Introduction of pre-exposure prophylaxis (PrEP) for HIV in Sri Lanka: a demonstration project (Pilot) to determine feasibility and acceptability of PrEP provision as part of strengthening sexual health services.

Final Report

Short Title: PrEP-4-SriLanka

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List of Abbreviations

AE/ADR	Adverse Event/ Adverse Drug Reactions
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy (for HIV positive individuals)
ARV	Antiretroviral medications
BMD	Bone Mineral Density
CBOs	Community-based organizations
CDC US	Centers for Disease Control and Prevention
CAI/CAS	Condomless anal intercourse/ Condomless anal sex
CT	Chlamydia
EDTA	Ethylenediaminetetraacetic acid.
eGFR	estimated Glomerular Filtration Rate
EIMS	Electronic Information Management System
ERC	Ethics Review Committee at the Faculty of Medicine, University of Colombo
FDA	U.S. Food and Drug Administration
FTC	emtricitabine
FU	Follow-Up
GC	Gonorrhoea
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
iPrEx study	The international multisite Pre-exposure Prophylaxis Initiative study
MSM	Men who have Sex with Men
NARI	National AIDS Research Institute
NSACP	National STD/AIDS Control Program
NSAID	non-steroidal anti-inflammatory drug
PEP	Post-exposure prophylaxis
PrEP	Pre-exposure prophylaxis
PSC	Protocol Steering Committee
PWID	People who inject drugs
PWUD	People who use drugs
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
STI	Sexually Transmitted Infection
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGM	Transgender men
TGW	Transgender women
TDF	tenofovir disoproxil fumarate
UADR	unexpected adverse drug reaction
UNAIDS	Joint United Nations Program on HIV/AIDS
UNFPA	United Nations Population Fund
WHO	World Health Organization

Contents

Summary

Background and rationale:

Sri Lanka is a low-prevalence country for HIV, with most infections occurring in men who have sex with men (MSM). Transgender (TG) persons also remain at higher risk for HIV in the country. In spite of significant investment and uptake of HIV prevention activities are implemented since past, the annual number of HIV notifications has shown an increase in recent years. Pre-exposure prophylaxis (PrEP) is the use of antiretroviral medicines to reduce the risk of acquiring HIV in HIV-negative persons, particularly in key populations. A decade of clinical trial research has resulted in the World Health Organization (WHO) strongly recommending the use of PrEP by individuals at substantial HIV risk. Over the past few years, in real-life settings, PrEP also has been shown to have population level benefits with reductions of HIV incidence. This public health benefit is particularly evident where PrEP is introduced and scaled-up rapidly in key populations. Given the lack of any formal PrEP service in Sri Lanka, this pilot project (entitled 'PrEP-4-SriLanka) provided the foundation to better understand how the health system can integrate PrEP in existing services, namely within sexually transmitted diseases (STD) clinics and with community led key populations (KP) interventions.

Aim:

PrEP-4-SriLanka was a pragmatic demonstration project that piloted the provision of PrEP to key populations at high risk for acquiring HIV; specifically MSM and TG persons. This pilot involved prescribing of PrEP by medical doctors at STD clinics and within the community. The pilot was critical in informing how PrEP services could be scaled-up in the rest of the country as part of a public health approach. A pragmatic approach was undertaken to ensure people starting PrEP on the same day as their baseline visit to the clinic ('same-day' PrEP initiation).

Methodology:

The pilot was commenced in September 2020, and was completed in end December 2021 (each participant was followed-up for 12 months). It was designed as a prospective, open-label cohort study. The term 'demonstration project' is synonymous with implementation studies in countries where PrEP is being introduced for the first time. Participants in this pilot were consented to enroll.

Prioritized populations:

The populations aimed to reach were MSM and TG persons at higher risk for HIV. Participants were recruited by two approaches. Clients/ patients directly visiting the STD clinics and using a referral system from a network of community-based organizations work for key populations interventions.

Intervention:

All participants were offered daily Tenofovir disoproxil and Emtricitabine (TDF/FTC) for PrEP. MSM had the option to also choose to take PrEP as event-driven (otherwise known as '211' or 'on-demand PrEP'), per the latest evidence-based WHO guidelines. Participants were allowed to switch, discontinue or restart regimens at follow-up visits after initial enrolment. At each visit, participants in this pilot received risk reduction counseling and provided samples to test for HIV and sexually transmitted infections (STIs). A subset of participants participated in a focus group as part of a qualitative assessment of PrEP use.

Project Schema

Participant identification and invitation

(Pre enrolment and enrolment)

Direct visit (Self-Referral), Referral from STD clinic/Colombo, Referral from district STD clinics, Through KP/ NGO/CBO, through https://know4sure.lk

1. Pre-Enrolment: People at risk were informed about the PrEP, then those became as participants and referred to the Colombo STD clinic for PrEP. Behavioral suitability assessed ("risk assessment"); after meeting suitability, individuals agreed to take part.
2. Refer to central clinic/ district clinics/community PrEP clinic for prescribing visit

↓

Baseline Visit (1st prescription)

1. Participant offered additional HIV/STI risk reductions including condoms, health education, and safer sex promotion
2. Medical history was taken
3. Clinical risk assessment performed (HIV, serum creatinine, hepatitis B testing, additional STI screening); clinician checked understanding of PrEP and determined appropriate dosing with participant (daily or event driven PrEP)
4. Prescribing clinician re confirmed eligibility and did prescription, dispensed PrEP reported on case reporting form
5. Next appointment for 1 month and subsequent visits were granted.

↓

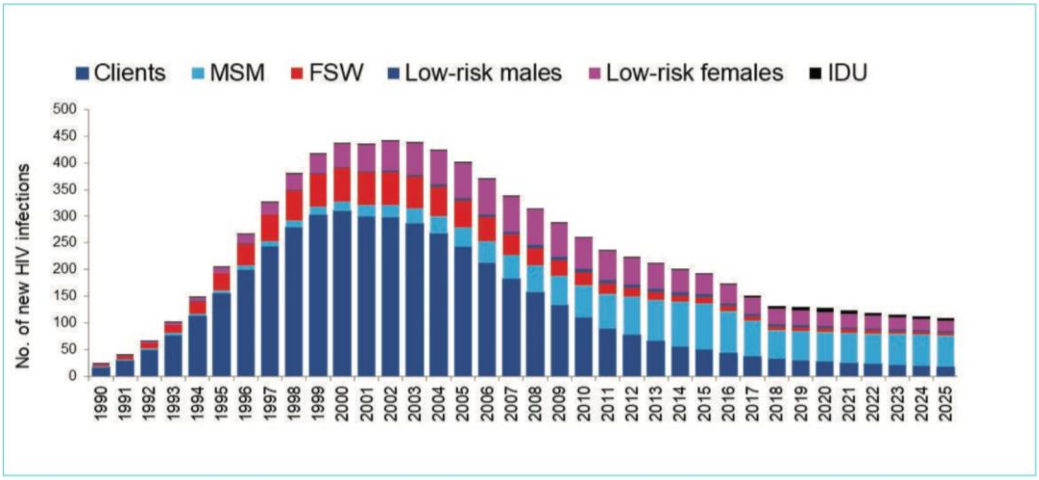
Ongoing follow-up

(1 month, 3 months, 6 months, 9 months, 12 months during ongoing risk)

1. Ongoing risk and adherence checked, and participant offered additional HIV/STI risk reduction intervention including condoms, health education, and safer sex promotion to reduce and modify high risk behavior
2. Tests conducted and behavioral suitability assessed per protocol
3. Prescribing clinician verified ongoing eligibility and generates prescription, dispensed PrEP report on case reporting form
4. Check for serious suspected adverse drug reaction if yes, report on case reporting register
5. Next appointment arranged

1. Background and rationale

Despite Sri Lanka's low HIV prevalence, new HIV infections have persisted, particularly among men who have sex with men (MSM) and transgender women (TWG) [1]. According to the latest AIDS epidemic model projections, there is a stagnation of this reduction of new HIV infections which will persist through 2024-2025 among MSM[2] (Figure 1). Globally, condom and lube distribution and programs, expanded HIV testing, treatment as prevention (TaSP), coupled with other harm reduction measures, remain central to HIV prevention efforts. In parallel, there has been an active pipeline of



research in the field of biomedical HIV prevention, which has included the use of antiretrovirals (ARVs) and monoclonal antibodies to prevent HIV acquisition, alongside HIV vaccines[3, 4]

Figure 1. Estimated number of new HIV infections in Sri Lanka by populations, 1990-2025 (MSM = men who have sex with men; FSW = female sex workers; IDU = injective drug users).

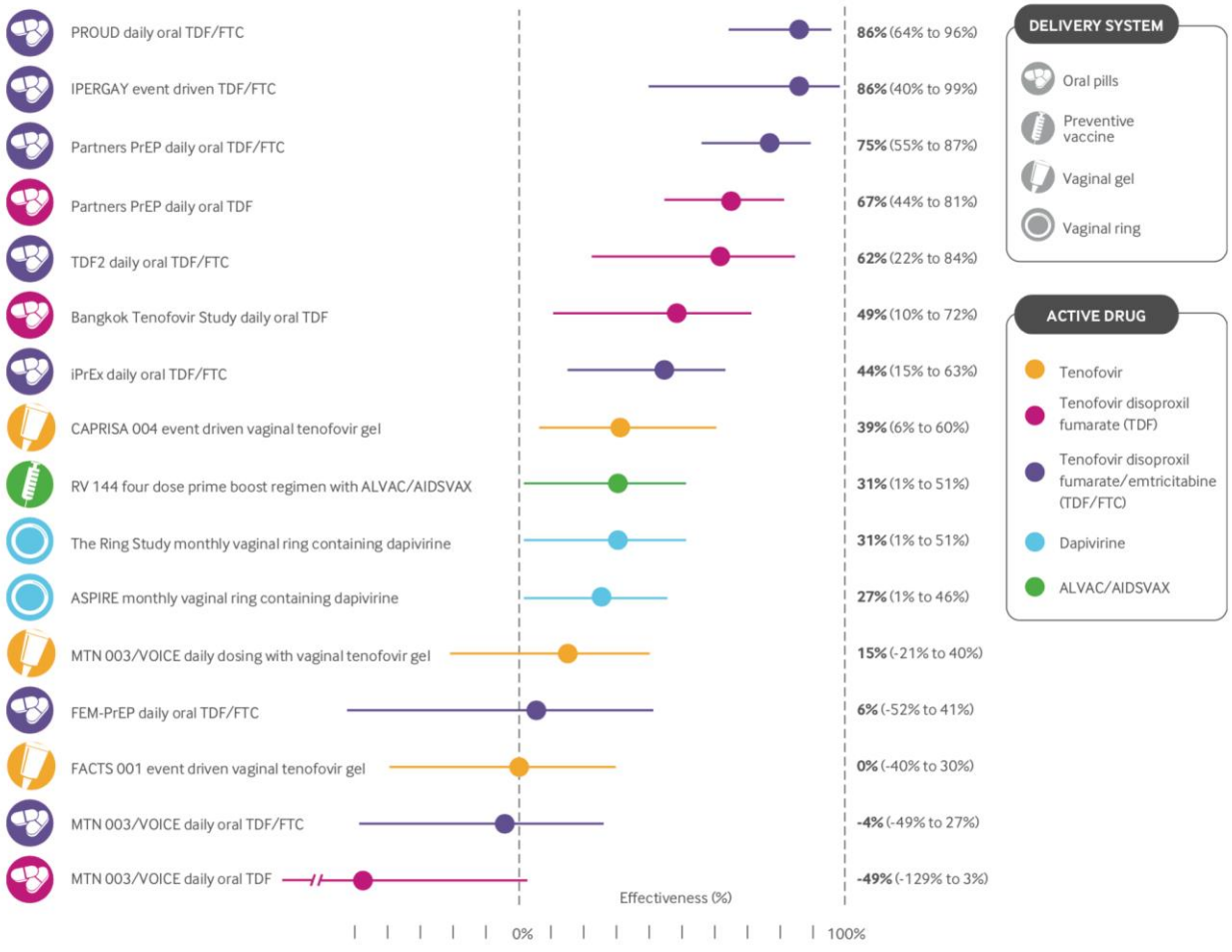
Pre-exposure prophylaxis (PrEP) is the use of antiretroviral medicines by HIV-negative persons prior to sexual exposure to HIV to reduce the risk of acquiring infection. Oral PrEP containing tenofovir has been strongly recommended by the World Health Organization (WHO) since 2015 [5, 6] and provides an additional option for individuals to protect themselves from HIV, particularly those who remain at substantial risk. PrEP should be offered as part of a comprehensive package of sexual and reproductive health (SRH) services, and in the context of HIV prevention, it is referred to as combination prevention. PrEP has been included since 2017 on the WHO's Essential Medicines List (EML); tenofovir in combination with either emtricitabine (FTC) or lamivudine (3TC); or tenofovir monotherapy[7]. PrEP can be taken on a daily basis for any person, irrespective of gender. Event-driven

dosing or otherwise referred to as 'on-demand PrEP' or '2-1-1' is also equally effective in preventing HIV transmission in MSM, and has been recommended by WHO since 2019 [8, 9]

The evidence

Extensive clinical and implementation research in a variety of populations has established high quality evidence supporting the safety, efficacy, and effectiveness of oral PrEP in reducing HIV transmission (Figure 2) in MSM, transgender women, heterosexual men and women and people who inject drugs (PWIDs) [10-18]. The efficacy of PrEP is directly correlated with medication adherence, with open label trials reporting high adherence and greater reduction in risk of HIV acquisition compared to earlier, blinded trials [19-21]. While PrEP is highly effective at reducing HIV transmission, it confers no protective effect against other bacterial and viral sexually transmissible infections (STIs), with the exception of HSV-2 infections [22, 23].

Figure 2. Summary of the effectiveness of biomedical prevention interventions, including oral PrEP



(Source: https://www.avac.org/infographic/evidence-hiv-prevention-options)[24]

In 2021, 144 countries reported that they had adopted the WHO recommendations on oral PrEP in national guidelines[25]. Most notably, Australia has been recording historic low HIV infection rates as a function of accelerating PrEP access since 2017 [26]. There are additional benefits that PrEP can confer beyond being highly effective in preventing HIV (up to 99% effective), which include uptake in HIV testing, and provision other SRH services, including vaccination for hepatitis B, and further counseling on reducing HIV risk [27, 28].

Why an STD clinic and NGO/CBO as a point of integrating PrEP

Sexually transmitted disease (STD) clinics are appropriate health care settings for PrEP provision, given STIs are associated with increased risk for HIV acquisition [29, 30]. In the United States, people attending STD clinics have high reported interest in PrEP [31, 32] and a PrEP demonstration project integrated with STD care showed good PrEP uptake and adherence [33]. Outside the US, STD clinics have been a critical entry point for PrEP access, particularly in the UK, Australia, and France. Integration of PrEP as an additional element of to an existing SRH package being offered in an STD clinic would be a pragmatic, public health approach.

Community outreach programs, educational programs, Condom distribution programs, NGO/CBO supported KP interventions have been highly successful in stabilizing the HIV epidemic in Sri Lanka, but a segment of people remain at risk for HIV and could benefit from additional evidence-based options, such as PrEP. PrEP was not available currently in Sri Lanka, and a pilot demonstration project served as a first step in access for people who are at risk for HIV. The pragmatic pilot model for PrEP provision being proposed was same-day PrEP initiation within a public STD clinic (at the National STD/AIDS Control Program (NSACP)).

Community engagement has emerged as a critical factor for education, demand generation, dispelling rumours, and supporting adherence and follow-up in PrEP demonstration projects [34]. PrEP services, to maximise benefits both to the individual and to public health, have to be meaningfully informed by communities most vulnerable to HIV, particularly key populations. These communities are ultimately the ones who will benefit from having PrEP available and accessible in the country.

Safety considerations

Use of oral PrEP containing TDF (TDF mono-therapy or in combination with FTC or 3TC) is very safe, with minimal side effects in a minority of individuals [10, 35-37] TDF has been used extensively worldwide

and is the most prescribed ARV drug for treatment of HIV infection [38]. The extensive data available demonstrate TDF-based PrEP is well tolerated and has a favourable safety profile.

Approximately 10% of people using PrEP may experience some short-term, mild side-effects. Side-effects may include gastrointestinal symptoms (diarrhoea, nausea, decreased appetite, abdominal cramping or flatulence) [37]. Dizziness or headaches have also been reported. Such side-effects are usually mild and resolve without stopping PrEP. Typically, these symptoms start in the first few days or weeks of PrEP use and last a few days, and almost always less than one month.

It is estimated that one in every 200 PrEP users will have an elevation of serum creatinine during PrEP use [39]. Therefore, renal function assessment had been recognized as an important element in prescribing PrEP. but also makes note that it can be considered more frequently if there is a history of conditions affecting the kidney, including diabetes or hypertension and if there are any chronic renal condition.
Serology testing for viral hepatitis B and C is also important in the context of PrEP initiation. If a screening test for hepatitis B is negative, a person wishing to initiate PrEP could benefit from a hepatitis B vaccination [40]; if the test result is positive, the client can have further blood tests to see if he/she would benefit from treating the HBV infection [41, 42]. Not everyone with detected HBsAg requires treatment. Treatment indications can be assessed in a variety of ways depending on which laboratory tests are available. TDF is recommended for treatment of HBV [41]; therefore, oral PrEP containing TDF can benefit people whose HBV infection warrants treatment. People who stop treatment for HBV infection are at risk of virological and clinical rebound of their HBV infection. This risk is higher in people who have liver fibrosis before starting treatment [43]. Clinical rebound after stopping PrEP was not observed in the limited data available from people with HBV infection who stopped oral PrEP containing TDF in trials [44, 45].

Consideration could be given to testing for evidence of HCV infection in MSM and people who inject drugs prior to initiation of PrEP and every 12 months thereafter. Testing for evidence of HCV infection is typically conducted by using a serological assay to detect antibodies to HCV (anti-HCV) [46].

In clinical trials, a statistically significant, albeit slight, decrease in bone mineral density has been seen in observed in people taking PrEP. PrEP has been associated with a small decrease in bone mineral density (0.5-1.5%) in the spine and hip in the first six months. It does not progress after that [47, 48]. In studies, there has been no increase in bone fractures [47]. Bone mineral density returns to normal when PrEP use ends [47]. People with a history of pathological bone fracture were excluded from PrEP trials; people with this kind of history who are considering PrEP should also consider treatment for low bone mineral density.

WHO also recommends the use of PrEP in pregnancy and breastfeeding, although this is more relevant in settings with higher HIV incidence settings, particularly in eastern and southern Africa. The risk of passing HIV infection onto a baby is higher if the mother becomes infected while she is pregnant. The existing safety data support the use of PrEP in pregnant and breastfeeding women who are at continuing substantial risk of HIV infection [49, 50].

2. Pilot Aim

With this demonstration pilot project, we aimed to assess the feasibility and acceptability of offering PrEP in a sexual health clinic setting in Sri Lanka, with a primary focus of service provision to MSM and TWG who are at increased risk for HIV infection. This pilot was conducted based on the current WHO guidelines on oral PrEP. In addition, the pilot adopted demonstration/implementation projects on PrEP, including the Impact trial in the UK, the AM-PrEP study in the Netherlands, the EPIC-New South Wales (EPIC-NSW) access trial, and PrEPX study in Australia [51-56.]

This pilot project was part of a comprehensive HIV-reduction package offered in the setting of a sexual health service.

3. Objectives

Primary

1. To Assess feasibility of PrEP provision in a sexual health clinic and other settings in Sri Lanka (uptake)
2. To Determine acceptability of PrEP to high-risk MSM and TGW (persistence)

Secondary

1. To Assess incidence of HIV infection during follow-up
2. To Assess the incidence of STIs (gonorrhoea, chlamydia and syphilis) among people prescribed PrEP
3. To Assess preferences of PrEP dosing (daily dosing vs. event-driven PrEP in MSM)
4. To Describe patterns of PrEP use and medication adherence to the recommended PrEP medication schedule in those prescribed PrEP
5. To Monitor behavioural risk practices among PrEP users in the cohort
6. To Determine if there are other health and social benefits in provision of PrEP (e.g. linkage into other health services, including mental health services)
7. To recommend similar HIV prevention interventions (PrEP) to Sri Lanka

4. Design and time period of pilot

The pilot was utilizing a protocol adapted from those in other PrEP demonstration projects, allowing for international comparisons. The design was an open-label, single-arm treatment cohort. People at risk for HIV based on an initial risk assessment were eligible to be prescribed PrEP on the same day as their baseline clinical visit. The pilot was commenced in early 2019 starting with stakeholder discussions, demand creation, community mobilization and first PrEP prescription took place on August 26.2020 by activating the clinical site where PrEP was prescribed, and completed in December 2021 (each participant was followed-up for 12 months). Therefore the pilot completed for the recruited participants as for end 2022. Participants in the pilot voluntarily consented to be enrolled.

5. Treatment/intervention

A fixed-dose combination of tenofovir/emtricitabine (TDF/FTC) was offered to everyone as their PrEP regimen. MSM were given the option to take it as daily dosing (single pill/each day during period of risk) or as event-driven PrEP (per the latest WHO guidelines). Transgender women, and any cis-women and cis-men were offered only the daily dosing option. The investigators anticipated and prioritized MSM and TGW for this demonstration project, although the prescribing medical doctors were given the freedom to identify individuals presenting at the clinic who were at substantial HIV risk.

6. Planned sample size

As this is a demonstration project, overall sample size was determined by capacity constraints and available funding rather than power calculations. A sample size of 250 participants was considered to be feasible within these parameters.

7. Prioritized population

The pilot enrolled individuals 18 years of age and older who were largely from key populations in Sri Lanka, and who were at substantial risk for HIV acquisition. Given the current epidemiology of HIV in the country, MSM and transgender women were prioritized. However, other people at substantial risk for HIV, based on WHO guidance and the discretion of the prescribing clinician, had the opportunity

to enroll in the study (e.g. beach boys, people who use drugs (PWUDs)/people who inject drugs (PWIDs), and HIV-negative people (MSM) who had HIV-positive partners who were not virally suppressed (Table 1). For this project, adolescents (Age 10-17) were not included.

Table 1: Populations MSM & transgender people (including behavioural risk criteria) those were eligible/suitable for PrEP in this pilot project

Men who have sex with men (MSM)	**Transgender people**	**Heterosexual people having bisexual relationship**	***People who inject/use drugs & MSM**
Suitability for PrEP could be based on the following:			
• Condomless anal sex (CAS) with any casual male partner. • Rectal gonorrhoea, rectal chlamydia or infectious syphilis. • Methamphetamine use. • CAS with a regular HIV+ partner who is not on treatment and/or has a detectable viral load.	• CAS with any casual male partner. • Rectal or vaginal gonorrhoea, chlamydia or infectious syphilis. • Methamphetamine use. • CAS with a regular HIV+ partner who is not on treatment and/or has a detectable viral load.	• CAS with any asual MSM partner. • CAS with a regular HIV+ partner who is not on treatment and/or has a detectable viral load.	• Shared injecting equipment with an HIV+ individual or with MSM of unknown HIV status.

8. Enrolment of participants (inclusion/exclusion criteria)

Study eligibility/suitability

Eligibility (or suitability) for this pilot was guided by the most up-to-date WHO guidelines on PrEP. To be eligible, participants must be aged 18 years or over, live or visit Colombo regularly enough to be able to attend clinical visits for follow-up assessments, be documented as HIV negative at enrolment or within 7 days of starting PrEP, and be at high risk of acquiring HIV through sexual exposure as established by the behavioural risk criteria (Table 1). Excluded from participation were individuals infected with HIV-1, with symptoms consistent with acute HIV infection, or indications for HIV post-exposure prophylaxis. If HIV status was indeterminate at the enrolment visit, the start of TDF/FTC was

delayed for at least 1 month, to confirm HIV negative status. The full list of inclusion and exclusion criteria is listed below.

Inclusion criteria

- Age ≥ 18 years with body weight ≥ 35 kg
- Men/transgender men/women who have sex with men
- HIV negative at enrolment, with a negative HIV test result documented within seven days of initiating PrEP
- Willing to be contacted via telephone or email (e.g. for reminder to attending follow-up visits)
- Willing to comply to visits schedule per protocol (*Note*: allowing for flexibility to stop and re-enter demonstration project if there is travel abroad for work or holiday)
- Motivated to strengthen prevention efforts, including willingness in starting to use pre-exposure prophylaxis
- Resident of Sri Lanka; visit Colombo regularly enough to be able to attend clinical visits for follow-up assessments
- Informed consent form signed
- Substantial risk of acquiring HIV infection, based on risk in the past 3 months or likely risk in the following 3 months:
    - For MSM and transgenders:
        - Condomless anal sex with a casual male partner over the last 3 months
        - And/or history of STI during the last 6 months (syphilis, gonorrhoea , chlamydia, HBV or HCV infection)
        - And/or using psycho-actives drugs during sexual intercourse (e.g. cocaine, gammahydroxybutyric acid (GHB), Methylenedioxymethamphetamine (MDMA), mephedrone)
        - And/or having an HIV-infected sexual partner with a detectable plasma viral load (> 50 copies (cp)/milliliter (ml))

Exclusión Criteria

- HIV-1 or HIV-2 infected
- Signs and symptoms of acute HIV infection with probable exposure
- Having an estimated creatinine clearance (glomerular filtration rate [GFR]) <60ml/min
- History of chronic renal disease, osteoporosis or osteopenia
- Allergy or contraindication to any medicine in the PrEP regimen (based on self-report or recorded)

9. Participating sites

For the initial phase of this demonstration project, the central STD clinic in Colombo was the site where clinicians were prescribing PrEP. Pre-enrolment and enrolment was initiated at other sites (e.g. community-based sites offering HIV testing; clinics such as FPA (Family Planning Association Sri Lanka); where information about the project was disseminated. Pre- enrolment demand generation was initiated within the communities & community –based sites.

10. Endpoints

Primary endpoints

- Feasibility: uptake of starting PrEP in those who meet both behavioural risk suitability and clinical suitability.
- Acceptability: persistence ('retention') of PrEP in those who start PrEP (total weeks taking PrEP)

Secondary endpoints

- Number of incident HIV infections
- Incidence of STI (gonorrhoea, chlamydia and infectious syphilis) per 100 person years among study participants
- Proportion of MSM participants choosing daily dosing vs. event-driven PrEP in MSM at baseline
- Proportion of MSM participants switching dosing strategy during follow-up PrEP use
- Rate of adverse events related to PrEP
- Adherence to the medication schedule among study participants
    - Daily PrEP group: proportion of correctly taken doses according to self-report, and pill-counts.
    - ED-PrEP group (for MSM): proportion of correctly taken doses according to self-report, and pill-counts.
- Viral resistance
    - Proportion of participants with incident HIV infection that has HIV drug resistance
    - Type of resistance mutations, proportion associated with TDF or FTC
- Changes in risk behaviour
    - Changes in number of sexual partners and type of sexual partner (steady or casual)
- Additional health and social benefits in provision of PrEP (e.g. linkage into other health services, including mental health services)

11. Procedures for providing PrEP to participants: assessment and follow-up

A referral network of community-based sites & regional grant implementing unit of Family Planning Association were able to provide information about the demonstration project (including through social media platforms and websites such as https://know4sure.lk) to members of key populations and other individuals that can benefit from PrEP. The actual prescribing/initiation of PrEP happened at the NSACP central clinic. Staff at the central NSACP clinic provided potential candidates with information on PrEP and other SRH services, including condoms/lubricant and additional risk reduction counseling. Table 2 lists the tests and procedures required prior to starting PrEP and throughout the duration of the demonstration project. To start someone on PrEP, the minimum HBsAg test. Within this pilot, molecular testing for gonorrhoea and chlamydia were provided at baseline, month 6, and month 12.

testing procedures included a 4th generation HIV rapid diagnostic test (RDT), a creatinine test, and a HBsAg test. Within this pilot, molecular testing for gonorrhoea and chlamydia were provided at baseline, month 6, and month 12.

Table 2: Baseline and follow-up testing and procedures during PrEP pilot

	Baseline / enrolment		**Follow-up**			
Test/procedure	Week -1 or 0	Month 1	Month 3	Month 6	Month 9	Month 12
HIV 4th generation RDT	Y	Y	Y	Y	Y	Y
Creatinine clearance (renal function)*	Y			Y		Y
HBsAg** (anti-HBs if available)	Y					
Syphilis serology	Y			Y		Y
N. gonorrhoea PCR	Y			Y		Y
C. trachomatis PCR	Y			Y		Y
HCV***	Y					Y
HBV vaccination**	Y					
HPV vaccination	Y					
Serious adverse events review		Y	Y	Y	Y	Y
Review eligibility	Y	Y	Y	Y	Y	
Review adherence	Y	Y	Y	Y	Y	
Drug dispensing	Y	Y	Y	Y	Y	

*creatine clearance was performed at baseline, 6 months, 12 months.

** HBV vaccination should be offered to anyone without HBV infection who is non-immune;

*** HCV testing for anyone with injecting drug risk.

PrEP initiation (baseline visit)

An initial consultation included confirmation of behavioural eligibility (meeting risk criteria in Table 1, clinical evaluation (medical history), education (counseling), and laboratory assessments, including either a 4th-generation HIV antibody/antigen test. An informed consent signed by the participant. A 1-month PrEP supply was provided at the first appointment, contingent on normal renal function and a negative HIV test. After initiation, follow-up appointments were scheduled at 1 month, month 3, month 6, month 9, and month 12.

PrEP continuation (ongoing follow-up)

Follow-up appointments entailed a 15-20 minute consultation with a clinician. The consultation l included an assessment of adherence, side effects, current medications and ongoing behavioural risk, laboratory tests, STI prevention counselling and up to 3 months PrEP supply (after the 1 month visit, 2 months PrEP supply was offered).

Participants with symptoms, and other issues requiring clinical management were managed accordingly.

All prescriptions were authorized by a medical doctor.

PrEP adherence & counseling

The risk to reduce drug resistance was ensured by that people actually a) take PrEP as it was indicated in the protocol; b) continued engagement and access to additional information and clarity by the PrEP investigators and the supporting community-based organizations; and c) PrEP users come back for their follow-up appointments. The rationale for the following up patients every 3 months was based on the fact that PrEP was not simply passing off pills to someone, but having meaningful engagement with a service provider and the clinical team. This engagement was based on trust. In addition, no more than 3 months of pills were dispensed to an individual, as the investigators wanted people to come back every three months to rule out any HIV infection, before offering a new prescription. Lastly, every visit on follow-up was an opportunity to assess if people wanted to continue taking PrEP.

Interrupted or discontinued PrEP

As this demonstration project attempts to be a 'real-world' implementation study, PrEP-4-SriLanka allowed participants the autonomy to continue, stop and restart PrEP in the course of the project

At each visit, participants provided with education about the importance of starting and stopping PrEP safely (daily dosing were offered to all and ED-PrEP were offered to only MSM if they were suitable for this dosing category). A missed appointment reminder was sent to anyone who had not

attended a scheduled follow-up visit. Participants re-presenting after a break in PrEP were reassessed and restarted on PrEP in accordance with the protocol, with a recommendation for HIV window-period testing and additional screening or management, depending on risk.

Abnormal results and other complications

Patients testing positive for HIV or other infections and those with abnormal renal function were flagged and urgently recalled for further assessment. HIV and renal function results were generally reported on the same day (or the next day).

Patients with impaired renal function, suspected HIV infection/seroconversion, or adverse events were referred and prioritised for medical review and follow-up. Additional support was made available to individuals with chronic viral hepatitis and other medical or psychosocial issues.

Arrangement was done to refer and actively link HBV-infected person in the PrEP project to specialized care by a hepatologist.

12. Procedure in the event of an HIV infection (seroconversion)

Arrangement was done in case if a participant became HIV infected during the project, they would be discontinued immediately from the project but decided to be followed up for safety. It was further decided that In this case, project staff would collect all unused pills, conduct the final visit procedures including testing for genotypic resistance and viral load testing, and refer the participant for ART initiation at NSACP.

It was decided to test Drug resistance and genotyping in this case. Routinely the NSACP send sample to National AIDS Research Institute (NARI), India. Three- five ml of blood sample is to be collected in an EDTA tube (Ethylenediaminetetraacetic acid) from the enrolled individual on the same day that the HIV diagnosis is made, and before ART is initiated. It was arranged or planned to send the blood sample to the laboratory at the National STD/AIDS Control Program, where the sample is processed as dried blood spot and send to NARI.

13. Recording and reporting of serious adverse events (SAEs)

Safety and tolerability of TDF/FTC was evaluated by recording adverse events (AEs) and grading laboratory and vital signs evaluations in the intake/follow-up forms; starting from enrolment until the final visit. Severity, causality, and outcome were also assessed. Any event that occurred before the enrolment visit was documented as medical history. All AEs were followed up until resolution to the extent possible. An HIV infection was not considered a serious adverse event (SAE), but required reporting to study team (see below). Due to the possible renal adverse effects of TDF/FTC, an elevation in serum creatinine was monitored closely. TDF/FTC as PrEP was interrupted when creatinine clearance is below 60 mL/minute/1.73 m^2 and was permanently discontinued when the clearance stays below 50 mL/minute/1.73 m^2 after repeat testing.

It was a requirement of this pilot that any serious adverse effects reported to the investigators, sponsors and generic manufactures

14. Packaging, labeling, storage, and accountability of pilot supplies

Medication supply

The study medication (Macleods Pharmaceuticals Ltd (generic TDF/FTC)) had been secured by the NSACP through formal procurement procedures. The medication storage and shipment/s was conducted under conditions specified by the manufacturers in the TDF/FTC Product Information.

Medication storage

TDF/FTC pilot study tablets must were stored below 25°C (as per TDF/FTC Product Information). TDF/FTC tablets were stored in the original container.

Prescribing

The study medications were prescribed only by an authorized prescriber trained to the study protocol. It was not allowed to be prescribed and/or used for purposes other than those described in this protocol.

Study Drug Dispensing

The study drug was distributed in the central clinic's pharmacy. The central clinic pharmacy was responsible for dispensing the drug to each study participant upon presentation of a valid

prescription. Drug dispensing was recorded in pharmacy dispensing logs. Distribution to participants was done as instructed.

15. Data collection, management and record retention

PrEP-4-SriLanka was a demonstration project that was attempting to mimic 'real world' implementation as closely as possible, and thereby to reduce the burden of data collection by clinical staff, at the NSACP central clinic and referral sites. Staff were asked to collect only critical information about study participants which allowed establishing study record and 'PrEP-Number (the unique identifier). The following information were collected at enrolment and in follow-up visits.

- Date of visit (e.g. enrolment/follow-up visit)
- Client ID (STD Number)
- PrEP-Number (the unique number generated after enrolment into the study)
- Confirmation check that all eligibility/inclusion criteria have been checked and confirmed in full (enrolment)
- Confirmation check that patient has signed and provided an informed consent form, including each
  component requiring additional consent (i.e., consent to participate in qualitative study, consent to be contacted with an invitation to complete behavioural questionnaire)
- Gender
- Date of birth
- Participant's telephone number
- Participant's email address (optional and collected only from those participants who consent to participate in optional on-line surveys described below)
- Medical history
- HIV/STI test and results
- Creatinine tests and results
- TDF/FTC regimen choice (daily or 211 for MSM; only daily for transgender persons)

Qualitative interviews of participants

A subset of participants (n=20) were invited to participate in in-depth, face-to-face interviews as part of the qualitative component of the pilot. Since the COVID 19 prevailed during this period these interviews took place through Zoom platforms. These took approximately one and a half hours and participants were asked questions about their personal experiences with taking PrEP. The face-to-face

interviews took place in a private office as part of small focus groups (n=4-5 people per group) at NSACP and in the participating community-based site.

These qualitative interviews were conducted among PrEP users and among the health care workers (doctors, Public Health Inspectors & Public Health Nursing Sisters) on separate dates and times for each different group.

Record retention

The NSACP central clinic took decision of continue to retain all study documents, including essential documents and participant files, for at least 7 years after the completion of the pilot.

It was agreed with NSACP central clinic that the clinic would inform the principal investigator in writing when the study related records are no longer maintained in the clinic.

16. Confidentiality of data

Individual subject medical information obtained as result of this pilot was considered confidential and disclosure to third parties was prohibited. Data generated as a result of this pilot were to be available for inspection on request by the participating physicians, including external site audits and inspections. All data were recorded with a client identification number.

All study-related information was stored securely at the study site. Adverse event reports were maintained in a register & participant confidentiality maintained. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, were stored with restricted access.

Forms, lists, logbooks, appointment books, and any other listings that link client IDs to identifying information were stored at the central clinic.

17. Analysis and statistical considerations

This was an implementation research, or a one-arm open-label treatment trial. No randomization or blinding procedures were used. One treatment was offered as an open label study, with the treatment being TDF/FTC. However, for MSM, study was offering two different dosing options (daily dosing and '211', otherwise known as event-driven PrEP),

Baseline data analysis

Descriptive statistical analyses were performed to describe uptake, choice of intervention strategy (e.g. daily vs 2-1-1), acceptability, usability, baseline characteristics and barriers and motives of choice.

Follow-up data analysis

Analyses were performed by intention to treat and per protocol. Both quantitative and qualitative analysis was performed.

Adherence was determined and compared within groups by using self-report.

Persistence (retention in care) at 1, 3, 6, and 12 months (yes/no), switched (yes/no) and adherence (>80% versus <80%) were further analyzed.

Changes over time were described for the following parameters: adverse events, risk behaviour, incidence of STIs.

The observed incidence rate of HIV and the occurrence of HIV resistance were described.

Changes between baseline and follow-up visits were described.

18. Ethics committee/regulatory approval and informed consent

Ethics committee/regulatory approval

Ethical approval was obtained from ethics review board of the University of Colombo. This nature of PrEP demonstration project is recommended by the WHO and the medications prescribed in this pilot is indicated in the WHO's Essential Medicines List.

The pilot was implemented without any deviation from, or changes to the protocol.

Informed consent

The study participants gave written informed consent before enrolling into the pilot and the start of any pilot-related procedure. The signed informed consent was retained by the clinic. A copy of the signed informed consent was given to the participant.

Potential risks

Study participants, verbally and also as part of the written consent form, were informed of the potential risk of participating this pilot, from the more commonly reported side effects of TDF and FTC when given as PrEP (e.g. headache, back pain, abdominal pain, unintentional weight loss, nausea, flatulence, and abdominal pain). They were also informed that after starting PrEP, symptoms in the majority of PrEP users resolve over the course of 4 weeks. As noted earlier, clinical trials have reported a small decline in kidney function, but this decrease is not likely to be clinically significant. A decline in the health of the kidneys may be more likely in older people and people with high blood pressure, or diabetes, or people who already have some mild kidney disease. Once PrEP is stopped, studies have shown that the kidneys return to normal.

PrEP has also been associated with a small decline in bone mineral density loss according to clinical trials, but this decrease is not likely to be clinically significant. The prescribing doctor may suggest that a participant have some additional tests (calcium concentration by serology) before starting PrEP, particularly in older persons, those with diabetes, or taking steroid tablets, or having chronic health problems. Once PrEP is stopped, studies have shown that the bone mineral density loss returns to normal.

TDF is active against HBV infection at the same dose used for PrEP. WHO recommends TDF for treatment of HBV infection in people for whom treatment is indicated. Not all people with chronic HBV infection have treatment indications. Indications for treatment of HBV can be assessed in a variety of ways depending on which laboratory tests are available. When HBV treatment is stopped, occasionally HBV infection can flare in the following one to three months. The risk of hepatitis flares after stopping HBV treatment is higher in people with liver fibrosis. Additional assessment can be considered for people with HBV infection who are considering PrEP. The event-driven (211) dosing is also not recommended for people with HBV, and in this pilot, it was not offered. Only daily dosing was the choice for anyone who have HBV.

There are at very limited reported cases in the world of a person became infected with HIV despite having evidence that they were taking PrEP during the period of risk. This is often described as a 'PrEP failure'. It is understood that the reason that PrEP failed was that the person was infected with a

strain of HIV that was resistant to TDF/FTC. The risk of being infected with a strain that is resistant to TDF and FTC is very low, but not zero.

If was instructed if a participant becomes infected with HIV during the pilot, the doctor would stop PrEP and refer individual for treatment initiation immediately.

WHO recommends the use of PrEP in pregnancy and breastfeeding, as it is both safe and effective in reducing HIV acquisition in women. However, for this pilot, cis-women were not included.

Counseling services or other appropriate support were arranged, if a participant becomes upset or distressed as a result of their participation in the pilot.

Lastly, having a blood sample taken may cause some discomfort or bruising, and this was clearly noted to participants.

Potential benefits

Conducting a demonstration project or pilot of this nature "Be-PrEP-ared" may in itself have an impact on HIV prevention that goes beyond providing ARV medication to participants. It had reinforced collaborations with community organizations and health care providers and helped in increasing PrEP awareness and influenced an impact strategy on HIV prevention. In the wake of Be-PrEP-ared, various sub studies have already started in Belgium such as a survey among health care providers to assess their PrEP knowledge, attitudes, and willingness to prescribe. New studies were show cased during the pilot. Those capacity building activities were important to for cross country learning during the pilot. To develop a good understanding of how to optimally implement and provide PrEP integrated into the existing health care structures, pilots like this helped a lot.

Risk/benefit ratio

PrEP is an intervention and service that is meant to be offered to people at high risk for HIV, which is a function of condomless sex. Therefore, the pilot aimed to minimize the risk of acquiring HIV in people by actually offering PrEP as part of a package of services, which included how to safely start and stop PrEP, the critical role of condoms in overall sexual health, and continuing education and sensitization on how PrEP is a responsible choice to protect oneself from HIV, and one's community and sexual network.

19. Results

PrEP-4 -Sri Lanka pilot was launched on August 26.2020. First PrEP prescription was done on September2nd 2020. Analysis was conducted twice an interim analysis after the last prescription on July15th 2021 and final analysis after last prescription on end December 2021.

Pilot outcome in summary

Table 3: Pilot summary

Characteristics	Number & % (Interim Analysis) As of July15. 2021	Number & % (Final Analysis) As of end December 2021.
Total Number enrolled for the pilot	47 Colombo – 47 *Hambantota – 2 *Ragama – 1 *Anuradhapura – 2 * Dropped in the analysis due to lack of further information	133
Retention Rate (1 month)	45/47 (97%)	128/133 (96%)
Retention rate (after 12 months) as of end December 2022.		44/133 (33%)
Daily Dosing prescription		90
Event Driven prescription		20
Prescription Data not filled		23

Implementation of the Pilot "PrEP-4- Sri Lanka

Pre- Activation steps & activation steps

- In early –mid April 2019, pilot co-chairs shared first PrEP pilot proposal with technical partners (WHO & UNAIDS) & Donor Global Fund.

a. Initial Demand Generation - Mobilizing Communities

- UNAIDS/UNFPA supported Community PrEP awareness sessions and consultative workshops July 2019– September 2020.
- PrEP awareness & demand generations activities were conducted by communities & UNAIDS/UNFPA focal point supported these activities; using a *Face book page,*

b. PrEP Webinar for Health care providers

- Pilot Co- Chairs organized a PrEP Webinar on July 22, 2019 taking The Regional advisor for PrEP from UNAIDS as resource.

c. Support from the International Technical Expert

- ITA recruited – visited twice to Sri Lanka in December 2019 & March 2020. Virtual ITA support obtained from March 2020.
- Pilot protocol & tools drafted
- Ethical clearance obtained from University of Colombo in September 2020.

d. Services activation geared trainings & demand generation

- Medical doctors, nurses, public health inspectors, and laboratory staff at NSACP and community-based organizations were trained to implement PrEP
- Knowledge-exchange on Australian PrEP experience: for clinicians and other stakeholders in the roll-out of PrEP in Sri Lanka; Webinar conducted on August, 2020

e. Community demand generation

- SKPA program conducted many community consultations & training programs in the view of creating demand for PrEP.
- A WhatsApp group (PrEP Community group) was created following the PrEP training for NGO/CBO to share knowledge with an online Google form for the potential clients to register for PrEP.
- Clients were directly contacted to enroll.

f. Further demand generations

- Two days PrEP demand generation workshop both MSM & TG groups and CBO - February 16 & 17, 2021.

✓ Mysore sex worker PrEP pilot expert shared her experiences, Workshop engaged sex worker community from Mysore India sex worker's pilot.
✓ Community PrEP evidence from Thailand is presented by Thailand experts in 2021
✓ PrEP information materials were distributed in the clinic from 2021
✓ Pilot progress was presented in the "PrEP Innovation and Implementation in Asia and the Pacific: Virtual Regional Discussion 15-16 December 2020" conference organized by UNAIDS & WHO
✓ Similarly pilot progress was presented in Asia-Pacific Workshop on PrEP Demand Generation in November 23.2021
✓ These regional conferences were a learning Opportunity for health care workers and communities.

g. Further scale up of PrEP implementation

- Interim analysis of PrEP pilot was presented among national & international implementers
- Pilot interim analysis, showed integrating PrEP services with the package of Key population interventions.
- NGO/CBO working in the case finder model (Gampaha & Colombo) were trained to refer clients from the available risk profiles data.
- Special KP friendly PrEP clinics were initiated at NSACP on Sundays from October 2021
- NSACP online platform https://know4sure.lk/ introduced booking systems for PrEP. This booking system facilitates clients to make booking for PrEP clinic.
- A mobile hot line has been in operation get information & make booking to PrEP clinic (+9471 637 9192)

- Pilot interim analysis was done twice, (bi annual). Based on these evidences, PrEP implementation was further intensified.
- Interim analysis of pilot revealed the importance of providing services through prevention & clinical care services and feasibility of integrating most needed population namely KPs through existing prevention models.
- PrEP is decentralized to other STD clinics namely Ragama, Jaffna, Hambantota & Anuradapura in early 2021.
- As part of the pilot, series of focus group discussions (FGD) were conducted in August to September 2021. FGD aim to assess their experience in PrEP provision; to better understand missed opportunities & bottle necks in the service delivery. Prescribing doctors, nurses, public health inspectors, outreach workers & MSM & TG communities participated both in Colombo & Gampaha. Semi-structured questionnaires with open-ended questions, and prompt questions within those primary questions were included to focus improve PrEP service delivery.
- Pilot interim analysis showing slow PrEP uptake & FGD indicating the requirement of flexible hours and minimum clinic waiting time pivoted Sunday PrEP clinics starting from October 2021. Sunday PrEP clinic resulted in accelerating PrEP uptake by nearly half of total clients initiated during October 2021-December 2021.
- Further PrEP demand generation was continued by recognized social media campaign.

Interim Analysis

Interim analysis was conducted in August 2021. Interim analysis was presented to the stakeholders. Based on the interim analysis PrEP pilot was progressively scaled up. Interim analysis is presented below.

Table 4: Interim analysis; PrEP enrollment details.

Characteristic	Details
First client Prescription	02.09.2020
Last prescription for interim analysis	15.07.2021
Total registered	
Colombo	47
Hambantota	2
Ragama	1
Anuradhapura	2

Table 5: Interim analysis; Mode of Referral

Mode of Referral	Number of clients (n=47)
Self-referred	24
STD clinic Attendee	10
Referred by NGO	04
Know4sure	05
Data not filled	02
Missing file	02

Table 6: Other Key funding of the interim analysis of the pilot

Characteristics	Number & %
Having sex with multiple partners	*40/47 (85%)*
Inconsistent or no condom use	*22/47 (47%)*
Didn't use a condom during sex in past 3 months	*32/47 (68%)*
Not using condoms for next 3 months	*18/47 (38%)*
Receptive anal	*21/47 (45%)*

Outcome of Focus group discussions (FGD)

Clinicians, transgender people, MSM, public health inspectors/nurses/outreach workers were participated in separate groups. 4-6 individuals involved in each FGD. Total of 4 FGD were conducted

Recommendations from the FGD

1. Further training required, particularly for PHIs/nurses
2. Hours matter (separate clinic one site was popular)
3. Opportunity for tele-health (openness to establish this as part of PrEP initiation/follow-up)
4. Gain framing messaging, instead overemphasis on side effects
5. Missed opportunities in clinics (referrals coming outside the clinic are more, within the clinics are less)
6. Differentiated service delivery (DSD) = better understanding for clinicians on PrEP delivery

Final Analysis

Final analysis was done in end December 2021. Total of 133 enrolled as of end December 2021.

Table 7: Final analysis; Mode of Referral

Mode of Referral	Number of clients (n=133)
Self-referred	27
STD clinic Attendee	16
Referred by NGO	78 (59%)
Know4sure	06
Data not filled	01
Missing file	05

Table 8: Final analysis; Gender composition

Gender	Number of clients (n=133)
Male	109(82%)
Transgender Female	12
Transgender Male	03
Missing file	05
Data not filled	04

Table 9: Final analysis; Age of the participants

Age	Number of clients (n=133)
20-25	31
26-30	31
31-35	17
36-40	12
>41	11
Data not filled	25
Missing file	05
Age 19 years	01

Age – 50% are < 30 years

Table 10: Final analysis; Previous history of taking PrEP

Gender	Number of clients (n=133)
Yes	05 (4 outside Sri Lanka, 01- online)
No	120
Not filled	03
Missing file	05

Table 11: Final analysis; Reason for starting PrEP

Reasons for PrEP	Number of clients (Multiple answers possible)
Has sex with > 1 partner	87 (65%)
Sex partner(s) high risk & HIV status is unknown	37(28%)
Inconsistent or no condom use	87(65%)
Recurrent sex under influence of alcohol/recreational drugs	13
Recent STI (past 6 months)	05
Sex partner(s) is HIV positive On ART < 6 months	04
Data not filled	05
Missing file	05

Reasons for starting PrEP – 92% reported multiple partners

Table 12: Final analysis; Number of partners in previous 3 months of starting PrEP

Number of partners in previous 3 months	Number of clients (n=133)
Less than 5	69
5-10	27
>10	22
Data Not filled	04
Missing file	05
>50	06

Condom Use at last sex – 75% have had condomless anal sex

Table 13: Final analysis; Condom use during the past 3 months prior to PrEP

Did you always use a condom when you had sex in past 3 months?	Number of clients (n=133)
Yes	22
No	100 (75%)
Data Not filled	06
Missing file	05

Table 14: Final analysis; Type of condom-less sex

Reasons for PrEP	Number of clients (Multiple answers possible)
Receptive anal	83(62%)
Insertive anal	55(41%)
Receptive vaginal	02
Insertive vaginal	11
Receptive oral with ejaculation	66
Not filled	06
Missing file	05

Anything else important for PrEP program in the sexual history

Table 15: Final analysis; Important points in the sexual history

Anything else you want to disclose about your sexual history?	Number of clients (Multiple answers possible)
More than 1000 partners	01
Works as a male commercial sex worker	03
Sex under the influence drugs	02
Didn't use condoms with partner he trusts	01
Practiced Group sex	02
have Sex with males on PrEP	01
All the sexual partners are foreigners	01
Mainly with female / only few males	01
Data not filled	117
Missing file	05

Table 16: Final analysis; Drug use and sex

Have you had Sex under the influence of drugs?	Number of clients (n=133)
Yes	28
No	91
Data Not filled	09
Missing file	05

Drugs used & Drug use practices

Drugs used - Ice,(methamphetamine), -(13), Ice, KG, Cannabis, - (01), Heroin,Ice,Cannabis, (01) , Ice (02), Cannabis (08), alcohol, Canabies (01), Marjuana (02)

Injecting-03

Bottlenecks for initiating clients on PrEP

- Lack of Awareness
- Poor Risk perception/risk assessment
- Prescription challenges; PrEP suitability ('eligibility'): daily dosing vs 211
- Convenience of visiting the clinics and obtaining PrEP
- COVID-19 surge
- Travel to clinic/time waiting in clinic

1. Limitations to the Pilot

2. Pilot Co-chair had limited access to the study site.
3. No training given to clinicians, anyone in the roster prescribe, thereby no uniformity.

4. When the pilot initiated, same data was entered in the Electronic Management Information system, however the pilot co-chair was only given the filled questionnaire. Due to this duplication of work and extra work load the data collectors/ clinicians did not fill out all information during data collection. Due to limited access to the study site data collection supervision was a challenge throughout the pilot.

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21. Annexures

Annex 1

Clinicians SOP for PrEP initiation and follow-up care

Introduction of pre-exposure prophylaxis (PrEP) for HIV in Sri Lanka: a demonstration project to determine feasibility and acceptability of PrEP provision as part of strengthening sexual health services.
PrEP 4 Sri Lanka pilot

This SOP is for doctors, nurses and public health inspectors who are involved in the PrEP pilot project.

Aim

With this demonstration pilot project, we aim to assess the feasibility and acceptability of offering PrEP in a STD Clinic setting in Sri Lanka.

Target Population
MSMs and TGW

Mode of recruitment/ referral

- Voluntary attendees requesting PrEP
- Referred clients from NGOs, district STD clinics, other hospitals, GPs and other methods for PrEP
- STD clinic attendees who are eligible for PrEP

At the registration desk

- Registered in the STD clinic via EIMS
- Issued a patient follow up card with the STD clinic number and a PHN number after which they are directed to a clinic room for consultation with the doctor, or to the PrEP room if they if they are attending only for PrEP

At the consultation with the doctor

- A paper based eligibility check list based on the inclusion/exclusion criteria***** is to be filled for all male clients and transgender women

**** Inclusion Criteria***

1. Age ≥ 18 years and weight ≥ 35 Kg
2. MSM/ TGW
3. HIV negative with rapid test at enrolment
4. Willing to be contacted via telephone or email (e.g. for reminder to attending follow-up visits)

5. Willing to comply to visits schedule per protocol (Note: allowing for flexibility to stop and re-enter demonstration project if there is travel abroad for work or holiday)
6. Motivated to strengthen prevention efforts, including willingness in starting to use pre-exposure prophylaxis
7. Resident of Sri Lanka;
8. Substantial risk of acquiring HIV infection,
    1. Condom less anal sex with a male partner over the last 3 months
    2. Or history of STI during the last 6 months (infective syphilis, gonorrhoea and chlamydia infection)
    3. Or having unprotected sex with an HIV-infected partner with a detectable plasma viral load (> 50 copies (cp)/milliliter (ml))

Exclusion Criteria

1. HIV-1 or HIV-2 infected
2. Signs and symptoms of acute HIV infection with probable exposure
3. Having an estimated creatinine clearance (glomerular filtration rate [GFR]) <60ml/min
4. History of chronic renal disease, osteoporosis or osteopaenia
5. Allergy or contraindication to any medicine in the PrEP regimen (based on self-report or recorded)

- If they are not eligible routine STD care given
- If they are eligible- discuss PrEP and given the information sheet on PrEP. If they are willing to participate in the PrEP pilot study, written consent is obtained in the same paper based document with the check list.
- If they are not consenting indicate the reason in the eligibility assessment tool and routine STD care given
- If the client is consenting, the STD patient record in EIMS is filled after taking a history and examination – for signs and symptoms of STI and BP
- Once they have consented the notes are sent back to the registration. At the registration desk,
    - Register in the PrEP register and PrEP number given (If EIMS has a PrEP module the doctor can assign the client to PrEP service)
    - A patient follow up card given with the STD Clinic number/ PHN number with a sticker pasted on it
    - The patient record is pasted with a sticker on its spine (the skeleton file)
    - Fill the Interviewer administered questionnaire or EIMS PrEP module

Fill the blood request forms – all forms should have a sticker pasted on the right upper corner (if we are sending a paper form)

- HIV 4th generation Ab/Ag RDT
- Hep B surface Ag RDT
- Serum Creatinine
- Hep C Ab RDT
- HIV ELISA (All the rapid tests are also to be performed from this sample)
- VDRL/TPPA

Sample collection for GC/CT

They will all be swabbed from urethra, anus and throat.

<u>Sample collection</u>

- Use disposable gloves for sample collection

- Throat – pharyngeal arches should be swabbed without touching the sides of the mouth
- Urethra – Swab should be inserted to the urethra and swabbed at least 10 secs
- Anus – should be inserted up to 2.5 cm and swabbed for 10-30 secs
- Use only dacron, rayon, calcium alginate tipped collection swabs with plastic or non aluminium wire shafts.
- Specimen container should be label appropriately after sealing the specimen container tightly or before sample collection.

If urine is collected instead of a urethral swab

- Collect 10-50 ml of first catch urine into a clean polypropylene container without preservatives
- Seal the container and label and add a PrEP sticker
- Urine samples are stable at 18-25^{0}c for 24 hours

Sample transport

- The specimen container should have a PrEP sticker
- The request form should have a PrEP sticker on the upper right hand corner
- Specimen containers should be kept on a tray that has been cleaned with alcohol based disinfectant prior to sample collection.
- Refrigerate swab specimens if transport to lab takes more than one hour.

Prescribing PrEP

- If the client has a negative HIV 4th generation Ab/Ag RDT result PrEP can be initiated on the same day pending the other investigation results
- Tenofovir Disoproxil Fumarate (TDF) 300 mg / Emtrcitabine (FTC) 200 mg fixed dose combination tablet once a day for 1 month will be prescribed by the medical officer using a EIMS after discussing the probable adverse effects and adherence counselling.
- Follow up date given as appropriate

Report tracing and entering and taking action

- This is a responsibility of the Senior Registrar who is allocated the duty for that month

Follow up

- Follow up will be done in 1 month, 3 months and three monthly thereafter for one year by the medical officer if all the laboratory test results are normal.
- During the follow up consultations assessment of adherence, side effects, current medications, ongoing behavioural risk and STI symptoms and STI screening will be done. Laboratory tests will be discussed and STI prevention counselling will be done.
- If there are new symptoms routine STD care and treatment will be given.
- PrEP drugs will be issued for 1 month at the first visit, for 2 months in the second visit and for 3 months thereafter if no abnormal results or adverse reactions.
- The summery of the laboratory testing and activities done at each visit are summarized in table 1.
- Hep B routine vaccination will be offered to those who are negative for Hep B S Ag

Table 1. Baseline and follow-up testing and procedures during PrEP pilot

	Baseline / enrolment		**Follow-up**			
Test/procedure		Month 1	Month 3	Month 6	Month 9	Month 12
HIV 3rd or 4th generation RDT	Y	Y	Y	Y	Y	Y
Serum Creatinine	Y			Y		Y
HBsAg RDT	Y					
Syphilis serology (VDRL/TPPA)	Y			Y		Y
N. gonorrhoea PCR	Y			Y		Y
C. trachomatis PCR	Y			Y		Y
GC culture	Y			Y		Y
HCV Ab RDT	Y					Y
HBV vaccination** (0, 1 , 6 months regimen	Y		Y	Y		
Serious adverse events review		Y	Y	Y	Y	Y
Review eligibility	Y	Y	Y	Y	Y	
Review adherence	Y	Y	Y	Y	Y	
Drug dispensing	Y	Y	Y	Y	Y	

Interrupted or discontinued PrEP

- This PrEP pilot project will allow participants the autonomy to continue, stop and restart
- Clients will be contacted through their preferred mode of communication after the first missed appointment.
- If there are no abnormal results participants will not be contacted after one reminder of a missed appointment
- Participants re-presenting after a break in PrEP will be reassessed and restarted on PrEP in accordance with the protocol, with a recommendation for HIV window-period testing and additional screening or management, depending on risk

Annex 2

Consent Form

Introduction of HIV pre-exposure prophylaxis (PrEP) in Sri Lanka: a demonstration project to determine feasibility and acceptability of PrEP provision as part of sexual health services.

PrEP-4-Sri Lanka

Part A - To be filled by the participant

The participant should complete the whole of this sheet herself.

1. Have you read the information sheet? (Please keep a copy for yourself) YES/NO
2. Have you had an opportunity to discuss this study and ask any questions? YES/NO
3. Have you had satisfactory answers to all your questions? YES/NO
4. Have you received enough information about the study? YES/NO
5. Who explained the study to you? ……..
6. Do you understand that you are free to withdraw from the study at any time, YES/NO without having to give a reason and without affecting your future medical care?

7. Other research assistants may examine information held by the investigators YES/NO All personal details will be treated as STRICTLY CONFIDENTIAL. Do you give your permission for these individuals to have access to your records?

8. Have you had sufficient time to come to your decision? YES/NO
9. Do you agree to take part in this study? YES/NO
   If 'NO', reason for declining……
10. Declaration by participant: consent to attending regular follow-up visits while taking PrEP
    I agree to have regular HIV and STI testing as part of the follow-up procedures, as described in the Participant Information Sheet, and as recommended by the study doctor
    YES/NO

11. I consent to participating in the face-to-face in-depth interviews if invited by the study team YES/NO

Name of participant _____

Signature_____ Date_____(DD/MM/YYYY)

Name of study doctor/senior researcher _____

Signature_____ Date_____(DD/MM/YYYY)

Part B - To be filled by the investigator

I have explained the study to the above volunteer and she has indicated her willingness to take part.

Signature of investigator: ……..... Date: …….

Name (BLOCK CAPITALS):

…….

Annex 3

Information Sheet

Introduction of HIV pre-exposure prophylaxis (PrEP) in Sri Lanka: a demonstration project to determine feasibility and acceptability of PrEP provision as part of sexual health services.

PrEP-4-Sri Lanka

The National STD/AIDS Control Programme (NSACP) would like to invite you to take part in the pilot project on Pre-Exposure prophylaxis to prevent HIV infection.

1. Purpose of the study

Sri Lanka has maintained a low prevalence of HIV infection. Certain populations are at a higher risk of HIV in spite of available prevention approaches. PrEP is a new intervention to Sri Lanka to prevent HIV among people who are most at risk. PrEP is a proven preventive strategy for HIV and currently being implemented successfully in many countries across the globe.

The medication (tablet) given to you contain combination of two HIV medications.

2. Voluntary participation

Your participation in this study is voluntary. Your withdrawal from this project at any point will not affect your right or access to receive routine care services available.

3. Duration, procedures of the study and participant's responsibilities

This pilot will be conducted over a period of one years (September 2020 to August 2021). By volunteering to participate in this study, you are expected to

a) take the prescribed medicines daily
b) undergo HIV testing and STI screening
c) undergo kidney functions tests
d) visit the STD clinic on the given follow up dates (in 1 month, 3 months and 3 monthly thereafter for 1 year)

4. Potential benefits

There is evidence that correct use of PrEP has significantly reduce the transmission of HIV infection. Correct and consistent use of condoms will help to further reduce the risk of HIV along with other STIs.

5. Risks, hazards and discomforts

The most commonly reported side effects of tenofovir and emtricitabine when given as PrEP are headache, back pain, abdominal pain, unintentional weight loss, nausea, and flatulence. After starting PrEP, symptoms typically resolve over the course of 4 weeks.

As a precaution, a blood test will be done to see kidney function before starting PrEP and every six months thereafter.

There are limited reported cases from other countries where a person became infected with HIV despite having evidence that they were taking PrEP on a daily basis (which means they were 'adherent'). This is often described as a 'PrEP failure'.

5. Reimbursements

You will not be paid for participating in this pilot.

6. Confidentiality

Confidentiality of all records on PrEP is guaranteed and no information by which you can be identified will be released or published.

7. Termination of study participation

If you decide to withdraw from the pilot, please notify a member of the research team before you withdraw. However being in the study for full period is beneficial for the reasons mentioned above.

8. Clarifications

If you have questions about any of the tests / procedures or information please feel free to ask any pilot team member/ National Co-ordinator for PrEP 4 Sri Lanka Pilot Project.

Dr Sathya Herath, National Co-ordinator for PrEP 4 Sri Lanka Pilot Project

Mobile: 0714152042

E mail: sathya_herath@yahoo.com

Annex 4

Withdrawal Form

Introduction of HIV pre-exposure prophylaxis (PrEP) in Sri Lanka: a demonstration project to determine feasibility and acceptability of PrEP provision as part of sexual health services.
PrEP-4-SriLanka

Form for Withdrawal of Participation

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with NSACP.

In the event that the participant's decision to withdraw is communicated verbally, the study doctor will need to provide a description of the circumstances in the participant's source documentation.

Name of participant (please print)_____

Signature_____ Date_____(DD/MM/YYYY)

Declaration by Study Doctor

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of study doctor/senior researcher (please print)_____

Signature_____ Date_____(DD/MM/YYYY)

Note: All parties signing the consent section must date their own signature

Annex 5

Introduction of pre-exposure prophylaxis (PrEP) for HIV in Sri Lanka: a demonstration project to determine feasibility and acceptability of PrEP provision as part of strengthening sexual health services.

PrEP-4-SriLanka

Interviewer administered questionnaire

Name of doctor completing this form : .....

Contact Number:.....

Annex 5

Baseline (intake form)

Epidemiological data

Name:

Date of visit:

PrEP No:

STD No:

Mode of referral: 1. Self-referred ☐ 2. STD Clinic attendee ☐ 3. Referred by NGO ☐ 4. Know4sure ☐

Age:

Gender: ☐ Male ☐ Transgender female

Weight (Kg):

BEHAVIOURAL checklist

- Had PrEP before? ☐ Yes ☐No
  - If yes, from where? ☐ Online
    ☐Received outside Sri Lanka
    ☐ Other:_____
- Reason for starting PrEP:
  ☐ Sex partner(s) is HIV positive and (mark all that apply)
    ☐ Not on ART
    ☐ On ART < 6 months
    ☐ Suspected poor adherence to ART

☐ Detectable HIV viral load

☐ Couple is trying to conceive

☐Sex partner(s) high risk & HIV status is unknown

☐Has sex with > 1 partner

☐Ongoing IPV/GBV

☐Transactional sex

☐Recent STI (past 6 months)

☐Recurrent use of post-exposure prophylaxis (PEO)

☐Recurrent sex under influence of alcohol/recreational drugs

☐Inconsistent or no condom use

☐Injection drug use with shared needles and/or syringes

- **Sexual history**
  - Number of partners in last 3 months _____
  - Did you always use a condom when you had sex in past 3 months?
    ☐ Yes ☐No
  - If no, what kind of condom-less sex have you had in the last 3 months (please see table below):

Receptive anal	☐
Insertive anal	☐
Receptive vaginal	☐
Insertive vaginal	☐
Receptive oral with ejaculation	☐

  - Are you planning to have sex and not use a condom in the next 3 months?
    ☐ Yes ☐No
  - Any HIV positive partner(s)?
    ☐ Yes ☐No ☐Unknown
  - If HIV positive partner, are they virally suppressed (VL<200 copies/mL)?
    ☐ Yes ☐No ☐Unknown

Anything else you want to disclose about your sexual history?

_____

_____

_____

- Have you had Sex under the influence of drugs? ☐ Yes ☐No
    - If yes, which drugs used? _____
    - Any injecting drug use? ☐ Yes ☐No
    - Any sharing of needles/works? ☐ Yes ☐No
    - Do you think sex under the influence of drugs is becoming a problem? ☐ Yes ☐No

MEDICAL HISTORY

- Blood pressure:
- Completed vaccination for hepatitis B?
  ☐ Yes ☐No ☐Unknown
- Past medical history:
  ☐ renal disease or complications
  ☐ bone disease
  ☐ diabetes
  ☐ hypertension
  ☐ viral hepatitis (e.g. Hepatitis A, B, or C)
  ☐ other (specify):_____

- Regular medications?
  ☐ Yes (please specify): _____ ☐ No

BASELINE CLINICAL TESTS

HIV result today (if available): Reactive* ☐ Non-reactive ☐

**If reactive, do not commence PrEP*

Baseline tests	**Tick if test ordered**	**Results** *(if referred for treatment, please indicate)*
HIV testing with combined antigen/antibody test		
Hepatitis B screening		
Hepatitis C screening		
Syphilis serology		
CT/GC molecular testing: - Urine - Pharyngeal - Anal		
GC Culture - Urine - Pharyngeal - Anal		
Renal function		Creatinine (plus units): eGFR: How was eGFR calculated: (i) ☐ Cockcroft–Gault (ii) ☐ CKD-EPI (iii) ☐ Lab estimate Abnormal renal function? ☐ Yes ☐ No Action taken:

OTHER PROCEDURES

Discussed the following points with study subject

☐ Dosing considerations: daily

☐ Common side effects/drug interactions

☐ Use of protein supplements which could impact creatinine clearance

☐ Need for HIV test and STI screen at every visit (1, 3, 6, 9, 12 months)

☐ Importance of adherence (e.g. setting mobile telephone reminders of taking PrEP)

☐ Sero-conversion symptoms

☐ HBV vaccination

Additional risk reduction strategies

☐ Advise use of condoms and lubricant to prevent other STIs

☐ Discussion on sex under the influence of recreational drugs

☐ Discussion on sex under the influence of alcohol

☐ Vaccines

FOLLOW UP SCHEDULED (please tick next visit):

☐ 1-month PrEP study visit
☐ 3-month PrEP study visit
☐ 6-month PrEP study visit
☐ 9-month PrEP study visit
☐ 12-month PrEP study visit

* Informed the client to make an additional visit if symptoms of STIs/HIV sero-conversion/ drug side effects occur ☐

If any other information is relevant for follow-up visits, please describe: _____

PREP DRUGS PRESCRIBED

Drug		**Quantity prescribed (no. of bottles)**	**Quantity dispensed (no. of bottles)**
TDF 300mg/FTC 200mg			

Annex 6

Follow up form

Introduction of pre-exposure prophylaxis (PrEP) for HIV in Sri Lanka: a demonstration project to determine feasibility and acceptability of PrEP provision as part of strengthening sexual health services.

PrEP-4-SriLanka

Name of doctor completing this form: .....

Contact Number.....

Follow-up form (m1, m2, m3, m6, m9, m12, additional)

Epidemiological data

Name:

Date of visit:

PrEP No:

STD No:

Visit number:..... ☐ Additional

Gender: ☐ Male ☐ Transgender female

☐ Female ☐ Transgender male

☐ Other

Weight (kg):

PrEP use checklist

- Do you want to continue taking PrEP? ☐ Yes ☐No
  - If no, why do you want to stop?
    - ☐ no more risk for HIV
    - ☐ side effects
    - ☐ prefer condoms
    - ☐ entered a monogamous relationship
    - ☐ other:_____
- Are you happier since you have been on PrEP? ☐ Yes ☐No
- Do you have less anxiety when having sex while on PrEP? ☐ Yes ☐No
- Do you think you are adhering to PrEP? ☐ Yes ☐ No

  If no, what have been the challenges in adhering to PrEP? _____
- How often did you use PrEP on average in past 30 days (4 weeks)?

  ☐ On all or almost all days (26 days or more)

☐ On many or most days (12-25 days)

☐ On a few days (1-11 days)

- Did you experience any of below Side effects?

☐ nausea
☐ diarrhoea
☐ abdominal pain
☐ weight loss
☐ weight gain
☐ vomiting
☐ flatulence
☐ skin rash
☐ hypersensitivity reaction
☐ burning
☐ numbness
☐ dizzy
☐ anxiety
☐ nightmare
☐ depression
☐ seizures
☐ fatigue
☐ headache
☐ fractures
☐ kidney dysfunction

BEHAVIOURAL checklist

- **Sexual history**
- Number of partners since last visit_____
- Did you always use a condom when you had sex since your last visit?

  ☐ Yes ☐No
- If no, what kind of condom-less sex have you had since your last visit (please see table below):

Receptive anal	☐
Insertive anal	☐
Receptive vaginal	☐
Insertive vaginal	☐
Receptive oral with ejaculation	☐

  - Are you planning to have sex and not use a condom in the next 3 months?

    ☐ Yes ☐No
  - Any HIV positive partner(s)?

    ☐ Yes ☐No ☐Unknown
  - If HIV positive partner, are they virally suppressed (VL<200 copies/mL)?

    ☐ Yes ☐No ☐Unknown
- Have you had Sex under the influence of drugs since last clinic visit? ☐ Yes ☐No
  - If yes, which drugs used? _____
  - Any injecting drug use? ☐ Yes ☐No
  - Any sharing of needles/works? ☐ Yes ☐No
  - Do you think sex under the influence of drugs is becoming a problem? ☐ Yes ☐No
  - Referral to additional drug services ☐ Yes ☐No

Anything else you want to disclose about your sexual history?

_____
_____
_____
_____

MEDICAL EXAMINATION

- Blood pressure:
- Past medical history:
  ☐ renal disease or complications
  ☐ bone health disease
  ☐ diabetes
  ☐ hypertension
  ☐ viral hepatitis (e.g. Hepatis A, B, or C)
  ☐ other (specify):_____

- New regular medications since last visit?
  ☐ Yes (please specify): _____ ☐ No

- Any symptoms of HIV seroconversion in past 4 weeks? ☐ Yes ☐No

CLINICAL TESTS

HIV result today (if available): Reactive* ☐ Non-reactive ☐

**If reactive, do not continue PrEP*

Baseline tests	**Tick if test ordered**	**Results** *(if referred for treatment, please indicate)*
HIV testing with combined antigen/antibody test		
Hepatitis C screening (at 1 ½ years)		
Syphilis serology (6month,1yr)		

CT/GC molecular testing: - Urine - Pharyngeal - Anal		
GC Culture (6 month/1 year) - Urine - Pharyngeal Anal		
Renal function (6 month/1 year)		Creatinine (plus units): eGFR: How was eGFR calculated: (iv) ☐ Cockcroft–Gault (v) ☐ CKD-EPI (vi) ☐ Lab estimate Abnormal renal function? ☐ Yes ☐ No Action taken:

OTHER PROCEDURES

Discussed the following points with study subject

☐ Importance of adherence (e.g. setting mobile telephone reminders of taking PrEP
☐ common side effects/drug interactions
☐ use of protein supplements which could impact creatinine clearance
☐ need for HIV test and STI screen at every visit
☐ Sero-conversion symptoms

Additional risk reduction strategies

☐ Advise use of condoms and lubricant o prevent other STIs
☐ Discussion on sex under the influence of drugs
☐ Discussion on sex under the influence of alcohol
☐ Vaccines

FOLLOW UP SCHEDULED (please tick next visit):

☐ 1-month PrEP study visit
☐ 3-month PrEP study visit
☐ 6-month PrEP study visit
☐ 9-month PrEP study visit
☐ 12-month PrEP study visit

* Informed the client to attend an additional visit if symptoms of STIs/HIV sero-conversion/ drug side effects occur ☐

If any other information is relevant for follow-up visits, please describe:

_____
_____
_____
_____

Clinical outcome of the visit

☐ Treated for STI
☐ PrEP discontinued
  ☐ HIV positive
  ☐ No longer at substantial risk of HIV
  ☐ Sero-conversion symptoms
  ☐ Drug side effects
  ☐ Client preference
  ☐ Other (Specify):.....
☐ PrEP continued

PREP DRUGS PRESCRIBED

Drug	Quantity prescribed	Quantity dispensed
TDF 300mg/FTC 200mg		

PREP DOSING CHOSEN

☐ Daily dosing

☐ 211 (event-driven PrEP)