Title
Pre-Exposure Prophylaxis Care Continuum among Men Who Have Sex with Men in Vietnam

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Publication Date
2020

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

Pre-Exposure Prophylaxis Care Continuum among Men Who Have Sex with Men in Vietnam

A dissertation submitted in partial satisfaction of

the requirements for

the degree Doctor of Philosophy in Epidemiology

by

Quang Loc Pham

2020

ABSTRACT OF THE DISSERTATION

Pre-Exposure Prophylaxis Care Continuum among Men Who Have Sex with Men in Vietnam

by

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Doctor of Philosophy Epidemiology

University of California, Los Angeles, 2020

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Background

Pre-exposure Prophylaxis (PrEP) is effective in preventing HIV acquisition and therefore is a key priority to ending the HIV/AIDS epidemic. Men who have sex with men (MSM) can largely benefit from the program because they are disproportionately affected by the epidemic. There is a paucity of studies conducted in Vietnam investigating barriers of PrEP uptake as well as the PrEP care continuum. The study aims to identify the challenges of PrEP implementation from the perspective of MSM and from the perspective of service providers working in antiretroviral therapy (ART) clinics, and to inform interventions to improve PrEP implementation.

Methods

A mixed-method design was used in the study. Sub-study 1 utilized the existing data of a cohort study of MSM and the ongoing PrEP-program data of an MSM-focused clinic in Hanoi, Vietnam to identify factors associated with PrEP initiation. Sub-study 2 was in-depth interviews of 30 discontinued MSM to explore multi-level challenges related to PrEP discontinuation. Sub-study 3 was a cross-sectional survey of service providers working in ART clinics in Hanoi, Ho Chi Minh, and Hai Phong Cities in Vietnam to investigate the association between service providers' acceptability of the PrEP program and concern about PrEP use.

Results

Study 1 found that 43% of HIV-negative MSM initiating PrEP. Four factors associated with increased PrEP initiation were revealed, that were, reported gender identity, no ATS use in the past three months or never, having more than two sexual partners in the last month, and ever tested for HIV in the last 12 months. Study 2 reported the challenges related to PrEP discontinuation in three levels: 1) Individual-level challenges were risk behaviors and risk perception, pill burden, side effects, and lack of motivation to treatment, 2) Institutional-level challenges were PrEP accessibility and logistical difficulties, 3) Structural-level challenges included cost due to the medication, stigma toward PrEP use, and the impact of the COVID-19 pandemic. Additionally, the study found that long-acting injectable PrEP was highly acceptable among discontinued MSM and that side effects and pain due to intramuscular injection were two major challenges related to injectable PrEP. Study 3 presented the high acceptability of PrEP implementation among ART service providers. The association between PrEP acceptability and concern about PrEP use was not observed, however, higher awareness of PrEP-related

information, lower stigma toward MSM, and higher job satisfaction were correlated with increased PrEP acceptability.

Conclusion

MSM faces multi-level challenges to initiate PrEP and to remain in the PrEP program. Interventions targeting the multi-level challenges should be developed and need to be delivered in a comprehensive package.

The dissertation of Quang Loc Pham is approved.

Roger Detels

Sung-Jae Lee

Chunqing Lin

Li Li, Committee Chair

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2020

To my dearest family

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Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ART	Antiretroviral Therapy
CASI	Computer-Assisted Self-Interview
CBO	Community-Based Organizations
HIV	Human Immunodeficiency Virus
HMU	Hanoi Medical University
IBBS	Integrated HIV/STI Biological and Behavioral Surveillance
MoH	Ministry of Health
MSM	Men who have sex with men
NGO	Non-Governmental Organizations
OPC	Out-Patient Clinic
PEPFAR	President's Emergency Plan for AIDS Relief
PrEP	Pre-exposure prophylaxis
STI	Sexually transmitted infections
UNAIDS	Joint United Nations Programs on HIV/AIDS
WHO	World Health Organization

Acknowledgment

First and foremost, I would like to express my sincere gratitude to Dr. Li who is my academic advisor and the doctoral committee chair for her uncountable supports, patient, and time during my Ph.D. journey at UCLA. Her commitment to my development, career as an independent researcher over the past four years has been invaluable. Her encouragement, guidance, and advice enabled me to complete this dissertation and to accomplish many great achievements. I am truly grateful to my committee members Drs. Roger Detels, Sung-Jae Lee, and Chunqing Lin for their insights and suggestions throughout my dissertation.

I would like to sincerely acknowledge Dr. Le Minh Giang and my outstanding colleagues in the Center for Training and Research on Substance Abuse – HIV, Hanoi Medical University for their advice and help for my fieldwork. Dr. Le Minh Giang was very supportive and generous to provide me with the existing data that I analyzed for the second chapter of my dissertation. I am also greatly appreciated all the studied participants who shared their information with me.

I would like to fully thank my friends and colleagues in the US and in the Fogarty program for always supporting each other in all aspects of life. You made my journey in the U.S. more special, more memorable, and more enjoyable.

I am truly grateful to Dr. Roberta Malmgren, Wendy Aft, and Lorin Chak for taking care of me and other Fogarty students and help us with the administrative issues. Besides, the UCLA/Fogarty AIDS International Training and Research program supported my training at UCLA and my dissertation implementation.

Last but not least, I would like to thank my dearest parents, Pham Quang Hung and Tran Thi Mai Huong for motivating, encouraging, and supporting me entire my first-time study abroad.

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Chapter 1: Background

1.1 Pre-exposure prophylaxis and its role in the 2030 goal

Pre-exposure prophylaxis (PrEP) is a bio-intervention approach that uses antiretroviral medications to prevent HIV infection in HIV-negative people. As of April 2020, two single-tablet medications were FDA approved as PrEP. The first one, which consists of emtricitabine and tenofovir disoproxil fumarate (FTC-TDF), was approved in 2012 (Gilead, 2012); the brand name is Truvada®. The second one, which consists of emtricitabine and tenofovir alafenamide (FTC-TAF), was approved in 2019 (FDA, 2019); the brand name is Descovy®. The idea of PrEP has followed the evidence of the effectiveness of post-exposure prophylaxis, of mother to child transmission, and of treatment as prevention strategies (TasP). If an HIV-negative person has sufficient levels of antiretroviral medications in their bloodstream, genital tracts, and rectum, they will be protected from HIV because the medication prevents the entry of HIV and the proliferation of viruses in our body.

PrEP has been shown to be an efficacious, safe HIV prevention strategy for at risk-populations (Chou et al., 2019; Fonner et al., 2016; Koechlin et al., 2017). The iPrEx study, which was the first randomized, double-blind, placebo-controlled trial of PrEP, demonstrated a 44% reduction in HIV infection among men who have sex with men (MSM) and transgender women in six countries (Grant, 2010). To attain that efficacy, medication adherence was found to be a critically important factor. Participants who took the pill more than 90% of the days were reduced to 73% risk of HIV acquisition; even more, PrEP achieved 93% efficacy among those with a detectable level of FTC-TDF compared to those without a detectable level (Grant, 2010). Similarly, a sub-study of participants in the Partners PrEP Study reported that high (>80%) PrEP

adherence was related to 100% PrEP efficacy (Haberer et al., 2013). Other studies conducted in different at-risk populations consistently showed PrEP significantly reduced the risk of HIV acquisition (Baeten et al., 2012; Choopanya et al., 2013; Thigpen et al., 2012). However, medication adherence is differently required for males and females as well as routes of transmission because of the different concentrations of medication in organs (Cottrell et al., 2016; Patterson et al., 2011). For example, the medication needs about 7 days of daily use to achieve a maximum protection for receptive anal sex and about 21 days of daily use for receptive vaginal sex and injection drug use. The safety of PrEP was also demonstrated in various studies. For example, serious adverse events were rare (less than 5%) and not different between both intervention and control arms (Grant, 2010; Thigpen et al., 2012). Other mild side effects such as increased creatinine level, nausea, headache, or dizziness were not uncommon among people who use PrEP, however, they were all manageable and typically went away in the first few weeks (Grant, 2010; Grohskopf et al., 2013; Hosek et al., 2017; Thigpen et al., 2012). HIV resistance was observed no more than 8% but it happened mostly among patients who took PrEP during the period of acute HIV infection (Lehman et al., 2015; Liegler et al., 2014). Changes in HIV risk behaviors, for example, condomless sex, more sexual partners, or increased STI rate, are observed in few studies but up to now, there is still no firm conclusion on where PrEP use is the reason for these changes (Maxwell, Gafos, & Shahmanesh, 2019; Montano et al., 2019).

Less-demanding PrEP approaches, for example, on-demand or time-driven PrEP, or injectable PrEP were recently proposed to overcome limitations of daily dosing. On-demand or on-event PrEP is in which the medication is taken before and after the anticipated HIV exposure, also known as the “2-1-1” regimen. Molina and colleagues found in the IPERGAY trial that participants using PrEP had an 86% relative reduction of HIV infection, compared to the placebo

group (Molina et al., 2015). In this study, participants were guided to take 4 tablets of PrEP, two in 2 to 24 hours before sex, one in 24 hours after the first take, and one in 24 hours after the third tablet. If participant anticipate having multiple consecutive sexual intercourses, they need to take PrEP daily until the day of the last sexual intercourse, and then take the last two tablets like the previous scenario. Time-driven dosing is where individuals take a pill two times a week on chosen days, following a post-intercourse pill. This approach has also been evaluated in different studies that reported intermittent dosing was as safe as daily dosing but seemingly achieved higher adherence levels (Kibengo et al., 2013; Mutua et al., 2012).

After the demonstration of safety and efficacy in various clinical trials, PrEP becomes one of five HIV prevention pillars to achieve the 2030 target by UNAIDS, which aims toward ending HIV/AIDS (AVERT, 2019; UNAIDS, 2016). In 2019, there were an estimated 1.7 million people newly diagnosed with HIV, raising the number of people who are living with HIV to 38 million (UNAIDS, 2020). Although the newly diagnosed cases were consistently declined since 2000, the progress is slow and disparate across at-risk populations (UNAIDS, 2019). Sexual transmission (both hetero- and homo-sexual) accounts for an increasing percentage of new HIV infection, and among the MSM population HIV prevalence is increasing (CDC, 2019a; UNAIDS, 2020). The mathematical model also showed that ART treatment is not sufficient to eliminate HIV/AIDS epidemic by 2030 (Cremin et al., 2013; Stover et al., 2016), so additional effective HIV prevention strategies are needed. A PrEP program, therefore, is evident to implement and will complement existing HIV prevention programs to meet the global target.

1.2 PrEP care continuum

PrEP was recommended for the first time in 2012 among specific populations at high risk of HIV (Gomez et al., 2013; San Francisco Department of Public Health, 2015; WHO, 2012). Three years later, a new guideline broadened PrEP indication, in which PrEP was recommended for people at "substantial risk", defined as "HIV incidence greater than 3 per 100 person–years in the absence of PrEP" (WHO, 2015). It implies that other than key populations, young people, adolescents, and women in high-HIV prevalence settings have an indication of PrEP. CDC also recommended PrEP to use among key populations as an additional HIV prevention method in 2014 (CDC, 2017). Despite the minor difference in recommended populations, these guidelines all emphasize that PrEP should be implemented as part of a package of combination prevention interventions. After some very first guidelines were published, PrEP has been accepted globally. As of 2019, PrEP was provided in 68 countries and almost half of the counties issued a national guideline for PrEP (PrEPWatch, 2019). In southeast Asia, five (Thailand, Vietnam, Laos, Philippines, Malaysia) of 11 countries provide PrEP, and of them, Thailand and Vietnam issued a national guideline for PrEP (PrEPWatch, 2019).

However, far fewer people who can benefit from PrEP uptake and a minority of the users are in low-and-middle-income countries (AIDSMAP, 2018; CDC, 2018; Maxwell et al., 2019; To & Lee, 2018). Among those who initiated PrEP, medication adherence widely varies from 9 to 100% across PrEP regimen (daily or episodic dosing) and populations (MSM, serodiscordant partners, female sex workers, PWUD), depending on how it was measured (Sidebottom, Ekstrom, & Stromdahl, 2018). Additionally, 12%-40% of those who initiated PrEP drop out after the first 6 months in the program and the drop-out rate appears to proportionate with the time

follow-up (Chan et al., 2016; Clement et al., 2019; Hojilla et al., 2018). It, therefore, highlights the need for understanding the challenges of PrEP programs.

PrEP care continuum, which consists of several consecutive benchmarks describing the natural process of the program, offers concrete and measurable indicators to identify gaps in the PrEP program (Ezennia, Geter, & Smith, 2019; Kelley et al., 2015; Nunn et al., 2017; Parsons et al., 2017). The concept is analogous to the HIV cascade of care (CDC, 2019b; Horn et al., 2016). The first definition of the PrEP care continuum crudely focused on 4 stages: awareness or willingness, access to care, prescribe and initiation, adherence and retention (Kelley et al., 2015). Building from that and combined with long-time practical experience, Nunn and colleagues proposed a more detailed PrEP care continuum that was summarized in three main stages, for example, PrEP awareness, uptake, and adherence & retention, and each stage consists of two to four steps (Nunn et al., 2017).

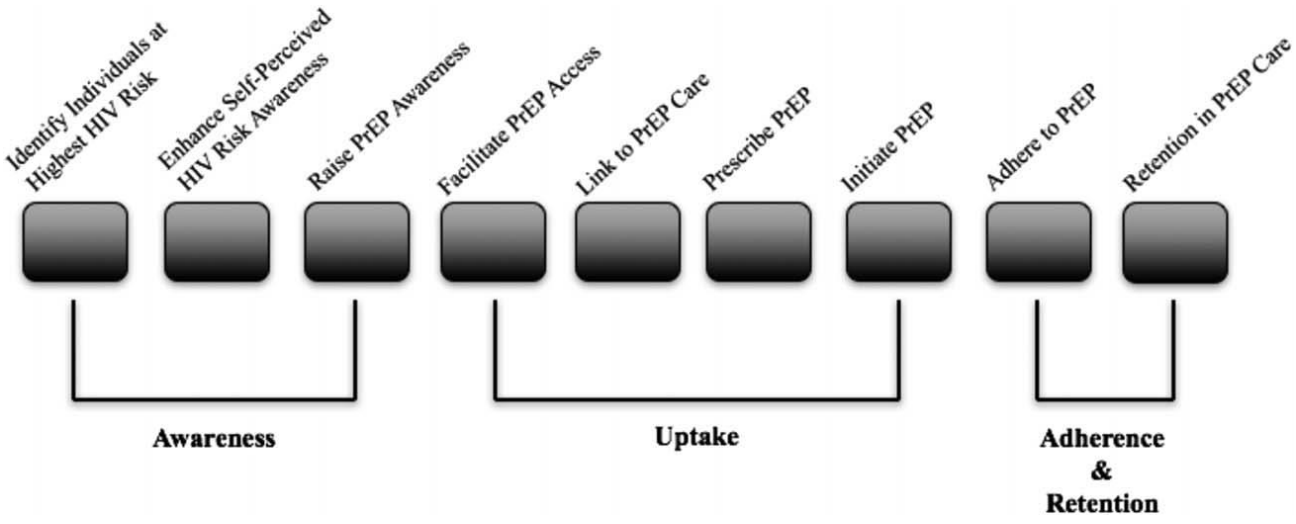

Figure 1.1. The proposed PrEP care continuum by Nunn and colleagues in 2017

1.3 HIV and MSM population in Vietnam

Vietnam is one of 11 countries in Southeast Asia and is a low-and-middle-income country (World Bank, 2019). Its Capitol is Hanoi city and its population was slightly more than 96 million in 2019 (VGSO, 2019). HIV epidemic was first reported in the 1990s; currently, the HIV epidemic in Vietnam concentrates among three key populations (people who use drugs, sex workers, and men who have sex with men), and in the general population HIV prevalence is approximately 0.3% (45 VMOH, 2020). As of October 2019, it was an estimated 212,000 people living with HIV, and of them, 8,500 were newly identified in the first 10 months of 2019 (45 VMOH, 2020). Ho Chi Minh City (HCMC) and Hanoi ranked first and second in the number of newly identified cases, accounting for 19% and 9% of the cases respectively (Vo, HIV/AIDS Epidemic in Vietnam). Though the decreasing trend of new HIV infection is consistently observed since 2007, HIV prevalence among MSM and transgender populations appears to increase significantly, from 2.3% in 2012 to 12.2% in 2017 (Vo, HIV/AIDS Epidemic in Vietnam). HIV infection acquired through unsafe sex alarmingly increased since 2015, it now accounted for 67% of the new HIV cases as compared to 63.2% in 2018 (45 VMOH, 2020). If that trend remains, MSM will sooner become the key population that drives the HIV epidemic in the years to come.

Vietnamese MSM aged 15 to 49 was estimated to be 178,000 (95% CI: 122,000-512,000), equivalently to 0.68% of 15-49 population (95% CI: 0.46-1.95) (Vo et al., 2019). They mostly populate in HCMC and Hanoi. The highest estimated number of MSM was in HCMC with 37,238 people (90% CI: 24,146–81,422) (Safarnejad, Nga, & Son, 2017). The second highest number was in Hanoi with 30,417 people (95% CI: 24,656-39,691) (Vo et al., 2019).

Drug use is not uncommon among MSM. There were 13.2% of MSM in Hanoi and 19.8% in HCMC self-reporting ever use of illicit drugs (VMOH, 2014). Amphetamine-type stimulant (ATS) was the most commonly used (12.7% in HCMC and 10.5% in Hanoi), followed by opiates (6.3% in HCMC and 5.3% in Hanoi) (VMOH, 2014). A cross-sectional study of 622 MSM in Hanoi and HCMC reported nearly one-third (30.4%) of the participants had ever used ATS, and of ATS users, 18% were classified as high-risk users (Vu, Holt, Phan, Le, et al., 2016). Drug use before or during sex is prevalent and appears to increase (Vu, Holt, Phan, Le, et al., 2016). That overlapped behavior contributes to the increased HIV infection up to five folds (Vu, Holt, Phan, La, et al., 2016).

Stigma and discrimination are still the main factors hindering MSM access to HIV/AIDS care (Berry et al., 2013; Colby, Cao, & Doussantousse, 2004; Philbin et al., 2018). MSM are afraid of their information will be disclosed to their family or friends, so they avoid visiting physicians or are reluctant to disclose homosexual behaviors with them (Philbin et al., 2018). That hinders health care providers to provide appropriate consultancy and health services, for example, HIV testing or PrEP initiation.

1.4 Current PrEP practice in Vietnam

Vietnam is the second country in Southeast Asia, after Thailand, adopting PrEP into the HIV prevention program. Vietnamese PrEP program was first piloted in 2017 in Hanoi and HCMC among MSM, partners of HIV-infected people who were not in ART, or who are in ART but their viral load exceeds 200 copies/ml, and transgender women. The demonstration project showed high acceptable and high efficacy (5866 VMOH, 2018), supporting the scaling up the PrEP program nationwide. The legal framework for the PrEP program was issued to support the

implementation. PrEP was first acknowledged as an HIV prevention modality that needs to implement in Vietnam in 2016 (1340 VMOH, 2016). By the end of 2017, the Vietnam Ministry of Health issues the Decision that specifies the regimen for PrEP treatment, which is the combination of TDF and FTC or TDF alone (5418 VMOH, 2017). In 2018, the Vietnam Ministry of Health issued the strategic plan for nationwide PrEP implementation (5866 VMOH, 2018). This document set the goals of recruiting 5,600 people in 2019 and 7,300 people in 2020 into the PrEP program, which, combining with existing HIV prevention programs, aims to bring HIV prevalence in the general population below 0.3% in 2020. The plan prioritized integrating PrEP into HIV-related clinics, for example, outpatient clinics (OPC, a clinic that provides ART), STI treatment facilities, and MMT clinics, and prioritized implementing PrEP services in where the number of populations at risk is high and HIV service is well-established.

The first national guideline for PrEP was issued in the early of 2019 (VAAC, 2019b). PrEP is recommended for at-risk populations, including MSM, transgender women, HIV-negative partners of people living with HIV who are not in the treatment or in the treatment but a viral load more than 200 copies/ml, sex workers, and people injecting drugs. To be eligible for PrEP, a patient should (1) have HIV-negative test result within the past seven days, and (2) having HIV risk behaviors such as having multiple sex partners, unprotected anal sex, commercial sex, sharing injection tools/needles, or being diagnosed with sexually transmitted infections. The exclusion criteria of PrEP are (1) having signs/symptoms of acute HIV infection, (2) having creatinine clearance less than 60ml/min, (3) weighing less than 35 kilograms, and (4) allergic to any PrEP medications or having PrEP contraindication. In the early of 2020, VAAC issued the updated version of the 2019 PrEP guideline (VAAC, 2020). The major update is

including the on-demand PrEP. On-demand PrEP is recommended only for the MSM population and among MSM who are less sexually active (≤ 2 times/weeks).

PrEP is provided in 43 clinics (35 public and 8 private clinics) in 11 cities/provinces in Vietnam by the end of 2019 (VAAC, 2019a). The medication is a generic type and Truvada is not registered in Vietnam yet. The number of MSM on PrEP accounts for 2% (3,300) of the MSM population (Nguyen & Green, 2019). There are two PrEP delivery models in Vietnam. The first model is a private clinic, which is usually run by MSM or has staff who is in the LGBT community (e.g., Lighthouse in Hanoi or Glink in HCMC – a social enterprise, CARMA – an MSM-based CBO). The second model is a public clinic, which is run by the government (e.g., ART clinics also known as OPC). International funds fully cover the cost of medication but partly cover the cost of doctor visits or monitoring services. Therefore, associated costs, such as HIV tests, hepatitis tests, STD tests, must be co-pay and are likely to become a huge financial burden if patients have no insurance.

There is a paucity of literature about the challenges of the PrEP program in Vietnam. Unpublished data from the HMU-affiliated Sexual Health Promotion (SHP) clinic reported that among 1,926 MSM invited to PrEP from May 2019 to April 2020, 47% of them initiated PrEP and among those initiated only 31% remained in the program after 6 months. Some challenges from other countries might not apply to Vietnam because of the difference in culture and healthcare delivery models. For example, the “purview paradox”, which was widely documented in the US (Krakower, Ware, Mitty, Maloney, & Mayer, 2014; Pinto, Berringer, Melendez, & Mmeje, 2018; Pleuhs, Quinn, Walsh, Petroll, & John, 2020; Zhang et al., 2019), is not relevant to Vietnam because, in the US, both HIV specialists and primary care providers can prescribe PrEP, while in Vietnam, only HIV specialist are trained so authorized to prescribe PrEP. Additionally,

during the COVID-19 pandemic, people must stay home so some barriers might arise and therefore might disturb PrEP treatment. Given that window opportunity and the need for evidence for PrEP implementation, we conducted this study to investigate barriers and facilitators associated with the PrEP care continuum.

1.5 Theoretical framework

In this study, we adopted the social-ecological model and health-belief model to comprehensively assess the challenges of the PrEP program. Both models have been applied in health research, including HIV (Barclay et al., 2007; McLaren & Hawe, 2005; Mugavero, Amico, Horn, & Thompson, 2013). The health-belief model guides the understanding of individual barriers associated with the PrEP program. Limitations of the health-belief model are overcome by using the social-ecological model, which conceptualizes the barriers from multi-level perspectives. We classified the challenges and facilitators of the PrEP program into individual, institutional, and social levels. Institutional factors represent the clinic climate that can hinder patients' access to care, and it includes clinic infrastructure (e.g., location, PrEP implementation model) and service providers (e.g., stigma, knowledge, skills to work with LGBT community, confidentiality). Social/structural factors represent the environment outside PrEP clinics, including barriers such as government regulations on PrEP implementation, stigma from society or patient's network, and facilitators such as social support.

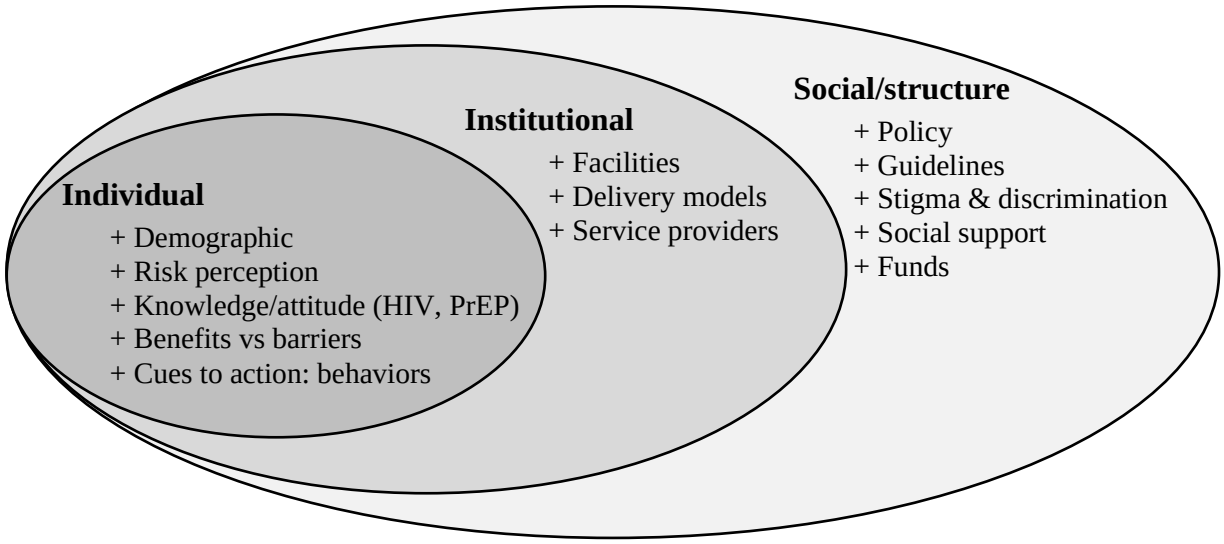

Figure 1.2. Multilevel influences of a four-level healthcare system

1.6 Study aims

The overall aim of this study is to identify the challenges of the PrEP program and to provide suggestions/evidence for multi-level interventions to improve PrEP implementation.

The study-specific aims are:

1) To investigate factors related to PrEP initiation among MSM in Vietnam
2) To explore challenges of PrEP continuum from the perspective of MSM who discontinued PrEP in Vietnam
3) To assess factors associated with service provider's acceptability of the PrEP program in Vietnam

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Chapter 2: Factors Associated with PrEP Initiation among MSM Population

Abstract

Background: Pre-exposure prophylaxis (PrEP) program is an effective measure to reduce HIV incidence but far few people at increased HIV risk have access to it. Data on PrEP initiation among the MSM population are limited. We described the PrEP initiation rate among MSM in an MSM-focused clinic in Hanoi, Vietnam, and the characteristics of those who did and who did not initiate PrEP. Factors associated with PrEP initiation were evaluated.

Methods: The study used the existing data of a cohort study of MSM who were recruited in a longitudinal study in an MSM-focused clinic in Hanoi, Vietnam between July 2017 and April 2019. The subset of participants who were recruited in 2019, older than 18, HIV-uninfected, and PrEP naïve was selected to analyze. The questionnaire included information on demographic characteristics, STI and HIV service utilization, sexual behaviors, drug-using behaviors, and homosexuality-related stigma. Since May 2019, all HIV-negative MSM in the cohort study were invited to start PrEP in the clinic. Cox proportional hazard model was used to evaluate factors associated with PrEP initiation defined as receiving the first PrEP prescription at the clinic.

Results: Among 335 HIV-negative PrEP-naïve MSM analyzed, 43% initiated PrEP. The overall incidence rate of PrEP initiation was 60 per 1000 person-month over 17 months of follow-up. MSM who reported their gender identity, ever tested for HIV, and had more than two sexual partners in the last month were more likely to initiate PrEP. However, those who used amphetamine-type stimulants in the past three months were less likely to initiate PrEP.

Conclusion: Interventions facilitating gender disclosure, enhancing risk perception, and increasing HIV testing coverage could improve PrEP initiation among the MSM population. It is

recommended to incorporate substance use such as amphetamine-type stimulants in the Vietnamese guideline of PrEP.

Keywords: MSM, PrEP, initiation, uptake

Introduction

PrEP is an effective measure to reduce HIV incidence among key populations (Chou et al., 2019; Fonner et al., 2016; Koechlin et al., 2017). It becomes one of the most prioritized pillars to achieve the UNAIDS goal – ending the AIDS epidemic in 2030 (UNAIDS, 2016). Previous studies suggest that widespread PrEP implementation could reduce HIV incidence in the United States by up to 33% (Desai et al., 2008; Jenness et al., 2016). Another modeling study, quantifying direct and indirect effects of PrEP coverage for at-risk populations, reported that if 70% of the populations use PrEP, the risk reduction in HIV incidence among those who did not use PrEP could be 15% (Buchanan et al., 2020). However, the proportion of people who can benefit from PrEP are using it remains low.

Few PrEP-eligible people have access to PrEP and a minority of PrEP users are in low-and-middle-income countries (AIDSMAP, 2018; CDC, 2018; Maxwell, Gafos, & Shahmanesh, 2019; To & Lee, 2018). Different statistics of uptake rates were reported depending on the type of programs and populations at risk (Chan et al., 2020; Kagaayi et al., 2020). For example, PrEP initiation was 29% among patients in a referral program at STI clinic in Chicago (Bhatia et al., 2018) but it was 39% among PrEP-eligible participants in rural Uganda (Mayer et al., 2019). In addition, studies investigating factors associated with PrEP uptake were scanty, especially in low-and-middle-income countries.

In southeast Asia, five (Thailand, Vietnam, Laos, Philippines, Malaysia) of 11 countries have PrEP program; Vietnam is the second country, after Thailand, adopting PrEP into the HIV prevention program (PrEPWatch, 2019). After piloting PrEP in 2017, Vietnam started scaling up the PrEP program national wide in 2019. As of December 2019, PrEP was provided in 43 clinics

(35 public and 8 private clinics) in 11 cities/provinces in Vietnam (VAAC, 2019a). However, statistics reported the number of MSM taking PrEP was under the target, accounting for 2% (3,300) of the MSM population by July 2019 (Nguyen & Green, 2019). Therefore, this study was conducted to describe the PrEP initiation rate among MSM in an MSM-focused clinic in Hanoi, Vietnam, and to identify factors associated with PrEP initiation. We also reported the cascade of the PrEP care continuum and the characteristics of those who did and who did not initiate PrEP.

Methods

Setting and study participant

Study 1 used the existing data of MSM who were recruited to a cohort study from January to April 2019 in Hanoi, Vietnam. The cohort study, the HIM study, was conducted at SHP clinic that was affiliated with Hanoi Medical University. SHP clinic is an MSM-focused clinic and specializes in providing counseling, testing, and treatment services for sexual health, substance abuse, and HIV/AIDS for MSM in Hanoi since 2013. The cohort recruitment was done by either internet-based sampling, time-location sampling, or respond-driven sampling method between July 2017 to April 2019. To be eligible, participants must age 16 and above, be male at birth, have sex with men in the past six months, and live in Hanoi. The fingerprint method was used to eliminate duplicating participation and to monitor participants' follow-up in the cohort study.

Participants were asked to complete the behavioral questionnaire using a computer-assisted self-interview (CASI) system in a private room in the clinic. The study staff was available outside the room to help with the administration. The administration took approximately 40-60 minutes to complete. Participants were paid 200,000 VND (approximately

10 USD) for the assessment. Since May 2019 when PrEP was available in the clinic, all MSM who were HIV-negative in the HIM study were contacted to recruit in the PrEP program at SHP clinic. MSM were contacted up to three times via phone calls or messages if they did not respond and the attempt ended in September 2019. MSM who visited the clinic were screened and those who were eligible based on the guideline were received the first PrEP prescription. The procedure was followed by the national guidelines for PrEP (VAAC, 2019b, 2020).

Measure

The outcome of the study was PrEP initiation that was defined as receiving the first PrEP prescription. Following the national guidelines for PrEP (VAAC, 2019b, 2020), those were indicated for PrEP must have an HIV-negative test in the past 7 days and engage in risk behaviors in the past 6 months or desire to take PrEP. Risk behaviors included, for example, having an HIV-positive sexual partner who was not in ART or was in ART but his/her viral load exceeded 200 copies/ml, having sexual activities with one at increase HIV risk (i.e., people who inject drugs or men who have sex with men), multiple sexual partners, unprotected anal sex, commercial sex, sharing injection tools/needles, or being diagnosed with sexually transmitted infections. The ineligibilities of PrEP were (1) having any signs or symptoms of acute HIV infection, (2) having creatinine clearance less than 60 ml/min, (3) weighing less than 35 kilograms, and (4) allergic to any PrEP medications.

Participants' sexual history and practices were collected by a structured questionnaire. Sexual history included, for example, types of sexual partners, the number of partners in the last month, or ever had sex with a male partner who was HIV-infected. Sexual practice questions were asked for each type of partner (causal or commercial and male or female). They included

the frequency of condomless sex or the frequency of drug use before or during sex (chemsex) in the past six months.

Drug-using behaviors were assessed by The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) version 3.1 developed by World Health Organization (WHO) (World Health Organization). The Vietnamese translation of the scale is available on the WHO website and has been widely used among key populations in Vietnam. The scale consists of eight questions that evaluate the frequency of usage of various substances and their impacts on respondents' life in the past three months. The substances are grouped into one of nine categories, for example, tobacco products, alcoholic beverages, cannabis, cocaine, or amphetamine-type stimulants (ATS). Each question provides 2 to 5 choices, each choice corresponds to a point from 0 to 6. The substance-specific score was summed across questions 2 to 7 to determine the need and type of intervention.

Homosexuality-related stigma was measured by a 28-item scale developed by Ha and colleagues for Vietnamese MSM (Ha, Ross, Risser, & Nguyen, 2013). The scale consisted of three domains: enacted homosexual stigma (9 items), perceived homosexual stigma (11 items), and internalized homosexual stigma (8 items). Each item was rated on a 4-point Likert scale. The score of enacted homosexual stigma domain ranged from 1 to 4, representing "Often," "Sometimes," "Rarely," "Never", respectively. The score in the other two domains also ranged from 1 to 4, but representing "Strongly Agree," "Agree," "Disagree," "Strongly disagree". All the codes were reversed. The total scores were summed, and the higher score indicated the higher level of stigma. (Cronbach's alpha of the overall score = 0.93)

Additionally, individual demographics and socio-economic characteristics were collected, for example, age, birthplace, education, employment, marital status, gender identity, and sexual orientation. Gender identity was assessed by the question "which of the following sentences mostly exactly characterizes the way that you think about yourself and your gender?" Those who reported either man or transgender were classified as the reveal-gender group. The other group comprised of the participants who chose "other gender" or "not sure about my gender identity." In addition, sexual orientation was dichotomized based on the question "Which of the following sentences most exactly characterizes types of people that you are sexually attracted to". Two groups were "exclusive attracted to men" vs "others" ("mostly attracted to men, sometimes women," "equally attracted to both men and women," "mostly attracted to women, sometimes men," or "exclusively attracted to women").

Data analysis

Of 1,704 participants in the HIM study, 407 were recruited from January to April 2019. We excluded 72 participants because 55 were diagnosed with HIV, 9 used to take PrEP, and 8 were currently on PrEP. Thus, the analyzed sample was a group of 335 MSM who were HIV-negative and never used PrEP (Figure 2.1).

The cascade of the PrEP care continuum was described. We presented five steps of care that were individuals at risk (the number of HIV-negative MSM in the HIM cohort study), access to PrEP care (the number of MSM who visited the SHP clinic), PrEP eligible (the number of MSM who visited the clinic and were identified as eligible for PrEP), PrEP initiation (the number of PrEP-eligible MSM who were received the first PrEP prescription), and retention in PrEP program (the number of MSM who returned within 30 days prior or after scheduled dates

to refill PrEP at 1 month, 3 months, 6 months, 9 months, and 12 months after the first prescription). To be counted as refilling PrEP at a follow-up visit, participants must return to refill PrEP at the immediately previous visit. For example, those who refilled the prescription at the six-month visit after the first prescription did refill the prescription at one-month and three-month visits.

Demographic characteristics of the participants were described by mean and standard deviation for continuous variables or by frequency and percentage for categorical variables. Because few participants self-reported ever used substances, we categorized their drug usage into either using a substance in the last 3 months or not using a substance in the last 3 months. The rate of PrEP initiation was reported with 95% confidence limits in every three-month interval as well as in the whole duration of the follow-up time. Cox proportional hazard models were fitted to analyze the association between risk behaviors and PrEP initiation, adjusting for covariates. The starting time was set on May 22, 2019, when PrEP was available at SHP clinic. For those who successfully initiated PrEP, the end date was the date of the first PrEP prescription. For those who did not start PrEP, the end date was the latest date when participants were contacted or visited the clinic. Hazard ratios with 95% confidence limits and p-values were reported. The final model was evaluated for the proportional hazard assumption. Data were analyzed using SAS software version 9.4 (SAS Institute, Inc., Cary, NC).

Results

Demographic characteristic of participants

Table 2.1 presents the demographic characteristics of 335 study participants. Most of them were from 16 to 24 years old (209, 62.4%), were born in Hanoi (133, 39.7%), and currently

employed (317, 94.6%). However, only about a third of the participants completed a university-level degree (101, 30.2%). Few were married to a woman (16, 4.8%). The majority of the participants reported their gender identity (227, 67.8%); of them, 216 were male (64.5%) and 11 were transgender (3.2%). The proportion of study participants who self-reported their sexual orientation to be "exclusively attracted to men" was slightly lower than "other" (48.7 % vs 51.3%).

HIV risk behaviors

Table 2.2 shows the drug-using behaviors of the study participants. Among nine different groups of substances assessed by the ASSIST tool, alcohol was the most commonly used substance in the past 3 months (74.6%), followed by tobacco (15.8%), sedatives or sleeping pills cannabis (4.5%), and amphetamine-type stimulants (ATS, 3.3%). Greater than three fourth of participants reported no usage of any substances among cannabis, cocaine, ATS, inhalants, sedatives, hallucinogens, or opioids in the past three months (262, 78.2%). Among 324 participants who did not use ATS in the past 3 months, 322 participants never used ATS in their lifetime and two used ATS not in the last 3 months.

Tables 2.3 and 2.4 present the sexual behaviors and STI history of the study participants. The majority of participants had exclusively male sexual partners (316, 94.3%) and did not know the HIV status of their same-sex partners (199, 59.4%). The number of sexual partners (regardless of sex and type) reported in the past month was between 0 and 38, and the proportion of respondents having two or more sexual partners was 30.8%. More than 50% of the respondents were occasionally or never used condoms in the past 6 months, group-sex practices accounted for 38.2%, and chemsex was 40.3%. One in ten participants were diagnosed with any

Chlamydia, Gonorrhea, or Syphilis in the past year (34, 10.2%). Of 195 participants who had ever been tested for HIV, more than half were tested in the past 6 months. The mean score of the homosexuality-related stigma scale was 67.1 and its standard deviation was 13.3.

PrEP care continuum

Figure 2.2 demonstrates the PrEP care continuum among 335 HIV-negative participants. Less than half of those who were potential for PrEP accessing to PrEP care. Among those who were assessed, 94% were eligible, and of them, only three did not receive the first PrEP prescription. There were 144 participants initiating PrEP before 14 September 2020 (i.e., 144 participants initiated PrEP for at least 1 month) and 70% of them returned to the clinic for the second PrEP prescription. 45% of participants who initiated PrEP for at least 6 months received the 6-month prescription and that proportion was 31% among those initiating PrEP for at least 12 months. The incidence rate of PrEP initiation was the highest in the first three months after PrEP was available at the clinic (486 per 1000 person-month). The rate during 17 months of the follow-up time was 60 per 1000 person-month (Table 2.5).

Factors associated with PrEP initiation

Table 2.6 reported the results of the multivariable Cox proportional hazard model. The model was controlling for the recruitment approach, age (years, continuous), birthplace (Hanoi vs not Hanoi), and education (university educated vs less than university educated). MSM who revealed their gender identity were 54% more likely to initiate PrEP (adjusted hazard ratio [aHR] 1.54, 95% confidence interval [1.04 – 2.30]). MSM who were ever tested for HIV before the baseline visit were 81% more likely to start PrEP (aHR 1.81, [1.24 – 2.65]). A higher number of sexual partners in the last month (aHR 1.44, [0.98 – 2.10]) were associated with a higher rate of

PrEP initiation but no ATS use in the past three months (aHR 0.28, [0.07– 1.19]) was associated with a lower rate of PrEP initiation; their p-values were slightly greater the statistically significant level (0.0619 and 0.0840, respectively) but confident intervals suggested the direction of the association.

Discussion

The study found that 43% of HIV-negative MSM participating in a cohort study in an MSM-focused clinic in Hanoi initiated PrEP. The PrEP initiation proportion was higher than that was observed in Vietnam in 2019 (Nguyen & Green, 2019) and that was reported in previous studies (Bhatia et al., 2018; Chan et al., 2020; Mayer et al., 2019). This could be due to three main factors. The first factor is the clinic model. SHP clinic is an MSM-focused clinic found in 2013 so the clinic staff has a lot of experience working with the MSM population. Additionally, the majority of the clinic staff are MSM peers, which makes outreaching and counseling easier. These characteristics create a non-discriminatory and non-stigmatizing environment, which can facilitate service delivery for this hard-to-reach population (Philbin et al., 2018). Second, participants already enrolled in a cohort study in the clinic so they might be more familiar with and trust the clinic staff. Third, the active usage of various strategies to introduce PrEP to the community may be one of the reasons for the high observed rate of PrEP initiation. For example, promoting PrEP was done by hosting multiple community-oriented activities, advertising on multiple social media channels (e.g., Facebook, Viber, Zalo, and the clinic website), or doing livestream talk shows about PrEP and related information.

Two risk behaviors that were associated with PrEP initiation in the inverse direction were ATS use in the past three months and having more than two sexual partners in the last month.

MSM who used ATS were less likely to initiate PrEP than those who did not use ATS or never used ATS while men who had a higher number of sexual partners were more likely to start PrEP. The relationship between ATS use in the past three months and the PrEP initiation in our study was not consistent with the previous results, in which engaging in high-risk behaviors often drives the PrEP initiation (Gombe et al., 2020; Hammoud et al., 2019; Holloway et al., 2017), though it is clear that ATS use is strongly associated with HIV acquisition among MSM population (Beyrer et al., 2012; Koblin et al., 2006). The contradictory results may be because our study participant's risk perception of HIV risk behaviors is not consistent with their practice of HIV risk behaviors. In other words, MSM practice high-risk behaviors but they do not perceive themselves as at high risk of HIV acquisition. They, therefore, do not take any HIV-prevention measures, including PrEP. Another possible explanation could be the “risk-taking” personality. They may perceive their behaviors as at high risk of HIV infection but they are willing to take risks so they do not uptake PrEP (Douglas & Calvez, 1990; Kalichman, Tannenbaum, & Nachimson, 1998). Thus, it is important that public health interventions address the issue by increasing the recognition of the high risk of substance use for MSM maybe through counseling.

Additionally, because Vietnamese guidelines for PrEP do not classify substance use as one indication for PrEP yet so it is recommended to include ATS or other substances use as an eligible criterion for PrEP initiation. One strategy to incorporate substance use in the future PrEP guideline is risk score. Calculating risk score to evaluate PrEP eligibility could be done rapidly and effectively to identify MSM at increased HIV risk (Menza, Hughes, Celum, & Golden, 2009; Smith, Pals, Herbst, Shinde, & Carey, 2012).

The results of the multivariable Cox proportional hazard model show that understand and willingness to reveal gender identity was one facilitator for PrEP initiation. Gender disclosure is impacted by several factors, for example, fear of discrimination, cultural norm, knowledge, family honor, social networks (Mansh et al., 2015; Saeed, Mughal, & Farooq, 2018). If MSM feel comfortable to share their gender identity with health workers, they will have better opportunities to be received more needed services (Kapanda, Jumbe, Izugbara, & Muula, 2019). Nonetheless, accepting and understanding their own gender identity is associated with risk perception, which is one of the most important factors driving the decision on starting PrEP (Becker, 1974; Gombe et al., 2020).

HIV testing plays an important role in both the spectrum of HIV prevention and treatment continuum (Horn et al., 2016). It can also be a gate to access other health care services, for example, mental health for HIV positive patients, or reproductive care for women (Bell, Mthembu, O'Sullivan, & Moody, 2007; Dowshen, Lee, Franklin, Castillo, & Barg, 2017). The proportion of our study participants having HIV tested in the past 6 months was quite low, which urges the need to continue expanding the testing for the MSM population, who also were disproportionately affected by the HIV epidemic. More importantly, using one strategy solely is less likely to succeed in increasing HIV testing so a multiple-approach strategy is recommended (Campbell, Lippman, Moss, & Lightfoot, 2018). One of the approaches could be normalizing HIV testing (Lin, Roy, Dam, & Coman, 2017; Mall, Middelkoop, Mark, Wood, & Bekker, 2013).

Study results should be interpreted with their limitations. First, all MSM in our analyzed sample initiated oral, daily PrEP so the results cannot be generalized to other PrEP regimens, which were indicated for different populations with distinct risk behaviors patterns. Second, we

might underestimate the proportion of PrEP initiation because we could only identify the outcome of those who received PrEP in the studied clinic. Some participants did not uptake PrEP in the SHP clinic but did uptake PrEP in another PrEP clinic. Third, the total of MSM who were eligible for PrEP was unknown because half did not visit the clinic even after several attempts. This might make our proportion of PrEP initiation conservative. For example, some might be diagnosed with HIV so they were not eligible for PrEP and never visited the clinic for PrEP uptake.

Conclusion

The study reported a high PrEP initiation rate among HIV-negative participants who had enrolled in a cohort study conducted in an MSM-focused clinic in Hanoi, Vietnam. Factors associated with increased PrEP initiation were identified, that were, reported gender identity, no ATS use, multiple sexual partners, and ever tested for HIV. Interventions that focus on improving risk perception and expanding HIV testing could improve PrEP uptake. Adding substance use into the PrEP guideline could engage more MSM into the PrEP program.

Figure 2.1. The description of the analyzed sample

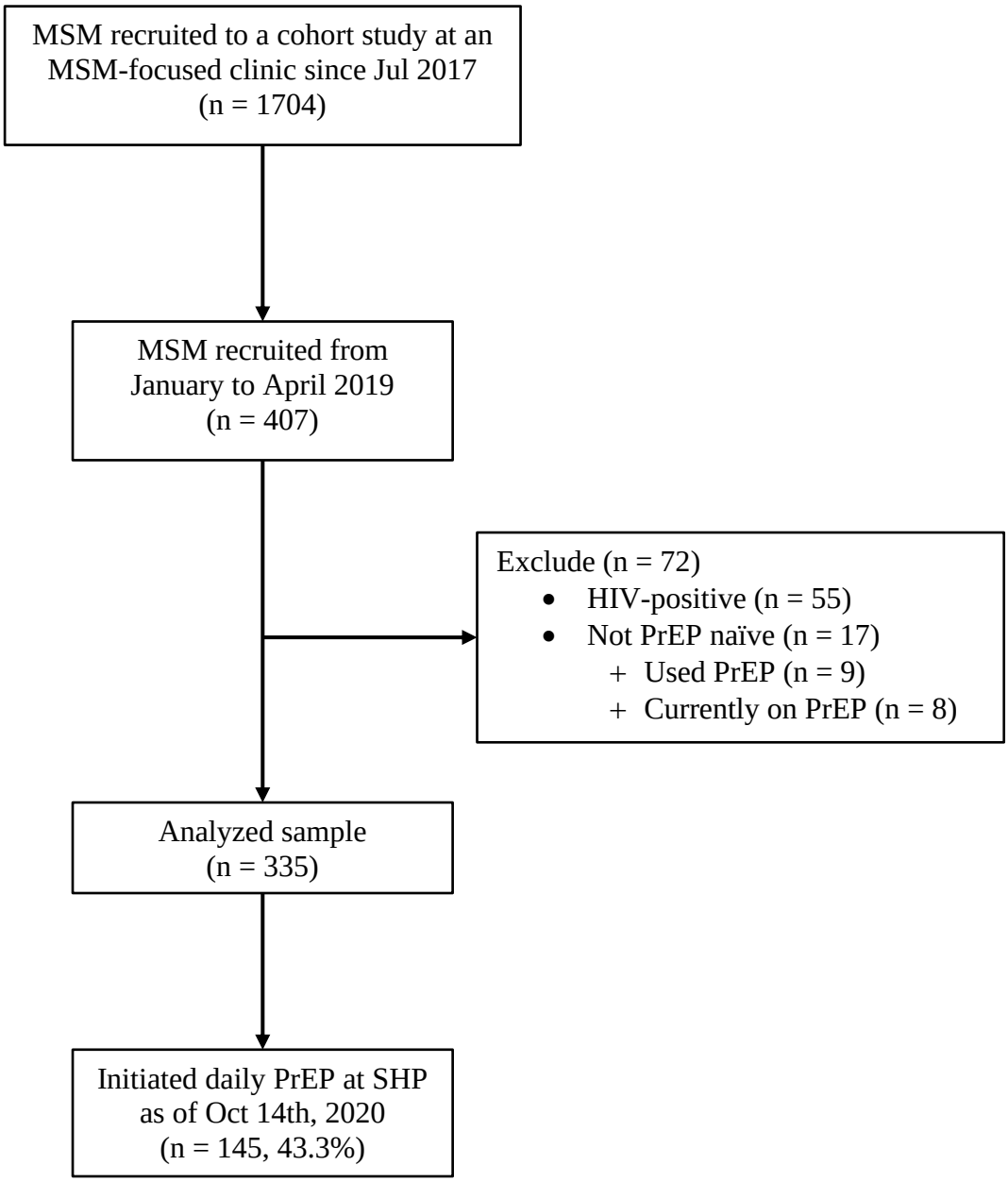


Table 2.1. Demographic characteristics of the analyzed sample (n = 335)

	None-PrEP initiators (N = 190)	PrEP initiators (N = 145)	Total (N = 335)
Recruitment method			
Time-location sampling	0	0	0
Respond-driven sampling	25 (13.2)	14 (9.7)	39 (11.6)
Internet-based sampling	165 (86.8)	131 (90.3)	296 (88.4)
Age			
16 – 24 years	124 (65.3)	85 (58.6)	209 (62.4)
25 – 29 years	47 (24.7)	45 (31.0)	92 (27.5)
≥ 30 years	19 (10.0)	15 (10.3)	34 (10.2)
Mean (SD)	23.8 (5.79)	24.0 (5.60)	23.9 (5.70)
Birthplace (Hanoi)	80 (42.1)	53 (36.6)	133 (39.7)
Educational attainment			
Less than university educated	134 (70.5)	100 (69.0)	234 (69.9)
University educated	56 (29.5)	45 (31.3)	101 (30.2)
Married to woman (yes)	9 (4.7)	7 (4.8)	16 (4.8)
Employment (yes)	178 (93.7)	139 (95.9)	317 (94.6)
Reported gender identity			
No (Other/Not sure)	73 (38.4)	35 (24.1)	108 (32.2)
Yes (Male/Transgender)	117 (61.6)	110 (75.9)	227 (67.8)
Sexual attraction			
Other	101 (53.2)	71 (49.0)	171 (51.3)
Exclusively to men	89 (46.8)	74 (51.0)	163 (48.7)

Table 2.2. Drug-using behaviors of the analyzed sample (N = 335)

	None-PrEP initiators (N = 190)	PrEP initiators (N = 145)	Total (N = 335)
Tobacco use, past 3 months	35 (18.4)	18 (12.4)	53 (15.8)
Alcohol use, past 3 months	146 (76.8)	104 (71.7)	250 (74.6)
Cannabis use, past 3 months	9 (4.7)	6 (4.1)	15 (4.5)
Cocaine use, past 3 months	1 (0.5)	0	1 (0.3)
ATS use, past 3 months	9 (4.7)	2 (1.4)	11 (3.3)
Inhalants use, past 3 months	8 (4.2)	2 (1.4)	10 (3.0)
Sedatives or sleeping pills use, past 3 months	9 (4.7)	11 (7.6)	20 (6.0)
Hallucinogens use, past 3 months	2 (1.1)	3 (2.1)	5 (1.5)
Opioids use, past 3 months	1 (0.5)	0	1 (0.3)
Any drugs use			
Never	149 (78.4)	113 (77.9)	262 (78.2)
Used, but not in the past 3 months	12 (6.3)	12 (8.3)	24 (7.2)
Used in the past 3 months	29 (15.3)	20 (13.8)	49 (14.6)

ATS: Amphetamine-type stimulants. Drugs included: Cannabis, cocaine, ATS, inhalants, sedatives, hallucinogens, or opioids.

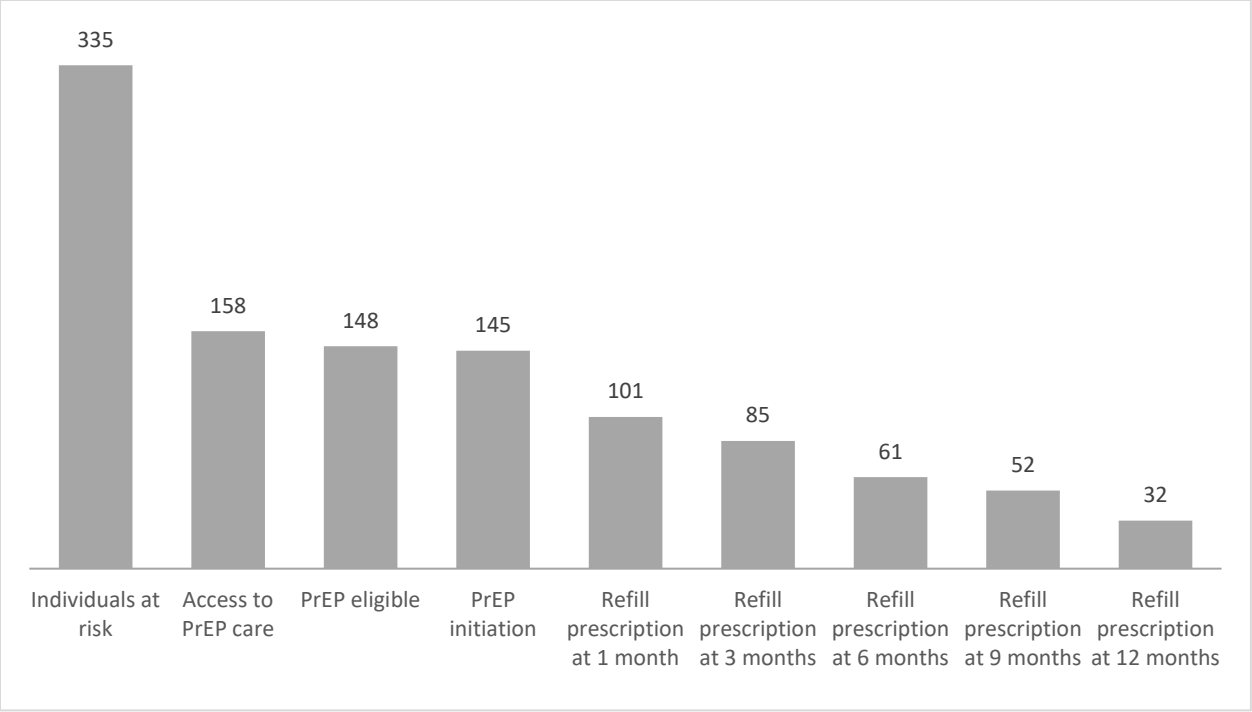
Table 2.3. Sexual behaviors of the analyzed sample (N = 335)

	None-PrEP initiators (N = 190)	PrEP initiators (N = 145)	Total (N = 335)
Sex of sexual partners			
Men and women	12 (6.3)	7 (4.8)	19 (5.7)
Men exclusively	178 (93.7)	138 (95.2)	316 (94.3)
Having sex with positive male sex partners			
Did not know their status	115 (60.5)	84 (57.9)	199 (59.4)
Never	69 (36.3)	55 (37.9)	124 (37.0)
Ever	6 (3.2)	6 (4.1)	12 (3.6)
Received payment for sex with money or goods (yes)	11 (5.8)	8 (5.5)	19 (5.7)
The number of partners, last month			
0 partner	59 (31.1)	44 (30.3)	103 (30.8)
1 partner	76 (40.0)	53 (36.6)	129 (38.4)
2+	55 (29.0)	48 (33.1)	103 (30.8)
Median (min – max)	1 (0 – 17)	1 (0 - 38)	1 (0 - 38)
Condomless anal intercourse, past 6 months			
No activity	20 (10.5)	11 (7.6)	31 (9.3)
Never	73 (38.4)	53 (36.6)	126 (37.6)
Occasionally or always	97 (51.1)	81 (55.9)	178 (53.1)
Group sex, past 6 months	76 (40.0)	52 (35.9)	128 (38.2)
Sexualized drugs, past 6 months	81 (42.6)	54 (37.2)	135 (40.3)

Table 2.4. STI history, HIV testing and the stigma score of the analyzed sample (N = 335)

	None PrEP initiators (N = 190)	PrEP initiators (N = 145)	Total (N = 335)
STI diagnoses, past year			
Chlamydia	11 (5.8)	9 (6.2)	20 (6.0)
Gonorrhea	10 (5.3)	6 (4.1)	16 (4.8)
Syphilis	1 (0.5)	3 (2.1)	4 (1.2)
Any of diagnosed STI	17 (9.0)	17 (11.7)	34 (10.2)
HIV test			
Never	95 (50.0)	45 (31.0)	140 (41.8)
Tested, but not in the last 6 months	41 (21.6)	47 (32.4)	88 (26.3)
Tested in the last 6 months	54 (28.4)	53 (36.6)	107 (31.9)
Homosexuality-related stigma scale			
Enacted homosexual stigma	18.4 (4.8)	18.2 (5.8)	18.3 (5.3)
Perceived homosexual stigma	28.7 (6.2)	28.5 (6.9)	28.6 (6.5)
Internalized homosexual stigma	19.8 (5.0)	20.6 (5.5)	20.1 (5.2)
Overall score	66.9 (12.5)	67.3 (14.3)	67.1 (13.3)

Any of diagnosed STI included: Chlamydia, Gonorrhea, and Syphilis.



Individuals at risk were HIV-negative MSM in the HIM study; Access to PrEP care was defined as visiting SHP clinic; PrEP initiator was the one who was received the first PrEP prescription in the SHP clinic; those who were counted as refilling PrEP at follow-up visits must return the immediately previous period, for example, those who were counted as refill prescription at 3 months were also received the prescription at 1 month. As of 14 October 2020, there were 145, 142, 137, 130, and 102 participants initiating PrEP for at least 1, 3, 6, 9, and 12 months, respectively.

Figure 2.2. Cascade of PrEP care among the analyzed sample

Table 2.5. The rate of PrEP initiation among the analyzed sample

	PrEP initiators	Person-month	Incidence rate per 1000 person-month (95% CI)
0 – 3 months	43	88.5	485.6 (360.2 – 654.8)
> 3 – 6 months	70	362.1	193.3 (153.0 – 244.4)
> 6 – 9 months	20	1403.0	14.3 (9.2 – 22.1)
> 9 – 12 months	7	105.8	66.2 (31.5 – 138.8)
> 12 – 17 months	5	86.0	58.1 (24.2 – 139.7)
Total	145	2045.4	60.2 (60.2 – 83.4)

Table 2.6. The adjusted Cox proportional hazard model of PrEP initiation (N = 335)

	aHR (95% CL)	p-value
Employment (Yes vs No)	1.68 (0.72; 3.90)	0.2305
Reported gender identity (Yes vs No)	1.54 (1.04; 2.30)	0.0320
Sexual attraction (Exclusively to men vs Others**)**	1.05 (0.74; 1.48)	0.7834
ATS use, past 3 months (Yes vs No)	0.28 (0.07; 1.19)	0.0840
The number of partners, last month (≥ 2 partners vs < 2 partner)	1.44 (0.98; 2.10)	0.0619
Having sex with a positive male sex partner		
Did not know their status	1	
Never	1.03 (0.72; 1.47)	0.8829
Ever	1.41 (0.59; 3.31)	0.4329
Condomless anal intercourse, past 6 months		
No activity	1	
Never	0.86 (0.44; 1.70)	0.6643
Occasionally or always	1.09 (0.56; 2.13)	0.7921
Sexualized drugs, past 6 months (Yes vs No)	0.94 (0.66; 1.35)	0.7521
HIV test (Ever vs Never)	1.81 (1.24; 2.65)	0.0022
Any of diagnosed STI, past year (Yes vs No)	0.97 (0.57; 1.66)	0.9186
Homosexuality-related stigma scale (Total score, continuous)	1.00 (0.99; 1.01)	0.9703

ATS: Amphetamine-type stimulants. aHR: adjusted Hazard ratio. The model was adjusted for recruitment approaches, age (years, continuous), birthplace (Hanoi vs not Hanoi), and education (university educated vs less than university educated).

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Chapter 3: MSM Perceived Challenges of PrEP Care Continuum

Abstract

Background: Pre-exposure prophylaxis (PrEP) is an antiretroviral medication that has been shown to be efficacious in HIV prevention among at-risk populations, including men who have sex with men (MSM). Challenges and barriers to scale up PrEP programs and retention of patients in those programs are not uncommonly documented worldwide. Few studies have been conducted in Vietnam to explore the challenges associated with the PrEP care continuum from the perspective of MSM.

Methods: In-depth interviews of 30 MSM who discontinued from the program were conducted in September 2020. Inclusion criteria were male at birth, living in Hanoi, 18 years old or above, self-reporting HIV-uninfected, and received oral PrEP for at least 2 months, and did not take PrEP for at least one month. Themes were deducted using Ground theory and reported with relevant quotes.

Result: Participants reported PrEP-continuation challenges that were summarized into three levels: individual, institutional, and structural levels. Individual-level challenges were risk behaviors and risk perception, pill burden, side effects, and lack of motivation to treatment. Institutional-level challenges were PrEP accessibility and logistical difficulties. Structural-level challenges were cost due to the medication, stigma toward PrEP use, and the impact of the COVID-19 pandemic on service continuation. Our interviewed MSM were highly aware of and highly acceptable to long-acting injectable PrEP, but they expressed concerns on side effects of the new regimen and pain due to intramuscular injection.

Conclusion: MSM in Vietnam are facing multilevel challenges along their PrEP care continuum. Providing risk education, assessing motivation, diversifying PrEP delivery models, addressing stigma, and developing strategic plans for national lockdown events can contribute to the improvement of the PrEP program. Long-acting injectable PrEP was highly aware of and highly acceptable among our study participants but caution about side effects and pain due to intramuscular injection should be addressed.

Keywords: HIV, PrEP, MSM, discontinuation, retention, long-acting injectable PrEP

Introduction

Pre-exposure prophylaxis (PrEP) is a bio-intervention approach that uses antiretroviral medications to prevent HIV infection in HIV-negative people. PrEP has been shown to be an effective, safe HIV prevention strategy for at-risk populations, including men who have sex with men (MSM), in both trial and real-world settings (Fonner et al., 2016; Koechlin et al., 2017). However, its effectiveness depends on medication adherence and retention (P. A. Chan et al., 2019; Chou et al., 2019; Riddell, Amico, & Mayer, 2018).

The retention rate of people who use PrEP has been documented low across many PrEP programs worldwide and it seems to proportionate with the time follow-up (Stankevitz et al., 2020). In an academic medical center in Manhattan in the US, the retention at the first follow-up visit and at the third follow-up visit among participants who initiated PrEP was 68% and 35%, respectively (Zucker et al., 2019). Chan and colleagues reported the retention defined regarding CDC guidelines was 54% at 3 months and 30% at 12 months after the first prescription in three clinical sites in the middle south US (Chan et al., 2019). Among participants who were referred from STI clinics to a federally qualified health center in North Carolina, 38% persisted in care for three months or more (Clement et al., 2019). However, in a lower resource setting, the retention rate at 10 months after the initiation was reported as 7% of the substantial HIV risk population and the medication retention was 45 days on average (Kagaayi et al., 2020). The high drop-out rate will compromise the efficacy of PrEP, which results in failing to reduce HIV incidence (Chou et al., 2019). Thus, it is necessary to investigate challenges related to retention and how to address that challenges in the real-world setting, especially in the low-and-middle-income countries where few studies have been conducted.

Reasons for PrEP discontinuation is complex (Ezennia, Geter, & Smith, 2019). Side effects of the medication, including mild to severe grades, are one of the most reported barriers associated with dropping out of the PrEP program (Gombe et al., 2020; Hosek et al., 2017; Smith, Toledo, Smith, Adams, & Rothenberg, 2012). Younger PrEP users are more likely to stop the treatment than those who are older (Chan et al., 2019; Zucker et al., 2019). Another barrier of the PrEP program is cost, which is mainly due to monitoring services (e.g., HIV test, liver function, kidney function), doctor's visits, or PrEP medication (Arnold et al., 2017). However, insurance and costs were not the factors associated with retention in the study conducted in the US (Chan et al., 2016). Additionally, service providers play pivotal roles in the successful implementation of PrEP (Krakower & Mayer, 2016), so their attitude toward and skills working with MSM would be one of the challenges of the discontinuation (Lankowski et al., 2019; Zhang et al., 2019). Other clinical factors may be reasons for stopping PrEP, including clinic location, or logistically challenges (Gombe et al., 2020). Stigma is an important factor associated with retention (Arnold et al., 2017; Dubov, Galbo, Altice, & Fraenkel, 2018). Stigma mainly comes from homophobia (Ayala et al., 2013), stereotypes of promiscuity (Collins, McMahan, & Stekler, 2017; Knight, Small, Carson, & Shoveller, 2016), and misconception of HIV-infection (Dubov et al., 2018; Lelutiu-Weinberger & Golub, 2016).

The PrEP program in Vietnam has recently been adopted and expanded so there have been few studies focusing on retention and its related challenges. Data from an MSM-focused clinic in Hanoi showed that among PrEP initiators, only 57% and 34% were retained in the program after 3 months and 12 months (Nguyen, Lung, & Bui, 2020). HIV prevalence among the MSM in Hanoi was raising three folds to 13.6% (PEPFAR, 2019). The MSM population in Hanoi was estimated 30,417 (95% CI: 24,656-39,691) (Vo et al., 2019). Given the need to better

understand challenges in order to maintain individuals in PrEP care in a real-world low-resource setting, especially among MSM population that was unevenly affected by HIV, the primary objective of this study was to explore challenges of the PrEP continuum from the perspective of MSM who discontinued PrEP in Vietnam. Additionally, because the randomized clinical trials of long-acting injectable PrEP conducted among MSM, transgender women (also known as HPTN083) and its sister conducted among women (also known as HPTN084) showed promising results (HPTN, 2020; Landovitz et al., 2020), it is a timely opportunity to investigate MSM attitude toward the new regimen.

Methods

Study settings and participants

In-depth interviews of 30 MSM who discontinued the PrEP program were conducted in September and October 2020. MSM discontinued the PrEP program were recruited by staff at PrEP clinics (both private and public clinics) and MSM-led CBO in Hanoi. To be eligible for this study, participants must be male at birth, living in Hanoi, 18 years old or above, self-report being HIV-negative in the latest test, and received oral PrEP for at least 2 months and did not take PrEP for at least one month. Those who were no longer indicated for PrEP (i.e., HIV positive, liver, or renal failure function or suffering severe side effects) were excluded. We contacted the referred MSM to verify their eligibilities and for MSM who were eligible and agreed to participate in the in-depth interview, we scheduled an appointment as soon as possible. In-depth interviewees were selected so that they were evenly distributed in each group of age (18-24, 25-34, or $\geq$ 35) and PrEP clinic type (private or public). The study was approved by the Institutional

Review Boards of the University of California, Los Angeles, the United States, and Hanoi Medical University, Vietnam.

Data collection

In-depth interviews were conducted in Vietnamese by trained, Vietnamese interviewers by phone or online (i.e., Zoom). Consent was orally obtained for every participant after providing them the study objectives, procedures, risk, and benefit. The interviews were audiotaped and took approximately 60-90 minutes. Participants were received 200,000 VND (approximately 10 USD) for their time and efforts.

A semi-structured guide was developed for the interview based on the theoretical framework and literature review to explore reasons for stopping PrEP treatment and MSM attitude toward the PrEP program. The interview topics were: (1) MSM knowledge and attitude about HIV/AIDS and PrEP; (2) MSM perception of susceptibility, severity of HIV/AIDS, and PrEP effectiveness; (3) reasons for taking PrEP (cues to action); (4) perceived barriers to initiate and continue PrEP; (5) experience in the PrEP program (e.g., duration on PrEP, changes due to the COVID-19 pandemic, counseling before the program, interaction with service providers); (6) experience while not in the program (e.g., concerns about risk, changes in behaviors); (7) reasons for dropping out PrEP program (e.g., PrEP-related stigma, distrust of the medical system, COVID19-related); (8) attitude toward long-acting injectable PrEP; (9) suggestions for the improvement of PrEP program and willingness to resume PrEP if the situation changed (different formulation of PrEP, different healthcare facilities). Additionally, participants' background information included age, gender identity, education, occupation, and living condition. We did not collect the name or any personally identifiable information of participants.

Data analysis

All recordings were de-identified and verbatim transcribed. All transcripts were read and cleaned to ensure accuracy before analysis. ATLAS.ti version 8 (Berlin, Germany) was used to manage and analyze the data. We applied the Grounded theory and thematic analysis approach to inform our data analyzing procedure (Glaser & Strauss, 2017). The draft of code lists was created based on the semi-structured guide and it was revised throughout the coding process based on the actual contents of the transcriptions. Themes were deducted from codes. The number/percentage of refusals and the background characteristics of the sample were reported. Relevant themes with supporting quotations were extracted and presented.

Results

There were 40 MSM were referred by PrEP clinic staff or MSM-led CBO. Of them, six were not eligible because of still using PrEP (only changing regimen from daily to event-driven PrEP), taking PrEP outside Hanoi or in the black market, or using PrEP for only one month. Among 34 eligible participants, four refused to participate or did not present at the scheduled interview. The demographic characteristics of 30 in-depth interviewers are presented in table 3.1.

We characterized the challenges relating to the PrEP program into three levels. The individual-level factors included sexual behaviors and risk perception, pill burden, side effects, and lack of motivation to stay on treatment. Institutional-level factors represented the clinic environment that can hinder patients' access to care, and they were PrEP accessibility and logistical difficulties. Social/structural-level factors represent the environment outside PrEP clinics, including cost, stigma toward PrEP use, and the impact of the COVID-19 pandemic.

1) Individual level

a. Sexual behaviors and risk perception

Sexual behaviors are not only the reason for initiating PrEP but the reason for stopping it. Participants perceived they were at risk of acquiring HIV so they initiated PrEP, but when they engaged in safe sex every time or at the acceptable proportion of the times, they felt it was not reasonable to continue using PrEP. Some stopped the treatment when practicing no sex, which could be due to the COVID-19 pandemic (the confinement order) or just breaking up with their lover.

"In the past 2 months or so, I have no risk, I feel that I am not in danger anymore. Now I focus more on studying than on relationships [to graduate]. Now I'm just hanging out for fun, not sex at all. Besides, when I'm taking PrEP, I have acne, it affects my appearance so I want to stop. You see, I have just recovered from this acne about 1 month." (P15, Transgender woman, 27 years old, 16 months on PrEP)

"I often forget, and not sure that much, but I more often forget to take pill in the some latest prescriptions, so I am worried that the medication will not work. […] Then I also had a sexual partner, he was not a lover but he was like a long-term partner. I used condom frequently, I did not have sex with any else but that partner." (P30, MSM, 37 years old, 7 months on PrEP)

b. Pill burden

Taking PrEP at the same time everyday creates a significant burden, especially for those who have been taking it for a long time. They were fatigued from doing the same thing over a long period of their life.

"It feels ok to take in the first year, when in the second year, I feel like, I am taking a lot, I feel bored so I do not want to take… I want to stop, because it has to be taken at fixed time. [...] Time is the main reason, the second is the low need of having sex." (P19, MSM, 35 years old, 27 months on PrEP since 2018)

"Sometimes I feel discouraged to take it [PrEP] for the rest of my life […] I was so frustrating when I think about it." (P33, MSM, 35 years old, 5 months mon PrEP since 2019)

c. Side-effects

Side effects were one of the most mentioned reasons for stopping the PrEP program. Though the side effects were not of the severe categories because we did exclude these patients, side effect did disturb the users for a long time, disrupted regular schedule (feel sleepy the whole day, or not sleep well) or in a way that they feel uncomfortable, especially increasing acne that affected participants' appearance. These participants seem to stay short in the program.

"But when I used it, I kept getting sleepy. I fell asleep while watching TV. I was not like that before. [...] I can feel its stomach boiling. I kept taking the drug but nothing changed. Every day I take, I suffer that, so I don't use it anymore. [...] Besides, I sweat a lot at night. So my sleep is not that good. For example, when I sweat at night, I am awake in the middle of the night, it will be very uncomfortable. Then, the mattress gets wet, the whole mattress is soaked too. So sometimes I have to change the sheets and then have to change clothes. Or maybe if I am more wake up, I take a shower." (P13, MSM, 25 years old, 3 months on PrEP)

"Around June [2020] I had a military term so I had to stop taking it for about a month. However, because of the another reason, after I finished taking it, it felt a bit hot inside, and then

my face got pimples, not to mention but I still feel a bit tired, or something similar in the morning right after taking the medicine. So I decided to stop." (P14, MSM, 19 years old, 2 months on PrEP)

d. Lack of motivation

While the majority of participants showed their clear motivation to initiate HIV PrEP, few participants did not. They just wanted to try PrEP to see how the mediation works or to help their friends to achieve the numbers of new PrEP users that they were requested by CBO or PrEP clinics.

"That thing is, "coincidentally" at the time I am using here [the first clinic], suddenly another friend asked me to register and take PrEP in another clinic. So I went to another site to take it." (P03, Transgender woman, 26 years old, 4 months on PrEP in two clinics)

"Basically, at that time [when I started taking PrEP] I thought that I had already had sex, so I try it, that's all. I knew at first that I will not take it for a long time. […] I'm sure I have a safe sex, but there is still a chance, a tiny chance, like a condom has broken during sex." (P20, MSM, 23 years old, 4 months on PrEP)

2) Institutional level

a. PrEP accessibility

PrEP services in Vietnam are only available in big cities such as Hanoi and HCMC, and in the central of the big cite, so it will be challenging for those who live in the suburban or rural areas to continue the treatment, or for those living in a province that did not have PrEP to access to PrEP.

"I think the clinic is fine right now, so is the PrEP medicine, so I think what I care about is going to get the medication and where to get it. Far distance and many provinces don't have PrEP, so they will be more afraid to travel. If more clinics are opened, the better." (P33, MSM, 35 years old, 5 months on PrEP)

No transferring system is available yet in Vietnam so one of our participants went to HCMC for a short training and discontinued PrEP because the clinic was far away from his accommodation and he did not receive adequate supports.

"I started taking PrEP in July or September [2019] or something, after 3 months I had to go to HCMC [for a three-month training], when I run out of the medication, my collaborator [in Hanoi] introduced me to a clinic to take the medication, the clinic was very far away the place I was living. I have arranged a time to get one bottle. After a time of lockdown, I texted and called, but no one answered." (P27, MSM, 28 years old, 4 months on PrEP)

Additionally, the working hours of the clinic discourage participants to refill the prescription. The majority of PrEP clinics were public so they open from 8 am to 4 pm, Monday to Friday.

"Some days I was free to come and pick it up but the clinic did not open, or did not open overtime [beyond the working hours], because of my job must be done during office hours. That's why going to get the medication is also a bit hard for me." (P02, MSM, 19 years old, 3 months on PrEP)

"There are a few times when I come to pick it up on a day the clinic is off, while that day is in the middle of the week. [...]I think the optimal time should be a full week. Sometimes opening on

Saturday and Sunday are better because these days are of people's free time, more of them can go." (P26, MSM, 20 years old, 11 months on PrEP)

b. Logistical difficulties

PrEP requires users to return to the clinic routinely for medical monitoring such as HIV tests, so some participants, especially among those who have been used PrEP for a longer time, commuting between their house and the PrEP clinic to refill the prescription is time-consuming.

"Take it is not difficult but going to refill it. […] Actually, my main cause of stopping PrEP is to be lazy to go, travel a lot of kilometers to go to the clinic." (P12, MSM, 35 years old, 10 months on PrEP)

"Another reason is that after I moved, I was far from [the PrEP clinic], so I wanted to stop. [...] I don't have a motorbike neither, so it's even further." (P15, Transgender, 27 years old, 16 months on PrEP)

The anticipated barrier, the distance between the participant's house and the clinic, seems to be more challenging when participants actually experienced it.

"[…] being lazy to go to the clinic is another reason. […] After I went to the clinic several times, I found that the clinic was actually far away [from my house]." (P08, MSM, 24 years old, 2 months on PrEP)

3) Social structural level

a. Cost due to the medication

In Vietnam, patients can receive HIV PrEP free of charge in Vietnam maybe till the end of next year depending largely on the availability of the international funds, so the medication cost was not an issue of dropping out from the program yet. However, some participants were aware of the financial burden in the future if they have to pay or co-pay for the medication. Some were willing to pay for the medication or related services but the cost should be affordable for them. Additionally, because a majority of the MSM population were young, the cost might be easy to over their affordability.

"I think it is okay if the price is reasonable. Because actually many of the community are students, in general they don't have enough economic resources to pay for the medication that are expensive. For example, if we can get a source of support that can minimize the cost of that medicine, I think there will be people who can buy and use the medication." (P09, MSM, 28 years old, 12 months on PrEP, full-time store assistance)

"With my economic condition right now, I think I can spend money to protect my health by using medication like that. But the one disadvantage is that it has to take quite long. If I take it every day and in a lifetime, I feel that the payment is not cheap." (P13, MSM, 25 years old, 3 months on PrEP, full-time dance teacher)

"I will accept [using PrEP] depending on how much it cost. If it is within my financial range, I will use, but if it exceeds my financial level, I will not participate." (P20, MSM, 23 years old, 6 months on PrEP. full-time insurance broker)

b. Stigma toward PrEP use

Stigma affects the quality of treatment and makes patients uncomfortable when visiting a clinic and when taking prep in front of others. The moral judgment of promiscuity is another factor contributing to stigma.

"If I answered it was the medication to prevent HIV transmission, right? Then they started to think: "Yeah, this guy must be seeing a lot of guys" or "He [our participant] might get infected [HIV] so he must take this medication." [...] Because my relationships are interrelated and so it affects my work and my life quite a bit, I have to hide it. Even if I tried putting PrEP in a smaller box, I didn't bring the whole bottle along, it was still the same." (P21, MSM, 27 years old, 18 months on PrEP)

"If I explain like that [a drug to prevent HIV], my parents surely know that I am like that [MSM]. Definitely everyone who hears about HIV freak out already, then surely people will think: you must do something so now you have to take preventive medication, you must be at very high risk so you are taking the drug. Then it will make me feel self-deprecation, self- inferiority. so I don't want to use it in front of people." (P26, MSM, 20 years old, 11 months on PrEP)

Participants experienced in lack of an LGBT-friendly environment, which then hesitate them access to care at such other clinics.

"They [nurses in a public hospital] don't respect me, a lot of nurses call my real name, they called me hey man, or bro, or dude." (P01, Transgender woman, 23 years old, 6 months on PrEP)

Our participants coped with that by explaining the purpose of PrEP, hiding the medication, or lying it as supplements. However, "PrEP" characters engraved on the pill makes the medication hard to hide. Some participants reported that they had to disclose their gender identity because people living with them noticed the characters on the pill and searched on the internet and then queried.

"When I was asked, I said that it was supplements.... usually, my family didn't ask any further questions. [...] Because I did not come out yet, I did not want to talk about this drug, because if anyone googles it, they will know what PrEP is for." (P04, MSM, 21 years old, 10 months on PrEP)

"I don't want to get many bottles, leaving that many bottles at home I am afraid that my family will notice. One bottle can be ok, but two or three bottles catch people' eyes easier, for example, when a family member clean the room, or friends come to hang out, they see it curious then ask… it is difficult to explain. [...] I usually put it [PrEP] in a drawer with lock." (P30, MSM, 37 years old, 7 months on PrEP)

However, after listening to the explanation, people persisted in not understanding because the more our participants explained, the more others were suspicious about the true purpose of PrEP.

"I see people are prejudice, old fashioned when they think that those who use PrEP are kind of going on in transient sexual relationships, or having sex with a lot of people. [...] Everyone sees me using it but people don't say it, but I know what they are thinking about my medication usage. So sometimes, I did not want to explain because the thought of Vietnamese people is the more we

explain, the more they disbelieve, or the more they explain, the more wrong they think about me." (P02, MSM, 19 years old, 3 months on PrEP)

Stigma and MSM-label can be due to how PrEP was advertised. Despite the fact that the medication is recommended for all people who are at higher risk for HIV infection, MSM are of the targeted population. It leads to the projection that those taking PrEP are MSM and therefore they are labeled as being at high risk of HIV.

"Actually, this drug is not for only MSM population, PrEP is also used for queer girl, like female prostitutes, they are still ok to take it, but so far this drug is still not known by many people [outside MSM community]." (P31, MSM, 29 years old, 6 months on PrEP)

"[…] I am the one who in the case of seeing my friends using [PrEP], I right away question whether my friend is gay or not (laughing)." (P26, MSM, 20 years old, 11 months on PrEP)

c. The impact of the COVID-19 epidemic on service continuation

The COVID-19 pandemic interrupted all services, including health care. The first confirmed COVID-19 case was identified in January 2020 in Vietnam. Since then, there were two waves of COVID-19 outbreak, one in March and the other in July. In March, due to several community transmission cases, the confinement order was imposed for approximately six weeks. People must strictly obey the stay-at-home order, only be allowed to go out for essential business. Not being excluded by the impact, our participants reported the COVID-19 pandemic was one of the reasons for stopping taking their medication.

"I think it [the COVID-19 pandemic] is the main reason that lead to that decision, it's more like a chance. Because I had idea to stop it anyway. Now, thanks to the epidemic, I have to stay

indoors anyway, so I don't take medicine anymore." (P18, MSM, 23 years old, living in Hanoi, 9 months on PrEP)

"I see there are both objective and subjective reasons. Objectively, it was due to the disease problem, so I couldn't get the medication, from there, the subjective reason is that I felt that I couldn't take PrEP for a while so when I come back I have to start from the beginning, it is very tired. Well, I said to myself that I don't take the medicine anymore, and also because I just broke up so I was very bored." (P26, MSM, 20 years old, not staying in Hanoi, 11 months on PrEP)

People who were not living in Hanoi stayed in their hometown where PrEP services were not available so they could not continue the treatment.

"During the time of COVID-19, I went back to my hometown and I did not bring medicine with me, so I stopped taking medicine." (P02, MSM, 19 years old, student, not living in Hanoi)

However, some clinics were flexible in delivering the medication to patients but it could not last long, patients still need to return to the clinic for clinical monitoring, such as HIV testing.

"During the time when COVID-19 occurred, for example, it was a very good thing that they gave me 4 bottles so that I did not be short of medication during that period of time." (P18, MSM, 23 years old, living in Hanoi, 9 months on PrEP)

"Well, that time I received PrEP without going to the clinic. That clinic did not open because of quarantine or something, but they sent to the address that I gave." (P13, MSM, 25 years old, 3 months on PrEP)

"I came back to my hometown around April [when national social distancing order was imposed]. I brought PrEP with me and used it until I run out, at that time I couldn't go get it, because if I go to [Hanoi], I had to quarantine for 14 days, right? [...] No, they [service providers] said I had to come in person, so I couldn't do that... Probably, other clinics, they have to do the same, they asked patients to return to run blood tests and then send medication, not only here." (P01, Transgender woman, 23 years old, not living in Hanoi, 6 months on PrEP)

Some were too afraid of going to health care settings to refill the prescription during the COVID-19 pandemic because doing that made them have higher chances of being contracted to the virus. Therefore, they decided to stop the treatment and reduce risk behaviors. Furthermore, during the first wave of COVID-19 in March 2020, the pandemic spread in one of the last-tier hospitals in Hanoi, which resulted in its closure for a month. That event was more likely to elevate the fear among our participants.

"[…] Besides, due to the [COVID-19] epidemic, I'm afraid to go out… Of course, without much going out, meeting others, the frequency of sexual activities decreased completely." (P30, MSM, 37 years old, living in Hanoi, 7 months on PrEP)

4) Attitude toward long-acting injectable PrEP

Long-acting injectable PrEP was highly aware of and highly acceptable among our study participants. Twenty-one (70%) ever heard about the new type of PrEP and after providing brief information about the long-acting injectable PrEP, most of them were willing to take PrEP if it is available in Vietnam (25 over 30 were willing and 1 were indeterminate). Those who knew the new medication received information from their peers, their service providers, social events.

"Actually, I heard about the injectable PrEP but I did not experience it on my own. I also heard that if you join the study in Yen Hoa clinic [the study site of HPTN083], half will receive the oral medication and the other half will be injected. Ngoc Ha gave me that information. At first she invited me to join. But I was busy, so I couldn't join. […] I do not learn carefully about the injection. I just knew that the injection is more directly into the body, and I do not have to drink that everyday, people just goes for routine injections." (P09, MSM, 28 years old, 12 months on PrEP)

"Injectable PrEP?... Yes, I heard about the injectable drug, I read it online, via Facebook and via friends. There were some of my friends using it, I have heard about PrEP injections from them." (P34, MSM, 25 years old, 6 months on PrEP)

However, maybe because long-acting injectable PrEP was not yet implemented in Vietnam, participants did not go further to look up information about it, and therefore, their knowledge about it was limited.

"Once I went out with a group of friends, I heard that one of them told that she had just received a shot. But I'm not sure so I don't ask. I just listen to it carelessly." (P08, MSM, 24 years old, 2 months on PrEP)

"That way [injection] it will be more convenient. I don't have to drink it every day, it's not like I have to drink every day. At that time, someone talked about injectable PrEP but I did not remember clearly because I did not pay much attention. It looks like it was just an injection, injecting every month or two months." (P16, MSM, 23 years old, 3 months on PrEP)

Among the concerns that participants expressed, side effects not only were the most mentioned but concerned most of the participants. Additionally, the medication is new so information about side effects is not prevalent and therefore participants seem to be more cautious about side effects.

"I'm 50% sure I'm ready to use that drug since the drug is new. First, I feel a bit more anxiety. The second, it is a substance that will be injected into my body, I fearly believe that it will affect my body at least something. And I'm a man of fear of injection, I don't dare to inject anything, I hate going to the hospital." (P02, MSM, 19 years old)

"I just worry about its [long-acting injectable PrEP] side effects only. Just worry about the side effects." (P06, MSM, 26 years old, 3 months on PrEP)

"Does it have any effect on your health? For example, it can make me fatigue or the feeling of being hot inside the body or is there any feeling that it is like an oral PrEP?" (P08, MSM, 24 years old, 2 months on PrEP)

Transgender participants who were using hormone replacement worried about the interaction between two medications, PrEP and hormone replacement therapy, and if it occurs, they preferred hormone replacement to HIV PrEP because the hormone is for the long run and more necessary to them.

"I've heard it for a long time, I heard it since November [2019], but I've already had hormone injections and now if I have one more injections, I'm afraid it will affect [the hormone], so I'm afraid of fighting each other […] I prefer hormones [to PrEP] because it's my life, I want to be a woman, I have to take hormones, so I can maintain everything to make me more feminine. If I

stop using it, I will be the man again." (P01, Transgender woman, 23 years old, 6 months on PrEP)

"The interaction [between PrEP and hormone] is very strong. Because PrEP has a stronger, more powerful substance, it will fight hormones and it will dissolve the hormone in my body and decrease that amount. […] My decision is whatever benefit for a long run should be prioritized. My priority is to use hormone therapy, which means longer periods of time." (P03, Transgender woman, 26 years old, 4 months on PrEP)

Pain due to the intramuscular injection makes long-acting injectable PrEP not suitable for everyone. Many of our participants strongly expressed their bad feeling and emotion about the pain due to injection. That rooted in their experiences in the past, which can be just due to their personality or could be due to service providers' skills when performing the procedure. Pain seems to be one of the major reasons for MSM to prefer oral to injectable administration, despite the benefits of long-acting injectable PrEP are over daily oral PrEP.

"Fear of injections! I knew the feeling when I got gonorrhea, I knew how painful it was to inject it [medication] into my butt. Medication to treat gonorrhea is kind of powder dissolved in water… it was so bitter. I'm like I'm haunted by that or something. So I felt terrible when seeing that needle, like I am going to be slaughtered as pig. So no injection, drink only. […] I have done a lot of blood tests, I used to it. But the needle for butt injection it too big. I am scared, really." (P12, MSM, 35 years old, 10 months on PrEP, intramuscular injections twice for gonorrhea)

"If I heard about butt injections or something injecting intramuscularly, I was already so scared and then I just want to give up. [...] Injections are very painful." (P23, MSM, 25 years old)

However, some who were afraid of injecting were willing to use the injectable PrEP after considering its potential advantages. They can apply some measures to overcome pain, such as using a pain killer before the follow-up visit.

"I feel worried about the pain only. Other than the pain, there should be nothing to worry about, because I have already taken PrEP so I know what side effects are, I think it will only be a flash pain for at most one day after injection. I don't think it can last every day. I think so. […] I guess I'm ready for the injection. I think I'll drink or will apply anesthetic or something before the injection." (P13, MSM, 25 years old)

"The advantage of injection is that the injection is faster, but the downside is that it hurts… So I am kinda hesitate. […] I will choose the Prep injection route because the injection will be ok, injection is fast, although it hurts but in a short time." (P19, MSM, 35 years old, HPTN08 participants, daily PrEP aim)

"For someone who doesn't like to inject like me, I don't like injectable PrEP. Because of the pain, I usually donated blood, I shouldn't have hated the injection, but in one blood donation, he [the nurse] poked several times to get blood, I guess he is new, he stabbed [the needle] in but did not reach the vein, then he pulled out, normally people slowly withdrawn but he pulled out so quick, and that made me a sharp pain [...] For me, if there is a need, I am ready to use it." (P20, MSM, 23 years old)

When comparing long-acting injectable PrEP and daily PrEP, there is no clear benefit regarding time participants have to spend for follow-up visits because, regardless of the route of administration, they must visit a clinic routinely for clinical monitors, for example, HIV testing and clinical examination. Additionally, for daily PrEP users, after the first two prescriptions, they

can get one prescription every three months. Therefore, daily oral PrEP users who retain in the PrEP program will not have to visit the clinic as frequently as injectable PrEP users.

"No, between the injection and the oral, I actually think they are the same [regarding follow-up visit]. Because the first time I took the oral PrEP, I was given 1 box, the second time I was given 2 boxes, the third time I was given 3 boxes, afterward every 3 months, I need to visit the clinic once, not every 2 months [like the injection]." (P01, Transgender woman, 23 years old)

"Regardless of injection, I still have to go to the clinic to get the prescription, so I think the time spent on taking the medicine is the same." (P02, MSM, 19 years old)

Many benefits of long-acting injectable PrEP were acknowledged. For example, it could provide a higher protection effect than daily oral PrEP, free of forgetting doses, avoid stigma related to PrEP pill. Beyond well-documented benefits, the injectable drug can eliminate the black market of PrEP so it can improve the effectiveness of PrEP for key populations.

"If that drug [long-acting injectable PrEP] was used in Vietnam, I felt that using it would be less time consuming in the process of using. During the management process, it will be 100% optimal, because if it is already injected into the body, there will be no missing or dumping as well as the chance that the drug is taken by many bad people and brought to the market for sale will no longer exist. And if the prevention it is higher, it will be very beneficial for the user, I think it would be much more accepted by the community." (P02, MSM, 19 years old, 3 months on PrEP)

Discussion

This study identifies the multi-level challenges that were related to PrEP discontinuation. At the individual level, four main themes emerged were risk behaviors and risk perception, pill burden, medication side effects, and lack of motivation to treatment. Pill burden and side effects have echoed the findings of previous studies (Arnold et al., 2017; Gombe et al., 2020). Resolution for this problem could be a less-demanding regimen. In addition to daily take the pill, individuals at "intermittent" risk (i.e., they engage in less sexual activities a week) can take event-driven PrEP. Although few interviewees reported they were lack motivation to continue PrEP in the beginning, this problem needs more attention. Because when the PrEP program is rapidly expanding, the number of people who start using PrEP might increase fast but the number of people who retain in treatment might not be a necessary increase, even decrease. That could result in a worse HIV preventive effectiveness because people at risk are not protected from the infection. In addition, the quota of new PrEP users might pressure on health workers and therefore, they have to recruit participants who might not be interested in PrEP. Therefore, it is necessary to increase communication and counsel patients about the options available at the clinic as well as the option that is the most suitable for them. It is noteworthy that people who discontinued due to no longer at risk of HIV but still need to be followed to restart the PrEP whenever they become at risk again (Rutstein, Smith, Dalal, Baggaley, & Cohen, 2020). Therefore, it is highly recommended to issue guidelines on how to make discontinuation safety and reengage discontinued patients.

At the institutional level, we observed challenges to access to PrEP care and logistical challenges such as transportation. Continuing to open more clinics and diversify the dispensing model may help reduce the drop-out rate, particularly, investing in the free community setting

model might be effective because the advantages of the model are "approachability" and "availability" (Lau, Hung, & Lee, 2020). For example, a novel model for PrEP care that was implemented in a community-based pharmacist setting, reporting a high in both initiation rate and retention rate, could be a promising candidate (Tung, Thomas, Eichner, & Shalit, 2018). A pharmacist-led program where clinical pharmacists were in charge of initial PrEP evaluation, PrEP prescription, and linking patients to clinicians could increase PrEP uptake and shorten the time to PrEP initiation (Khosropour et al., 2020). Such a model makes PrEP is more accessible to people who are not able to visit the traditional healthcare setting or where the PrEP system is not available yet. In addition, we found that the change in living place or workplace was one of the reasons for the treatment disruption. As PrEP becomes more widely available, a referral system for PrEP treatment, which can be similar to ARV referral where patients can request a refill in different clinics, should be established.

At the social level, the COVID-19 pandemic profoundly interrupted health care services so responsive plans for similar events in future need to be developed (Chenneville, Gabbidon, Hanson, & Holyfield, 2020). In light of other studies, our study findings reported that PrEP use was declined due to changes in risk behaviors, probably to avoid COVID-19 infection (Chow et al., 2020; Hammoud et al., 2020). Though some clinics were allowed to send medications to patients by mail, this is temporary and not systematic across the PrEP clinics in Vietnam. Therefore, structured and systematic strategies need to be devised to minimize the interruption of health service delivery, for example, applying telemedicine and revising policies (Quirke et al., 2020). Additionally, measures to protect patients who come for re-examination at health facilities should be focused to address patients' concerns about the risk of acquiring the infection. Some studies alerted that, after the end of the COVID-19 pandemic, the number of HIV or STI will

increase dramatically (Arafat, Alradie-Mohamed, Kar, Sharma, & Kabir, 2020; Sanchez, Zlotorzynska, Rai, & Baral, 2020); therefore, the impact of the COVID-19 pandemic on PrEP programs as well as other health services should be taken into consideration synchronously.

We found some differences between our study and previous studies. None of the participants reported they have any issues with the doctor's appointment for follow-up visits. It was contracted to Morgan's study which reported it was one of the primary reasons for PrEP discontinuation (Morgan, Ryan, Newcomb, & Mustanski, 2018). Additionally, due to PrEP medication is still free in Vietnam, we did not observe any challenges with the medication cost, which is often cited as a profound barrier to start and continue using PrEP from both service providers and service receivers' perspective (Emmanuel et al., 2020; Ezennia et al., 2019; Koechlin et al., 2017; Pleuhs, Quinn, Walsh, Petroll, & John, 2020). However, the funding cannot provide PrEP without charge perpetually, it is anticipated that patients will have to pay or co-pay after the next year. In fact, many of our participants were already aware of the policy and raised their concerns about the cost when the program is no longer subsidized. Therefore, it is crucial to greatly consider the financial burden in implementation plans. One promising strategy could be integrating PrEP in social health insurance like ART treatment.

Long-acting injectable PrEP seems to be quite well known among our studied MSM as well as they were willing to participate. However, individuals' concerns about the injection should be addressed. Two concerns standing out among them were pain related to intramuscular injection and side effects. More specifically, among transgender women who were using hormone therapy, they strongly concerned about the interaction between PrEP and hormones, and if any interaction occurs, hormones will be prioritized. Though the interaction is a myth, his attitude was replicated in other studies (Sevelius, Deutsch, & Grant, 2016; Sevelius, Keatley,

Calma, & Arnold, 2016). Pain from the intramuscular injection can originate from negative experiences that are possibly due to the technique of injection or from the fact that that type of injection is not a common procedure, or from the recalling of going to the hospital. Providing comprehensive information about the medication, particularly emphasizing on side effects, interaction with hormone therapy to patients, and pain, and thoroughly training staff who will administer the injection should be focused.

The study should be interpreted with its limitations. First, the study was conducted among individuals who ever received PrEP from clinics in Hanoi so some barriers in other provinces, for example, HCMC, might not be reported. Second, due to the inclusion criterion that our study eligible participants must take PrEP for at least two months, some distinctive reasons for individuals who used PrEP for only one month may not completely be captured. Third, the study only included individuals who were MSM or transgender women, so other at-risk populations might have different perspectives and attitudes to the challenges of the PrEP program.

Conclusion

The study highlighted multi-level challenges related to discontinuation of the PrEP program. At the individual level, challenges were risk perception, pill burden, side effects, and lack of treatment motivation; while at the institutional level, they were PrEP accessibility and logistical difficulties; and at the social level, barriers were stigma toward PrEP use, the impact of the COVID-19 pandemic, and cost due to the medication. Future research and intervention strategies should comprehensively address the challenges at different levels. Implementation of

long-acting injectable PrEP is supportive among our studied MSM, given the concerns of side effects and pain due to intramuscular injection.

Table 3.1. Demographic characteristics of the in-depth interview participants (N = 30)

	Count (%)
Age	
18 – 24 years	12 (40.0)
25 – 34 years	12 (40.0)
> 34 years	6 (20.0)
Received PrEP in a private clinic	16 (53.3)
Born in Hanoi	11 (36.7)
Currently single	17 (56.7)
Transgender	3 (10.0)
Full-time employment	23 (76.7)
Duration on PrEP	
0 – 3 months	8 (26.7)
4 – 6 months	10 (33.3)
7 – 9 months	3 (10.0)
10 – 12 months	5 (16.7)
> 12 months	4 (13.3)
Mean (SD)	8 (5.9)

Table 3.2. Challenges associated with PrEP discontinuation

Individual-level factors	Institutional-level factors	Structural-level factors
○ Sexual behaviors and risk perception ○ Pill burden ○ Side effects ○ Lack of treatment motivation	○ PrEP accessibility ○ Logistical difficulties	○ Cost due to the medication ○ Stigma toward PrEP use ○ The impact of the COVID-19 pandemic on service continuation

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Chapter 4: Factors Associated with Service Providers' Acceptability

Abstract

Background: Service providers play crucial roles in the implementation of the HIV PrEP program, so it is important to understand their attitude and concern about it. Vietnam piloted PrEP in 2017 and scaled up PrEP since 2019, but few studies about PrEP have been conducted in Vietnam, and even fewer studies among service providers. The study aims to evaluate the association between the acceptability of the PrEP program and concern about PrEP use among service providers in Vietnam. We hypothesized service providers who concern more about PrEP use are more likely to accept the implementation of the PrEP program.

Methods: A cross-sectional study was conducted in Hanoi, Ho Chi Minh City (HCMC), and Hai Phong in September 2020. Service providers individually completed an online questionnaire about their demographic characteristics, training and work experience, the acceptability of the PrEP program, concern about PrEP use, the awareness of PrEP-related information, comfort in performing clinical activities for MSM, stigma toward MSM, stigma toward PrEP users, institutional support, and job satisfaction. PrEP acceptability was measured by a two-item scale and concern about PrEP use was evaluated by a 17-item scale. The multiple linear regression model was used to investigate the association between PrEP acceptability and concern about PrEP use.

Results: There were 270 eligible service providers in 46 ART clinics participating the survey. The average age of the participants was 39 (SD: 9.4). The majority of the participants were from HCMC (66.3%), female (66.7%), counsellor (48.5%), ever received addiction training (72.6%), and ever provide PrEP-related service (68.2%). The average scores of PrEP acceptability and

concern about PrEP use were 8.6 (SD: 1.41) and 51.8 (SD: 10.06) respectively. In the multiple linear model, awareness of PrEP-related information (β = 0.04, 95% CL: 0.01; 0.07), stigma toward MSM (β = -0.04, 95% CL: -0.07; 0.0002), and job satisfaction (β = 0.02, 95% CL: 0.001; 0.04) were correlated with PrEP acceptability. However, no association between PrEP acceptability and concern about PrEP use were observed (β = 0.02, 95% CL: 0.001; 0.04).

Conclusion: PrEP acceptability was high among ART service providers and it was positively associated with PrEP awareness and job satisfaction but negatively associated with stigma toward MSM. Providing training related to PrEP and LGBT for service providers, more importantly for those who never provide or even know about PrEP, could improve the acceptability of the PrEP program.

Keywords: PrEP acceptability, concern, service provider, Vietnam

Introduction

Service providers play pivotal roles in the successful implementation of pre-exposure prophylaxis (PrEP) so understanding service providers' attitude toward and concern about the PrEP program is of importance (Krakower & Mayer, 2016). Similar to other bio-behavioral interventions, PrEP requires a wide range of health services, including screening, prescription, clinical examination, adherence counseling, supports, and education, that must be performed by healthcare professionals. Service providers might have high awareness and willingness to prescribe PrEP but a small proportion of them prescribed it (Krakower & Mayer, 2016; Pleuhs, Quinn, Walsh, Petroll, & John, 2020). A study of 1175 doctors in the US and Canada reported that a majority of the participants supported PrEP but only 9% had actually provided it (Karris, Beekmann, Mehta, Anderson, & Polgreen, 2014). The result was replicated in an online survey of 189 members and credentials of the American Academy of HIV Medicine. The study reported that 78% of the participants were aware of PrEP but only 19% had prescribed PrEP (Tellalian, Maznavi, Bredeek, & Hardy, 2013). Additionally, patient-provider interaction is crucial in any type of treatment. In the PrEP program, screening is the first step to initiate PrEP treatment. An online survey of 1,394 men who have sex with men (MSM) reported that 43% of the participants were not comfortable discussing homosexual behaviors with their primary care providers (PCP) and 76% believed that their PCP would not be willing to prescribe PrEP (D. Krakower et al., 2015). A qualitative study of providers, administrators, and case managers in South Florida reported that they hesitated to bring up sexual topics and affirmed that other providers will feel the same (Doblecki-Lewis & Jones, 2016). Recently, a study conducted in the Netherlands including 209 STI professionals and HIV specialists found that the acceptability of the PrEP

program was only moderate (Bil et al., 2018). That moderate level of acceptability may impede the implementation of the PrEP.

PrEP was first piloted in 2017 in Vietnam among at-risk populations, for example, MSM, partners of HIV-infected people who are not in ART, and transgender women. Given the demonstration project showed high acceptable and high efficacy (VMOH, 2018), the PrEP program started scaling up nationwide. As of 2019 PrEP was available in 43 clinics (35 public and 8 private clinics) in 11 cities/provinces in Vietnam (VAAC, 2019) but the number of people who used PrEP accounted for a small proportion of at-risk populations, thought the number exponentially increased (Nguyen & Green, 2019). In Vietnam, PrEP is delivered via two official models. The first model is via a private clinic, which is often led by MSM or has staff who is in the LGBT community. The second model distributes PrEP via a public clinic, which is run by the government (ART clinics - OPC) and accounts for the majority of the PrEP clinics. The second model outnumbers the first model because of the priority in integrating PrEP into HIV-related clinics, for example, outpatient clinics (OPC, a clinic that provides ART, also called as ART clinic). The reasons for prioritizing are that ART clinics are more sustainable and already meet all the requirements for prescribing PrEP – a combination of ARV medications. For example, an ART clinic has an established reporting system, qualified HIV testing facilities, trained health care workers who can perform and counsel HIV test, and trained physicians who can prescribe antiretroviral drugs.

Little is known about service providers' attitude and their concerns about the PrEP program in Vietnam. Therefore, we conducted this study to investigate the association between the acceptability of the PrEP program and concern about PrEP use. We hypothesized that service

providers who express more concern about PrEP use are less likely to accept the implementation of the PrEP program.

Methods

Study participants

The cross-sectional survey was implemented in Hanoi, Ho Chi Minh City (HCMC), and Hai Phong in September 2020. These three cities are among the most populated MSM and have the highest number of service providers in Vietnam. Hanoi and Hai Phong are located in the northern part of Vietnam, while HCMC is in the south. MSM population in HCMC is the biggest in Vietnam, it was an estimate of 37,000 in 2017 (Safarnejad, Nga, & Son, 2017); MSM population in Hanoi ranked second with an estimation of 30,417 and Hai Phong MSM population was approximately 3,300 people (Vo et al., 2019).

All service providers who were physicians or physician assistants, counselors or educators, and pharmacists in 46 ART clinics were invited to participate in this survey. Inclusion criteria were 18 years old or above, directly providing services to MSM, and working for at least three months in the clinics. Exclusion criteria were temporarily working in ART clinics as interns/residences, or leave of absence (for example, maternity leave). The study was approved by the Institutional Review Boards of the University of California, Los Angeles, the United States, and of Hanoi Medical University, Vietnam.

Data collection

Data collection was conducted online. We collaborated with Centers for Disease Control and Prevention at selected cities and heads of ART clinics to obtain the roster of potential service

providers. They then were approached by email or phone call to inform about study objectives, procedures, risks, and benefits as well as voluntariness. Service providers who agree to participate were received a structured questionnaire via email to self-administer. Participants who could not self-administer were interviewed by our study staff via phone call or Zoom. The survey included three sections. The first section provided the study information, emphasizing privacy, and voluntariness. The second section was a set of questions evaluating study eligibilities. Responders who were identified as eligible were asked to give consent for participation. Those who agreed to participate then self-answered questions in the third section. Our staff was available via Zoom or phone call to address any question composed by participants.

The questionnaire was created using the KoBoToolbox platform and separately implemented for each city. The assessment took between 30 to 45 minutes to complete. After finishing the questionnaire, each participant was received 150,000 VND via bank transfer or phone card (approximately 7 USD) for their time and effort.

Measures

The acceptability of the PrEP program, the outcome variable, was measured by two questions ("I am willing to provide PrEP-related services" and "PrEP should be implemented in Vietnam as a new HIV intervention strategy"). Each question offered a 5-point scale, ranging from 1 = "completely disagree" to 5 = "completely agree". The higher sum of scores indicated higher levels of acceptability.

PrEP awareness was assessed by 9 questions asking whether responders were aware of PrEP-related information such as the guideline or regulation about PrEP, clinics that can provide

PrEP, the procedure of PrEP provision and follow-up, PrEP side effects, and so forth (Table 4.1). We adapted this scale from Bil and colleagues' work (Bil et al., 2018). Participants rated on a scale of 5, from 1 = "Very poor" to 5 = "Very good" to reflect how aware they were for each of the PrEP-related information. The score was then summed, and the higher score indicated a higher awareness of the PrEP program.

Comfort in performing clinical activities for MSM was measure by a 6-item scale (Cronbach's alpha = 0.94). Each item in the scale is a clinical activity that is important precursors to PrEP provision, for example, discussing sexual orientation, sexual activities, HIV risk assessment (Table 4.2). The scale was adapted from an 8-item scale originally used among physicians, nurse practitioners, and physician assistants in the US (Petroll et al., 2017). Five-point Likert scales, from 1 = "completely uncomfortable" to 5 = "completely comfortable", measured participant's level of comfort when performing each clinical activity for MSM. The score was summed, and a higher total score indicated a higher level of comfort in performing clinical activities for MSM.

Stigma toward MSM was assessed by a 10-item scale (Cronbach's alpha = 0.73). The original scale was the Provider Perception Inventory that had 39 items evaluating health services providers' stigma toward three aspects, namely, HIV/AIDS, substance use, and MSM (Windsor, Benoit, Ream, & Forenza, 2013). Participants completed all items on a 5-point Likert scale with responses ranging from 1 = "completely disagree" to 5 = "completely agree". Before summing the score, two questions were reverse-coded were "I believe that discussing sex can be normalized" and "MSM clients feel comfortable participating in services". A higher summed score indicated a higher level of stigma toward MSM.

Stigma toward PrEP users was measured by a six-item instrument from Kambutse and colleagues (Kambutse, Igiraneza, & Ogbuagu, 2018). The instrument questioned responders' attitude toward people using PrEP. Responses ranged from 1 = "completely disagree" to 5 = "completely agree". The codes of two of the six items were reversed ("If a patient was taking PrEP, that patient would feel comfortable telling a close friend", and "My patients would feel comfortable telling others that they are taking PrEP"). The overall score was constructed by summing scores of all the items, with higher scores indicating higher levels of stigma toward PrEP users (Cronbach's alpha = 0.64).

Concern about PrEP use was assessed by a 17-item scale, adapted from Kambutse and Petroll (Kambutse et al., 2018; Petroll et al., 2017). The scale inquired different topics of PrEP use, for example, cost of the PrEP, short-term or long-term side effects for PrEP users, an increase of HIV-drug resistance, an increase of condom-less sex while using PrEP. The items are presented in Table 4.5. Participants were asked to rate each of the items on a 5-point Likert scale (1 = "completely disagree" to 5 = "completely agree"). A higher score indicated more concern about PrEP use. (Cronbach's alpha = 0.89)

Institutional support was measured by a 4-item scale. The questions were "Generally speaking, your supervisor thinks much about your own protection", "ART drugs are available for post-exposure prophylaxis if occupational exposure happens", "You would have sufficient health insurance coverage if you were infected with HIV on your job", and "Providers at your clinic can remain confidential if occupational exposures happen to them". This scale was adapted from previous work that was implemented in China and Vietnam (Li, Liang, Wu, Lin, & Wu, 2008). The original scale was specially developed to evaluate the availability of support for service providers working in HIV/AIDS, including HIV-protection supplies, or post-exposure

prophylaxis testing and treatment. Each item was rated on a scale of 5, from 1 = “completely disagree” to 5 = “completely agree”. The higher summed score indicated more institutional support. (Cronbach’s alpha = 0.73)

Job satisfaction was measured by a 23-items scale (Bellingham, 2004). The scale evaluated job satisfaction in different aspects, for example, motivation to work, interaction with colleagues, and self-fulfillment. Response categories ranged from 1 = "completely disagree" to 5 = "completely agree". All scores were summed, and a higher total score indicated more satisfaction with the job. (Cronbach’s alpha = 0.94)

All aforementioned scales were piloted in a sample of 10 people including service providers and experts in the field. Their feedback was used to improve the cultural appropriateness and the Vietnamese translation of the scale. In addition, service providers’ demographics, job-related characteristics, and experience on HIV treatment and PrEP program were collected. Demographic information included age, gender, and ethnicity. Job-related information included the name of the clinic, the current position in the clinic, length of work, and years of medical training. Experience in HIV and PrEP programs included years of work in the field, training in HIV and PrEP programs, experience in PrEP-related services (e.g., receiving questions or counseling PrEP from clients/patients in the past 6 months, ever prescribe PrEP for physicians), willingness to prescribe PrEP for those who have never prescribed and the number of patients served.

Data analysis

The dataset was downloaded from the KoboToolbox server in an excel file and then was imported to SAS version 9.4 (SAS Institute, Cary, NC) to manage and analyze. For continuous

variables such as age or scales, mean and standard deviation were reported. For categorical variables such as gender and job position in the clinic, frequency and percentage were reported.

The correlation matrix was used to explore the relationship among continuous covariates and the outcome variable (the acceptability of the PrEP program). A multiple regression model of the acceptability of the PrEP program on service providers' concerns toward PrEP use was fitted, controlling for covariates. Covariates in the final model were selected based on the literature and based on their correlation in the dataset. Model fitting and model diagnoses of the final model were evaluated, including influential points, model assumptions (homoscedasticity, linear relationship, normality of residual errors). Model results were reported with the estimate of coefficients (β), 95% confidence limits, and p-values. The statistically significant level was set at 0.05 ($\alpha = 0.05$).

Results

Hanoi, HCMC, and Hai Phong had a total of 59 ART clinics. Of them, 13 were excluded from the study because they were in a hospital or in jail so could not be potential for providing PrEP (Figure 4.1). Among 46 clinics, nearly two-third (29 clinics) were providing PrEP to patients. Among eight ART clinics in Hanoi that had the PrEP program, two newly started the program in September 2020. One of two clinics that were providing PrEP in Hai Phong launched the PrEP program in August 2020. HCMC had the broadest PrEP program, as showed by the highest number of PrEP clinics as well as the highest percentage of PrEP clinics among ART clinics (19/24, 79.2%). Additionally, two new PrEP clinics will be opened by the end of October 2020.

Figure 4.2 presents the recruitment of the study participants. There was a total of 288 service providers working in 46 ART clinics in three study sites. Of them, nine refused to participate in the survey after three attempts. Among 279 service providers who agreed to participate, nine were ineligible because of insufficient time working in the clinic (3 service providers) and not directly providing services to MSM (6 service providers).

Socio-demographics and professional characteristics of the study participants

Table 4.6 presents the demographic characteristics of the study participants. Among 270 responders, most were from ART clinics in HCMC (66.3%), followed by Hanoi (21.5%) and Hai Phong (12.2%). The study sample included 131 counselors (48.5%), 63 pharmacists (23.3%), and 76 physicians or physician assistants (28.2%). The average age was 39.0 (SD 9.4) and approximately one-third of the participants were younger than 35 years old. Female service providers were double male service providers (66.7% vs 33.3%). Kinh ethnicity was the most popular (97.4%). Slightly more than half of the participants had more than four years of training in medical school (51.1%) and of them, most were physicians or physician assistants (72, 52.2%).

Tables 4.7 and 4.8 show the professional characteristics and PrEP-related experience of the service providers. The average year service providers working in the current clinics and HIV/AIDS field was 9.3 (SD 6.3) and 7.7 (SD 5.6), respectively. Hanoi and Hai Phong had more new staff in the HIV/AIDS field; service providers who worked less than five years in the field accounted for 51.7% in Hanoi and 63.8% in Hai Phong; while it accounted for 34.6% in HCMC (data not showed). The median of time working with the LGBT population was three years. The majority of the participants ever received training about substance use disorder (72/6%), about

the LGBT population (71.9%), and about PrEP-related services (78.2%). Among 184 participants who ever provided PrEP-related services to patients, the median of patients who provided services a month was 23 (IQR: 10 – 50). Among 50 physicians who ever prescribed PrEP, the median of patients they prescribed a month was 20 (IQR: 10 – 32).

Description of scales of interest

Table 4.9 reports the average score and standard deviation of service providers' acceptability of the PrEP program and its potentially related factors, which were PrEP awareness, comfort in performing clinical activities for MSM, stigma toward MSM, stigma toward PrEP users, concern about PrEP use, institutional support, and job satisfaction. PrEP acceptability had a mean of 8.6 and a standard deviation of 1.4; its median was 8 and nearly one in ten subjects had a total score of 7 or below. Haft of the participants was scored 53 and below in the concern about the PrEP use scale and its mean was 51.8 (SD: 10.1).

Table 4.10 presents bivariate comparisons between continuous variables and PrEP experience (ever vs. never providing PrEP-related services). Participants who ever provided PrEP had higher levels of awareness of PrEP-related information and institutional support but had lower levels of stigma toward MSM, stigma toward PrEP users, and concerns about PrEP use, as compared to those who never provided PrEP (p-values of t-tests < 0.05). No statistical difference in PrEP acceptability, comfortable in discussing sexual topics with MSM, and job satisfaction was found (p-values of t-tests ≥ 0.05).

Correlation of PrEP acceptability and scales of interest

Table 4.11 presents the correlation coefficients and p-values of every pair of eight continuous variables, including the outcome variable. The acceptability of the PrEP program was positively associated with awareness of PrEP-related information ($r = 0.18$, $p = 0.003$), comfort in performing clinical activities for MSM ($r = 0.21$, $p = 0.001$), institutional support ($r = 0.31$, $p < 0.001$), and job satisfaction ($r = 0.21$, $p < 0.001$), and negatively associated with stigma toward MSM ($r = -0.19$, $p = 0.002$) and stigma toward MSM users ($r = -0.15$, $p = 0.012$). The correlation between PrEP acceptability and concern about PrEP use was very weak and non-significant ($r = -0.03$, $p = 0.650$).

Concern about PrEP use was moderately correlated with job satisfaction ($r = 0.44$, $p < 0.001$). It was weakly inversely correlated with awareness of PrEP-related information ($r = -0.24$, $p < 0.001$) and comfort in performing clinical activities for MSM ($r = -0.18$, $p = 0.003$) but weakly positively related to stigma toward MSM ($r = 0.34$, $p < 0.001$), and stigma toward MSM users ($r = 0.26$, $p < 0.001$).

Factors associated with PrEP acceptability

Table 4.12 reports estimated coefficients and confident limits of covariates in the multiple linear regression model of PrEP acceptability on concern about PrEP use. After adjusting for covariates, no association between the acceptability of the PrEP program and concerns toward PrEP use was observed. However, a higher level of awareness of PrEP-related information was related to a higher level of the acceptability of the PrEP program ($\beta = 0.04$, 95% CL: 0.01; 0.07). Similarly, participants who were more satisfied with their job had higher levels of the acceptability of the PrEP program ($\beta = 0.02$, 95% CL: 0.002; 0.04). Contradictory, stigma

toward MSM were negatively associated with PrEP acceptability (β = -0.04, 95% CL: -0.08; -0.002).

Discussion

It is one of the few studies conducted in Vietnam investigating the association between service providers' attitude toward HIV PrEP program and concern about its use. Our study achieved a high response rate among service providers who were working in ART clinics in Hanoi, HCMC, and Hai Phong city in Vietnam. The study found that service providers were at a high level of acceptability, demonstrating a high average acceptability score (the average score was 8.6 while the maximum score was 10). However, it was different from the result reported in Bil and colleagues' study conducted in the Netherlands: The acceptability level was only moderate among STI professionals and HIV specialists (Bil et al., 2018). The difference could be largely due to the time when data were collected. In the latter study, the survey was conducted from January to August 2015 when PrEP was just recommended by WHO to use among at-risk populations, and more importantly, PrEP was not yet routinely available in the Netherlands (Bil et al., 2018). While in our study, data collection occurred during September 2020, five years after the WHO recommendation. Additionally, our study participants might overrate their acceptability just due to social desirability, a common phenomenon in health care research (Larson & Bradshaw, 2017; Latkin, Edwards, Davey-Rothwell, & Tobin, 2017). Though a high level of acceptability among ART service providers in Vietnam was observed, it still needs to be improved. A high level of acceptability can be a positive indicator for the PrEP implementation but one caution should be noted, that is, the positive attitude toward PrEP might not be actually correlated to provide PrEP services (Karris et al., 2014; White, Mimiaga, Krakower, & Mayer, 2012).

Concerns about PrEP use was not associated with the acceptability of the PrEP program in the multiple regression model. It is not in light of our hypothesis that concern about PrEP is negatively related to the PrEP acceptability. In the bivariate comparison, we observed a higher level of concerns among service providers who never provided PrEP-related services than those who ever provided. The results suggested that the anticipated concern about PrEP use of service providers diminished once they actually provide it. Concerns about PrEP use in our study encompassed different aspects, for example, side effects of PrEP, drug resistance, or changes in sexual behaviors and STI rate, so it can be seen as challenges for the PrEP implementation. Bil and colleagues reported the negative association (Bil et al., 2018), and they highlighted concerns was about changes in sexual behaviors and STI diagnoses, which are still debatable because of mixed results (Liu et al., 2016; Marcus et al., 2016; Montano et al., 2019).

In order to increase PrEP acceptability among service providers in Vietnam, awareness of PrEP-related information, stigma toward MSM, and job satisfaction are barriers that need to be addressed. Stigma toward MSM and PrEP awareness can be changed by providing information about PrEP and MSM population via training or other channels. Health care professionals reported that after knowing PrEP knowledge and skills, 91% would discuss PrEP with patients, and 85% would prescribe PrEP (Petroll et al., 2017). The sigma toward MSM is not new and has been persisting in HIV/AIDS care for a long time. Service providers' stigma can aggravate fear in the MSM population and impede the likelihood that MSM seek and receive services (Valdiserri, 2002; Washington & Brocato, 2011). Because more and more MSM need to access the treatment, reducing the stigma becomes more important. Additionally, the undue burden of the HIV epidemic among the MSM population might increase stigma from the community

toward MSM. From the perspective of service receivers, MSM reported one of the facilitators for the PrEP program is MSM-friendly providers (Wong et al., 2019).

This study should be interpreted in light of several limitations. First, the data were collected online so there was a chance of misinterpreting questions. However, we believe it was minimal because we piloted the questionnaire before data collection, and responders were emphasized that our study staff was always available to provide clarification. In fact, of 270 participants, 7 were interviewed by our staff via phone due to their limits in technologies. Second, service providers might be more likely to select desirable answers for questions related to their job or their attitude such as PrEP acceptability or stigma toward MSM. Finally, the study survey among service providers working in the ART clinic in three big cities of Vietnam so the study findings might not be applicable to service providers working in different settings or other cities.

Conclusion

The acceptability of the PrEP program among service providers working in ART clinics in Vietnam was high. By examining the acceptability of the PrEP program, this study identified opportunities to improve PrEP quality and to expand the PrEP program. The awareness of PrEP-related information and job satisfaction were positively associated with the acceptability of the PrEP program while stigma toward MSM was negatively associated with the acceptability. Studies about the relationship between PrEP acceptability and concern about PrEP use among service providers should be conducted to provide insight information on why concern about PrEP use was not correlated with PrEP acceptability among service providers. Training that focuses on PrEP and MSM population should be provided for service providers in ART clinics

regardless of their PrEP experience because it could not only reduce the stigma toward the MSM population but also the concern toward PrEP use. Providing more supports to increase job satisfaction could enhance service providers' acceptability.

Table 4.1. Scale to measure PrEP awareness

1	National guidelines for PrEP treatment
2	Locations that can provide PrEP
3	Procedures to provide PrEP
4	Indication and contraindication of PrEP
5	PrEP follow-up procedure
6	Currently available PrEP regimen
7	Knowledge about PrEP efficacy
8	The frequency or severity of side effects
9	Ability to inform or discuss PrEP with patients
10	Knowledge about MSM population

Table 4.2. Scale to measure comfort in performing clinical activities for MSM

1	Discussing sexual orientation
2	Discussing sexual activities
3	Screening for sexually transmitted infections (STIs) and HIV
4	Assessing HIV risk
5	Providing risk reduction counseling
6	Diagnosing acute HIV

Table 4.3. Scale to measure stigma toward MSM

1	I would be upset if I learned that my brother or sister was homosexual
2	Gay men are either feminine or on the "down low."
3	I believe that discussing sex can be normalized (Reversed coding)
4	Real men don't show their emotions
5	MSM have opposite-sex relations to "keep up appearances"
6	I would feel uncomfortable being seen in a gay bar
7	I would feel that I had failed as a parent if I learned that my child was gay
8	Gay men are “weak”
9	In my workplace there is no safe space for MSM
10	MSM clients feel comfortable participating in services (Reversed coding)

Table 4.4. Scale to measure stigma toward PrEP users

1	If a patient was taking PrEP, people would think less of that patient
2	If a patient was taking PrEP, people would avoid that patient
3	If a patient was taking PrEP, that patient would feel comfortable telling a close friend
4	If a patient was taking PrEP, the patient would think less of oneself
5	If a patient was taking PrEP, people will think that patient has HIV
6	My patients would feel comfortable telling others that they are taking PrEP

Table 4.5. Scale to measure concern about PrEP use

1	Adherence to PrEP will be insufficient to prevent HIV infection
2	The use of PrEP will lead to an increase in STIs
3	The costs of PrEP are a problem
4	I would worry that some people have to use PrEP life long
5	It is unethical to prescribe antiretroviral therapy to healthy individuals
6	I'm worried about the long-term side effects of PrEP
7	I'm worried about the short-term side effects of PrEP
8	I am concerned that PrEP will not protect patient 100%
9	I am concerned about the potential side effects of PrEP for my patients
10	I think patients will not be interested in PrEP
11	I think patients will not adhere PrEP
12	I think patients will come to the clinic monthly to get PrEP
13	I am concerned that patients will not use condoms if they take PrEP
14	I am concerned that patients will have more sexual partners if they take PrEP
15	I am concerned that patients using PrEP will no longer get tested for HIV
16	I am concerned that taking PrEP continuously would be too expensive for patients
17	I am concerned that using PrEP would cause HIV drug resistance

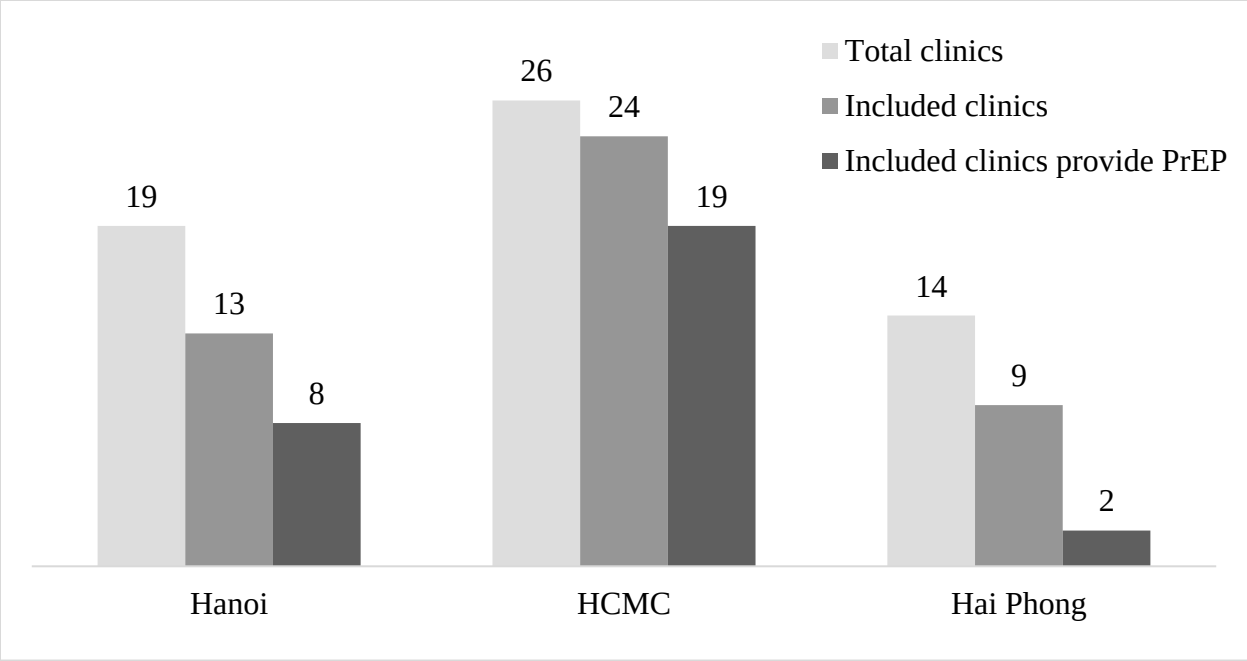

Figure 4.1. The number of clinics in study 3 and the PrEP ability among them

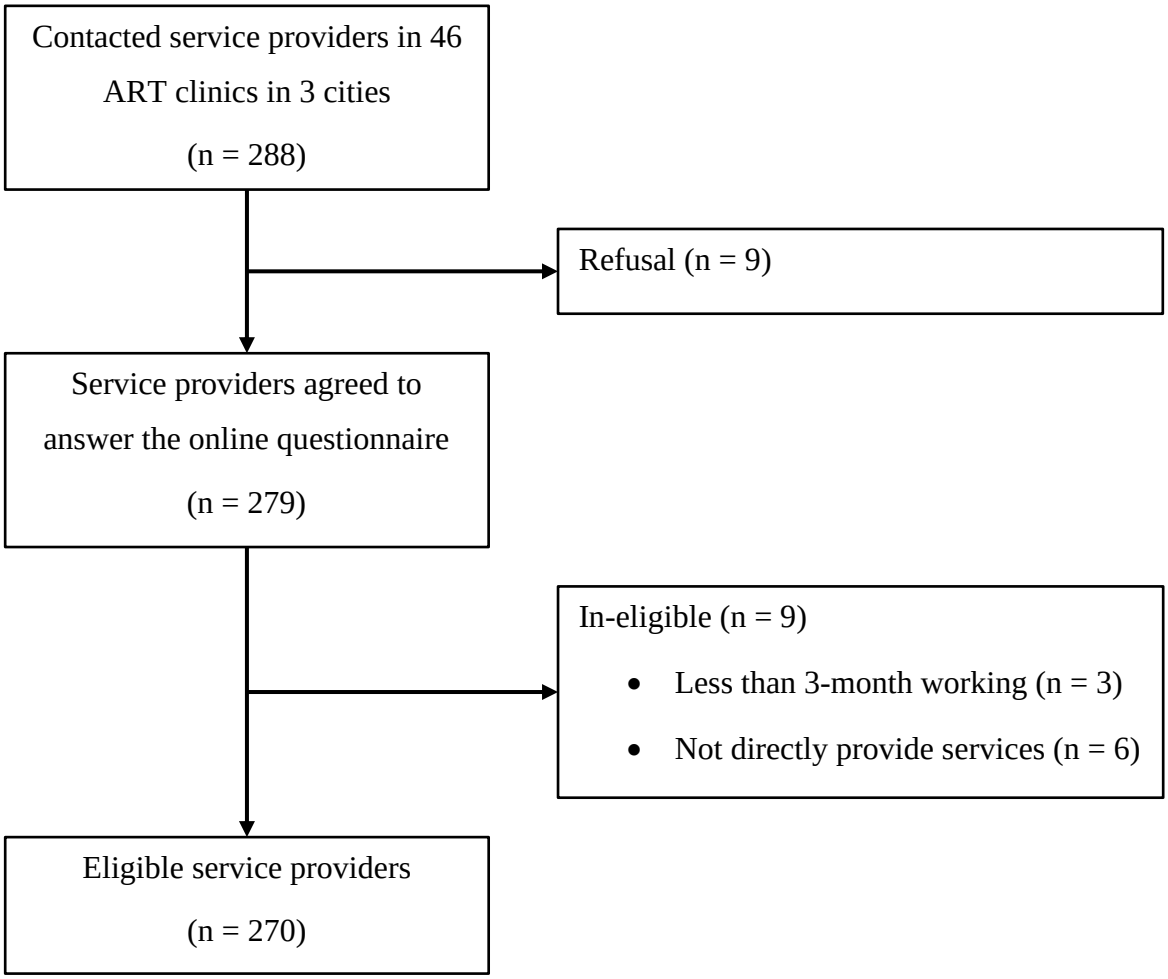

Figure 4.2. The recruitment process of the study participants

Table 4.6. Demographic characteristics of the study participants (N = 270)

	Count (%)
Participants in each site	
Hanoi	58 (21.5)
Ho Chi Minh City	179 (66.3)
Hai Phong	33 (12.2)
OPC position	
Counselor or Pharmacist	164 (71.8)
Physician or Physician assistant	76 (28.2)
Age	
18 – 34 years	99 (36.6%)
35 – 44 years	103 (38.2)
>44 years	68 (25.2)
Mean (SD)	39.0 (9.4)
Gender	
Male	90 (33.3)
Female	180 (66.7)
Ethnicity	
Kinh	263 (97.4)
Other	7 (2.6)
Highest medical education	
College or lower (≤ 3 years)	132 (48.9)
Graduate (≥ 4 years)	138 (51.1)

Table 4.7. Professional characteristics of the study participants (N = 270)

	Count (%)
Time in the current clinic	
<5 years	76 (28.2)
5-10 years	69 (25.6)
>10 years	125 (46.3)
Mean (SD)	9.3 (6.3)
Time in the HIV field	
<5 years	113 (41.9)
5-10 years	57 (21.1)
>10 years	100 (37.0)
Mean (SD)	7.7 (5.6)
SUD-related training	
Never	74 (27.4)
Ever	196 (72.6)

Table 4.8. PrEP-related experience of the study participants (N = 270)

	Count (%)
Time working with LGBT population	
<5 years	181 (67.0)
5-10 years	52 (19.3)
>10 years	37 (13.7)
Median (IQR)	3 (1 – 6)
LGBT training	
Never	76 (28.1)
Ever	194 (71.9)
PrEP training	
Never	59 (21.8)
Ever	211 (78.2)
Provide PrEP-related services to patients	
Never	86 (31.8)
Ever	184 (68.2)
Among 184 service providers, number of patients they provided PrEP-related services a month (median, IQR)	23 (10 – 50)
Among 184 service providers, number of MSM patients they provided PrEP-related services a month (median, IQR)	15 (5 - 30)
Prescribe PrEP among physicians (n = 76)	
Never	26 (34.2)
Ever	50 (65.8)
Among 50 physicians, number of patients they prescribed PrEP a month (median, IQR)	20 (10 – 32)
Among 50 physicians, number of MSM patients they prescribed PrEP a month (median, IQR)	11 (6 – 27)

Table 4.9. The description of the scale used in the study

	Number of items (score range)	Mean (SD)	Min – Max
PrEP acceptability	2 (1-5)	8.6 (1.41)	2 - 10
PrEP awareness	9 (1-5)	28.2 (7.58)	9 - 45
Comfort in performing clinical activities for MSM	6 (1-5)	24.5 (3.70)	6 - 30
Stigma toward MSM	10 (1-5)	24.9 (5.05)	11 - 37
Stigma toward PrEP users	6 (1-5)	13.8 (2.87)	6 - 23
Concern about PrEP use	17 (1-5)	51.8 (10.06)	17 - 85
Institutional support	4 (1-5)	16.1 (2.22)	6 - 20
Job satisfaction	23 (1-5)	91.4 (9.82)	51 - 115

Table 4.10. Comparisons of PrEP acceptability and interested variables among service providers who never or ever provided PrEP (n = 270)

	Never provide PrEP (n = 86)	Ever provide PrEP (n = 184)	p-value of t-test
PrEP acceptability	8.4 (1.48)	8.6 (1.37)	0.2751
Awareness of PrEP-related information	22.1 (7.12)	31.0 (5.97)	<0.0001
Comfortable in discussing sexual topics with MSM	23.9 (4.20)	24.8 (3.40)	0.0807
Stigma toward MSM	26.4 (4.23)	24.2 (5.18)	0.0008
Stigma toward PrEP users	14.4 (3.27)	13.6 (2.63)	0.0466
Concern about PrEP use	54.9 (9.31)	50.4 (10.10)	0.0005
Institutional support	15.7 (2.17)	16.3 (2.23)	0.0436
Job satisfaction	90.8 (11.1)	91.7 (9.20)	0.4627

Table 4.11. The correlation matrix of PrEP acceptability and continuous covariates (n = 270)

	1	2	3	4	5	6	7
1. PrEP acceptability							
2. Awareness of PrEP-related information	0.181[b]						
3. Comfortable in discussing sexual topics with MSM	0.206[c]	0.310[c]					
4. Stigma toward MSM	-0.190[b]	-0.275[c]	-0.229[c]				
5. Stigma toward PrEP users	-0.153[b]	-0.201[c]	-0.127[b]	0.393[c]			
6. Concern about PrEP use	-0.028	-0.236[c]	-0.178[b]	0.338[c]	0.261[c]		
7. Institutional support	0.312[c]	0.217[c]	0.142[b]	-0.228[c]	-0.187[b]	-0.097	
8. Job satisfaction	0.214[c]	0.258[c]	0.227[c]	-0.273[c]	-0.252[c]	-0.113	0.438[c]

[a]$p<0.05$; [b]$p<0.01$; [c]$p<0.001$

Table 4.12. The multiple regression model of PrEP acceptability on concern about PrEP use (n=270)

	β	95% CL	p-value
Physician/Physician assistant vs. Counselor/Pharmacist	-0.08	-0.59; 0.43	0.7670
≥ 4 years medical education vs. Lower	-0.18	-0.60; 0.22	0.3751
Ever provide PrEP vs. Never	-0.13	-0.56; 0.30	0.5523
Concern about PrEP use	0.01	-0.01; 0.03	0.2402
Awareness of PrEP-related information	0.04	0.01; 0.07	0.0199
Stigma toward MSM	-0.04	-0.08; -0.002	0.0350
Job satisfaction	0.02	0.002; 0.04	0.0277

The model was adjusted for study sites, participants' age (years, continuous), gender (male vs female), and time in HIV/AIDS field (< 5 years, 5-10 years, > 10 years).

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Chapter 5: Summary

This study timely investigated the challenges related to the PrEP care continuum among men who have sex with men (MSM). Studying both service receiver and service providers and using the mixed-method design, we were able to identify complex, multi-level factors associated with PrEP implementation.

Regarding PrEP initiation stage, reporting gender identity, no ATS use, having multiple sexual partners, and ever tested for HIV were associated with increasing PrEP uptake. Regarding PrEP continuation stage, addressing challenges from different levels could mitigate the high drop-out rate. In the individual level, we found the challenges included risk perception, pill burden, side effects, and lack of motivation to treatment. In the institutional level, the challenges were PrEP accessibility and logistical difficulties. In the structural level, cost due to the medication, stigma toward PrEP use, and the impact of the COVID-19 pandemic on health service delivery barricaded the PrEP service continuation. Additionally, the PrEP implementation can be strengthened by interventions targeting service providers. Increasing their awareness of PrEP information and their job satisfaction as well as decreasing stigma toward MSM, interventions could enhance service providers' acceptability of the PrEP program. Beyond the daily oral PrEP, we timely explored MSM attitude toward long-acting injectable PrEP, which has been recently demonstrated as effective in HIV prevention in HPTN083 and HPTN084 trials. Long-acting injectable PrEP was widely accepted among our study participants but many reported their concerns about side effects and pain related to the intramuscular injection, which could impede its implementation. The study findings provide recommendations for upcoming strategies that aim to improve the quality and coverage of the PrEP program in order to avert a significant number of new HIV infections.

Recommendation

1. It is recommended to improve risk perception among MSM population.
2. Broadening PrEP indication by including substance use in the criteria is recommended. One possible solution is evaluating participants' different risk behaviors in a compound score.
3. The continuation of intensifying HIV testing to the MSM population is urged to increase PrEP initiation.
4. Opening more facilities that can provide PrEP and diversifying PrEP delivery models will create opportunities for more people accessing and retaining PrEP.
5. Building a referral system among PrEP clinics can limit the treatment discontinuation.
6. Initiatives to address the cost of PrEP in the context where PrEP will not be free of charge are particularly important to strengthen the PrEP implementation.
7. Development of systematic plans to keep health care system operate functionally in lockdown circumstances is needed to cope with the COVID-19 pandemic or similar outbreak in the future.
8. Stigma toward PrEP use and homosexuality should be addressed to improve the quality of the PrEP program and reduce PrEP discontinuation.
9. More training and support for ART service providers could enhance their acceptability of PrEP implementation.
10. Willingness to use long-acting injectable PrEP in our sample of the discontinued MSM was high, suggesting the implementation of the new PrEP medication is promising. However, challenges on side effects and pain due to intramuscular injection should be addressed.

Limitation

There were some general limitations that should be taken into consideration when interpreting the dissertation results. First, cross-sectional design in studies 2 and 3 could limit our ability to draw causal inferences. Second, studies 1 and 2 were conducted in MSM in Hanoi, Vietnam so caution should be noted when generalizing the study findings to different populations in different settings in different locations. Third, our MSM participants solely took daily oral PrEP so the study finding might not be applicable to other PrEP regimens. Fourth, our study data were all self-reported so were subject to information bias that was probably driven by social desirability or recall bias.