Original Article

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Low willingness and actual uptake of pre-exposure prophylaxis for HIV-1 prevention among men who have sex with men in Shanghai, China

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Summary **Little is known about the acceptance and actual uptake of pre-exposure prophylaxis (PrEP) and associated factors in men who have sex with men (MSM) in China. This study is the baseline survey of an intervention study designed to evaluate the effectiveness of tenofovirdisoproxil fumarate (TDF) on a daily use for human immunodeficiency virus (HIV) prevention among MSM in Shanghai, China. From October 2012 to December 2013, a total of 1,033 MSM in Shanghai were recruited by local district Centers for Disease Control and Prevention (CDC) and a MSM community-based non-governmental organization (NGO). Among them, 197 (19.1%) participants expressed willingness to use the TDF group at baseline survey, but only 26 (2.5%) participated in the TDF group and took TDF one tablet a day. Higher willingness to use PrEP was associated with being 45 years or older, non-local residents, having more male sex partners in the past 6 months and not using condom at last anal sex with man. Acutal uptake of PrEP was associated with having ≥ 11 male sex partners in lifetime and reporting no female sex partners in lifetime. Reasons for not participating in TDF group among those who expressed willingness to use PrEP at baseline survey included loss of contact, ineligiblity because of abnormal results for liver or renal function tests, change of mind, and HIV seroconversion before uptake of PrEP. Our findings suggest that promotion of PrEP in MSM remains challenging at current circumstancein China. Future research is needed to solicit effective education and intervention programs to promote acceptance of PrEP among Chinese MSM.**

Keywords: Pre-exposure prophylaxis (PrEP), HIV, prevention, willingness, MSM, China

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1. Introduction

Although the overall human immunodeficiency virus (HIV) incidence has decreased in China, men who have sex with men (MSM) remains disproportionally affected by HIV. The percentages of newly reported HIV infections in China that were attributable to homosexual transmission have increased from 12.2%

in 2007 to 25.8% in 2014 (*1*). According to recent national sentinel surveillance data, HIV prevalence in MSM population was 1.4% in 2005, increasing to 8.0% in 2015 (*2*). Recent studies also revealed an increasing trend of HIV incidence in MSM population in various areas of China (*3-5*). Although sexual risk reduction interventions have proven to be effective in increasing HIV/AIDS knowledge, condom use, and HIV testing in MSM population (*6-7*), it seems that these strategies are not enough to curb the HIV epidemic.

The pre-exposure prophylaxis (PrEP) is a biomedical approach for the prevention of HIV infection using antiretroviral drugs before exposure and its efficacy has been evaluated in clinical trials of tenofovir disoproxyl fumarate (TDF) and emtrictiabine/tenofovir (FTC/TDF) (*8-10*). But, the success of any new prevention or treatment method depends on the potential users' acceptance of this method. Earlier studies in China demonstrated that 11.2% to 22% of MSM participants reported having heard of PrEP, and 64% to 91.9% would accept PrEP if available and proved to be safe and effective (*11-13*). However, in most of these studies willingness to use was assessed for a future hypothetical PrEP program and therefore the actual acceptance rate of PrEP could not be assessed (*11-13*). In this study, we investigated the willingness and actual uptake of PrEP as HIV prevention and associated factors among a sample of HIV-negative MSM in Shanghai, China. Our findings will provide implication for promoting PrEP as HIV prevention among MSM in China.

2. Methods

2.1. *Study participants*

This study was a baseline survey of an intervention study designed to investigate the willingness and actual uptake of PrEP as HIV prevention and associated factors among MSM in Shanghai, China. Participants made their own choices to participate in the TDF group or control group at baseline. Those in the control group would not be given any other antiretroviral drugs for prevention or placebo pills. From October 2012 to December 2013, MSM in downtown area of Shanghai were recruited by local district Centers for Disease Control and Prevention (CDC) and a non-governmental organization (NGO) working with MSM. To be eligible, participants must be at least 18 years, self-identified as a male, have ever had oral and/or anal sex with man in the past 6 months, screened negative for HIV, and be able to give written consent. Participants were verbally informed the nature and purpose of the baseline survey as well as the forthcoming clinical trial study, follow-up surveys, and confidentiality parameters. Participants were also explained the risks and benefits (including referrals to other services), and the freedom to cease participation at any time without penalty. Upon agreement, they signed a consent form and were given a copy of the signed consent form. This study was approved by the institutional review board (IRB) of Fudan University, Shanghai, China.

2.2. *Data collection*

Each participant was administrated with a face-to-face questionnaire interview by an experienced and trained public health worker in a private place. Questions were developed to obtain information about demographic characteristics, HIV/AIDS knowledge, drug use, sexual behaviors, and willingness to participate in the TDF group. HIV/AIDS knowledge was measured by six questions (two about reducing number of sex partners and promoting condom use for HIV prevention, one about blood testing for HIV, one about whether HIV/AIDS was curable, and two about misconceptions about mosquito bites in HIV transmission and lubricant use for HIV prevention). The total score for HIV/AIDS knowledge ranged from 0 to 6 with a score of 1 for a correct answer and 0 for a wrong answeror an answer of unknown or unsure.

Willingness to take TDF as prevention was measured by asking participants at enrollment "Are you willing to participate in the TDF group (*i.e.*, take one tablet of TDF each day) of the forthcoming PrEP program over a 24-month period to prevent HIV infection?". All participants were asked to undertake liver and renal function tests. Those with abnormal results but expressed their willingness to participate in the TDF group were encouraged to participate in the control group. Actual uptake of PrEP refers to those finally participating in the TDF group of the trial.

2.3. *Laboratory tests*

Venous blood was collected from each participant by professional nurses using disposable sterile needles and tubes. The serum was frozen in 500 μl aliquots to a -80°C refrigerator. Serum samples were screened for anti-HIV IgG antibody using an ELISA technique (Kehua Biotechnology Co. Ltd., Shanghai, China) according to the manufacturer's instructions. If a participant tested HIV-positive, he/she would be referred to a local CDC for further HIV confirmation by a western blot assay (HIV BLOT 2.2; Genelabs Diagnostics Pte Ltd., Singapore) as well as post-test HIV counseling. Only HIV-negative MSM were invited to participate in the intervention study. Liver and renal functions were measured by automatic biochemistry analyzer (Hitachi, Japan).

2.4. *Data analysis*

All statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC). Age was stratified

to four groups: 18-24, 25-34, 35-44, and ≥ 45 years (*14*). Differences were assessed by chi-square test or Fisher's exact test was used for categorical variables as appropriate. Univaraite and multivariate logistic regression analyses were performed separately to examine the factors associated with willingness to use PrEP and actual uptake of PrEP. Univariate regression analysis was performed at first, followed by multiple logisitic regression analysis including those with a p-value < 0.1 in univariate analysis. Odd ratios (ORs) and 95% confidence intervals (95% CI) were calculated.

3. Results

3.1. *Characteristics of participants*

A total of 1,033 MSM were included. The majority were younger than 35 years (76.7%), non-local residents (59.3%), with at least college education (62.5%), never married (74.2%), and self-identified as a gay (76.0%). Overa half of the participants had HIV/AIDS knowledge score of 5 to 6, only a few participants (5%) had ever used drugs (Table 1).

In terms of sexual behaviors, 93.5% of the

Table 1. Participant characteristics of 1,033 cases enrolled in this study*

Items	Total, *N* (%)	Willingness to use PrEP Events/Total (%)	Uptake of PrEP Events/Total (%)	*p*-value[a]	*p*-value[b]
Age (year)				0.002	0.154
18-24	297 (28.8)	59/297 (19.9)	5/297 (1.7)		
25-34	494 (47.9)	77/494 (15.6)	11/494 (2.2)		
35-44	154 (14.9)	33/154 (21.4)	5/154 (3.2)		
≥ 45	86 (8.3)	28/86 (32.6)	5/86 (5.8)		
Permanent legal residency				0.026	0.419
Local (Shanghai)	416 (40.7)	66/416 (15.9)	13/416 (3.1)		
Non-local	606 (59.3)	130/606 (21.5)	13/606 (2.1)		
Occupation				0.085	0.438
Company employees	335 (32.4)	54/335 (16.1)	11/335 (3.3)		
Factory workers	206 (19.9)	43/206 (20.9)	2/206 (1.0)		
Freelancers	259 (25.1)	53/259 (20.5)	6/259 (2.3)		
Students	98 (9.5)	13/98 (13.3)	2/98 (2.0)		
Others	135 (13.1)	34/135 (25.2)	5/135 (3.7)		
Education				0.019	0.061
Middle school or below	127 (12.3)	33/127 (26.0)	5/127 (3.9)		
High school or equal	260 (25.2)	57/260 (21.9)	2/260 (0.8)		
College or above	646 (62.5)	107/646 (16.6)	19/646 (2.9)		
Marital status				0.378	0.206
Never married	767 (74.2)	139/767 (18.1)	18/767 (2.3)		
Currently married	194 (18.8)	41/194 (21.1)	4/194 (2.1)		
Divorced/widowed	72 (7.0)	17/72 (23.6)	4/72 (5.6)		
Sexual identity				0.331	0.360
Gay	780 (76.0)	155/780 (19.9)	22/780 (2.8)		
Non-gay	246 (24.0)	42/246 (17.1)	4/246 (1.6)		
HIV/AIDS knowledge score				0.293	0.297
0-2	73 (7.1)	16/73 (21.9)	0/73 (0.0)		
3-4	374 (36.2)	79/374 (21.1)	8/374 (2.1)		
5-6	586 (56.7)	102/586 (17.4)	18/586 (3.1)		
Ever used drugs				0.629	0.639
No	971 (95.0)	183/971 (18.8)	26/971 (2.7)		
Yes	51 (5.0)	11/51 (21.6)	0/51 (0.0)		
No. male sex partners in lifetime				0.209	0.055
1	67 (6.5)	10/67 (14.9)	0/67 (0.0)		
2-10	660 (64.3)	79/660 (18.4)	13/660 (2.0)		
≥ 11	300 (29.2)	67/300 (22.3)	13/300 (4.3)		
No. male anal sex partners in the past 6 months				0.005	0.466
0-1	480 (47.1)	73/480 (15.2)	9/480 (1.9)		
2-5	446 (43.8)	97/446 (21.7)	13/446 (2.9)		
≥ 6	92 (9.0)	25/92 (27.2)	3/92 (3.3)		
Condom use at last anal sex with man				0.949	0.261
No	265 (26.9)	63/265 (23.8)	16/719 (2.2)		
Yes	719 (73.1)	128/719 (17.8)	10/265 (3.8)		
No. female sex partners in lifetime				0.397	0.065
0	529 (52.7)	95/529 (18.0)	17/529 (3.2)		
1	249 (24.8)	50/249 (20.1)	8/249 (3.2)		
≥ 2	226 (22.5)	50/226 (22.1)	1/226 (0.4)		

*: numbers may not add up to 1,033 due to missing values. [a]: *p*-value for comparing willingness to use PrEP by listed variables. [b]: *p*-value for comparing actual uptake of PrEP by listed variables.

Table 2. Logistic regression analysis of factors associated with willingness to use PrEP for HIV prevention

Items	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age				
18-24	1.00	0.123	1.00	
25-34	0.74 (0.51-1.08)	0.696	0.70 (0.46-1.06)	0.091
35-44	1.10 (0.68-1.78)	0.014	0.96 (0.56-1.63)	0.868
≥ 45	1.95 (1.14-3.32)	0.026	2.18 (1.13-4.23)	0.021
Non-local residents	1.47 (0.67-3.21)		1.69 (1.16-2.45)	0.006
Occupation				
Company employees	1.00	0.172	1.00	
Factory workers	1.36 (0.87-2.13)	0.184	0.99 (0.58-1.70)	0.977
Freelancers	1.33 (0.87-2.02)	0.436	1.09 (0.67-1.77)	0.737
Students	0.77 (0.40-1.48)	0.026	0.75 (0.40-1.51)	0.421
Others	1.74 (1.07-2.83)		1.38 (0.79-2.41)	0.251
Education				
Middle school or below	1.00	0.375	1.00	
High school or equal	0.80 (0.49-1.31)	0.013	0.83 (0.48-1.43)	0.832
College or above	0.56 (0.36-0.88)		0.76 (0.43-1.31)	0.755
Marital status				
Never married	1.00	0.337		
Currently married	1.21 (0.82-1.79)	0.254		
Divorced/widowed	1.40 (0.79-2.50)	0.332		
Sexual identified as gay	1.20 (0.83-1.75)	0.119		
HIV/AIDS knowledge score ≥ 3	0.78 (0.57-1.07)	0.629		
Ever used drugs	1.18 (0.60-2.35)			
No. male sex partners in lifetime				
1	1.00	0.512		
2-10	0.79 (0.39-1.59)	0.130		
≥ 11	1.30 (0.93-1.81)			
No. male anal sex partners in the past 6 months				
0-1	1.00	0.011	1.00	
2-5	1.55 (1.11-2.16)	0.006	1.53 (1.07-2.17)	0.020
≥ 6	2.08 (1.23-3.51)	0.036	1.82 (1.05-3.17)	0.034
Condom use at last anal sex	0.69 (0.49-0.98)		0.68 (0.47-0.97)	0.034
No. female sex partners in lifetime				
0	1.00	0.479		
1	1.15 (0.78-1.68)	0.184		
≥ 2	1.30 (0.88–1.91)			

OR, odds ratio; CI, confidence interval.

participants reported having two or more male sex partners in lifetime with 29.2% having 10 or more male sex partners, and 52.8% having two or more male anal sex partners in the past 6 months, and 26.9% not using condom at last anal sex. About 52.7% reported no female sex partners in lifetime, whereas 22.5% reported having two or more female sex partners in lifetime (Table 1).

3.2. *Willingness to use PrEP and associated factors*

Overall, 197 (19.1%) participants reported that they were willing to use PrEP for HIV prevention. There were significant higher proportions of reporting willingness to use PrEP among those who were aged ≥ 45 years (32.6%), non-local residents (21.6%), had middle school education or below (26.0%) and had ≥ 6 male anal sex partners in the past 6 months (27.2%) ($p < 0.05$) (Table 1).

Univariate analysis indicated that significant variables associated with willingness to use PrEP included age, permanent legal residency, occupation, education, number of male sex partners in the past 6 months, and condom use at last anal sex. In multivariate analysis, those who were aged ≥ 45 years (OR = 2.18; 95% CI: 1.13-4.23), non-local residents (OR = 1.69; 95% CI: 1.16-2.45), 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 significantly more willing to use PrEP, whereas those reporting condom use at last anal sex with man were significantly less willing to use PrEP (OR = 0.68; 95% CI: 0.47-0.97) (Table 2).

3.3. *Acutal uptake of PrEP and associated factors*

Only 26 (2.5%) participants finally enrolled in the TDF group and took TDF one tablet a day, *i.e.*, actual uptake of PrEP (Table 1). There were only marginally significant higher proportions of uptake of PrEP among those who were ≥ 45 years (5.8%), had middle school education or below (3.8%), had ≥ 11 male sex partners in lifetime (4.3%) and had no more than one female sex partner in lifetime (3.2%) ($0.05 < p < 0.10$) (Table 1).

Univariate analysis indicated that significant variables included age, education, number of male sex partners in lifetime. In multivariate analysis, those who had ≥ 11 male sex partners in lifetime were significantly

Table 3. Logistic regression analysis of factors associated with uptake of PrEP for HIV prevention

Items	Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age (years)				
18–24	1.00		1.00	
25–34	1.33 (0.46-3.87)	0.600	1.10 (0.37-3.28)	0.863
35–44	1.96 (0.56-6.88)	0.293	2.15 (0.57-8.05)	0.258
≥ 45	3.61 (1.02-12.76)	0.047	3.69 (0.79-17.33)	0.097
Non-local residents	0.69 (0.32-1.48)	0.331		
Occupation				
Company employees	1.00			
Factory workers	0.29 (0.06-1.31)	0.108		
Freelancers	0.70 (0.25-1.91)	0.482		
Students	0.60 (0.13-2.78)	0.519		
Others	1.13 (0.39-3.31)	0.825		
Education				
Middle school or below	1.00		1.00	
High school or equal	0.19 (0.04-0.99)	0.048	0.20 (0.04-1.12)	0.068
College or above	0.74 (0.27-2.02)	0.556	0.93 (0.27-3.23)	0.910
Marital status				
Never married	1.00			
Currently married	0.88 (0.29-2.62)	0.813		
Divorced/widowed	2.45 (0.80-7.44)	0.114		
Sexual identifiedas gay	1.76 (0.60-5.15)	0.305		
HIV/AIDS knowledge score ≥ 3	1.74 (0.75-4.03)	0.174		
No. male sex partners in lifetime				
1	-	-	-	
2-10	1.00		1.00	
≥ 11	2.26 (1.03-4.93)	0.041	2.40 (1.07-5.37)	0.033
No. male anal sex partners in the past 6 months				
0-1	1			
2-5	1.57 (0.66-3.71)	0.303		
≥ 6	1.76 (0.47-6.64)	0.402		
Condom use at last anal intercourse	1.73 (0.77-3.85)	0.184		
No. female sex partners in lifetime				
0	1.00			
1	1.00 (0.43-2.35)	1.000	0.77 (0.28-2.13)	0.614
2	0.13 (0.02-1.01)	0.051	0.12 (0.02-0.91)	0.040

OR, odds ratio; CI, confidence interval.

more likely to participate in the TDF group (OR = 2.40; 95% CI: 1.07-5.37), whereas those had two or more female sex partners were significantly less likely to participate in the TDF group (OR = 0.12; 95% CI: 0.02-0.91). A marginal significance was also observed for the association between actual uptake of PrEP and lower education level (high school or equal vs. middle school or below) (OR = 0.20; 95% CI: 0.04-1.12; $p = 0.068$) (Table 3).

3.4. *Reasons for not participating in TDF group*

Of the 171 participants who reported being willing to use PrEP but finally not participating in the TDF group, the reasons were summarized as below: 85 (49.7%) were lost of contact, 47 (27.5%) were ineligible because of abnormal results for liver or renal function tests, 35 (20.5%) changed their mind to not using PrEP, 4 (2.3%) experienced HIV seroconversion before uptake of PrEP.

4. Discussion

We found a significant number of MSM engaged in risky sexual behaviors, *e.g.*, having multiple anal sex partners and non-condom use at last anal sex. HIV behavioral interventions including HIV/AIDS education and voluntary counselling and testing (VCT) services have been scaled up for a number of years in China (*6*). These suggest that existing educational and behavioral interventions may be insufficient to prevent HIV transmission in MSM population, and alternative biomedical interventions such as PrEP are warranted.

Previous studies conducted in China observed high proportions of willingness to use PrEP among MSM (*11,12*). In contrast, we found that less than one-fifth of participants showed their willingness to take TDF on a daily basis for HIV prevention. Such differences were very likely attributed to the fact that the PrEP program was hypothetical in the reference studies but was really available in the present study, and thus ours more realisticly reflects the actual willingness of MSM participating in the PrEP program, which usually requires a long-term period of taking pills and follow-up visits.

Several factors have found to be associated with the willingness to take TDF for HIV prevention. MSM

reported more anal sex partners were more willing to participate in the TDF group, consistent with previous studies (*11,12,15*). This suggests that those with high-risk behaviors were more likely to accept PrEP for HIV prevention. We also found that compared to the younger MSM, older MSM were more willing to participate in the TDF group, which is consistent with a previous study (*16*). The possible explanation was that younger MSM were more likely to worry about the long term side effects of TDF. However, younger MSM are at higher risk of HIV infection compared to the older MSM (*17,18*) and playing an important role in the transmission of HIV in China (*18,19*). In addition, we found that non-local residents were more willing to use TDF for HIV prevention than local residents. It was possible that non-local residents have more freedom and less worries about potential risks of disclosing sexual orientation to their family members because they are less likely to live with family members.

Furthermore, we found that only 2.5% of participants finally participated in the TDF group and took the pills. This was unexpectedly low even though some of participants were ineligible to participate in the TDF group due to abnormal results for liver or kidney function tests. MSM who had more sex partners in lifetime were more likely to participate in the TDF group. Same as previous studies which indicated that men who have sex with men and women (MSMW) were less likely to participate in HIV prevention and intervention activities despite at similar or even higher risk of HIV infection compared to MSM only (*20,21*), we also found that those reporting more female sex partners in lifetime were less likely to use PrEP.

These data indicate that implementation of PrEP to prevent HIV transmission among MSM at current circumstance in China remains challenging. Previous surveys in China showed that less than one quarter of MSM have heard of PrEP (*10,11*), which was associated with willingness to accept PrEP (*10*). In fact, the present study was a baseline survey for one of the first clinical trials of PrEP in China. Therefore, there is an urgent need to raise MSM population's awareness of PrEP and increase their knowledge about the safety and efficacy of PrEP through the internet and social media.

There were several limitations of this study. First, participants were recruited solely from Shanghai; caution should be taken in generalizing the findings to MSM population to other areas. Second, sexual behaviors were self-reported and therefore subject to information bias. Third, the reasons for unwillingness to use TDF for HIV prevention, except loss to follow-up and changing mind to not taking TDF, were not fully elaborated. Despite these limitations, the present study provides important information for implementation of PrEP among MSM population in China. Our findings suggest that promotion of PrEP in MSM remains challenging at current circumstance in China. Future research is warranted to solicit effective education and intervention programs to promote acceptance of PrEP among Chinese MSM.

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