

Awareness and Willingness to Use Pre-Exposure Prophylaxis (Prep) Amongst Men Who Have Sex with Men (MSM) in China: A Mini-Review

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Abstract

The purpose of this review is to research the awareness of and willingness to use pre-exposure prophylaxis (PrEP) to protect themselves from HIV infection amongst MSM in China. In addition, we explored the potential impact factors and evaluated the need and user preferences related to access and utilization of PrEP in China. PUBMED, EMBASE, and CNKI were accessed to search for the relevant articles published before August 2019. The studies included in this review were conducted in 9 cities in China. The awareness of PrEP use was from 11.2% (Zhou et al., 2012) to 52.7% (Peng et al., 2019). The lowest willingness to use PrEP was 19.1% (Ding et al., 2016), the highest is 91.9% (Wei et al., 2011) provided the drug is safe, effective and free. Assuming HIV prevention medicines are effective and safe, the willingness to use PrEP was in the range of 63%-89.8%. Factors associated with willingness to use PrEP include the factors of drug products (e.g., perceived safety, efficacy, price and dosing schedule, etc.); sociodemographic characteristics (e.g., age, education, income, sex identity and sex role, etc.); behavioral factors (e.g., drug use, condom use, STI history and sex partner, etc.), and the awareness and knowledge of HIV treatment and prevention. Results indicate that as more MSM in China are becoming aware of PrEP, the willingness to use PrEP is higher than 63% if the medicine is safe and effective. Future research is needed to solicit effective education and intervention programs to support the access and use of PrEP.

Keywords: pre-exposure prophylaxis (PrEP); men who have sex with men (MSM); Human immunodeficiency virus (HIV); Acquired immune deficiency syndrome (AIDS); awareness; willingness.

Introduction

In 2018, 1.7 million people became newly infected with HIV, 37.9 million people were living with HIV, the risk of acquiring HIV is 22 times higher among men who have sex with men [1]. Global HIV epidemic among men who have sex with men (MSM) remained uncontrolled [2].

Epidemic in China

Human immunodeficiency virus (HIV) infection has caused a huge burden and imposed a serious public health challenge to China. The National Health and Family Planning Commission (now renamed the National Health Commission) of China recently published data regarding the national (excluding Hong Kong, Macao, and Taiwan) infectious disease epidemic situation in 2018. This report indicated that 64,170 cases of new HIV infection were reported and the incidence of HIV infection was 4.6195 per 100,000, the number of deaths was 18,780 and the mortality was 1.352 per 100,000 [3]. A meta-analysis reported a pooled incidence of HIV incidence among Chinese MSM is 5.61/100 person-years, with an increasing trend over time [4]. Unprotected anal intercourse is common and puts MSM in China at high risks of acquiring and transmitting HIV [5]. In Sichuan province, the average survival time of HIV/AIDS cases was 11.51 years during 1991–2017 [6]. With education, HIV counseling and testing, and increasing use of highly active anti-retroviral therapy (HAART) in China, HIV infected individuals have been discovered early, the mortality of HIV/AIDS patients has been significantly reduced after treatment.

In the past ten years, the transmission of HIV infection in China has changed significantly. In 2005, HIV infection was mainly through injecting drugs, transfusion, and heterosexual intercourse. By the year 2015, heterosexual/homosexual intercourse and illicit drug injection have become the main route of transmission. The proportion of homosexual in newly identified HIV subjects has increased from 0.3% in 2005 to 27.6% in 2015 [7]. Further, a systematic review showed that HIV prevalence in men who have sex with men (MSM) increased from 1.77% (1.26–2.57) in 2000 to 5.98% (4.43–8.18) in 2010, with a national incidence of 0.98 (0.70–1.25) per 100 person-years in 2010 [8]. From 2010 to 2015, HIV antibody positive rate amongst MSM at sentinel surveillance sites increased from 5.73% to 7.98% [9]. MSM had quickly become a high-risk population for HIV infection and the growing epidemic amongst MSM is one of the new challenges regarding HIV prevention/treatment in China.

Pre-Exposure Prophylaxis (PrEP)

Antiretroviral agents remain the cornerstone of HIV treatment and prevention [10]. HIV pre-exposure prophylaxis (PrEP) typically refers to the use of antiviral drugs as a strategy to prevent the acquisition of HIV amongst HIV-uninfected people [11,12]. Randomized placebo-controlled trials [13], as well as the PROUD study [14], have shown that daily oral PrEP reduces the risk of HIV infection when medications are taken as indicated. PrEP has been shown to be effective and acceptable amongst MSM in multiple clinical trials [15,16]. WHO recommends PrEP to be used as part of a package of prevention interventions that also include male and female condoms, voluntary medical male circumcision, prevention of mother-to-child HIV transmission (PMTCT) and harm reduction strategies such as the provision of sterile injecting equipment and opiate substitution therapy for people who inject drugs [11]. PrEP is not only highly effective within the MSM subject population at the individual level, but it is also effective on population-level, for example, intensive promotion of PrEP within the MSM population in Australia has reduced the overall incidence in this population [17]. HIV/AIDS strategy emphasizes the importance of bringing prevention to the most at-risk populations. While, PrEP may be particularly challenging among key populations such as MSM in low- and middle-income countries where healthcare infrastructure and socio-cultural contexts are extremely different from that in developed countries [18].

As of March 2018, PrEP has been approved in more than 50 countries globally [19]. Despite the effectiveness of PrEP, it has not been adopted in many countries including China. Within China, numerous activities have been initiated in order to address the growing problem of HIV infection, including condom use, voluntary HIV testing and counseling services, HIV treatment as prevention (TasP) [20]. A compartmental model for HIV suggested that without PrEP, there will be 1.1–3.0 million new infections and 0.7–2.3 million HIV-related deaths in the next two decades in China [21]. To achieve HIV elimination in the next 10, 15 and 20 years in China, the required PrEP coverage rates would be 65%, 32% and 19%, respectively, if 100% PrEP compliance [22]. It is necessary to strengthen the comprehensive intervention in MSM, including improving PrEP adherence.

One study identified moderate acceptability (57.8%) of PrEP in MSM worldwide, showed efficacy, perception of HIV risk and experienced stigma determine its acceptance [23]. However, very few surveys exploring PrEP use amongst MSM population have been published and there are not any guidelines or medicines approved for PrEP in China. The goal of this review

is to understand the awareness of and willingness to use PrEP amongst Chinese MSM. In addition, for those showing a willingness to use PrEP, we examined the factors involved in that decision, including the user preferences to access and utilize PrEP. The data may help to better understand the motivations and willingness to use PrEP beyond clinical trials amongst MSM.

Materials and Methods

Both PUBMED and EMBASE were used to research the relevant articles using the keywords "PrEP or pre-exposure prophylaxis", "MSM or men who have sex with men" and "China or Chinese", and searched CNKI (National Knowledge Infrastructure) to identify the relevant Chinese-language articles using the keywords "暴露前 (Bao Lu Qian) or PrEP" and "男男 (Nan Nan) or MSM" on human subjects published from 2008 to February 2018. Two reviewers (Y. R. and J. P.) independently extracted and tabulated all data. Discrepancies were resolved by discussion and agreement.

Results and Discussion

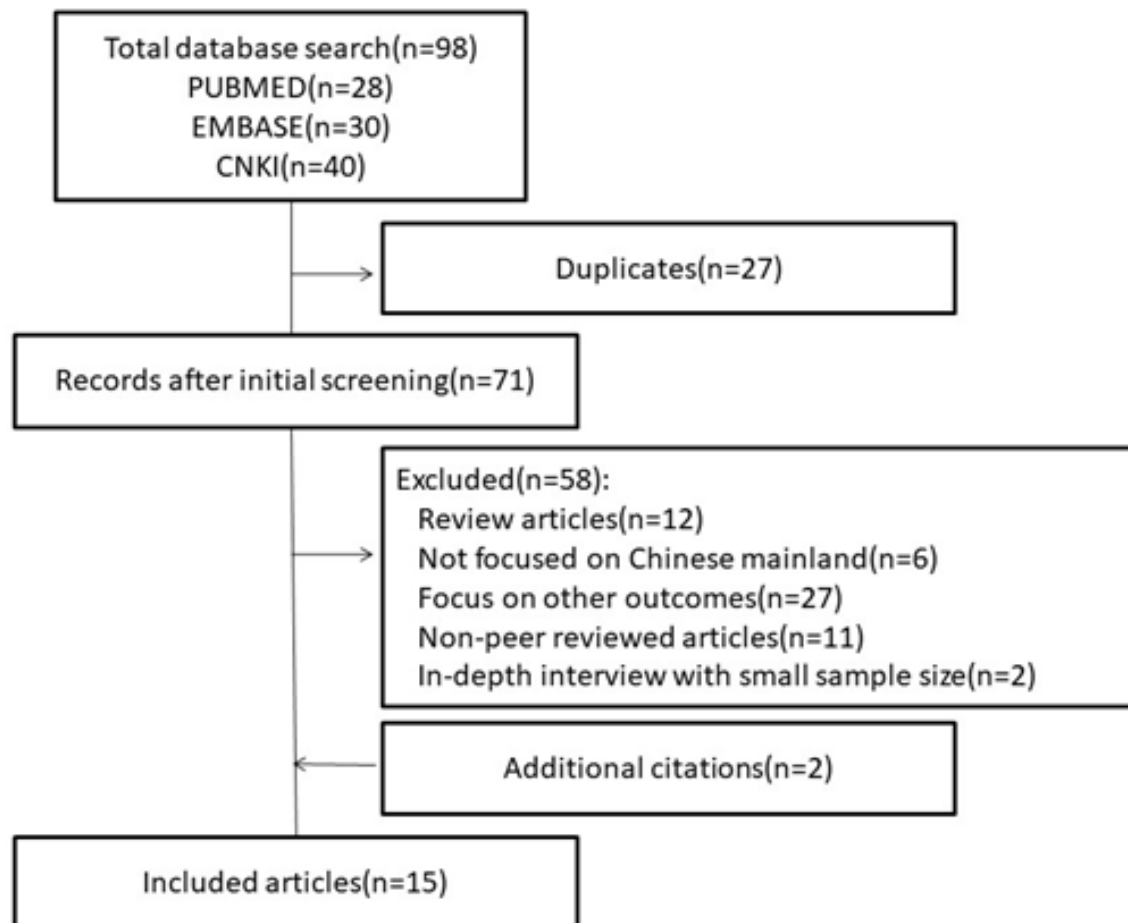
Results

Summary of included studies

This review involved a total of 98 identified publications and 27 articles were excluded due to duplication. Additional exclusions ($n = 58$) were due to a variety of reasons, including (i) review articles, (ii) not focused on the Chinese mainland, (iii) articles focussed on other outcomes or (iv) non-peer reviewed articles, (v) in-depth interview which has small sample size. Two more Chinese language articles were added additionally.

Finally, 15 publications were included in the analysis which reports data from the following cities; Shanghai, Beijing, Shenyang, Wuhan, Chengdu, Wulumuqi, Guangxi, Chongqing, and Sichuan. A flow diagram illustrating the literature search, article selection, and final included studies is shown below (Figure 1).

Figure 1, Study selection.



The 15 studies involved about 12,000 Chinese MSM. The MSM describe their sexual orientation as gay, bisexual or heterosexual. 13 studies only explored oral PrEP, "PrEP" in the articles regards to "oral PrEP", while 2 studies explored both oral and long-acting injectable (LAI) PrEP.

Table 1: Characteristics and findings of the included studies.

Author AND publication year	Data collection period	Country/ City	Sample size	Participants' characteristics on age	Awareness to PrEP	Willingness to use PrEP (combined different form)
Han et al. (24), 2019	19 th Jan to 6 th Feb 2017	China	4581MSM	Age \geq 15 years. The majority of participants were 18 to 25 years old (54.6%).	22.4%	75.6%
Peng et al. (25), 2019	Nov 2018 to March 2019	Chengdu	524MSM	Mean age=27.65(\pm 8.1). 50.9% of the participants were younger than 25 years old.	52.7%	84.9%
Zheng et al. (26), 2019	Not reported	Guangzhou	541MSM	50.8% of participants were younger than 30 years of age.	Not reported	64.7% willing to use PrEP or uncertain about uptake
Wang et al. (27), 2018	May 2015 to Dec 2015	Wuhan, Shanghai	487MSM	Mean age=27.68 (\pm 7.15 years). Age range=18-61 years.	Not reported	71.3%
Meyers et al. (28), 2018	Oct 2013 to Jan 2014	Beijing, Shenyang	200MSM	Mean age=31.6 years. Age range=18-56 years	33%	78.5%
Xie et al. (29), 2017	Aug 2015 to Nov 2015	Wuhan	301MSM	Age range=18-61 years.	17.28%	77.42%
Mao et al. (30), 2017	Nov 2015 to May 2016	Shenyang	292MSM	Mean age=29 years	34.2%	61%
Wei et al. (31), 2016	Sep 2014 to Feb 2016	Guangxi	295MSM.	Mean age=23 years. Age range=18-26 years.	19.7%	89.8%
Ding et al. (32), 2016	Oct 2012 to Dec 2013	Shanghai	1033MSM	Age range= \geq 18 years 76.7% were younger than 35 years.	Not reported	19.1% (197/1033)
Xue et al. (33), 2015	Nov 2013 to Dec 2013	China	760MSM	Age range=18-60 years	Not reported	32.1%
Zhang et al. (34), 2015	Not reported	Wulumuqi	379MSM	Age range=18-68 years.	Not reported.	68.3%
Zhang et al. (8), 2013	July 2009 to April 2010	Chongqing, Guangxi and Sichuan	1402MSM	Age range=18-74 years, 18-24 years comprised 41.5% of the sample.	22%	63.6% absolutely and 16.8% somewhat willing to use PrEP
Zhou et al. (35), 2012	Aug 2009 to Jan 2010	Beijing	152MSM	Age range=18-61 years.	11.2%	67.8% were 'definitely' or 'probably' willing to take PrEP
Jackson et al. (36), 2012	Dec 2009 to Feb 2010	Chongqing, Guangxi and Sichuan	570MSM	Mean age=27.6 years. Age range=18-62 years	Not reported.	63% had a high willingness to use PrEP
Wei et al. (37), 2011	Not mention	Guangxi	650MSM.	Mean age=28 years	19.7%	91.9%

Awareness and willingness of PrEPamongst MSM in China

Awareness: Amongst the 15 publications, 9 reported the results on awareness of PrEP. These studies gathered information on awareness by asking participants whether they were aware of or have had heard of PrEP. Overall awareness of PrEP was low, ranging from 11.2% [35] in Beijing to 52.7% [25] in Chengdu. Other cities showed similar levels of PrEP awareness such as 17.28% [29] in Wuhan, 19.7% [37] in Guangxi, 19.7% [31] in Guangxi's university students, 22% [38] in western China (Chongqing, Guangxi, and Sichuan), 22.4% [24] in China online survey, 33% [28] in Beijing/ Shenyang and 34.2% [30] in Shenyang. In general, there doesn't appear to be a significant difference in awareness by regions.

Willingness

All the involved publications reported the willingness of PrEP use. Approximately half of the studies assessed by simply asking binary measures, while six studies rated by five-level scales and one study rated by four-level scales. The question within the studies with five-level scale was "Assuming HIV prevention medications are safe and effective, how willing are you to use them to prevent HIV?". The response options were "very unwilling, somewhat unwilling, neither willing nor unwilling(uncertain), somewhat willing (probably willing) and

very willing (definitely willing)". In addition, one study evaluated willingness by four-level scales (very unwilling, unwilling, willing and very willing). Those who "somewhat (probably)" and "very (definitely)" willing on the five-level scale were grouped "willing" on a four-level scale for analysis purpose.

Amongst the 15 studies, the lowest willingness to use PrEP was 19.1% [32]. The highest is 91.9% with prerequisites of the drug being safe, effective and free [37]. If the HIV prevention medicines are effective and safe, the willingness to use PrEP was in the range of 63%-89.8%, including 63% [36] and 80.4% [38] in western China (Chongqing, Guangxi, Sichuan), 64.7% [26] in Guangzhou, 67.8% [35] in Beijing, 68.3% [34] in Wulumuqi, 77.4% [29] in Wuhan and 89.8% [31] in Guangxi university students respectively 71.3% [27] MSM in Wuhan and Shanghai would be willing to use PrEP if it were made available for use in China. In the Meyers et al. study [28], 54% (108/200) of the surveyed MSM would be willing to use oral PrEP, 76% (152/200) to use LAI PrEP and the combined interest in using oral and LAI PrEP was 78.5% (157/200) in Beijing and Shenyang. In the Peng et al. study [25], willingness to use oral PrEP, LAI PrEP is 60.1% and 60.8% respectively. In general, the willingness to use PrEP is greater than 63% if the medicine is safe and effective. In contrast, an on-line study that recruited subjects throughout China [33] showed a lower willingness to use PrEP

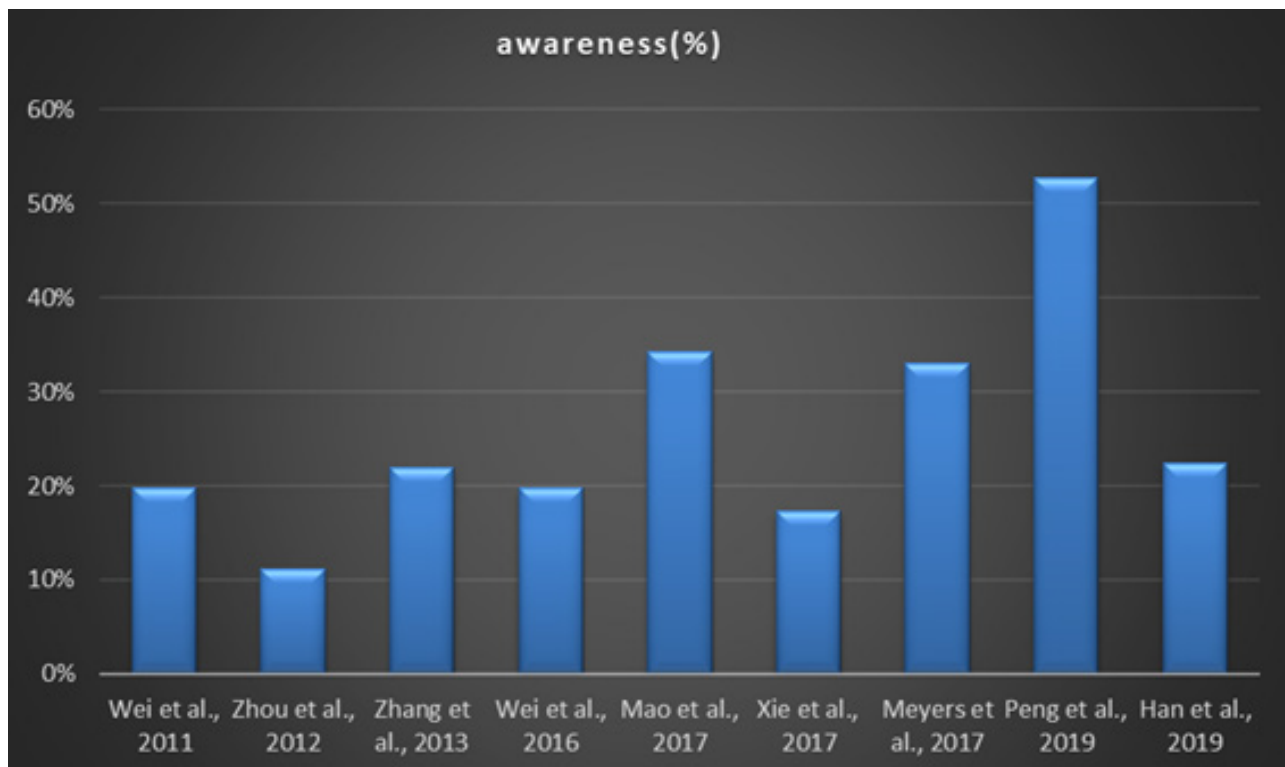


Figure 2, Awareness to use PrEPamongst MSM in China. Data were from 9 publications.

(32.1%). Moreover, combining the “daily” use and “on-demand” use of PrEP, the willingness to use was 61% in Shenyang [30]. In general, there does not appear to be a significant difference in willingness to use PrEP by regions or years.

Impact factors on the willingness of using PrEP

Based on included studies, I summarized 4 kinds of factors which are potentially associated with willingness to use

PrEP among MSM (Table 2). Included studies were variety in regions, years, enrolled population, the documented impact factors were lack of standard wordings, showed different meanings in different studies, they may bring big bias when doing analysis. These factors may play an important role in the prevention of HIV among MSM, we list the information here without analysis to provide references for future study.

Figure 3. Willingness to use PrEP amongst MSM in China. Data were from 15 publications.

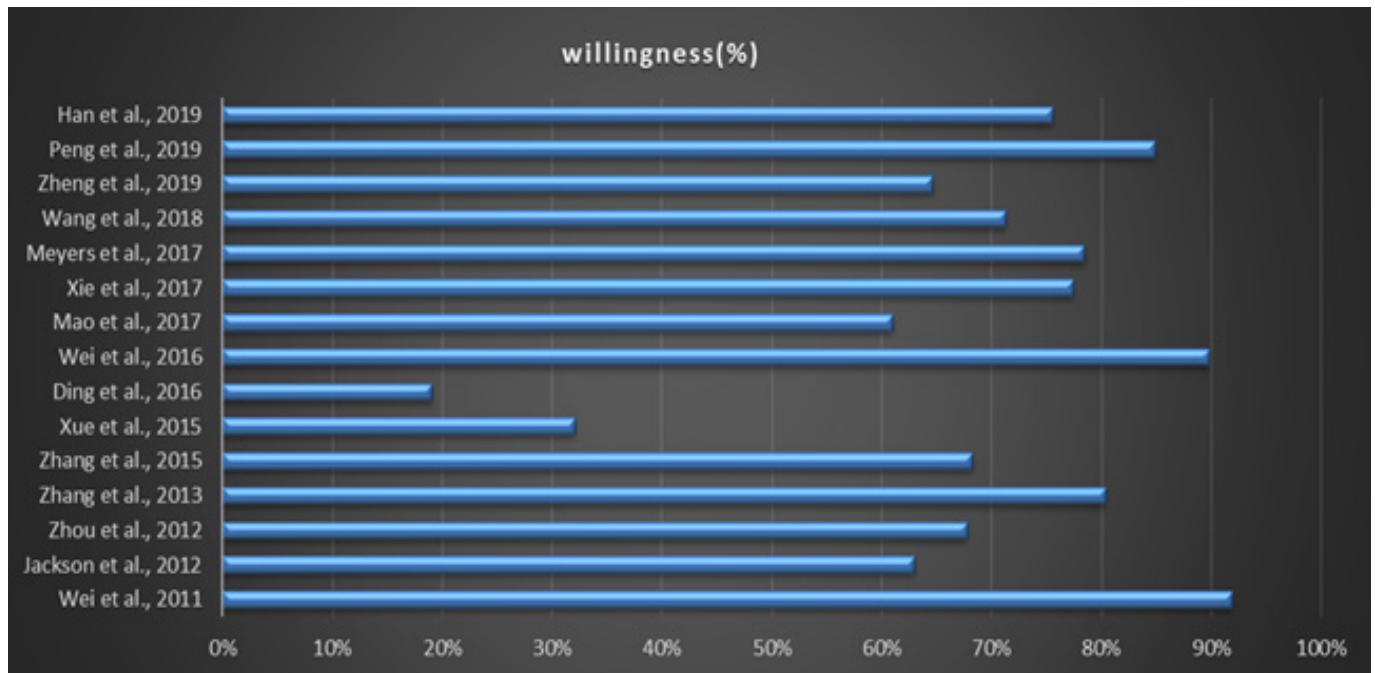


Table 2: Factors affecting willingness to use HIV pre-exposure prophylaxis (PrEP) amongst men who have sex with men (MSM) in China.

	Associated factors	Source studies which analyzed the factors	Source studies which showed the factors affecting willingness to use PrEP*
Product-level factors	Perceived safety	(24, 30, 31, 35)	(24, 30, 35)
	Efficacy	(24, 30, 31, 35)	(31)
	Price	(31, 35)	-
	Dosing schedule	(24, 30, 31)	(30, 31)
Sociodemographic factors	Age	(24, 25, 28-33, 35, 36, 38)	(24, 32)
	Education	(24, 25, 28-30, 32-36, 38)	(28, 36, 38)
	Income	(24, 25, 29, 30, 33, 35, 36, 38)	(33, 38)
	Sex identity	(24, 25, 28-33, 35, 38)	(29)
	Sex role	(25, 28, 30, 31, 33-35, 38)	(34)
Awareness and knowledge	Awareness of PrEP	(24, 25, 28, 30, 31, 35, 38)	(24, 30, 38)
	HIV/AIDS knowledge	(25, 32, 35, 38)	(25, 38)
Behavioral factors	Drug use	(28, 30, 32, 38)	-
	Condom use	(24, 25, 27, 28, 30-32, 34-37)	(24, 25, 27, 31, 32, 34-36)
	STI history**	(25, 28, 30, 34-36, 38)	(30, 34, 38)
	Multiple sex partner	(25, 28, 30-32, 38)	(25, 30, 32)
	Stable sex partner	(28-30, 36-38)	(30)

* The associations of willingness to use PrEP with impact factors were shown in the multivariate model, $p < 0.05$.

** STI means sexually transmitted infection

PrEP drug-level factors(eg.perceives safety, efficacy, price and dosing schedule)

Amongst the 15 publications, 14 mentioned safety or side effect, 13 mentioned efficacy. 72.9% [27] and 31.8% [26] participants worried about side effects as the reason for not willing to use PrEP. 3 studies analyzed safety or side effect as an influencing factor. One study in Beijing [35] showed those who were aware of the potential side effects of ARV drugs (OR=0.30, 95% CI: 0.14–0.67) were less likely to initiate prep. Those who had no worries about side effects were more probably use PrEP (aOR=1.3, 95% CI: 1.1–1.5). More specifically, 44.7% of MSM participants expressed worry that PrEP would disrupted their diet and sleep. Similarly, another study in Shenyang [30] showed that in contrast to efficacy, MSM who were concerned about side effects were less likely to use PrEP.

Only one study [31] showed by multivariate logistic regression analysis that those who suspected drug efficacy (OR=0.010, 95%CI: 0.001–0.112) were less likely to use PrEP. Mao et al. [30] showed that compared with "on-demand" use, less MSM prefers to choose "daily" use ($\chi^2=5.785$, $P=0.02$), and amongst MSM who prefer "daily" use, only 50.3% expressed they can adhere to take medicine every day. Another study in Guangxi [31] showed by multivariate logistic regression analysis that those who felt they could adhere to daily medicine (OR=88.245, 95% CI: 10.237–760.696) were more likely to use PrEP.

Sociodemographic factors (Age, Education, Income, Sex identity and Sex role)

As essential elements of the questionnaire, sociodemographic characteristics were mentioned in most of the studies.

Age: Studies showed that those who were aged ≥ 45 years (OR=2.18, 95% CI: 1.13–4.23) [32] and aged ≥ 40 years (OR=2.0, 95% CI: 1.1–3.6) [24] were significantly more willing to use PrEP.

Education: Low education level was a predictor for willingness to use PrEP. One study showed that people with lower education (OR=1.50, 95% CI: 1.18–1.92) are more willing to use PrEP than people with college or higher education [38]. The other study showed that who attend post-secondary education (OR=0.72, 95% CI: 0.55–0.94) are less will to use PrEP than lower education [36]. In general, high willingness to use HIV PrEP was related to lower education. Also, one publication [28] showed by the multivariate model that those with higher education (aOR=0.5, 95% CI: 0.2–1.0) had lower odds of being interested in LAI-PrEP only, compared with any type of PrEP.

Income: Seven studies examined the association between willingness to use PrEP and socioeconomic status/income. Xue et

al. showed that MSM who have an annual income of less than 60,000 yuan (OR=0.64, 95% CI: 0.45–0.92) are less likely to use PrEP [33]. And another study [38] shows that subjects with moderate-income (1000–3000yuan per month) (OR=1.31, 95% CI: 1.02–1.67) compared with the lowest income (<1000yuan per month) are more willing to use PrEP. This seems to be in direct contrast to the education level data.

Sex identity and Sex role: One study [29] showed that bisexuals (OR=0.22, $p<0.05$) are less likely to use PrEP than homosexuals amongst MSM who have regular homosexual partners. Whereas MSM who were "not sure" about their sexual identity were less likely to be a willingness to use PrEP (aor=0.6, 95% CI: 0.4–0.9). Additionally, compared with receptive sex, MSM who prefer insertive sex (OR=0.34, 95% CI: 0.19–0.60) are less likely to use PrEP [34].

Awareness and Knowledge (Awareness of PrEP, HIV/AIDS knowledge)

Awareness of PrEP: In most studies, initial awareness of PrEP was low, after the introduction of the concept, most of MSM express willingness to use it. Six studies mentioned awareness as a potential factor to a willingness to use PrEP amongst seven studies which reported awareness. After analysis, only Zhang et al. [38] and Mao et al.[30] showed that having previously heard of PrEP (OR=1.33, 95% CI: 1.01–1.75 and aOR=1.7, 95% CI: 1.0–2.8 respectively) is one of the relevant factors for willingness to accept PrEP amongst MSM. MSM who had heard of PrEP were more "definitely and probably" (aOR=1.7, 95% CI: 1.4–2.2 and aOR=1.2, 95% CI: 1.0–1.5) [24] willing to use PrEP compared to those who had never heard of PrEP.

HIV/AIDS Knowledge: Zhang et al.' study [38] showed that these were more knowledgeable about AIDS (OR=1.49, CI: 1.18–1.88) were more willing to use PrEP. Peng et al., [25] showed who possessed a higher literacy in HIV prevention (aOR = 1.49, 95% CI: 1.03–2.16) were more willing to use PrEP.

Behavioralfactors (Drug use, Condom use, STI history, Multiple sex partner, Stable sex partner)

Drug use: No publication showed that willingness to use PrEP amongst MSM is associated with drug use.

Condom use: Amongst 15 publications include, 8 studies believed that inconsistent condom use is one of the predictors of willingness to use PrEP. MSM who report condom use during their last anal sex act (OR=0.68, 95% CI: 0.47–0.97) [32], who consistently used condom in homosexual behavior in the past 6 months (OR=0.31, 95% CI: 0.13–0.70) [35] or in sexual intercourse with regular partners (aOR = 0.47; 95% CI: 0.23–0.95) [25], prefer using condom as prevention for HIV (aOR=0.5, 95%

CI: 0.4-0.5) [24] and reject sex with someone who will not use a condom (OR=0.34, 95% CI: 0.16-0.72) [37] were significantly less willing to use PrEP. In the multivariate logistic regression model, those who use condom occasionally (OR=1.46, 95% CI: 1.01-2.09) [34], and those who report barriers to condom use (OR=1.11, 95% CI: 1.06-1.17) [36] were willing to accept PrEP. In addition, compared to always using condoms, MSM who reported never using condoms with their regular sexual partners were more likely to explain their willingness to use PrEP in terms of "problems using condoms" (39.4% versus 6.3%, $\chi^2 = 22.93$, $p < 0.01$) [27].

STI history: Five studies considered STI history as a factor for willingness to use PrEP, three of them showed a significant difference. Zhang et al. [38] and Mao et al. [30] showed that having STI history (OR=1.61, 95% CI: 1.09–2.39 and aOR=11.8, 95% CI: 1.4-99.0 respectively) was the predictor for willingness to use PrEP. Zhang et al. showed that MSM who don't have STI history (OR=0.20, 95% CI: 0.07-0.56) are less willing to use PrEP [34].

Multiple sex partner: In multivariate analyses, MSM who had two or more male sex partners in the past 6 months (OR=1.53, 95% CI: 1.07-2.17 for 2 to 5 and OR=1.82, 95% CI: 1.05-3.17 for ≥ 6 , respectively) were more willing to use PrEP [32]. Mao et al.'s [30] and Peng et al., reported similar results: (aOR=1.8, 95% CI: 1.1-2.9) and (aOR = 3.36, 95% CI: 1.10–10.26) respectively.

Stable sex partner: Mao et al. [30] showed that MSM who have stable male sex partner (aOR=1.9, 95% CI: 1.1-3.3) are more likely to use PrEP.

Discussion

At the community-level in China, many do not know that HIV is a manageable disease, and there is a severe lack of awareness and correct knowledge of the benefits of ART [39], even among MSM living with HIV [40, 41]. Despite PrEP being initially low amongst MSM in China, once they become aware of PrEP, many MSM is willing to use it. Even though the willingness to use PrEP is relatively high, the actual reported use is low (<1%–3.1%) [32, 38, 42]. Perception of low HIV risk, mistrust of the national PrEP program, and concerns of side effects, lack of main sexual partner's support, difficulties in adhering to the daily oral PrEP regimen, and the inconvenient schedules in securing the medicine were the major reasons for not wanting to use or quitting the use of PrEP [43]. On the other hands, the effectiveness of oral HIV preexposure prophylaxis (PrEP) strongly depends on maintaining adherence [44]. One study showed the median adherence rate of daily oral PrEP in clinical trials was 64.29%, the main objective factor in non-adherence was forgetting to take the medicine [45], LAI PrEP may improve PrEP ad-

herence to some extent and may further reduce the incidence of HIV. Qu, et al. [46]. explored the impact factors to the low-level PrEP self-efficacy (Self-efficacy, as the determinant of individual behavior, is also the center of individual factors that often influences the choice and continuation of individual behavior [47] in China, age and anxiety score were negatively related to PrEP self-efficacy, AIDS-related knowledge and PrEP-related motivation were activities related to PrEP self-efficacy. One more potential reason may be a lack of community's attention or availability of approved medicine for PrEP in China. The strategy to improve PrEP actual use and adherence requires further study, such as a more robust HIV prevention care network in China may help potential uninfected subjects to understand the importance of, and how to get and use PrEP. Data from New York City indicates that delivering provider training, raising awareness and ensuring Medicaid (insurance) coverage, resulting in the number of Medicaid beneficiaries increasing from 259 in 2013 to 1330 in 2015 [48].

One study [27] showed that the top 2 reasons for willingness to use PrEP are "efficacy to sexual health" and "problems using condoms" and the top 3 reasons for unwillingness to use PrEP are "concern about side effects, long dose schedule", "confidence in protecting themselves" and "cost and stigma". Our findings suggested that several factors could potentially prevent or facilitate participants' willingness to use PrEP. Price, safe and efficacious medicine and ease of use are common concerns amongst the MSM population. If HIV prevention medicines are effective and safe, 63%–89.8% MSM are willing to use PrEP. Further, if reimbursement and insurance can cover the medicine for PrEP, make the price more affordable, PrEP utilization may increase. One study suggested that to achieve cost-effectiveness and realize the public health good of preventing HIV infections among MSM, current Truvada PrEP regimen in China would need to be reduced by half [21].

MSM that is age ≥ 45 years have lower education, in a moderate-income bracket, participate in receptive anal sex, and who have more awareness of PrEP and knowledgeable about HIV/AIDS may have a greater willingness to use PrEP. Compared to MSM with higher education, those with lower education may be less confident to avoid risky behavior, and less knowledgeable to protect themselves by traditional methods. MSM with moderate-income may be less worried about the price of PrEP compared with the lowest income. A Boston [49] study also showed that MSM with a lower education and moderate-income are more intent to use PrEP compared to those with higher education and the lowest income category. For MSM of diverse educational and demographic backgrounds, accessibility of community educa-

tional messages should be considered [49]. Besides traditional methods, Han et al. clearly indicated that young MSM in China prefers the Internet to looking for general health information. Therefore, online educational efforts can greatly facilitate PrEP uptake among young Chinese MSM [50]. For MSM with higher education, PrEP seems to be another reliable method for them to protect themselves. PrEP would need to be integrated into existing prevention strategies, however, rather than replacing them [51]. Additionally, in order to encourage the use of PrEP, an accessible price is necessary to consider because of the cost may be a big burden for those with lower income. Negotiating with the industry and striving for subsidies from the government to make reimbursement and insurance cover medicine is a positive method to control the price. As the data reported here is limited, future studies among Chinese may be conducted more thoroughly. An interesting point in our study is the association of between MSMEs behaviors and willingness to use PrEP. While a study in Hongkong [52] showed that there were no significant associations between risky behaviors (eg. the practice of condomless sex) and PrEP acceptance which is different from mainland China.

In mainland China, recreational drug use has increased considerably amongst MSM and became a high-risk factor for HIV infection [53]. As reported by Lauby, et al. [55] and Tweed, et al. [56], recreational drug use is related to an increase in unprotected sex and HIV risk. Even though drug use did not seem to have a significant influence on the willingness to use PrEP in our review, once drug users realized they are in high HIV risk, prevention methods including PrEP may become popular among the population, further study on this factor is needed. Current literature has also identified barrier of condom use, STI history, multiple sex partner and stable sex partner as potential factors for willingness to use PrEP. It's likely that these with stronger self-perceptions of risk are more willing to explore additional protection methods, including PrEP. Condom use greatly decreases the risk of gonorrhea, chlamydia, HIV/AIDS, as well as to a lesser extent to protect against syphilis [57]. MSM who use condoms regularly regard themselves as already protected against the acquisition of HIV. Of concern, however, one study in India [58] found that availability of PrEP could reduce the use of condoms, one study showed STI is on the rise in PrEP Users [59]. Mansegh et al. [60] concluded that as PrEP becomes more available among MSM, HIV prevention programs can be enhanced in a way that reinforces condom use and helps men perceive PrEP as a supplementary biomedical intervention. For HIV and STI prevention, we should clarify if and how condoms should be used in combination with PrEP. Ongoing screening

and timely treatment of STIs is both a part of broader PrEP intervention and a potential method for decreasing STI burden in the face of decreasing condom use [61]. As China begins to thinking about using PrEP targeting MSM at high risk for HIV, it will be increasingly important to evaluate ways in which we can use PrEP programs to engage MSM in sexual health and comprehensive STI prevention programs that do not solely focus on condom use [62]. For sex partner, a study in Malaysia showed that having 2 or more male anal sex partners in the past 6 months (aOR=1.98, 95% CI: 1.29-3.05) were independently associated with greater willingness to use PrEP [63]. This is expected as other studies have shown that STI incidence increases with multiple sex partners [64]. In contrast, MSM who have stable sex partner also have a higher willingness to use PrEP in one of the six publications which analyzed this factor. One possible explanation may be that partner in such a stable same-sex relationship may have sex without a condom, but may also not be clear as to the HIV infection status of their partner. One study indicated that people were less likely to inform their main partner when they had unprotected sexual intercourses with casual partners [65]. It is reasonable for someone who has both stable and casual partners, PrEP is an attractive option for self-protection and for protection of the partner. Also, Hu, et al. suggested that integrated delivery of sexual partners' PrEP and early ART could nearly eliminate HIV transmission and reduce costs [66].

As highlighted by the WHO guideline [67] there are some other potential issues among potential PrEP users, such as not taking up HIV testing regularly, not seeking medical consultation before they decide to start or discontinue using PrEP which should be monitored and prevented to ensure the effectiveness of PrEP and safety of PrEP users.

For MSM in China, we should deepen their understanding of the safety and effectiveness of PrEP and increase their confidence in PrEP, thereby improving their medication adherence [68]. Clinicians also need to be knowledgeable about PrEP as an HIV prevention tool to provide more effective sexual health services [69]. Wei, et al. [18] systematically summarized the way of successful PrEP rollout: First, health authorities should more fully engage and support community-based organizations to establish an equitable process among stakeholders. Second, broader campaigns to address lack of knowledge around PrEP medications' safety and efficacy, negative beliefs as well as HIV and sexual minority stigma. Third, government and community clinics should provide PrEP as well as MSM community partners can provide supporting counseling and monitoring. Fi-

nally, guidelines and policies should be implemented to protect the health rights of sexual minority groups.

Conclusions

PrEP for HIV has been available since 2012 outside of China, which is a promising prevention option to prevent the acquisition of HIV for non-infected people. WHO has endorsed the use of PrEP by MSM and other populations at substantial risk of HIV [11,12]. To introduce and scale-up the usage of PrEP, it is important to learn more about user preferences and potential demand.

While willingness is not always a good indicator of future use, this helps to identify cultural values and beliefs, and concerns that need to be addressed to adequately counsel HIV high-risk individuals who would benefit from PrEP use [70].

This review contributes to knowledge around the awareness and willingness to use PrEP in China, by reporting factors that impact willingness such as product information, sociodemography, knowledge, awareness, and behavior.

In China, the awareness of PrEP is low, ranging from 11.2% to 34.2% based on these 11 studies, and one in-depth personal interview [71] even showed that no one had heard PrEP amongst the 31 subjects. In contrast, amongst those aware, the willingness to use PrEP is higher than 63% if the medicine is presumed safe and effective. Our review also found that several factors could potentially prevent or facilitate participants' willingness to use PrEP. Drug use, unprotected (condomless) anal intercourse, STI history, and multiple sex partner are a potential predictor to a willingness to use PrEP in our study which is consistent with the target situation of PrEP. But few studies have investigated the potential use PrEP in China and the small number of studies included in our review is the biggest limitation. From the studies focused on MSM, we can further understand this population and provide appropriate advice and help for their HIV prevention. In general, future research is needed to solicit effective education and intervention programs to support access and utilization of PrEP.

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