remains to be the major route of transmission.

4. HIV-negative men having sex with men (MSM) who report condomless anal sex in the previous 6 months and on-going condomless anal sex, along with one or more the following factors are considered at high risk for HIV acquisition[2,3,4]

- Diagnosis of bacterial sexually transmitted infections (STIs) (e.g. chlamydia, gonorrhoea, syphilis) or viral hepatitis
- Practice of chemsex*
- Use of post-exposure prophylaxis following sexual exposure in the previous year, particularly where repeated courses have been used

Figure 1. Assessing indications for PrEP in sexually active MSM[2,3,4]



* Defined as the use of drugs before or during sexual activity to sustain, enhance, disinhibit or facilitate sexual experience.

5. Reasons for risky sexual behaviours should be explored and counselling be offered where appropriate. The prospective client should understand the side effects and limitations of PrEP as well as the extent of effectiveness based on the prerequisite of good adherence. This process of assessment and counselling should be repeated in subsequent visits.

6. For HIV-negative individuals having condomless sex with partners who are HIV positive and have been on antiretroviral therapy with an undetectable plasma viral load for 6 months or more, PrEP is generally not indicated as the risk for HIV transmission through condomless sex is essentially zero as proven in multiple large scale studies[5,6,7,8]. PrEP could be considered on a case-by-case basis for people with other factors that place them at increased risk for HIV acquisition.

7. It is imperative that pre-existing HIV infection be excluded prior to PrEP initiation. A negative HIV test by a fourth generation ELISA antigen-antibody test should be obtained within the last 7 days before PrEP initiation. Point-of-care tests should not be used for such HIV screening due to a lower testing sensitivity. Individuals should also be reminded and reviewed for symptoms suggestive of HIV seroconversion throughout the course of PrEP use. When in doubt, PrEP should be withheld until acute HIV infection can be definitively excluded with repeat testing. Until then, the client should be counselled to cease all risk practices.

II. If prescribed, PrEP adherence should be carefully monitored

8. Fixed-dose combination of TDF/FTC has been widely approved as oral PrEP for healthy adults and adolescents with studies supporting its efficacy in the prevention of HIV transmission[9,10,11].

9. TAF/FTC was approved by the US Food and Drug Administration (FDA) as an option for oral daily PrEP in men and transgender women with sexual risks for HIV acquisition[12,13]. In cisgender women with risks for HIV acquisition through receptive vaginal sex, TAF/FTC should not be used due to limited data.

10. Studies have demonstrated TDF/FTC or TAF/FTC, when taken daily with good adherence, could offer effective protection against HIV acquisition. The time to clinical protection in anal sex is estimated as 2-24 hours following a double dose of TDF/FTC[14]. Data extrapolated from pharmacokinetic studies of TDF/FTC [15] suggested daily TDF/FTC should be started 7 days prior the potential sexual risk exposure and continued for 7 days after the last sexual risk in cisgender women with risk of HIV acquisition through vaginal sex. With daily dose TAF/FTC, time to clinical protection is currently unknown. Clients should be educated on use of additional protection for HIV during the lead-in period.

11. For MSM anticipating less frequent high-risk activities, on-demand, also known as event driven PrEP, could be discussed as an alternative[14,16]. Two tablets of fixed dose TDF/FTC should be taken 2-24 hours prior to sexual exposure, followed by a third tablet at 24 hours and a fourth tablet at 48 hours after the event. When there are on-going exposures prone to HIV acquisition, one tablet per day should be continued until the last sexual intercourse, followed by two post-exposure tablets. TAF/FTC is not recommended for on-demand use due to limited data on efficacy.

III. If prescribed, PrEP should be used as an addition to other HIV prevention strategies

12. PrEP is an additional option; it never supplants a comprehensive prevention package for those at risk. This principle has been previously addressed by this Committee and continues to uphold[1].

13. Risk compensation, defined as an increase in condomless sexual intercourse or other risky sexual behaviours due to a perceived protection from HIV acquisition, has been observed among PrEP users[17]. The number of sex partners could also potentially increase. Some studies had demonstrated increase in STI incidence among PrEP users, especially among those with more frequent engagement in high-risk sexual activities[18,19]. On the other hand, a recent cohort from Australia showed STI incidence was highest in the early months of PrEP implementation and stabilised at a slightly lower rate thereafter following wider PrEP uptake[20]. Widespread PrEP implementation coupled with timely STI screening and early treatment might have led to shortened duration of infection

and reduction in onward transmission.

14. A non-judgmental approach to elicit behavioural risks and their reasons, followed by advice towards effective prevention may suffice for some clients without the need of PrEP. Even for those on PrEP, risk reduction counselling should be continued as part and parcel of each client visit.

15. The use of recreational drugs, with or without the practice of chemsex, has to be addressed by a harm reduction approach, in which recourse should be made to professional and community services. The impact of substance use on the physical, as well as mental health of an individual should be addressed, and followed up with appropriate counselling and referral, when being assessed for PrEP use.

16. Clients on PrEP should be educated on sexual health and the importance of prevention, early diagnosis and treatment of STIs and sexually transmissible viral hepatitis, including hepatitis A, B and C. Vaccination should be offered to those who are hepatitis A or B susceptible and Human Papillomavirus (HPV) vaccination could be discussed where appropriate.

IV. Optimising the safety and effectiveness of PrEP use

17. Prior to PrEP initiation, clients should be educated on the following:

- Potential side effects of the medication and corresponding management;
- Possible drug-drug interactions with other medications and recreational drugs;
- Importance of adherence to effectiveness of PrEP;
- Risks of breakthrough HIV infection and antiretroviral resistance from suboptimal adherence; and
- Symptoms of HIV seroconversion that warrant assessment.

18. Regular follow-up should be arranged for clients while on PrEP, with an interval not longer than 3 months.

19. TDF/FTC and TAF/FTC are generally well tolerated. Common side effects include nausea, flatulence, abdominal pain, dizziness and headache. These symptoms are usually self-limiting, but some may need symptomatic management. Sleep disturbances and depression resulting from PrEP use could be severe and should be addressed promptly. Data from local studies[21,22] demonstrated approximately 9% of daily PrEP users suffered from mild to moderate sleep disturbances. Depression was reported in 2% of daily PrEP users. As PrEP requires high level of adherence to be effective, monitoring of adherence using different strategies should be employed during every visit, and more intensive counselling to address factors impacting adherence should be offered.

20. To date, studies have demonstrated a small but statistically significant decline in renal function from baseline[23] following the use of TDF/FTC as daily PrEP, which was reversible after stopping the medication[24,25]. However, limited data is available for people with estimated GFR <60 ml/min and hence TDF/FTC should not be given under such circumstances. On the other hand, TAF/FTC is associated with less renal toxicities[26] and could be used as PrEP for people with estimated GFR ≥30ml/min. While on PrEP, renal function as reflected by serum creatinine level should be monitored regularly. Clients with risk factors for renal impairment such as old age, hypertension, diabetes and concurrent use of nephrotoxic agents would require more thorough assessment of their renal function and test for proteinuria.

21. Both TDF/FTC and TAF/FTC are useful in the treatment of chronic hepatitis B. Cessation of medication may result in a flare of underlying chronic hepatitis. Limited data had suggested daily TDF/FTC was safe with monitoring of liver enzymes while on PrEP and after cessation[27]. Clients known to be chronic hepatitis B carrier should be counselled on the above risk prior to PrEP initiation. On-demand PrEP should not be used in individuals with chronic hepatitis B.

22. Despite a possible decrease in bone mineral density (BMD) in HIV-infected persons treated with TDF containing regimen, dual-energy X-ray absorptiometry (DXA) scan is not routinely recommended for monitoring for PrEP users. Studies demonstrated a small decline in BMD occurred within first few months of TDF-containing PrEP initiation, which either stabilised or returned to normal[28]. Clinicians should discuss the risk of bone loss with individuals with pre-existing risk factors or demonstrated osteoporosis, osteomalacia or osteopenia and manage accordingly.

Table 1. Monitoring for MSM prescribed with oral PrEP

(Adapted from Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States – 2021 Update: a clinical practice guideline.)

Test	Baseline	Every 3 months	Every 6 months	Every 12 months	At cessation of PrEP
HIV testing	X	X			X
Serum creatinine/ eGFR/ urinalysis	X		If age ≥50 or eGFR <90 ml/min at PrEP initiation	If age <50 and CrCl ≥90 ml/min at PrEP initiation	X
Sexually transmitted infections (e.g. chlamydia, gonorrhoea, syphilis)	X	X			X
Hepatitis B serology	X (Discuss on vaccination if uninfected and non-immune)				X (For individuals non-immune to Hepatitis B at baseline and not receiving vaccination)
Hepatitis C serology	X (For MSM, TGW and PWID; refer for treatment as indicated)			X (Testing frequency can be increased to every 3 months for those with ongoing potential exposure[3,4])	

Local experiences

23. The awareness of PrEP among local MSM has increased over the past years. Local surveys had found an increase of PrEP use among respondents of the MSM community, increasing from 1.1% reporting PrEP use within the past 12 months in 2018 to 6.3% in 2020. Only 9.3% respondents in 2020 had never heard of PrEP, compared with 26.3% in 2018[29].

24. Several local studies have found good overall acceptability of oral PrEP among MSM. A pilot study conducted by the Chinese University of Hong Kong (CUHK) demonstrated good adherence to daily oral PrEP with self-limiting adverse effects[21]. Commonly reported side effects include dyspepsia, increased bowel movements, fatigue and headache. Risk compensation was observed with a reduction of condom use with both newly acquainted and known partners. Cost was the main reported concern by PrEP users.

25. In the follow-up study comparing daily and on-demand PrEP use in Hong Kong by CUHK, both regimens were found to have high prevention-effective adherence as demonstrated in the coverage of condomless anal intercourse[22]. Participants on either daily or on-demand PrEP were associated with high STI incidence. More adverse events were reported by MSM using daily PrEP. The study concluded that MSM's individual preference and sexual behaviours should be considered when choosing between daily versus on-demand PrEP. Flexible PrEP regimen with switching could be an approach for effective programme implementation.

26. A PrEP implementation study by CUHK is currently underway to explore on a local service model for PrEP delivery and test its operability in the real-world local setting.

Other drug options

27. Besides TDF/FTC and TAF/FTC, there are other oral agents, injectable treatment and different delivery systems for HIV pre-exposure prevention in the pipeline. Among them is cabotegravir (CAB) which is a long acting antiretroviral given as intramuscular injection which has been recently approved by the FDA and World Health Organization (WHO) for use as PrEP[30,31].

28. Following an optional 4-week oral CAB lead-in, the medication should be given by intramuscular injection into the gluteal region every 2 months. Injection site reactions, e.g. pain, tenderness and indurations are most common following the first 2-3 injections. Hepatotoxicity has been reported in a small number of people receiving CAB injection, at a similar rate as in those receiving placebo injections in clinical trials. Liver function tests should be performed prior to CAB initiation and during its use. It should not be initiated in individuals with advanced liver diseases or acute viral hepatitis. Regular follow-up should be arranged for monitoring of tolerance, counselling on other behavioural risks, and screening of HIV and other STI. Individuals receiving intramuscular CAB as PrEP should be advised on the potential drug-drug interaction while on medication and risks of HIV acquisition during the "tail" phase after cessation of injection. For those anticipating ongoing risks of HIV exposure after cessation of CAB injection, counselling on other HIV preventive strategies should be provided.

29. Results from cost-effective analysis on the role of injectable PrEP in HIV prevention have been mixed. While the cost-effectiveness may be limited by its relatively high drug cost [32], preliminary results from mathematical modelling have also demonstrated that an increase in PrEP uptake and the resultant, impact on reducing HIV incidence could allow the cost-effectiveness to be maintained, especially when its use is being prioritised among certain populations[33]. Further studies are required to review its acceptability and overall prevention effectiveness.

Conclusion and way forward

30. With good adherence, oral PrEP is highly effective in preventing HIV infection. Nevertheless, regular monitoring on physical, mental and sexual health are essential in PrEP delivery. Corresponding counselling should be given. Condom use and other harm reduction strategies should be offered as a comprehensive package during each assessment. STIs should be screened and treated in a timely manner.

31. HIV-negative heterosexuals having condomless sex with HIV positive partners who have not been on antiretroviral therapy for at least 6 months and

plasma viral load is detectable are at risk of HIV acquisition. Transgender population (TG) and people who inject drugs (PWID), with presence of other indicators such as risky sexual behaviours, practice of chemsex, repeated episodes of STIs and sharing of injecting equipment[2,3,4] etc., are also considered at risk for HIV infection. However, there are limited local data on the acceptance and overall prevention effectiveness of PrEP use in these populations. The use of PrEP in other at risk populations should be kept in view with reference to local data and emerging needs.

32. In Hong Kong, healthcare providers in public and private sectors and NGOs may all have their roles in the provision of care and support to PrEP users, while service delivery models that could fit the unique social and cultural background of the community are to be explored. Integration of PrEP delivery (and follow-up) to conventional HIV/STI services, as part of combination prevention, could also be considered to achieve synergism of the preventive efforts. Further work is needed to enhance the awareness and knowledge among population at-risk, and capacity building of service providers.

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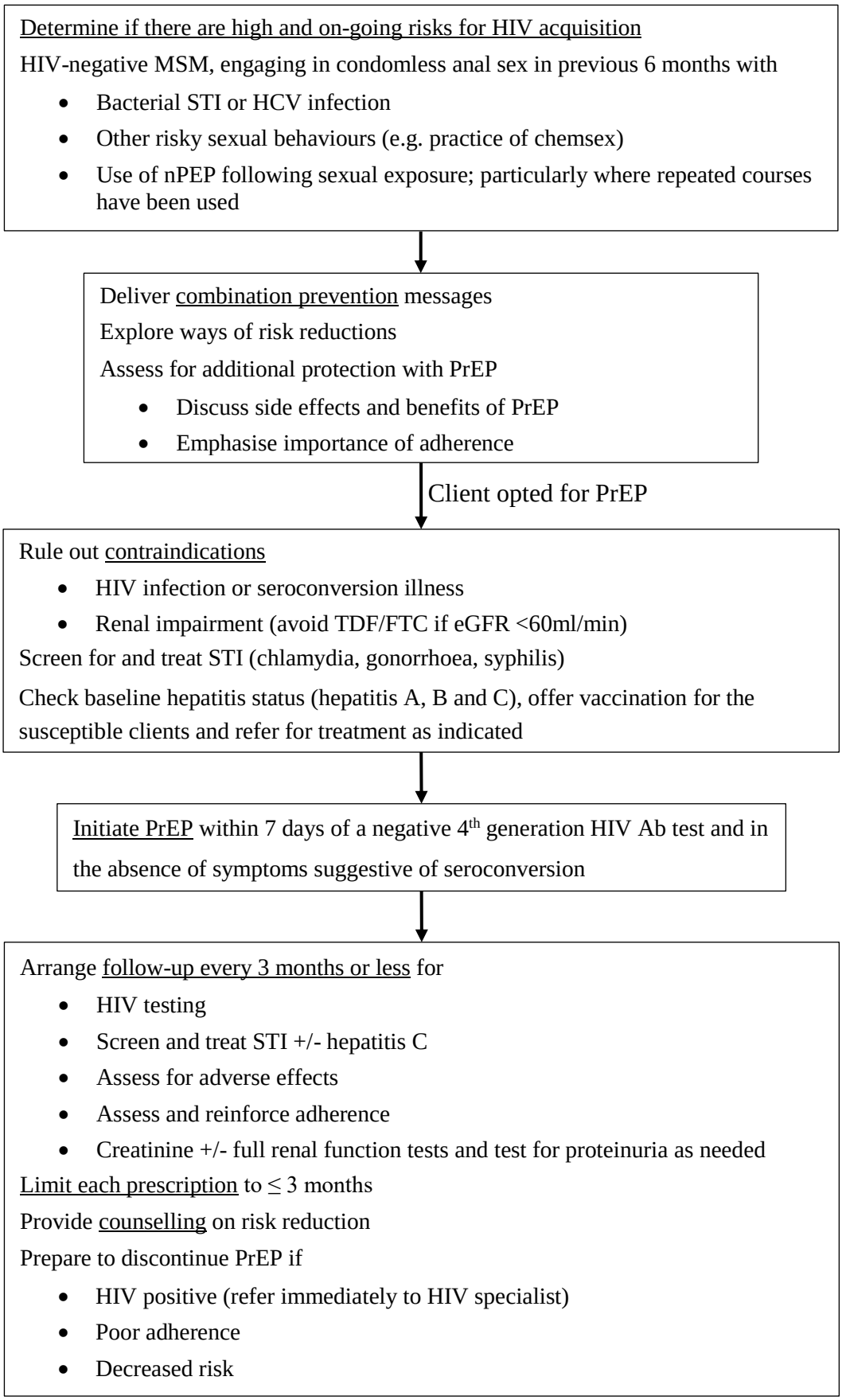
Appendix. Suggested clinical approach to using PrEP



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