Piloting a partially self-financed mode of human immunodeficiency virus pre-exposure prophylaxis delivery for men who have sex with men in Hong Kong

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ABSTRACT

Introduction: Pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate (TDF) 300 mg/emtricitabine (FTC) 200 mg is a proven strategy for preventing human immunodeficiency virus (HIV) transmission in men who have sex with men (MSM). This study aimed to test the feasibility and acceptability of PrEP delivered at a pilot clinic for MSM in Hong Kong, where PrEP service is currently unavailable.

Methods: Partially self-financed PrEP was provided to HIV-negative adult MSM with high behavioural risk of HIV transmission after excluding hepatitis B infection and renal insufficiency. Participants received daily TDF/FTC for 30 weeks at 13.3% of the drug cost. Adherence and behaviours were monitored through questionnaires while creatinine and HIV/STI (sexually transmitted infection) incidence were monitored with point-of-care and laboratory tests. Preference for continuing with PrEP was evaluated at the end of the prescription period.

Results: Seventy-one PrEP-naïve MSM were included in the study, of whom 57 (80%) were retained at the end of 28 weeks. Satisfactory adherence and self-limiting adverse events were reported, while none of the participants contracted HIV. Risk compensation was observed, with an STI incidence of 3.17 per 100 person-years. At the end of the prescription period, a majority (89%) indicated interest in continuing with PrEP. Preference for PrEP was associated with age ≥28 years and peer influence (P=0.04), while stigma was a concern. Price was a deterrent to self-financed PrEP, and only half (51%) considered a monthly cost of ≤HK$500 (US$1=HK$7.8) as reasonable.

Conclusions: A partially self-financed mode of PrEP delivery is feasible with good retention in MSM in Hong Kong.

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New knowledge added by this study

- A workable model for delivering affordable pre-exposure prophylaxis (PrEP) to men who have sex with men (MSM) at high risk of human immunodeficiency virus (HIV) infection in Hong Kong is important.
- Risk compensation as reflected by diagnosis of sexually transmitted infections (STIs) following PrEP is a concern in a proportion of MSM.
- Adverse events from the use of tenofovir disoproxil fumarate 300 mg and emtricitabine 200 mg for PrEP are not uncommon though normally self-limiting, but cessation may be required in a small proportion of PrEP users.

Implications for clinical practice or policy

- Partially self-financed daily PrEP administered in conjunction with STI/HIV monitoring is operationally feasible and acceptable to MSM in Hong Kong, where PrEP is currently otherwise unavailable as a service.

Introduction

Pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate (TDF) 300 mg/emtricitabine (FTC) 200 mg is a key strategy for protecting people at high risk of human immunodeficiency virus (HIV) transmission. The effectiveness of PrEP for HIV prevention has been demonstrated in large-scale national studies[1-3] and extensively reviewed in the literature.[4] Mathematical modelling parameterised by data from the Netherlands concluded that PrEP for men who have sex with men (MSM) is cost-effective in the context of a stable HIV

epidemic.[5] Following approval of the Food and Drug Administration in the US, PrEP guidelines have been promulgated by the World Health Organization,[6] the Centers for Disease Control and Prevention,[7] and the European AIDS Clinical Society.[8] Despite promotions and advocacies at different levels, uptake of PrEP has remained low internationally, with wide disparities across countries. Of note, Asia has been reported to account for fewer than 5% of all PrEP initiations recorded worldwide.[9] Notably, cost remains an important deterrent to its introduction in most cities/countries where generic TDF/FTC cannot be prescribed legally, and Hong Kong is no exception. Elsewhere, different service models for PrEP delivery have been developed,[10] but there exists a "purview paradox" causing obstructions in societal implementation.[11]

In Hong Kong, PrEP is currently unavailable as an HIV prevention service, where MSM have continued to account for a high proportion of newly reported HIV infections (67% in 2017; www.aids.gov.hk). A study was conceptualised to test the feasibility and acceptability of PrEP delivery by piloting a designated clinic to deliver lower-cost TDF/FTC to MSM at high risk of HIV transmission. The results of this study are expected to serve as a useful reference for the future development of sustainable PrEP programmes in Hong Kong.

以部份自費模式在香港設立為男男性接觸者提供愛滋病事前預防用藥試點

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引言：服用TDF 300 mg / FTC 200 mg作為事前預防用藥是一種經證實的策略，可以預防愛滋病病毒在男男性接觸者之間傳播。目前香港尚無此等服務，本研究旨在設立試點診所測試事前預防用藥的可行性和可接受性。

方法：研究針對具高風險行為而沒受愛滋病病毒感染的成年男男性接觸者，在排除乙型肝炎感染和腎功能不全後，為他們提供需部分自費的事前預防用藥。參與者一連30週每天服用TDF / FTC，並付藥費的13.3%。參與者需填答問卷以監察用藥依從性和行為風險，並以快速測試和實驗室測試檢測腎功能、愛滋病病毒和性病感染發生率。在處方期結束時評估參與者對繼續使用事前預防用藥的傾向。

結果：71名從未服用事前預防用藥的男男性接觸者被納入研究，其中57人（80%）持續用藥28週。參與者的依從性令人滿意，對藥物只產生自限性不良反應，沒有參與者感染愛滋病病毒。觀察期間出現風險補償現象，性病發病率為每100人年3.17。在處方期結束時，大多數人（89%）表示有興趣繼續事前預防用藥。對事前預防用藥的偏好與年齡28歲或以上和同伴影響相關（P=0.04），而感覺污名化則是一個擔憂。藥物價格是自費模式的一種威懾，只有一半（51%）認為每月低於500港元（1美元=7.8港元）的費用是合理。

結論：以部分自費模式推行事前預防用藥是可行的，得到香港的男男性接觸者接受並持續使用。

Methods

Pre-exposure prophylaxis clinic

A research clinic was set up at Prince of Wales Hospital, the teaching hospital of The Chinese University of Hong Kong. In collaboration with HIV services and community-based organisations, eligible HIV-negative MSM were referred or self-referred to join the study. A bilingual (Chinese and English) website was set up to provide information about PrEP, with linkages to eligibility screening and behavioural and adherence surveys through the online system.

Participant recruitment

Participants were MSM aged ≥18 years who were normally resident in Hong Kong and could communicate in written and spoken English or Chinese. Potential participants who had not previously used PrEP were targeted. The main inclusion criteria were: firstly, history of unprotected anal sex in the preceding 6 months; and secondly, negative HIV antibody test result within the last 3 months; plus at least one of the following in the past 6 months: (a) diagnosis of sexually transmitted infection [STI], (b) sex partner(s) with positive or unknown HIV status, (c) history of recreational drug use during sex, ie, "chem-sex"; and/or (d) multiple sex partners. The exclusion criteria were: (a) having any form of mental illnesses; (b) inability or refusal to give consent; (c) incarceration; (d) known hepatitis B virus infection; and (e) known renal insufficiency with creatinine clearance <60 mL/min/1.73 m^2.

Pre-exposure prophylaxis regimen and monitoring

Participants completed a pre-assessment to confirm their eligibility for inclusion in the study. A 2-week course of daily TDF/FTC was given free at the first visit to evaluate tolerance before the participant was asked to provide partial payment by instalment, covering a total prescription period of 30 weeks. The prescription was partially self-financed, as each person was required to pay HK$1316 (US$1=HK$7.8) 4 times for four consecutive prescription periods. As an incentive, the same payment entitled the participant to receive an increasing duration of medication. At week 28, a 2-week supply of medication was given free. The total cost was equivalent to 13.3% of the market price of patented TDF/FTC, or HK$702 per month, in Hong Kong.

Three forms of monitoring were implemented: (a) questionnaires for periodic data collection on HIV risk behaviours, adverse reactions to antiretrovirals, and adherence to daily self-administered PrEP by tablet PC, at each consultation; (b) point-of-care and laboratory tests: fourth-generation HIV antibody/antigen tests; plasma creatinine and estimated

glomerular filtration rate; STI: syphilis serology, and urine tests for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* by nucleic acid amplification test (NAAT); and (c) online diary for tracking daily intake of TDF/FTC and sexual activities. Finger prick was used for monitoring HIV, creatinine, and syphilis serology at selected time-points. Archived blood samples collected at baseline and week 28 were tested for hepatitis C virus antibody. A weekly email reminder was sent to participants requesting completion of the online diary.

Analyses

Complete case analyses were performed addressing: (a) acceptability/feasibility: characteristics of participants; proportion of MSM interested in continuing with PrEP following the study; retention in the programme; (b) outcome evaluation: drug adherence; coverage of unprotected sex; adverse reactions; detection of STIs at baseline; subsequent diagnoses while on PrEP; and preference for continuing PrEP use and service delivery models including price, setting, and regimen. Variables were assessed using univariate analysis. Categorical variables were tested with the Chi squared test if the expected value in each cell was at least 5; otherwise, Fisher's exact test was used. Continuous variables were examined using the Mann-Whitney *U* test. The STROBE guideline was implemented in reporting the study.

Results

Between September 2017 and May 2018, 292 MSM were assessed.[12] A total of 71 (median age, 32 years) MSM were included in the study. Their demographic and behavioural profiles are shown in Table 1. Half of the participants were self-referred; the rest were referred from community-based organisations and collaborating HIV services. Thirty-three (46%) participants reported a history of STIs, 15 of whom had a diagnosis in the preceding 6 months. All participants were PrEP-naïve, but 10 (14%) had previously been put on post-exposure prophylaxis after high-risk sexual exposure. Engagement in chem-sex was reported by 25 (35%) of the participants. The self-perceived risk of HIV infection was high in one-fifth of the participants. Over the 30-week prescription period, there was a total follow-up of 1639 person-weeks. At the end of the study period, 57 (80%) participants remained in the programme. Fourteen withdrew from the study, nine of whom (64%) did so within the initial 2 months. The following reasons for withdrawal were given by 10 participants: low or no perceived risk (6); adverse events (2); concern about adverse drug effects or drug interactions (1); unaffordability (1); inconvenience or too busy to attend the clinic (1); and on the advice of friends (1).

TABLE 1. Demographic characteristics and behavioural profile of men who have sex with men who participated in the study (n=71)*

Demographics	
Age (years)	32 (27-40)
Ethnicity	
Local Chinese	63 (89%)
Mainland Chinese	3 (4%)
Southeast Asian	2 (3%)
Overseas non-Chinese	3 (4%)
Attainment of postsecondary level education	60 (85%)
Work status	
Full-time employment	52 (73%)
Self-employed	4 (6%)
Part-time working or freelancer	6 (8%)
Student	5 (7%)
Unemployed	4 (6%)
Monthly income (US$1=HK$7.8)	
<HK$15 000	14 (20%)
HK$15 000-30 000	27 (38%)
HK$30 001-50 000	16 (23%)
>HK$50 000	14 (20%)
Source of referral	
Self-referred	35 (49%)
Community-based organisations	27 (38%)
Public HIV services	9 (13%)
Health status	
History of sexually transmitted infection diagnosis	33 (46%)
Having chronic illnesses	0
On long-term medications	5 (7%)
Age of first sexual intercourse with men (years)	20 (18-22)
Behavioural profile	
Usual sexual role	
Insertive	21 (30%)
Versatile	30 (42%)
Receptive	20 (28%)
Ever on HIV post-exposure prophylaxis	10 (14%)
Behavioural risk in the past 6 months	
Diagnosed with sexually transmitted infections	15 (21%)
Engaged in recreational drug use	25 (35%)
Had more than one male partner	63 (89%)
Perceived risk of HIV infection	
High	14 (20%)
Medium	33 (46%)
Low	24 (34%)

Abbreviation: HIV = human immunodeficiency virus

* Data are shown as No (%) or median (interquartile range)

Full adherence to attending all visits was achieved by all participants who completed the study, though 16% (74/460) of the pre-arranged appointments required rescheduling. The rates of adherence to HIV testing (six time-points), plasma creatinine testing (three time-points), and STI screening (three time-points) were 100%, 99.5%, and 100%, respectively. Adherence to daily use of TDF/FTC, as derived from the questionnaires administered at each visit, is shown in Table 2. Overall, 60 out of 69 (87%) participants with diary data reported having ever omitted at least one dose. A median of two to three doses was missed between each pair of consultations, which took place at intervals of 4 to 8 weeks. The total number of doses omitted ranged from 1 to 71 (median, 6; interquartile range=3-14). Occasions of condomless sex without concurrent use of TDF/FTC were noted, which occurred in 20 out of 953 (2%) person-days. While participants were advised to take the TDF/FTC tablet at about the same time each day, some 14% to 25% reported not being able to stick to the strict 24-hour dosing interval.

Adverse events relating to the use of TDF/FTC were reported by 35 (52%) out of the 67 participants who attended the clinic at least twice (Table 3[13]). The main adverse events were: dyspepsia (18%), loose stool or increased bowel motions (16%), fatigue (15%), headache (12%), and nausea with or without decreased appetite (12%). Other adverse events included difficulty falling or staying asleep, dizziness, and anxiety or depression. These adverse events were generally mild (grade 1), self-limiting, and did not bother the participants, and the majority resolved within the first week. Two participants withdrew from the study because of grade 2 adverse events that lasted over 2 weeks. One complained of nausea, diarrhoea, stomach upset, and anxiety, which resolved 2 days after stopping TDF/FTC at week 8. The other had headache shortly after initiation on PrEP and depressed mood and fleeting suicidal ideation in the ensuing 2 weeks, which resolved upon stopping at week 4. Separately, plasma creatinine was measured at baseline, week 12, and week 28; there was a >20% increase of plasma creatinine in 7/63 (11%) and 6/57 (11%) of the participants compared

TABLE 2. Adherence of men who have sex with men to pre-exposure prophylaxis use*

Markers for non-adherence	Weeks 2-6 (n=64)†	Weeks 7-12 (n=61)	Weeks 13-20 (n=58)†	Weeks 21-28 (n=57)
Ever forgotten to take PrEP	24 (38%)	33 (54%)	36 (62%)	29 (51%)
Ever decided to skip PrEP	4 (6%)	8 (13%)	7 (12%)	8 (14%)
Reported missed dose	23 (36%)	34 (56%)	35 (60%)	31 (54%)
No. of missed doses	2 (1-4)	3 (2-5)	3 (2-5)	3 (2-5)
Did not take PrEP tablet at the correct time	13 (20%)	14 (23%)	8 (14%)	14 (25%)
Took more than one tablet per day	5 (8%)	5 (8%)	4 (7%)	13 (23%)

Abbreviation: PrEP = pre-exposure prophylaxis
* Data are shown as No. (%) or median (interquartile range)
† Data missing for one participant

TABLE 3. Adverse events related to the use of pre-exposure prophylaxis (n=67)*

	Grade†[13]				Total
	1	2	3	4	
General					
Fatigue	10 (15%)	0	0	0	10 (15%)
Dizziness	4 (6%)	0	0	0	4 (6%)
Gastrointestinal					
Loose stool or increased bowel motions	11 (16%)	0	0	0	11 (16%)
Nausea with or without decreased appetite	8 (12%)	0	0	0	8 (12%)
Dyspepsia	12 (18%)	0	0	0	12 (18%)
Neurological					
Headache	8 (12%)	0	0	0	8 (12%)
Anxiety or depression	2 (3%)	1 (1.5%)	0	0	3 (4.5%)
Difficulty falling or staying asleep	5 (7.5%)	1 (1.5%)	0	0	6 (9%)

* Data are shown as No. (%)
† Grade 1: mild, 2: moderate, 3: severe, 4: potentially life-threatening

with baseline, respectively. Three (5%) participants who completed the study had a 20% increase in plasma creatinine readings at both weeks 12 and 28. None had an estimated glomerular filtration rate level <60 mL/min/1.73 m^2 at any time in the course of receiving PrEP.

None of the participants contracted HIV in the course of the study. Condomless sex was reported by 70 out of 71 (99%) of the participants. Their behavioural profiles and STI diagnoses at different time intervals are shown in Table 4. Out of the 59 MSM followed up through week 20 or beyond, compared with baseline, condom use decreased in 22 (49%), increased in 9 (20%), and was unchanged in 14 (31%) for sex with known partners (n=45), and the corresponding rates for newly met partners (n=47) were 19 (40%), 7 (15%), and 21 (45%), respectively. Reduction of condom use with newly met partners was associated with the attainment of postsecondary education (odds ratio [OR]=2.00, 95% confidence interval [CI]=1.46-2.75, P=0.07 by Fisher's exact test). There was no association between reduction of condom use and demographic characteristics, reasons for taking PrEP, or history of risk behaviours. The proportion of PrEP users engaging in chem-sex was similar before (41%) and after PrEP (32%-40%).

With regard to STIs, 2 (3%), 3 (4%), and 16 (23%) were positive for *N gonorrhoeae* (NAAT), *C trachomatis* (NAAT), and syphilis serology (nine treponemal only, seven treponemal and non-treponemal) at baseline, respectively. One of the 16 (6%) syphilis serology-positive MSM was a newly diagnosed infection. Over a follow-up period of 1639 person-weeks among those retained in the study for at least 12 weeks, 13 incident STIs (one *N gonorrhoeae* [incidence rate=3.17 per 100 person-years], three *C trachomatis* [incidence rate=9.52 per 100 person-years], and nine syphilis [incidence rate=28.55 per 100 person-years]) had occurred. The participants with incident STI were more likely to be poppers users (46% and 18% of participants with and without incident STIs used poppers, respectively; OR=3.81, 95% CI=1.03-14.10, P=0.06). None of the participants had positive results for hepatitis C virus antibody at baseline or follow-up.

At the last visit during the prescription period, participants (n=65) were asked about their future intentions regarding PrEP. Fifty-eight (89%) responded that they would like to continue with PrEP after the study. The MSM who preferred to continue PrEP after the study were more likely to be aged ≥28 years (OR=6.03, 95% CI=1.06-34.17, P=0.04) [Table 5]. Peer influence was important, as none of those uninterested in continuing on had discussed PrEP use with their boyfriends (P=0.04) or sex partners (P=0.04). Price (83%) was the most concerning factor affecting their PrEP-using decision, followed by efficacy (46%) and potential adverse drug effects (42%) [Table 6]. Some 14% were worried about embarrassment or stigma related to

TABLE 4. Condomless anal sex and diagnoses of sexually transmitted infections at baseline and during the 28-week observation period*

	12 weeks before PrEP (n=71)	Week 2-6 (n=65)	Week 7-12 (n=61)	Week 13-20 (n=59)	Week 21-28 (n=57)
No. of male sex partners					
Total	4 (3-10)	4 (2-6)	4 (2-6)	4 (2-7)	4 (2-7)
Newly acquainted	2 (1-5)	2 (1-4)	2 (1-4)	2 (0-5)	2 (1-5)
Had receptive anal sex	45 (63%)	45 (69%)	41 (67%)	36 (61%)	37 (65%)
Engagement in recreational drug use	29 (41%)	21 (32%)	23 (38%)	23 (39%)	23 (40%)
Condomless sex all or most times					
With newly acquainted partner	15/64 (23%)	24/55 (44%)	29/58 (50%)	20/49 (41%)	28/51 (55%)
With known partners	21/62 (34%)	28/57 (49%)	32/57 (56%)	27/52 (52%)	33/52 (63%)
Person-days of sex without PrEP	NA	20	20	4	11
Self-reported STI symptoms	7 (10%)	2 (3%)	3 (5%)	5 (8%)	6 (11%)
Incident bacterial STI†					
Syphilis	16 (23%)	-	3 (5%)	-	6 (11%)
Chlamydia	3 (4%)	-	2 (3%)	-	1 (2%)
Gonorrhoea	2 (3%)	-	0	-	1 (2%)
Person-episodes of STI	21	-	5	-	8

Abbreviations: IQR = interquartile range; NA = not applicable; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infections

* Data are shown as No. (%) or median (IQR), unless otherwise specified

† STI not screened at weeks 2, 6, and 20

TABLE 5. Factors associated with preference for continuing PrEP after completion of study*

	Uninterested in continuing PrEP (n=7)	Interest in continuing PrEP (n=58)	OR (95% CI)	P value (Fisher's exact test)
Demographics				
Age ≥28 years	2 (29%)	41 (71%)	6.03 (1.06-34.17)	0.04
Local Chinese	6 (86%)	52 (90%)	1.44 (0.15-14.11)	0.57
Attained postsecondary education	6 (86%)	48 (83%)	0.80 (0.09-7.40)	1.00
Full-time or self-employed	4 (57%)	47 (81%)	3.21 (0.63-16.43)	0.16
Monthly income ≥HK$30 000	2 (29%)	24 (41%)	1.77 (0.32-9.87)	0.69
Six months before baseline				
History of STI diagnosis	0	14 (24%)	-	0.33
No HIV+ sex partners	1 (14%)	17 (29%)	2.49 (0.28-22.26)	0.66
Engagement in recreational drug use	1 (14%)	21 (36%)	3.41 (0.38-30.24)	0.41
Having >1 sex partner	7 (100%)	50 (86%)	-	0.58
Risk profiles				
Ever had sex with HIV+ partners	2 (29%)	24 (41%)	1.77 (0.32-9.87)	0.69
Ever had sex with females	2 (29%)	10 (17%)	0.52 (0.09-3.08)	0.60
Ever had group sex	4 (57%)	47 (81%)	3.21 (0.63-16.43)	0.16
Engagement in sex while on recreational drugs	1 (14%)	29 (50%)	6.00 (0.68-53.01)	0.11
High perceived HIV risk	2 (29%)	11 (19%)	0.59 (0.10-3.42)	0.62
Reasons for joining PrEP study				
Protection from HIV infection	7 (100%)	54 (93%)	-	1.00
High anticipated HIV risk	4 (57%)	25 (43%)	0.57 (0.12-2.77)	0.69
Desire to reduce/avoid condom use	1 (14%)	19 (33%)	2.92 (0.33-26.04)	0.42
Sex partner being HIV+	0	12 (21%)	-	0.33
Following others' recommendations	2 (29%)	15 (26%)	0.87 (0.15-4.98)	1.00
Discussions about PrEP with				
Friends	7 (100%)	40 (69%)	-	0.18
Health workers other than doctors	0	5 (9%)	-	1.00
Sex partners	0	24 (41%)	-	0.04
Boyfriends	0	23 (40%)	-	0.045
Family members	1 (14%)	1 (2%)	0.11 (0.006-1.91)	0.21
Risk/behaviours while on PrEP as reported at the last visit				
Completed the study	2 (29%)	55 (95%)	45.83 (6.14-342.01)	<0.001
Incident STI during study period	1 (14%)	11 (19%)	1.40 (0.15-12.88)	1.00
Engagement in sex while on recreational drugs	1 (14%)	22 (38%)	3.67 (0.41-32.52)	0.41
Sex partners also taking PrEP	3 (43%)	20 (35%)	0.70 (0.14-3.45)	0.69
Always used condoms with new partners	3/5 (60%)	11/52 (21%)	0.18 (0.03-1.21)	0.09
Always used condoms with known partners	1/5 (20%)	14/52 (27%)	1.47 (0.15-14.34)	1.00
Used ecstasy	0	13 (22%)	-	0.33
Used poppers	1 (14%)	13 (22%)	1.73 (0.19-15.72)	1.00
PrEP preferences				
Daily regimen	5 (71%)	34 (59%)	0.57 (0.10-3.17)	0.69
On-demand regimen	2 (29%)	29 (50%)	2.50 (0.45-13.94)	0.43
Time-driven PrEP	0	17 (29%)	-	0.18
Injectable PrEP	2 (29%)	16 (28%)	0.95 (0.17-5.42)	1.00

Abbreviations: 95% CI = 95% confidence interval; HIV = human immunodeficiency virus; OR = odds ratio; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection

* Data are shown as No. (%), unless otherwise specified

TABLE 6. Preference for PrEP delivery models (n=65)

Preferred service characteristics	
Price (HK$)*	
Free	13 (20%)
1-500	20 (31%)
1000	24 (37%)
2000	8 (12%)
Delivery setting†	
Current pilot clinic with university affiliation	50 (77%)
Department of Health HIV service (Integrated Treatment Centre)	17 (26%)
Community-based organisation	43 (66%)
Another public hospital	24 (37%)
Private clinic	18 (28%)
Others	2 (3%)
PrEP regimen†	
Daily	39 (60%)
On-demand	31 (48%)
Time-driven	17 (26%)
Injectable	18 (28%)
Factors affecting PrEP using decision†	
Efficacy	30 (46%)
Price	54 (83%)
Regimen	10 (15%)
Adverse drug effects	27 (42%)
Service organisation	17 (26%)
Service location	20 (31%)
Service time	20 (31%)
Privacy	20 (31%)
Embarrassment or stigma related to PrEP	9 (14%)

Abbreviations: HIV = human immunodeficiency virus; PrEP = pre-exposure prophylaxis

* Price: US$1=HK$7.8

† Multiple selections possible

PrEP. The majority, 63 of 68 (93%), had disclosed their PrEP status to their partners, and 9 (14%) of them reported ever experiencing stigma. Half (51%) considered a monthly cost for PrEP of ≤HK$500 reasonable. Two-thirds (66%) accepted community-based organisations as the portal for receiving PrEP and monitoring. Over half (60%) and about half (48%) favoured daily mode and on-demand PrEP, respectively. Fewer than one-third favoured injection (28%) and time-driven PrEP (26%).

Discussion

Men who have sex with men have continued to be the hardest-hit population by the global HIV epidemic,[14] and Hong Kong is no exception. While PrEP has not yet been implemented, its acceptance is generally high, at 78.6% among MSM in late 2016,[15] but only 1% have been reported to have accessed PrEP.[16] Our study was the first that has piloted PrEP delivery to MSM in Hong Kong. Our results showed that the operation of a PrEP clinic in Hong Kong is feasible and acceptable to the MSM community, as evidenced by our high retention rate of 80% among users of a daily regimen over the 7-month observation period. Severe adverse reactions were uncommon in our study, echoing the conclusion on the safety profile of PrEP, as illustrated in clinical studies and confirmed in reviews.[4,17]

None of the MSM in the study contracted HIV, but the small sample size did not allow the efficacy of PrEP to be evaluated. Elsewhere, a meta-analysis of multiple studies with different regimens concluded that PrEP reduced the HIV infection risk by 70% in the presence of high adherence.[4] The failure of PrEP is very uncommon, as shown by a large-scale PROUD study[2] and by evaluating real world data.[18] In our pilot study, adherence to daily TDF/FTC, creatinine testing, and HIV/STI monitoring was high. Non-adherence to TDF/FTC could potentially lead to resistance if HIV infection occurs in the course of PrEP, though its incidence has remained low.[19] Condomless sex in conjunction with the omission of TDF/FTC, which can be referred as PrEP-unprotected condomless sex, was relatively uncommon. Risk compensation, defined as the increased practice of condomless sex in PrEP users, is an emerging concern.[20,21] Our results did not confirm any consistent increase of risk compensation behaviours, an observation shared by other recent studies.[4,22,23] Increased incidence of STI could be more prevalent in the initial period of PrEP introduction[19,24] or restricted to a subpopulation of MSM regardless of PrEP use.[20] It is uncommon to see MSM starting to engage in condomless anal sex after PrEP initiation.[23] One modelling study showed that STI incidence would decline with increased PrEP coverage.[25] With increasing PrEP coverage, non-PrEP users may become a neglected community when planning STI/HIV interventions.[26]

The present results highlight that the major obstacle to PrEP implementation is its cost, as patented TDF/FTC is too expensive for out-of-pocket acquisition.[16] In our study, requiring participants to pay an amount closer to the cost of generic products (HK$750 or <US$100 per month) appealed to only a fraction of the MSM approached. About half of the eligible MSM did not join this project because of the high cost incurred.[12] Making PrEP free or affordable should be an effective strategy for preventing HIV transmission through high-risk behaviours. Taking reference to the situation in the US, different models for PrEP could be considered, including services at STI clinics, community

health centres, community-based organisations, pharmacies, and private primary care providers.[10] This study highlighted issues for consideration in the establishment of a local PrEP service. The need for dispensing prescription medicine alongside HIV/STI testing and toxicity monitoring has made access to PrEP complex. Vertical programmes that have conventionally offered HIV testing to high-risk populations have been more prepared to implement PrEP than overburdened primary care services tend to be.[27] Other innovative models of PrEP delivery have been reported in other countries, such as pharmacy-based clinics in Seattle in the US,[28] community health centres in Bangkok, Thailand,[29] and integrated sexual reproductive health services in Wales.[30] While those models provide lessons, they may not be relevant to the situation in Hong Kong. Finally, stigma could be a major deterrent to accessing PrEP, as expressed by some of the MSM who refused to participate.[31] In rolling out PrEP, a marketing strategy that focuses on health protection rather than risk reduction may be more appropriate.[32] A non-targeting approach regarding behavioural risk could be less stigmatising and may still be cost-effective at achieving HIV prevention in low-HIV incidence settings.[33]

The current study has some limitations. First, the sample size was small, such that the results may not be generalisable to the situation of the entire MSM community in Hong Kong. Second, sampling bias could not be eliminated, as the study included self-referred MSM and those referred from collaborating organisations. Individuals reluctant to participate in a clinical trial and those unwilling or unable to pay for TDF/FTC were excluded. Nevertheless, the study did manage to recruit MSM with high-risk behaviours, including those who engaged in chem-sex. Finally, we relied on self-reporting for tracking of HIV/STI risk, a strategy that might have underestimated high-risk behaviours. By subjecting the participants to STI screening at multiple time-points, we detected otherwise-hidden STIs both at baseline and during the course of PrEP. For maximum effectiveness, PrEP should go hand in hand with community-based STI/HIV monitoring, so that prompt treatment can be offered to those diagnosed with infections, while those testing negative can continue to be prescribed TDF/FTC for HIV prevention.

Conclusion

While cost is a major obstacle to scaling up implementation of PrEP, making it available free may pose an added challenge to countries or cities where a policy decision to introduce PrEP as a public health service has yet to be made. Our results suggested that a partially self-financed mode of delivery is feasible and could appeal to a proportion of risk-taking MSM. Fee-based PrEP provision has been available in other Asian Pacific countries like Thailand.[34] A partially self-financed model could be an interim measure, and this is less demanding of resources in locations where generic TDF/FTC is not available (as in Hong Kong). Operationally, PrEP cannot be implemented in isolation but must be provided in conjunction with periodic HIV/STI testing, as reflected in our study. Provision of PrEP serves the dual purpose of HIV prevention and opportunistic STI screening, which enables prompt treatment to be given so as to reduce reinfections and the infection burden in the MSM community. Rectal *C trachomatis* or *N gonorrhoeae* infection has been shown to be associated with an increased risk of HIV transmission[35] and should therefore be considered as part and parcel of the HIV prevention package. Finally, as PrEP is a biomedical form of HIV prevention, our results confirm that severe adverse events are uncommon, but moderate but intolerable reactions may occur in a small proportion of people on TDF/FTC, who would require clinical advice on cessation.

Author contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Concept or design: SS Lee, TH Kwan, TTN Lam.
Acquisition of data: TH Kwan, NS Wong, SS Lee, GCY Lui, DPC Chan, KCK Lee.
Analysis or interpretation of data: TH Kwan, NS Wong, SS Lee.
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Declaration

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Conflicts of interest

GCY Lui has served as advisory committee member for Gilead Sciences, Merck, Sanofi Pasteur, and ViiV; and as a speaker for Gilead Sciences and Merck; and has received research grants/donations from Gilead Sciences, Merck and GSK. SS Lee has served as advisory committee member for Gilead Sciences, GSK and Merck; and as a speaker for Gilead Sciences sponsored events; and has received funding from Gilead Grants for community education activities.

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Ethics approval

The study was approved by The Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (Ref CREC 2016.470) and registered at the Centre for Clinical Research and Biostatistics Clinical Trials Registry of The Chinese University of Hong Kong (Ref CUHK_CCRB00533). A Clinical Trials Certificate was obtained following application to Department of Health of the Hong Kong SAR Government (Ref 100860).

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