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Uptake and challenges with daily oral pre-exposure prophylaxis among men who have sex with men and transgender women, suburban Yangon, Myanmar

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Background: Pre-exposure prophylaxis (PrEP) is effective for human immunodeficiency virus (HIV) prevention in risk groups. We assessed PrEP uptake and 12-month retention among men who have sex with men (MSM) and transgender women (TGW) in Myanmar during the coronavirus disease 2019 pandemic and a political crisis.

Methods: Using prospectively collected data, we assessed the proportion of persons eligible, initiated and retained 12 months on PrEP. We calculated HIV and syphilis incidence among those initiated on PrEP. Predictors of compliance to scheduled visits were assessed with fractional logistic regression.

Results: Among 652 persons screened between July and December 2020, 85.3% were eligible and 38.8% initiated PrEP. The daily pill burden was the main reason (86.5%) for refusing PrEP. A history of HIV post-exposure prophylaxis (PEP) and having an HIV-positive partner not on anti-retroviral therapy (ART) was associated with PrEP uptake ($p<0.05$). The 12-month retention among those initiating PrEP was 43.0%. Age ≥25 y, a history of PEP and having an HIV-positive partner not on ART predicted better compliance with scheduled visits ($p<0.05$). HIV incidence among PrEP initiators was 3.1 per 100 person-years (95% confidence interval [CI] 1.3 to 7.4) and syphilis incidence was 17.6 per 100 person-years (95% CI 12.3 to 25.1).

Conclusions: A PrEP program for MSM and TGW in Myanmar was implemented successfully under difficult circumstances. Alternative strategies are needed addressing PrEP uptake and retention.

Keywords: daily oral PrEP, HIV incidence, HIV prevention, men who have sex with men, pre-exposure prophylaxis, transgender women.

Introduction

Pre-exposure prophylaxis (PrEP) has proven to be highly effective in reducing human immunodeficiency virus (HIV) transmission and decreasing new HIV infections.[1] Since 2014, the World Health Organization (WHO) has recommended PrEP as a key component of the combination prevention strategy for all population groups at substantial risk of HIV infection.[2] Men who have sex with men (MSM) from the South and Southeast Asia regions are infected with HIV 5–15 times more often than the general population.[3] According to a global 2012 study that included six countries from Asia and the Pacific region, transgender women (TGW) were 49 times more likely to have HIV than other adults of reproductive age.[4] It is important to offer comprehensive HIV care to MSM and TGW, including optimal preventive strategies to reduce infection rates in these affected groups.

Thailand was the first country to start a PrEP program in the region, but apart from Thailand, access to PrEP has been poor.[5] In Myanmar, MSM and TGW have the second highest HIV prevalence (8.8%) after people who inject drugs (PWID) (19%).[6] Thirteen percent of new HIV infections were among MSM and TGW populations in 2016.[7] In late 2019, the Myanmar National AIDS Programme approved daily oral PrEP for MSM and TGW.[8] The

uptake of PrEP and challenges in carrying out PrEP programs in Myanmar's MSM and TGW populations have not yet been studied.

Medical Action Myanmar (MAM) is a medical non-governmental organization that has focussed on HIV prevention and treatment activities for key at-risk populations in Myanmar. In 2020, MAM was one of the first organizations to start a daily oral PrEP demonstration program for MSM and TGW. To better understand the potential and challenges of PrEP among MSM and TGW in Myanmar, we analysed the PrEP service cascade, including uptake and 12-month retention, and the HIV seroconversion and syphilis incidence among PrEP users.

Methods

Study design, period and population

This was a prospective cohort study among self-identified MSM or TGW who presented at a clinic in Yangon, Myanmar between June and December 2020. Persons who accepted PrEP were followed until December 2021. PrEP eligibility criteria were being ≥18 y of age, testing HIV negative, being at low risk of acute HIV infection, being at substantial risk of HIV infection, having a creatinine clearance >30 ml/min, being willing to use daily oral PrEP as prescribed, accepting regular HIV testing and giving informed consent. Presumptive acute HIV infection (AHI) was defined as presenting signs and symptoms, including a flu-like illness such as fever, sore throat, aches and pains, lymphadenopathy, mouth sores, headache or rash and potential exposure to HIV in the past 4 weeks. A substantial risk of HIV infection in our target population was defined as having had either sex work as the primary source of income, a history of injecting drugs, vaginal or anal sexual intercourse without condoms with more than one partner, a history of sexually transmitted infection (STI; by lab testing, self-report or having received syndromic STI treatment), a history of PEP, requested PrEP, having an HIV-positive partner who is not on suppressive ART or having a sexual partner who has a substantial risk (having one or more HIV risk factors) in the last 6 months.[8]

Study setting

MAM operates a clinic that specifically focusses on health services for MSM and TGW in Hlaingthaya township, one of Yangon's largest suburban slum areas. The population of this township is at the lowest end of the socio-economic spectrum, with a high burden of HIV infection. In 2016, the HIV prevalence among MSM and TGW in Yangon was high, at 28.4%, surpassing rates observed in other regions in Myanmar.[7] MAM has been providing HIV prevention and treatment services in Myanmar since 2009. These services include a comprehensive HIV prevention package comprising health education, condom distribution, HIV testing, counselling, screening and treatment of STIs, PEP, initiation of ART and free distribution of sterile needles and syringes to female sex workers (FSWs), MSM, TGW and PWID. In June 2020 this package of services was expanded with the addition of PrEP.

Study procedures

As PrEP was new for Myanmar, awareness had to be raised first. This was mainly done through trained peer MSM and TGW who reached out to their network and informed them about PrEP. People who self-identified as MSM or TGW were contacted during routine HIV prevention activities online and offline and informed about the PrEP project. The project also used an online Facebook page, managed by the peer staff, that was already popular among MSM and TGW. All MSM and TGW who presented at the clinic were invited to join the PrEP project.

The different steps between screening and PrEP enrolment in the MAM clinic are shown in Figure 1. The clinic PrEP team included a trained medical doctor, a lay counsellor and a peer educator. A doctor performed the clinical assessment, ordered a blood investigation and prescribed PrEP. The lay counsellors explained PrEP use, safety, risks and efficacy. Reasons for not accepting PrEP were recorded. The peer educators were peer staff who acted as a PrEP 'buddy' for PrEP users (approximately 1 peer educator for 50 PrEP users), by providing moral support, reminding them about regular appointments and conducting phone calls or home visits. HIV was tested with third-generation rapid antibody tests; Determine HIV-1/2 as the first test, followed by Uni-Gold HIV and HIV 1/2 STAT-PAK if the first test was positive.[9] Additional laboratory testing before the start of PrEP included a blood test for syphilis, rapid tests for hepatitis B surface (HBs) antigen and anti-hepatitis C virus (HCV) antibody and serum creatinine.

The PrEP regimen was tenofovir disoproxil fumarate 300 mg in combination with lamivudine 300 mg or emtricitabine 200 mg (Ricovir-EM; Mylan, Maharashtra, India), depending on the availability from the National AIDS Programme.[8]

All procedures, including patient follow-up and laboratory investigations for the study, were performed at the clinic. The clinical and laboratory investigations during the initial visit and follow-up visits are shown in Table 1.

Study definitions and variables

Baseline variables for age, biological sex at birth (male, female) and gender expression (MSM, TGW) were collected during PrEP screening and initiation.

PrEP uptake was assessed as the proportion of persons who were eligible and who subsequently initiated PrEP. Retention of PrEP was defined as the proportion of persons initiating PrEP who attended a follow-up visit at 12 months (10.5–13.5 month window) after initiation. Compliance with scheduled appointments was determined by tracking adherence to five appointments following PrEP initiation at months 1, 3, 6, 9 and 12. The composite STI indicator was considered positive if the person had a history of an STI within the last 6 months, received treatment for syphilis or tested positive for HBs antigen or anti-HCV antibody at Baseline.

Data collection and management

The study used PrEP program data collected from standardized PrEP forms in hard copy, designed for use with the MAM-owned PrEP project database. The substantial HIV risk assessment and reasons for PrEP refusal and discontinuation were self-reported by participants during interviews performed by staff. Any PrEP-initiated participant at the clinic received a numeric code (PrEP code) for the PrEP database. Doctors and counsellors kept paper-based PrEP patient files updated and trained data clerks entered the data into the PrEP database. No direct identifying information

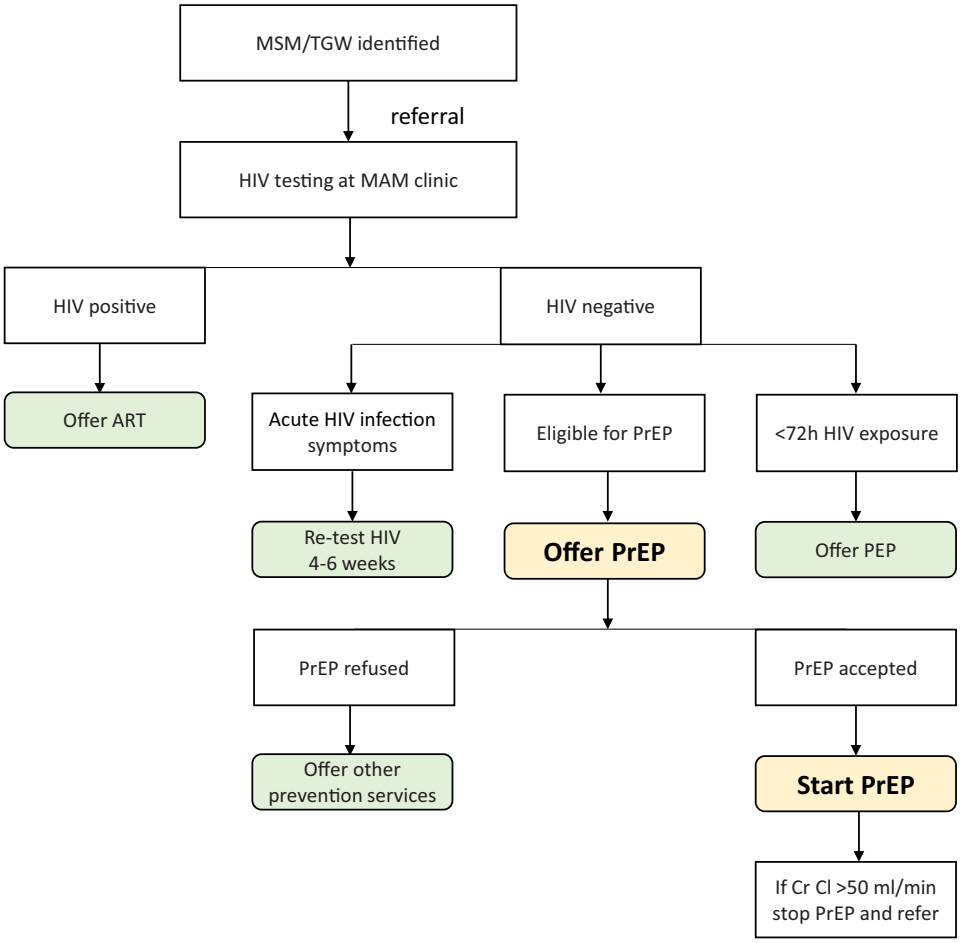

Figure 1. PrEP implementation flow in a MAM PrEP clinic. CrCl: creatinine clearance.

was recorded in the database, and the PrEP code was used for any medical communication, including linking laboratory results with PrEP persons' files. Each PrEP person received a separate study code before data were extracted into Excel (Microsoft, Redmond, WA, USA) to create the study database. The key to linking study codes with PrEP codes was password protected and only accessible to the first author. The first author conducted data cleaning and verification. In case of discrepancies between the PrEP database and the study database, original records were verified and corrections were made.

Data analysis

Categorical variables were summarised with frequencies and proportions, while continuous variables were summarised with medians and interquartile ranges (IQRs) or means and standard deviations (SDs), as appropriate. PrEP persons transferred out were censored the day they were assigned.

With survival analysis, we calculated the HIV incidence per 100 person-years for those who initiated PrEP in the last 12 months and who had at least one follow-up HIV test, in line with WHO recommendations.[10] The time under observation for the calculation of HIV incidence was the time from the initiation of PrEP until the last visit, censored at 13.5 months for those attending a 12-month visit, or the midpoint between the last HIV-negative test and the first positive HIV test for those who seroconverted. The time until a positive HIV test was the time from the initiation of PrEP until the positive HIV test result. For calculation of syphilis incidence and assessment of factors associated with incidence, we used an Anderson–Gill model for ordered failure events.[12] All treated syphilis cases (based on lab tests [rapid plasma reagin {RPR}, new positive RPR or a fourfold increase in RPR] and/or clinical manifestations in line with national STI guidelines[11]) were considered as an event. Syphilis incidence was defined as the number of syphilis events during the time under observation among those who had initiated PrEP. In this analysis, the time under observation was defined as the time between the initiation of PrEP and the end of the follow-up period (ultimately December 2021) or the time between the previous syphilis episode and the next episode. We assessed the factors associated with compliance to five scheduled visits (after PrEP initiation) using fractional logistic regression. For both models, we started from a saturated multivariable model, stepwise dropping variables with $p>0.2$ and retaining those with $p>0.05$ in the final model. Model comparison was performed using R^2 and Akaike's and Bayesian information

Table 1. Monitoring MSM and TGW at baseline and after initiating PrEP

Type of monitoring	Month 0	Month 1	Month 3	Every 3 months
HIV test[a]	x	x	x	x
HIV substantial risk assessment[b]	x	x	x	x
Acute HIV infection screening[c]	x	x	x	x
Informed consent for initiating PrEP	x			
Provide PrEP pills	x	x	x	x
PrEP utilization assessment[d]		x	x	x
PrEP pill side-effect assessment[e]		x	x	x
Syphilis clinical assessment[f]	x	x	x	x
Syphilis RDT	x	x[g]	x[g]	x[g]
Syphilis RPR[h]	x	x	x	x
Serum creatinine[i]	x			
HBs antigen test[j]	x			
HCV antibody test	x			

RDT: rapid diagnostic test; TDF: tenofovir.
[a]HIV-positive cases were initiated on ART in line with national guidelines.
[b]If there was no risk, participants were informed that they did not need or could discontinue daily oral PrEP.
[c]If symptoms of presumptive acute HIV infection were present, PrEP initiation was delayed and the person was retested for HIV after 4–6 weeks.
[d]If PrEP utilization was low (<95%), participants were reminded to take it regularly.
[e]If the participants experienced intolerable side effects they were asked to discontinue PrEP.
[f]If clinical features of primary or secondary syphilis were present, syphilis treatment was given.
[g]If no previous positive RDT.
[h]For confirmation of syphilis infection in case of a positive RDT and follow-up in case of a previous positive RPR.
[i]If the creatinine clearance result was <30 ml/min, PrEP was stopped and the participants referred to a renal specialist.
[j]If HBs antigen-positive participants did not accept PrEP, the person was referred to a hepatologist for a prescription of TDF.

criteria. All analyses were done in Stata 16.1 (StataCorp, College Station, TX, USA).

Results

PrEP service cascade

PrEP eligibility and uptake

Between July and December 2020, 652 persons (94% MSM) sought screening for PrEP eligibility at the MAM clinic. Among them, 19 (2.9%) were screened twice and 1 (0.2%) underwent screening three times. Of the 652 persons, 96 (14.7%) were deemed ineligible to start PrEP. Eleven (11.5%) were <18 y of age, 47 (49.0%) tested HIV positive, 35 (36.5%) had a suspicion of AHI (27 had symptoms in the past 28 d, 6 engaged in high-risk behaviour in the past 72 h and 2 had both), 2 (2.1%) had a renal disease and 1 (1.0%) had an inconclusive HIV test result. Of 556 (85.3%) persons eligible for PrEP, 216 (38.8%) initiated PrEP (Figure 2).

Baseline characteristics of eligible MSM and TGW who accepted and refused daily oral PrEP

Among the 556 persons eligible for PrEP, the median age was 24 y, with 303 (54.5%) being <25 y of age. Younger persons (<25 y) were more likely to accept PrEP compared with those ≥25 y (44.2% vs 32.4%, p<0.01). The median ages among those who accepted and those who refused PrEP were 23 y (IQR 10–28] and 25 y (IQR 20–30), respectively. Uptake was significantly higher among TGW than among MSM (75.0% versus 37.2%, p<0.001). All five persons with a history of PEP and four persons with an HIV-positive partner not on ART accepted PrEP. At the time of PrEP initiation, among 216 persons who started PrEP, 4 tested positive for HCV antibodies (1.8%), 11 tested positive for HBs antigen (5.1%) and 32 (14.8%) were on syphilis treatment. The composite STI indicator was positive in 73 (33.8%) of the 216 enrolled persons. The details are shown in Table 2.

Reasons for PrEP refusal among those who were eligible to take PrEP

Of 556 persons eligible for PrEP and offered daily oral PrEP, 340 (61.2%) declined to accept it. The reasons are described in Table 2. Among those who did not want to take PrEP, 86.5% mentioned the burden of taking a daily oral pill as the primary reason, while 9.1% did not want to take PrEP because they believed they had a low risk of HIV transmission (Table 3).

PrEP retention

Among 216 persons who started PrEP, 93 (43%) attended a follow-up visit at 12 months (range 10.5–13.5) after the initiation of PrEP. Among the 123 persons who did not attend the

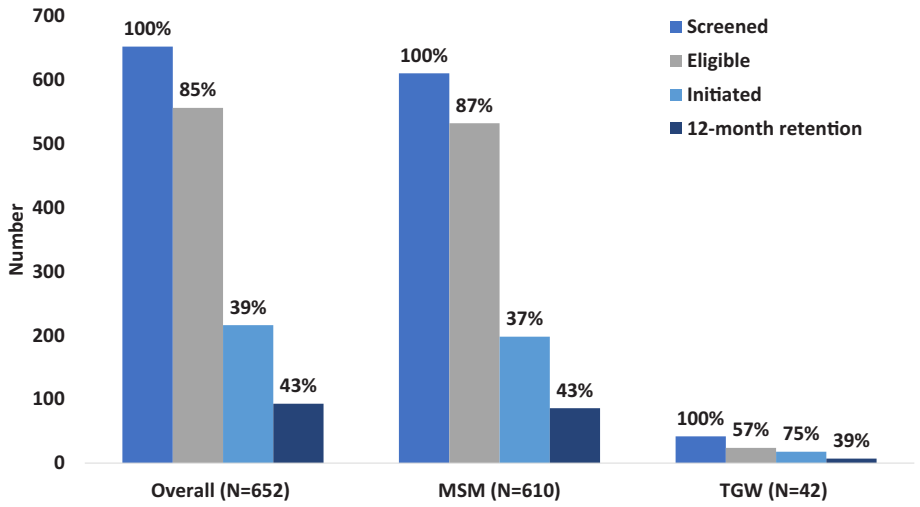

Figure 2. Daily oral PrEP uptake and retention among MSM and TGW in 2020 in Myanmar.

12-month follow-up visit, 58 (47%) were considered lost to follow-up. Among the remaining 65 persons, when asked about their decision to stop PrEP, 21 (32%) said they left town, 18 (28%) stopped because of the burden of taking daily tablets and 15 (23%) mentioned that they were no longer at risk as reasons to discontinue (Table 4).

Compliance to scheduled appointments

Among persons who initiated PrEP, those >25 y of age (adjusted odds ratio [aOR] 1.90 [95% confidence interval {CI} 1.38 to 1.62]), with a history of an STI (aOR 1.63 [95% CI 1.07 to 2.48]), with PEP use within the last 6 months (aOR 3.27 [95% CI 1.40 to 7.64]) or having an HIV-positive partner not on ART (aOR 6.94 [95% CI 1.19 to 40.42]) were more likely to adhere to scheduled appointments during the 12-month follow-up period. The details are shown in Table 5.

HIV seroconversion among people initiated on PrEP

Among 191 persons who started PrEP and had at least one follow-up HIV test, 5 persons had an HIV seroconversion, all of whom were MSM. The details of these five cases are shown in Figure 3. Person 1 had an inconclusive test result 4 weeks after starting PrEP and tested HIV positive 2 weeks later. The other four persons tested HIV positive after they had discontinued PrEP. Person 4 had stopped taking PrEP because he had moved out of town due to security concerns and person 5 discontinued PrEP because he felt he was no longer at risk. All five persons who seroconverted had reported condomless sex or inconsistent condom use at baseline. The total follow-up time of persons on PrEP was 161.8 years and HIV incidence was 3.1 per 100 person-years (95% CI 1.3 to 7.4). None of the five persons who seroconverted was treated for STIs during follow-up.

Incidence of syphilis infection among people initiated on PrEP

Among the 216 persons who initiated PrEP, 27 had at least one new episode of syphilis infection (12.5%), while 3 persons had two episodes (1.4%) during the observation period. The syphilis incidence among those who started PrEP was 17.6 per 100 person-years (95% CI 12.3 to 25.1), based on a total follow-up time of 170.8 years. In univariable and multivariable Anderson–Gill analysis, no variables were associated with syphilis incidence (Supplementary Table S1).

Discussion

This is the first study to analyse a daily oral PrEP program among MSM and TGW in Myanmar. We found that 39% of eligible MSM and TGW accepted daily oral PrEP and, within this group, 43% remained under care for at least 1 y. Five persons who started PrEP seroconverted, with one case occurring during the first month on PrEP, while the other seroconversions happened while the persons were off PrEP.

Acceptance to start PrEP in our study was higher compared with initial programs conducted in the Netherlands and Thailand from 2015 to 2017, which reported uptakes of approximately 8–10%.[13,14] However, our acceptance rate was lower than that of a PrEP program in Thailand that was initiated later (2017–2019).[15] The latter included a study population of whom 54% were university educated and 89% reported sufficient funds for basic needs, which is in stark contrast to the low-income study population in the area where we implemented our project.

Willingness to use PrEP was substantial (62%) among 434 MSM and TGW interviewed in Myanmar in 2014, when PrEP was not yet available.[16] This was higher than the actual uptake in our study, which can be explained by practical hurdles or confirmation bias by those who had attended the interviews in 2014.

Table 2. Baseline demographic characteristics and risk behaviours of MSM and TGW eligible for taking PrEP in 2020, disaggregated by people who accepted and declined PrEP

Variables		Total (N=556), n	Accepted PrEP (n=216) n	Accepted PrEP (n=216) %	Declined PrEP (n=340) n	Declined PrEP (n=340) %	p-Value[a]
Age at PrEP initiation (years)							
Age category (years)	<25	303	134	44.2	169	55.8	<0.01
	≥25	253	82	32.4	171	67.6	
Gender	MSM	532	198	37.2	334	62.8	<0.001
	TGW	24	18	75.0	6	25.0	
Self-reported risk behaviour in the last 6 months							
Sex work as the primary source of income	Yes	32	10	31.3	22	68.8	NS
	No	524	206	39.3	318	60.7	
Injected drugs	Yes	3	3	100.0	0	0.0	NS[b]
	No	553	213	38.5	340	61.5	
Condomless sex with more than one partner or inconsistent condom use	Yes	391	154	39.4	237	60.6	NS
	No	165	62	37.6	103	62.4	
History of STI[c]	Yes	113	42	37.2	71	62.8	NS
	No	443	174	39.3	269	60.7	
History of PEP	Yes	5	5	100.0	0	0.0	<0.01[b]
	No	551	211	38.3	340	61.7	
HIV-positive sexual partner not on ART	Yes	4	4	100.0	0	0.0	0.02[b]
	No	552	212	38.4	340	61.6	

[a]The p-value for χ^2 test.
[b]The p-value for Fishers exact test.
[c]Based on self-report, laboratory result or treatment received for gonorrhoea and/or chlamydia and/or syphilis.
NS: not significant.

Table 3. Reasons for not accepting PrEP among eligible MSM and TGW in 2020 in Myanmar

Answer to the question: Why do you not want to take PrEP?	Total (N=340) n	Total (N=340) %	MSM (n=334) n	MSM (n=334) %	TGW (n=6) n	TGW (n=6) %
I do not want to take daily pills	294	86.5	290	86.8	4	66.7
I no longer feel at risk for HIV	31	9.1	29	8.7	2	33.3
I am afraid of side effects	9	2.6	9	2.7	0	0
I am afraid of what other people think of me	2	0.6	2	0.6	0	0
I do not have time to come for a 3-monthly visit	2	0.6	2	0.6	0	0
No specific reason	2	0.6	2	0.6	0	0

Of the persons who did not want to start PrEP, most (86.5%) mentioned the daily pill burden as the most important reason, followed by a perception of low risk (9.1%). The same reasons were reported for stopping PrEP. This needs further attention. The reluctance to take pills daily and the perception of low risk could potentially be mitigated by alternative PrEP strategies such as event-driven PrEP (ED-PrEP) for MSM or TGW who are not taking exogenous oestradiol-based hormones, where tablets are taken for 3 d around a high-risk encounter, or starting and stopping PrEP, which requires tablets only during periods of high risk. These approaches offer flexibility and could address the concerns associated with daily pill consumption and risk perception.[2]

In a pooled analysis of two projects in Belgium and the Netherlands, where both daily PrEP and ED-PrEP were offered as options, a quarter of MSM chose ED-PrEP.[17] In another study in the Netherlands among 376 persons, 27% chose ED-PrEP. Persons switched 53 times to ED-PrEP and 56 times to daily PrEP, and daily PrEP was

Table 4. Reasons for stopping PrEP among MSM and TGW

	Total (N=123)		MSM (n=112)		TGW (n=11)	
Answer to the question: Why do you want to stop PrEP?	n	%	n	%	n	%
Lost to follow-up (no contact)	58	47.2	49	43.8	9	81.8
I moved out of Yangon	21	17.1	21	18.8	0	0.0
I did not want to take daily pills	18	14.6	18	16.1	0	0.0
I am no longer at risk for HIV	15	12.2	13	11.6	2	18.2
I had an HIV-positive result	5	4.1	5	4.5	0	0.0
I was afraid of what other people thought of me	3	2.4	3	2.7	0	0.0
I was afraid of side effects	2	1.6	2	1.8	0	0.0
No specific reason	1	0.8	1	0.9	0	0.0

Table 5. Fractional logistic regression of predictors of compliance with five scheduled visits within 1 y after starting PrEP in MSM and TGW

	Univariable analysis			Multivariable analysis		
Variable	OR	95% CI	p-Value	aOR	95% CI	p-Value
Age at PrEP initiation (years)	1.1	1.02 to 1.07	0	NA		
Age ≥25 y (vs <25 y)	2	1.45 to 2.78	0	1.9	1.38 to 1.62	<0.001
Gender MSM (vs TGW)	0.9	0.54 to 1.40	NS	NA		
Self-reported risk behaviour in the last 6 months						
Sex work as the primary source of income	1.3	0.65 to 2.52	NS	NA		
Injected drugs	1.5	0.17 to 3.39	NS	NA		
Condomless sex with more than one partner or inconsistent condom use	0.8	0.52 to 1.09	NS	NA		
History of STI[a]	1.7	1.11 to 2.67	0.015	1.63	1.07 to 2.48	0.024
History of PEP	4.1	1.77 to 9.31	0.001	3.27	1.40 to 7.64	0.006
HIV-positive sexual partner not on ART	11	1.75 to 63.5	0.01	6.94	1.19 to 40.42	0.031
STI assessment results at PrEP start						
HCV antibodies	0.5	0.19 to 1.10	NS	NA		
HBV antibodies	0.9	0.37 to 2.16	NS	NA		
Initiated syphilis treatment	0.8	0.51 to 1.23	NS	NA		
Composite STI indicator[b]	1.5	1.08 to 2.12	0.017	NA		

[a]Based on self-report, laboratory results or treatment received for gonorrhoea and/or chlamydia and/or syphilis.
[b]STI in the last 6 months or STI treatment, HBV or HCV antibodies at enrolment.
NA: not applicable; NS: not significant.

temporarily stopped 161 times.[18] Motives behind PrEP choices differ between persons and choices can change over time. Offering different PrEP regimens could be essential to match users' priorities and increase both uptake and retention.

PrEP uptake was notably higher among TGW (18/24 [75%]), persons with a history of PEP (5/5 [100%]) and those with an HIV-positive sexual partner not on ART (4/4 [100%]). This could be related to their higher risk perception and awareness. The high proportion of HIV-positive TGW in the region might have alarmed the TGW community.[4] Persons with a history of PEP use were more likely to accept PrEP, and also more likely to be retained at 12 months. The correlation was also shown in the findings of

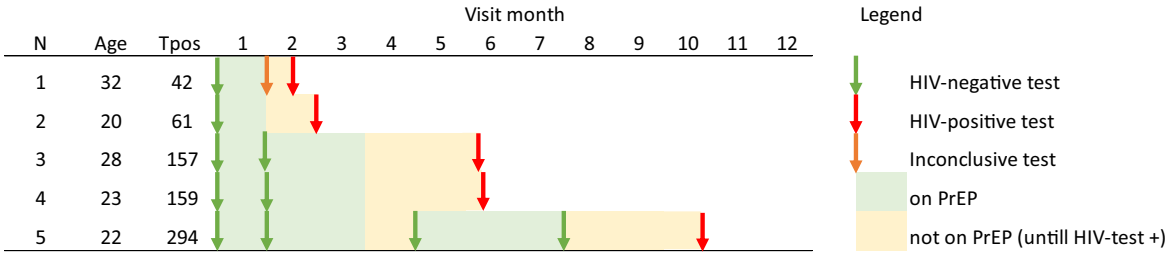

Figure 3. Details on MSM who started PrEP and seroconverted in 2020 in Myanmar. Age: age of the person at the time of PrEP initiation (years); N: serial number of the person; Tpos: time until positive test (number of days from PrEP start to positive HIV test).

two reviews.[19,20] It suggests that previously exposed persons are more aware of HIV infection, have a better understanding of HIV transmission and thus are more willing to take oral medication.

Of the 123 persons who discontinued PrEP, 58 (47%) were lost to follow-up and 21 (17%) moved out of town. We were unable to determine the reasons for this. However, the project coincided with a particularly challenging period marked by the coronavirus disease 2019 (COVID-19) epidemic (2020–2021) and a political conflict (2021), causing significant security concerns.[21] This coincided with lockdowns, the loss of jobs and insecurity, which affected peoples' mobility and accessibility of healthcare services.[22] Anecdotal evidence from other MAM clinics providing integrated services for primary health and HIV care, revealed a substantial decrease in patient attendance throughout 2020 and 2021. When reaching out to chronic patients, many expressed a reluctance to visit clinics for fear of COVID and insecurity. Some people mentioned that they left the area because they lost their job or expressed fear of fighting and returned to their places of origin. It is likely that this contributed to a lower recruitment for PrEP and a higher dropout rate.[22]

The overall HIV incidence in this cohort was 3.1 per 100 person-years (95% CI1.3 to 7.4). Comparable findings were observed in a daily oral PrEP program in Thailand, which reported a similar HIV incidence of 3.4 per 100 person-years (95% CI 1.64 to 6.30), and also showed that HIV infection only occurred in persons who had discontinued PrEP.[15] This confirms that we targeted the appropriate population for PrEP and underscores the importance of adherence to the medication.

At PrEP initiation, the prevalence of syphilis, defined by the prescription of treatment based on RPR test results and/or clinical suspicion, was 14.8%, and, over time, the cumulative incidence was 17.6 per 100 person-years (95% CI 12.3 to 25.1). Notably, this prevalence was higher than the pooled prevalence reported in a meta-analysis of 66 studies among MSM in Asia (9.9% [95% CI 8.3 to 11.4]).[23] This underscores that our cohort is a high-risk population, highlighting the potential importance of PrEP for their protection. However, since we used prescription of treatment to define an episode of infection, including prescriptions based on a clinical diagnosis, diverging diagnostic skills and treatment practices might have influenced our reported incidence of syphilis. The high syphilis incidence rate might be associated with PrEP use, as users might feel protected, and PrEP use has been associated with increased condomless sex and higher STI diagnoses.[24] However, the syphilis prevalence of the study population was already high before PrEP initiation, suggesting that the observed high incidence rate might be more attributed to pre-existing infections rather than solely resulting from increased condomless sex facilitated by PrEP usage. We found no variables associated with syphilis treatment during PrEP at the 0.05 level, which may be linked to the limited syphilis episodes.

Our study has limitations. As mentioned, the project coincided with the COVID-19 pandemic (2020–2021) and security concerns in 2021, potentially impacting the uptake and retention of PrEP.[25] We were unable to measure the true impact of these crises on our results. We managed to reach only 54% of persons who discontinued PrEP. Among them, 32% reported leaving town, indicating a notable high migration rate within a brief period, strongly suggestive of a link with an acute crisis. Another 23% mentioned that they perceived their risk as lower than before, possibly influencing their decision to discontinue PrEP. This is in line with a large review of 46 studies published in 2022 that showed the COVID pandemic and its associated measures created barriers to sexual health services and PrEP, and it noted a decrease in sexual behaviours, fewer sexual partners and a reduced perception of HIV infection risk, all contributing to a decline or discontinuation in PrEP uptake.[25] There is a potential for social desirability bias among participants who reported to staff about their HIV risk or reasons for refusing or discontinuing PrEP. The HIV tests we used were third-generation antibody rapid tests, which have a large window period (median 26 d [IQR 22–31], with 99% detection within 50 d), which affects the precision of estimating the PrEP prevention period.[26] In one instance, an individual had an inconclusive test result 4 weeks after starting PrEP and subsequently tested HIV positive 2 weeks later. Determining the timing of infection remains uncertain, leaving the possibility that this infection occurred before starting PrEP, while the baseline test was negative due to the test's window period. HIV incidence was not recorded among MSM and TGW who were not initiated on PrEP.

On the other hand, our study has a notable strength. The first author, who initiated the PrEP program, maintained close involvement in patient management, data collection and source file review to address any missing data or uncertainties. This close involvement instils confidence in the accuracy of the database, ensuring that it correctly reflects the data.

Conclusions

In conclusion, we successfully implemented one of Myanmar's first PrEP programs for MSM and TGW, despite substantial external disruptors. PrEP's substantial impact on HIV

transmission was evident and we demonstrated a very high level of protection among adherent PrEP users. However, as in projects performed in other settings, we identified that the burden of daily pill intake and a perception of low risk of HIV transmission were key barriers to PrEP uptake and retention. This knowledge can be used to broaden and tailor the PrEP implementation strategy and improve the PrEP cascade in Myanmar and in similar settings.

Supplementary data

Supplementary data are available at *International Health* online (http://inthealth.oxfordjournals.org).

Authors' contributions: NNT conceived the idea and designed and conducted the study. FS supervised the program and data acquisition. LL, TD, EF and TG supported the study design. NNT, MMMH and NLT performed data acquisition and analysis. NNT, FS, LL, TD, EF and TG performed data interpretation. TG supported the statistical analysis and manuscript writing. NNT and FS drafted the first version of the manuscript, which was subsequently critically revised, edited and approved by all authors.

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Ethical approval: The study procedures were in accordance with the ethical standards of the Helsinki Declaration (1964, amended most recently in 2008) of the World Medical Association. All persons provided written consent and all information, including illustrations, were anonymised. The study received ethical approval from the local Institutional Review Board, Ministry of Health, Myanmar; the Institute of Tropical Medicine, Antwerp, Belgium; the University of Antwerp, Antwerp, Belgium and the Oxford Tropical Research Ethics Committee of the University of Oxford. The study is registered at clinicaltrials.gov (NCT04781426).

Data availability: None.

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