

AN EXPLORATION OF HIV TESTING, LINKAGE-TO-CARE AND  
ANTIRETROVIRAL THERAPY INITIATION AMONG CHINESE MEN WHO HAVE  
SEX WITH MEN

By

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Dissertation

Submitted to the Faculty of the  
Graduate School of Vanderbilt University

in partial fulfillment of the requirements

for the degree of

DOCTOR OF PHILOSOPHY

in

Epidemiology

August, 2015

Nashville, Tennessee

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## DEDICATION

To my beloved family and parents

For their continuing encouragement and support.

## ACKNOWLEDGEMENTS

Striving through the vigorous and challenging trail of accomplishing the highest degree in my devoted area of interest, I have always been grateful for numerous people who have been providing me with valuable training, mentorship, assistance, opportunities and support. My progress would not be accomplished without these efforts and blessings.

First and foremost, I would like to express the most sincere gratitude to my research mentor and Chair of my dissertation committee, Dr. Sten H. Vermund. I greatly appreciate and learn from every conversation with Dr. Vermund to discuss my research projects and dissertation for his critical challenge, creative idea, visionary suggestions and tremendous patience. I am also very grateful for Dr. Vermund's generosity and caring for inviting me to a variety of symphonies, concerts, operas and Christmas parties, which truly added warmth and color to my life living in this music city. I am also very thankful for my mentor, Dr. Han-zhu Qian, for his great efforts to address every question I had during my research activities, and his timely revisions and feedbacks for all the manuscripts and dissertation drafts. I would also like to thank other committee members for their time and effort on my dissertation, including Dr. Chandra Y. Osborn, especially for her guidance of doing qualitative data analysis; Dr. Pingsheng Wu, especially for her statistical support; and Dr. Yujiang Jia for his input about HIV cascade modeling in China.

I sincerely owe my earnest thankfulness to the Ph.D. program in Epidemiology at Vanderbilt University that provided me a stage for further training; and the

current/former faculty members at Vanderbilt (Drs. Katherine Hartmann, Sandra Deming-Halverson, Robert Greevy, Aaron Kipp, Christ Slaughter, Meira Epplein, Alicia Beeghly-Fadiel, Melinda Aldrich, Kristin Archer, Stephen Deppen, and Yu Shyr) who provided me with cutting-edge coursework training for the growing of my intellectual curiosity and academic ability. My thankfulness also goes to the former program coordinator, Ms. Toye Spencer, who offered generous assistance for all the academic logistics and management work.

I am also grateful for all the faculty and staff at Vanderbilt Institute of Global Health, with whom I felt embraced in a comfortable and supportive environment every day. Specifically, I would like to thank Ms. Jennifer St. Clair for her arrangements of my meetings with Dr. Vermund; Ms. Bea Smith for helping me with a variety of logistics; Ms. Holly Cassell for all the administrative efforts; and Mr. Clay Wilson for the travelling and purchase coordination.

I would like to thank our Chinese collaborators at National Center for AIDS/STD Control and Prevention, Beijing Center for Disease Control and Prevention, Chaoyang District Center for Disease Control and Prevention and Xicheng District Center for Disease Control and Prevention, and Chaoyang Chinese AIDS Volunteer Group for their efforts in participant recruitment, study implementation and data collection.

Finally, this work was supported by the generous support of Vanderbilt Clinical & Translational Research Scholars (VCTRS) Program (UL1TR000445 and KL2TR000446), the U.S. National Institutes of Health (R01AI09462 and R34AI091446), the Ministry of Science and Technology of China (2012ZX10004-904, 2012ZX10001-

002), the Chinese State Key Laboratory for Infectious Disease (Development Grant 2012SKLID103), and the National Natural Science Foundation of China (81273188). My stipend was supported, in part, by the endowment from the Amos Christie Chair in Global Health, held by Dr. Vermund.

## TABLE OF CONTENTS

	Page
DEDICATIONS.....	ii
ACKNOWLEDGEMENTS.....	iii
LIST OF TABLES.....	viii
LIST OF FIGURES.....	ix
LIST OF ABBREVIATIONS.....	x
Chapter	
I. BACKGROUND.....	1
HIV/AIDS and global patterns.....	1
Global HIV epidemics among men who have sex with men.....	2
HIV/AIDS in China.....	4
HIV epidemics among Chinese MSM.....	6
HIV prevention intervention among Chinese MSM.....	12
II. SPECIFIC AIMS AND SIGNIFICANCE.....	16
Specific aims.....	16
Significance of Aim 1.....	18
Significance of Aim 2.....	20
Significance of Aim 3.....	23
III. DATA AND METHODOLOGY.....	26

IV. REPEAT HIV TESTING IS ASSOCIATED WITH A LOWER LIKELIHOOD OF HIV INFECTION AMONG CHINESE MEN WHO HAVE SEX WITH MEN: A MULTIVARIABLE ANALYSIS WITH PROPENSITY SCORE ADJUSTMENT .....	39
Abstract.....	39
Introduction .....	40
Methods .....	43
Results .....	47
Discussion.....	50
V. BARRIERS AND FACILITATORS OF LINKAGE TO AND ENGAGEMENT IN HIV CARE: A QUALITATIVE STUDY AMONG HIV-POSITIVE MEN WHO HAVE SEX WITH MEN IN CHINA.....	65
Abstract.....	65
Introduction .....	66
Methods .....	69
Results .....	71
Discussion .....	81
VI. PREDICTORS OF ANTIRETROVIRAL THERAPY INITIATION: A CROSS-SECTIONAL STUDY AMONG CHINESE HIV-INFECTED MEN WHO HAVE SEX WITH MEN .....	88
Abstract.....	88
Introduction .....	90
Methods .....	92
Results .....	95
Discussion .....	97
VII. SYNOPSIS .....	113
REFERENCES .....	119

## LIST OF TABLES

Table	Page
1. Demographic and behavioral characteristics of men who have sex with men in Beijing, China, 2013 (N=3,588) .....	56
2. Logistic regression analyses of the association between prior HIV testing and risk HIV infection among Chinese MSM (N=3588) .....	61
3. Socio-demographic characteristics of HIV-positive men who have sex with men in Beijing, China (N=40) .....	86
4. Perceived barriers and facilitators for HIV testing among HIV-positive men who have sex with men in Beijing, China (N=40) .....	87
5. Sociodemographic and behavioral characteristics of HIV-infected men who have sex with men in Beijing, China .....	102
6. Sociodemographic and behavioral characteristics of HIV-infected men who have sex with men by CD4+ cell count (<350 cells/ $\mu$ L eligible for free antiretroviral treatment at the time of the study) in Beijing, China .....	105
7. Bivariable and multivariable logistic regression analyses of factors associated with initiation of antiretroviral therapy (ART) among HIV-infected men who have sex with men by CD4+ cell count (<350 cells/ $\mu$ L eligible for free ART at the time of the study) in Beijing, China .....	109



## LIST OF FIGURES

Figure	Page
1. HIV care continuum and presentation of each stage .....	15
2. Association between frequency of prior HIV testing and odds ratios of being infected with HIV .....	62
3. Perceived facilitators for enhancing HIV testing among men who have sex with men in Beijing, China (N=3,588) .....	63
4. Barriers to test for HIV identified by men who have sex with men who never tested for HIV in Beijing, China (N=1,054) .....	64
5 . HIV care counseling services received among participants by ART initiation status .....	112

## LIST OF ABBREVIATIONS

AIDS	Acquired immunodeficiency syndrome
AOR	Adjusted odds ratio
ART	Antiretroviral therapy
ARV	Antiretroviral drug
CBO	Community-based organization
CCAAG	Chaoyang Chinese AIDS Volunteer Group
CDC	Center for Disease Control and Prevention
CSW	Commercial sex workers
DAG	Directed acyclic graph
ELISA	Enzyme-linked immunosorbent assay
FG	Focus group
FGD	Focus group discussion
FSW	Female sex workers
HBCT	Home-based counseling and testing
HIV	Human immunodeficiency virus
IgG	Immunoglobulin G
IQR	Interquartile range
IRB	Institutional review board
MOH	Minister of Health
MSM	Men who have sex with men
MTCT	Maternal-to-child transmission
NCAIDS	National Center for AIDS/STD Control and Prevention
PITC	Provider-initiated testing and counseling
PLWHA	People living with HIV/AIDS

PLHIV	People living with HIV
PWID	Persons who inject drugs
RPR	Rapid plasma regain
RR	Relative risk
STD	Sexually transmitted diseases
STI	Sexually transmitted infection
TLC	Testing and linkage-to-care
TP	<i>Treponema pallidum</i>
UAI	Unprotected anal intercourse
UNAIDS	Joint United Nations Programme on HIV/AIDS
VCT	Voluntary counseling and testing
WHO	World Health Organization

## CHAPTER I

### BACKGROUND

#### HIV/AIDS and global patterns

Human immunodeficiency virus (HIV) is a virus that may lead to irreversible damage to the human immune system, and results in the loss of CD4+ T-lymphocytes (CD4 cells) (Cunningham, Donaghy, Harman, Kim, & Turville, 2010). If not virally suppressed through timely and continuous treatment, it may ultimately result in the Acquired Immune Deficiency Syndrome (AIDS). AIDS is the final stage of HIV infection, occurring in at least 98% of untreated HIV-infected persons with severely damaged immune systems that can no longer fight against infections effectively (Sepkowitz, 2001).

Since the first cases reported in the *Morbidity and Mortality Weekly Report* by U.S. Centers for Disease Control and Prevention (CDC) in June, 1981 (MMWR, 1981), HIV/AIDS has been spreading rapidly worldwide, which threatens diverse populations and constitutes a significant public health burden (Cohen, Hellmann, Levy, DeCock, & Lange, 2008; De Cock, Jaffe, & Curran, 2012). By the end of 2013, an estimated 35 (33.2-37.2) million people were living with HIV worldwide, 2.1 (1.9-2.4) million people were newly infected with HIV in 2013, and 1.5 (1.4-1.7) million people died from AIDS-related causes. ("The Gap Report. UNAIDS. 2014.,")(The Gap Report. UNAIDS. 2014.)

An estimated 78 million people have been infected and 39 million have died of HIV since the advent of the epidemic (Organization, 2013).

There is an optimistic side of the epidemics. With global efforts in the advancement of treatment and care sciences (Beyrer et al., 2013), and the expansion of HIV/AIDS prevention and intervention programs, we are observing encouraging declines in HIV/AIDS morbidity, mortality and new infections as compared to early years. ("The Gap Report. UNAIDS. 2014.,") (The Gap Report. UNAIDS. 2014.)

#### HIV epidemics among men who have sex with men

Nonetheless, there has been an increasing global concern about the resurging spread of HIV driven by men who have sex with men (MSM) in the past decade (Baral, Sifakis, Cleghorn, & Beyrer, 2007a; Murray et al., 2014; Supervie & Ekouevi, 2014; van Griensven, de Lind van Wijngaarden, Baral, & Grulich, 2009a). Although HIV surges among MSM are seen at a global level (van Griensven & de Lind van Wijngaarden, 2010), current prevention efforts have been minimally effective in containing the spread of the disease among this population. MSM are extremely vulnerable to HIV infection because of biological susceptibility from unprotected anal intercourse, high frequency of risky behavior taking, and burden of STI co-infection (Baggaley, White, & Boily, 2010; Mayer et al., 2013). MSM continue to be overrepresented in newly identified HIV cases in many developed and developing countries (Beyrer, Baral, et al., 2012), while the infection rates among the general population and other high-risk subgroups have been declining since 2001. ("GLOBAL REPORT.UNAIDS report on the global AIDS

epidemic 2013. Available at <http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport/>," ) (GLOBAL REPORT.UNAIDS report on the global AIDS epidemic 2013. Available at <http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport/>) In some low- and middle-income countries, the odds of being HIV infected is 19.3 times higher among MSM compared with the risk of an individual in the general population (Baral, Sifakis, Cleghorn, & Beyrer, 2007b). Some recent review data revealed the drastic differences and expanding trajectories of the HIV epidemics among MSM in low, middle and high income countries (Beyrer, Baral, et al., 2012; Beyrer, et al., 2013). Male-to-male homosexual transmission has become the major and stable contributor to the existing and new HIV cases in developed countries/regions such as the United States, Western Europe and Australia (Jansson & Wilson, 2012; Nakagawa, Phillips, & Lundgren, 2014; Vermund & Leigh-Brown, 2012). HIV incidence and prevalence among MSM has also become evident in underdeveloped or developing regions (Caribbean, Sub-Saharan Africa, Latin America and East/south East Asia), where the epidemics were originally driven by female sex workers (FSW), maternal-to-child transmission (MTCT), illegal plasma donor and/or persons who inject drugs (PWID) (Baral et al., 2011; Beyrer, et al., 2013; Clark et al., 2008; Hladik et al., 2012; Y. F. Huang et al., 2013; Pham et al., 2012; van Griensven et al., 2010; Wu et al., 2013b).

Asia has the second largest number of people living with HIV/AIDS (PLWHA), after Sub-Saharan Africa, with 4.8 (4.1-5.5) million PLWHA across the region and 888,000 of whom resided in East Asia ("The Gap Report. UNAIDS. 2014.," ; Suguimoto et al., 2014). Although HIV prevalence is low in East Asia (0.1%), the emerging and

booming prevalence of male-to-male homosexual contact plays a significant role in driving the epidemic upwards rapidly. HIV prevalence among MSM has also been increasing in this region—recent data published in China, Taiwan and Vietnam have lifted the estimated HIV prevalence among MSM from 5.3% in 2012 to 10.3% in 2013 this region. Of particular note, China accounts for 89% of PLWHA in East Asia. ("GLOBAL REPORT.UNAIDS report on the global AIDS epidemic 2013. Available at <http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport/>,") (GLOBAL REPORT.UNAIDS report on the global AIDS epidemic 2013. Available at <http://www.unaids.org/en/resources/campaigns/globalreport2013/globalreport/>) The HIV epidemic is also climbing rapidly among Chinese MSM. ("State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2012.,")(State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2012.) This situation presents new challenges for the combat against HIV in China.

### HIV/AIDS in China

As the country with the world's largest population, ("Central Intelligence Agency: The World Factbook 2013-14. ,")(Central Intelligence Agency: The World Factbook 2013-14. )China has been facing noticeable social and public health challenges deriving from the HIV/AIDS epidemic during the past two decades. By the end of 2008, unpublished government reports documented that HIV/AIDS had become the leading

cause of death among infectious diseases in China. According to the joint national report by the Chinese Ministry of Health (MOH), together with the Joint United Nations Programme on HIV/AIDS(UNAIDS) and the World Health Organization (WHO), by the end of 2011, there were an estimated 780,000 (620,000-940,000) people PLWHA in China. ("State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2012.,") (State Council AIDS Working Committee Office (SCAWCO): China 2012 UNGASS Country Progress Report. Beijing, China: Ministry of Health of the People's Republic of China; 2012.) Although the HIV/AIDS prevalence among the general Chinese population maintains at a low level (0.033%), the number of PLWHA has been increasing noticeably with a substantial proportion of undiagnosed cases. During 2009 -2013, the actual reported cases of PLWHA from both hospital and surveillance increased from 272,000 in 2009 to 307,000 in 2010, 352,000 in 2011, 386,000 in 2012, and 437,000 in 2013 (State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing).

Although blood transfusions and injecting drug use were the dominant routes in China, sexual transmission has become the primary mode of HIV transmission since 2005 (Z. Huang et al., 2013). Compared to statistics in 1998 where 60%-70% of the reported infections were due to injecting drug use, 63.9% of the estimated 780,000 PLWHA and 81.6% of 48,000 new infections in 2011 were transmitted via sexual contact (Y. Li et al., 2013; "State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2012.," ; Zhang KI & Ma, 2002). In recent years, while the



HIV positive antibody rate among other high-risk subgroups (FSW, PWID and illegal plasma donors) have been decreasing or remaining stable, HIV transmission via male-to-male homosexual contact showed an upward trend, with the proportion among all new cases increasing from 2.5% in 2006 to 21.4% in 2013 (State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing). In the meantime, the estimated HIV prevalence among Chinese MSM also increased from 3.0% in 2006 to 7.6% in 2013, according to the national report (State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing).

### HIV/AIDS epidemics among Chinese MSM

Findings from observational studies also demonstrated an increasing trend of the HIV epidemics among Chinese MSM, despite the heterogeneity of the magnitude of the results. Chow et al. summarized 94 studies up to 2009 and revealed a pooled HIV prevalence increasing from 1.4% (0.8%-2.4%) in 2001 to 5.3% (4.8%-5.8%) in 2009 (Chow, Wilson, Zhang, Jing, & Zhang, 2011); another study by Meng et al. reported that the pooled HIV prevalence among MSM in China increased from 0.6% (0.0-2.1%) in 2003 to 7.4% (5.7-9.2%) in 2009 (Meng et al., 2013). A more recent meta-analysis of 84 studies published between 2009-2013 showed an overall pooled HIV prevalence of 7.2% among MSM in China (Zhou et al., 2014). Although HIV incidence is suggested to be substantial among Chinese MSM, relevant studies with summary of such measurement across the country remain limited. The most recent meta-analysis of 12 studies published

through 2011 indicated an incidence density among Chinese MSM varying from 2.6% (1.1%–4.1%) to 9.4% (6.3%–12.5%), with a pooled HIV incidence of 3.5% (1.7%-5.3%) and 6.7% (4.8%-8.6%) among included cohort (3 studies) and cross-sectional studies (9 studies), respectively (H. M. Li et al., 2011).

All regions in China have been experiencing a significant increase in PLWHA among MSM in the past decade (Chow, et al., 2011). However, as a result of the difference in social concept, cultural value and openness towards homosexuality, the prevalence of male homosexual behaviors may vary across different regions in China , leading to the geographic variation in terms of the trend and magnitude of HIV epidemics among Chinese MSM (Chow, et al., 2011). A review paper suggested that, in general, HIV epidemics among MSM in China are more robust in socioeconomically less developed areas than in developed cities; MSM in Southeast (11.4%;9.6%-13.5%) had the highest HIV prevalence, while those in Northwest had the lowest (1.0%;0.5%-3.7%) (Zhou, et al., 2014). Nonetheless, some recent studies showed a high HIV prevalence rate (ranging from 10.7% to 19.6%) in metropolitan cities (e.g. Beijing, Shanghai, Guangzhou and Chongqing) (Bai, Xu, et al., 2014b; X. Li et al., 2014a; Long et al., 2014a; Tao et al., 2014; Yan, Ding, et al., 2015; G. Zeng et al., 2014; Zhong et al., 2014). Despite the inconsistencies, it reflects the fact that the acceleration of the HIV epidemics among Chinese MSM has become one of the most critical public health and social challenges in China's fight against HIV/AIDS.

It is estimated that there are 5-10 million MSM living in China and this estimate is still growing (Wong et al., 2009; Zhang BC, 2002; Zhang Kl & Ma, 2002).

Homosexuality has existed in the Chinese history for more than 3,000 years, with the

earliest record traceable back in Shang Dynasty (1523-1027 BC) (F. F. Ruan & Tsai, 1987; Tao et al., 2013b). Since the ‘Reform and Opening Up’ revolution from late 1970s, Chinese has become more tolerant to a variety of activities and concepts that were previously considered as anti-social by Chinese culture. However, male-to-male homosexual activities are yet not socially acceptable because of the traditional taboo and historical discrimination against homosexuality that is influenced by the Confucianism (H. Liu et al., 2006). As a result of this situation, Chinese MSM are often under tremendous psychological burdens and social pressures that directly or indirectly isolate them from socialization and exposure to the general public. In addition, to fulfill family responsibilities of reproduction to carry on a family line and avoid being stigmatized, Chinese MSM often are pressured to marry women, disguising their sexual orientation (He et al., 2006b; Neilands, Steward, & Choi, 2008; Qian, Vermund, & Wang, 2005). In the meantime, these married MSM often remain sexually active with their male partners (Tao et al., 2013a). This situation not only makes Chinese MSM a ‘hidden’ and ‘hard-to-reach’ subgroup that introduces difficulties for the implementation of prevention interventions (Beyrer, 2010), but also makes it highly likely to transmit HIV and sexually transmitted infections (STI) from this high risk population to their low risk wives and general populations (He et al., 2006a).

Sexual networks have proven to be complex among Chinese MSM compared to other high-risk groups like FSW (Y. Li, et al., 2013; J. Liu, Qu, Ezeakile, Zhang, & Liang, 2013; H. Lu, Han, et al., 2013a; Y. Ruan, Luo, et al., 2009a; Tang et al., 2013b). In practice, Chinese MSM often seek their sexual partners in public locations such as parks and public toilets, entertainment facilities (e.g., gay bars, pubs, bathhouses, and

saunas), gay websites, and chatting platforms (e.g., QQ, MSN, WeChat, online chat rooms) (Lau, Zhao, Wu, Gu, & Hao, 2013; Qi et al., 2015). Although many MSM reported knowing high HIV prevalence among Chinese MSM, a majority of them do not perceive themselves to be at high risk of being infected with HIV (Fan et al., 2014; Ma et al., 2013). In the past few years, many project-based prevention interventions have been widely and specifically implemented among Chinese MSM and were demonstrated to be efficacious (Z. Huang, et al., 2013; H. Lu, Liu, et al., 2013; Ye et al., 2014; Zheng & Zheng, 2012). Nonetheless, evidence from recent observational studies suggested that known high-risk behaviors, such as having multiple partners, unprotected anal intercourse (UAI), alcohol or illicit drug use and not routinely test for HIV, are still highly prevalent among Chinese MSM (Bai, Luo, et al., 2014; Y. H. Chang et al., 2013; Q. Q. Wang et al., 2014a; Zhong, et al., 2014).

UAI is one of the high-risk behaviors that contributed substantially to the HIV transmission (J. Wu et al., 2014). In China, it was estimated that regular partnerships exist among 47.2%-62.1% of the MSM population (B. Zhang, Li, & Hu, 2001; B. C. Zhang et al., 2007). According to several studies in both Western countries and China, UAI was more likely to occur when regular partners are involved (Davidovich, de Wit, & Stroebe, 2000; Elford, Bolding, Maguire, & Sherr, 1999; Fitzpatrick, McLean, Dawson, Boulton, & Hart, 1990; Hays, Kegeles, & Coates, 1997). A recent meta-analysis of 62 articles published through September, 2013 showed a pooled prevalence of UAI to be the following: with any male partner 53% (95%CI: 51–56%); with regular male partners 45% (95%CI: 39–51%); with non-regular male partners 34% (95%CI: 24–45%); with casual male partners 33% (95%CI: 30–36%); and with commercial male partners 12% (95%CI:

5–26%) (J. Wu, et al., 2014). Evidence also suggested that UAI was even more prevalent among some MSM subgroups in China. A meta-analysis of a pooled sample of 1,603 HIV-positive Chinese MSM from 19 studies indicated a drastically high UAI prevalence among this subgroup (75.4% ;95%CI: 67.5%-82.5%) (He, Peng, Zhang, Wang, & Wang, 2012). A study of 2,812 older MSM (>50 years old) showed that 79.5% (95% CI: 72.7%-84.9%) of them had engaged in UAI in past 6 months (Y. Z. Li et al., 2014). Therefore, UAI is a significant concern among Chinese MSM that entails specific and effective interventional efforts.

Having multiple sexual partners is another highly prevalent risky behavior among Chinese MSM. Evidence suggests that a great proportion MSM who have regular partners are in active sexual relationship with other men at the same time (D. Li, Li, Wang, & Lau, 2015; Mitchell & Petroll, 2013; Z. Wang et al., 2013). Several studies has suggested more than half of the surveyed participants had multiple concurrent sexual partners in the past 6 months prior to study participation (Chu et al., 2013; D. Song et al., 2013; Xu, Zhang, et al., 2014). Some previous observational studies suggested that UAI was highly prevalent among Chinese MSM who had regular partners (42.9% to 78.1%) (H. Yang et al., 2010; Zeng ZL, 2008; X. Zhang et al., 2007), and it is a significant predictor of HIV seroconversion (H. Yang, et al., 2010). Under the circumstance of UAI, multiple sexual partnerships would dramatically increase the transmission of the virus within this key population.

Alcohol consumption and illicit drug use is also a common high risk behavior that is often associated with other risk factors among Chinese MSM. The prevalence of alcohol drinking varies among different studies due to sample size and measurement

discrepancies (H. Lu, Han, et al., 2013b). A recent meta-analysis of 19 independent studies published through September 2013 showed a pooled prevalence of 32% (effect size: 0.32; 95% CI: 0.25–0.4) of alcohol drinking, with the individual findings ranging from 16.5% to 79.7% (Y. Liu et al., 2014b). Alcohol has been proven to be associated with the dynamics of sexual arousal, expectation of casual sex and thus HIV/STI transmission because of its psychogenic nature and influence on decision making (R. L. Cook & Clark, 2005; Jones-Webb, Smolenski, Brady, Wilkerson, & Rosser, 2013; Woolf-King & Maisto, 2011). Several studies also found that Chinese MSM who drank alcohol more than once a week or before sex were more likely to have unprotected insertive or receptive anal sex with men, have more lifetime male sex partners, trade sex for money and use illicit drugs (Y. Liu, et al., 2014b; H. Lu, Han, et al., 2013b; Y. Ruan, Luo, et al., 2009b; Tang et al., 2013a). Recent studies also observed that illicit drug use for a recreational purpose has been gaining popularity among Chinese MSM (D. Li et al., 2014; Nehl et al., 2015; Xu, Qian, et al., 2014; Xu, Zhang, et al., 2014). A study of 3,830 MSM from six Chinese cities showed that 28% of them reporting ever using drugs (popper, ecstasy, methamphetamine, amphetamine, tramadol, and ketamine) at least once in the past 6 months (Xu, Zhang, et al., 2014). Consumption of such recreational/illicit drugs may result in ‘cognitive escape’ with judgment impairment, which leads to disinhibiting behaviors and subsequently increase the risk of HIV/STI transmission (Catania et al., 2008; Drumright et al., 2006; McKirnan, Venable, Ostrow, & Hope, 2001).

### HIV prevention intervention among Chinese MSM

Because of the prevalent high-risk behaviors and potential bridging role in transmitting disease to the general population (Chow et al., 2013), Chinese MSM have become a unique subgroup that is driving the HIV epidemic in China (Lau, Lin, Hao, Wu, & Gu, 2011). Without effective prevention interventions to reduce the risk, MSM could result in China contributing more substantially to regional and even global HIV transmission (Ma et al., 2012).

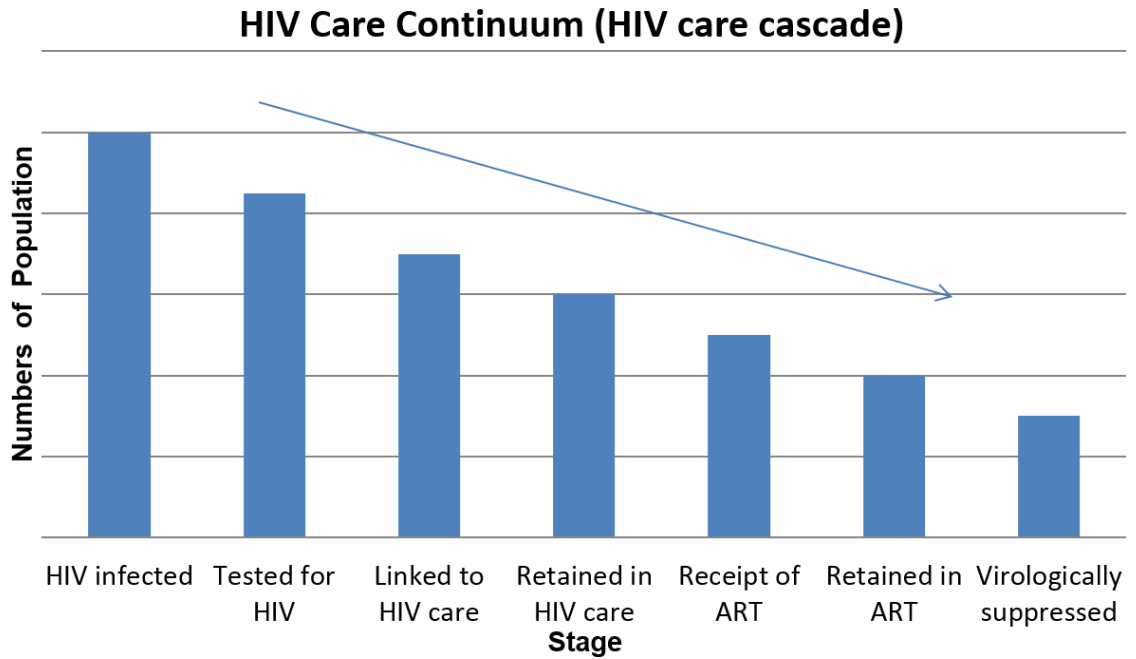
In the past decade, Chinese government has spent tremendous efforts in scaling up the HIV prevention intervention via surveillance system enhancement and policy establishment. One of the most important actions was the expansion of sentinel surveillance. Sentinel surveillance actively monitors HIV epidemics among several key populations through venue-based sampling, such as commercial sex workers (CSW) including both FSW and male sex workers, MSM, and PWID (Y. Mao et al., 2010; L. Wang & Wang, 2010; L. Zhang, E. P. Chow, et al., 2013; L. Zhang, Chow, Zhang, Jing, & Wilson, 2012). Since the establishment of sentinel surveillance pilot spots in 2000, there were 1884 sites throughout China by 2013 covering 13 at-risk population groups (L. Zhang, E. P. Chow, et al., 2013; L. Zhang, E. P. Chow, J. Zhang, et al., 2012). To accelerate HIV/AIDS control and prevention, China initiated the ‘Four Free and One Care’ policy (free ARV drugs, free prevention of mother-to-child HIV transmission [PMTCT], free voluntary counseling and testing, free schooling for children orphaned by AIDS, and care to people living with HIV/AIDS) in 2003. Further efforts have been made by implementing ‘Five Expands, Six Strengthens’ approach. This consists of expanding information/education/communication activities, surveillance and testing, PMTCT,

comprehensive interventions, coverage of ART, strengthening of blood safety management, and expanding health insurance, care and support, rights protections, organizational leadership, and response teams. However, MSM were not explicitly marked for special attention when the initial prevention intervention efforts were initiated (Choi, Lui, Guo, Han, & Mandel, 2006), which left a large proportion of MSM untested for HIV, even though they were active in risky behaviors, resulting in gaps in care including too few early diagnoses and too few infected persons linked to HIV/AIDS care and treatment, with a resulting low proportion of MSM being virologically suppressed. Moreover, knowledge about factors associated with active access to HIV testing and care remains limited among this population. Thus, studies need to be conducted to better understand the HIV epidemic, HIV testing, the pattern of HIV care, and the connection of these elements in order to ameliorate the growing rates of HIV infection among Chinese MSM.

Recent HIV intervention paradigm requires a high HIV testing rate, from the perspective that people who are aware of their positive HIV status would possibly modify high-risk behaviors and seek HIV care services with antiretroviral therapy (ART) (Choi, et al., 2006; Chow, et al., 2013; Granich, Gilks, Dye, De Cock, & Williams, 2009; Rotheram-Borus, Leibowitz, & Etzel, 2006). This may result in reduction in onwards transmissions at partnership level, a public health benefit termed ‘test-and-treat’ or ‘treatment-as-prevention’, even as ART mitigates damage to the patients’ own immune systems via timely viral load suppression (Crepaz et al., 2009; Das et al., 2010; X. Li, H. Lu, H. F. Raymond, et al., 2012; Montaner et al., 2010; Venkatesh, Flanigan, & Mayer, 2011; Vermund & Hayes, 2013a; Zou, Hu, Xin, & Beck, 2012). Experts also presented a



prevention intervention model indicating the success in curtailing HIV spread and maximizing the effect of HIV treatment entails efforts in optimizing each stage of the continuum of HIV care, or HIV care cascade (Burns, Dieffenbach, & Vermund, 2010; Gardner, McLees, Steiner, Del Rio, & Burman, 2011). These stages include HIV diagnosis (HIV testing), linkage to care, retention in care, initiation of ART, adherence to ART, and ultimate viral load suppression (Figure 1.1). Suboptimal presentation in any stages of the HIV care cascade, such as late diagnosis, loss of linkage to HIV care, poor retention, low ART initiation, and poor adherence, would ultimately impede the overall public health intervention goal (viral suppression) (Gardner, et al., 2011; Nosyk et al., 2014). Transmission modeling experts suggest that early identification of HIV-infected individuals, timely initiation of ART, and appropriate action to increase retention in care and ART adherence can lead to substantial reduction in community HIV transmission (Charurat et al., 2015). However, this objective could not be fully realized unless well designed qualitative and quantitative assessments are conducted within each spectrum of the continuum, and the plausible factors resulting in the ‘leaky pipe’ are understood. My thesis addresses these questions.



**Figure 1.HIV care continuum and presentation of each stage**

\*Attrition exists throughout the HIV care cascade. For example, among participants who test for HIV and are confirmed positive, only some of them will seek HIV care; among those who seek HIV care only some may consistently retain in HIV care, etc. (the same mechanism applies to later stages). As the proportion of patient is shrinking when entering further stages, only a minority of person with HIV actually achieve suppression of their viral infection. This explains the reason the decreasing trend shown in the bar graph above. The overall goal of the prevention interventions is to maximize the presentation for each stage with patients rolling from the previous stage(s).

## CHAPTER II

### SPECIFIC AIMS AND SIGNIFICANCE

#### Specific Aims

The overall goal of this study was to use the novel modeling framework of HIV care cascade and explore important aspects of three key stages among Chinese MSM, including HIV testing, linkage to care and use of antiretroviral therapy. The findings from the study are expected to strengthen the existing evidence of ‘test-and-treat’ and ‘treatment-as-prevention’ strategy in China, which has been widely discussed in the recent years (Muessig et al., 2012). The specific objectives include: (1) Assessing the association between history of HIV testing and HIV risk among Chinese MSM; (2) Qualitatively exploring personal as well as structural determinants of linkage to and engagement in HIV/AIDS care among HIV-infected Chinese MSM; (3) Quantitatively examining factors associated with use of antiretroviral therapy (ART) among HIV-infected Chinese MSM.

**Aim 1: To assess the association between history of HIV testing and HIV risk among Chinese MSM. Hypothesis #1:** HIV-negative Chinese MSM with a history of HIV testing are less likely to be HIV-infected detected in the most recent test than those without a history of HIV testing. The data are from an ongoing NIH-supported project (“Multi-component HIV Intervention Packages for Chinese MSM,” or “China-MP3

Project”), which collected both questionnaire and laboratory testing data among 3,588 MSM in Beijing City, China.

**Aim 2: To analyze the barriers to and facilitators of linkage to and engagement in HIV care among HIV-infected Chinese MSM.** Four focus group discussions (FGD) among 40 HIV-positive and two FGDs among 20 HIV-negative MSM were conducted in the China-MP3 project. Key questions were asked among HIV-infected groups about HIV risk, testing, care and treatment, risk reduction and intervention efforts, and perspectives on HIV care utilization improvement. We qualitatively explored the barriers and facilitators of linkage to and engagement in HIV care among HIV-infected Chinese MSM. Finding from this qualitative research may be used for formulating theories to guide future intervention efforts.

**Aim 3: To examine factors associated with ART initiation among HIV-infected Chinese MSM. Hypothesis #2:** Social-demographic (e.g., age, educational level), behavioral (e.g., number of sexual partners, sex role preference, unprotected anal sex), and clinical (e.g., CD4 count, HIV infection-related symptoms) factors are associated with ART initiation among HIV-infected MSM in China. Specifically, we hypothesize that MSM with Beijing ‘Hukou’ (residence) are more likely to use ART than those without Beijing ‘Hukou’. Data for this study aim came from another epidemiological survey conducted in 2011 among 1,155 MSM in Beijing, China, where a sub set of HIV-infected participants (N=238) were previous diagnosed. In the 2011 survey, data on use of ART were collected. Analysis among 238 HIV-infected MSM was performed to test hypothesis #2 and assess other factors associated with ART initiation.

## Significance of Aim 1

HIV/AIDS has been increasing among MSM in China during the past decade. By the end of 2011, male-to-male homosexual transmission accounted for 29.4% of newly reported HIV infections (D. Li et al., 2012; Y. Ruan, Jia, et al., 2009), and 17.4% of 780,000 people living with HIV/AIDS. ("State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2012.,")(State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2012.)Chinese MSM are not traditionally in favor of testing for HIV since the advent of the epidemic in this population. A study conducted in Jinan (Bond, Lauby, & Batson, 2005) suggested that more than 80% of MSM had never tested for HIV during the past 12 months. Although the Chinese government has been investing tremendous resources to promote HIV testing during the past decade, utilization rates still remain relatively low among hard-to-reach populations, including MSM. A recent study published in 2012 reported that approximately 40% of 500 MSM in Beijing, where HIV care resources are abundant, had not tested for HIV during the past 12 months (X. Li, H. Lu, H. F. Raymond, et al., 2012). A meta-analytic study published in 2013 aggregating findings from 54 independent studies showed that 53% of Chinese MSM had never tested for HIV in their lifetimes; 62% had no HIV testing during the past 12 months (Zou, et al., 2012). Since people who are aware of their HIV infection status are far more likely to seek early access to social and medical services (Rotheram-Borus, et al., 2006), timely identification of individuals with HIV infection is the key initial step to glean the documented health advantages of early

ART, addressing damage to patients' psychological health and immune systems (Zou, et al., 2012). Early access to care also can be expected to provide the public health benefits of reducing HIV transmission and spread (Cohen et al., 2011). Moreover, evidence also shows that frequent and repeated HIV testing has been linked to higher CD4+ cell counts when first diagnosed positive and is significantly associated with a reduced the mortality rate (Gras et al., 2011; Sobrino-Vegas et al., 2009; Walensky et al., 2010). Thus, from the perspective of prevention, it is extremely important to maximize HIV testing rates and strengthen repeated HIV testing among high risk populations, such as MSM, along with linking to care.

HIV testing may also reduce the likelihood of engaging in HIV high risk behaviors. Published studies suggested that frequent testers were more likely to be aware of their last sexual partner's HIV status and taking subsequent precautions, and seeking a healthcare provider historically; conversely, frequent testers had lower risk of being newly diagnosed as HIV positive and having any causal or exchange partners (Phillips et al., 2013). The possible mechanism could be, compared to non-testers or less-frequent testers, individuals who frequently undertake HIV testing are more likely to have interaction with doctors, healthcare workers and other peers. During this process, they might be able to gain more knowledge on appropriate HIV prevention, enhance HIV awareness, and re-adjust HIV risk perception (Straub et al., 2011). Therefore, frequent testers might be more attentive to avoid risky sexual behaviors (e.g., unprotected sex, substance use before sex, multiple concurrent partners, trade sex for money etc.) during homosexual activities, which lead to a lower risk of being HIV infected. Alternatively, frequent

testers may be better informed to begin with, with a greater propensity to get regular testing.

Only a few studies have investigated important correlates of HIV testing, comparing testers vs. non-testers, among Chinese MSM (X. Li, H. Lu, X. Ma, et al., 2012; X. Li, H. Lu, H. F. Raymond, et al., 2012; Y. Song et al., 2011). None of these studies has assessed factors related to the history of HIV testing and how this might be associated with risk of contracting HIV among MSM in China. Although many researchers have proven the need to have MSM test for HIV, we consider it valuable to bolster current HIV testing policy if our hypothesized association of having prior repeat HIV testing and a lower risk of being HIV-infected exists among Chinese MSM.

This study aimed to examine these factors and the hypothesized association using a cross-sectional sample of 3,588 MSM in Beijing. In addition, we quantitatively summarized reasons that are reflected as either advantages or disadvantages for active HIV testing. Positive findings will add to the evidence to strengthen the expansion of test and treat strategy among Chinese MSM, and mobilize HIV testing activities among this subgroup.

### Significance of Aim 2

The scale-up of free HIV/AIDS testing and care in China since 2003 has been one of the major intervention and prevention strategies being used to minimize HIV transmission among high risk subgroups, such as commercial sex workers (CSW), persons who inject drugs (PWID), illegal plasma donors (infected by unhygienic

reinfusion of red blood cells), and MSM (Chow, Wilson, & Zhang, 2012; Y. Song, et al., 2011). However, when this policy was established, MSM did not receive adequate attention from the government commensurate with the focus on other key populations; thus MSM-friendly programs were late in development, without a clear risk reduction policy strategy. It is not surprising, therefore, that MSM had low utilization of HIV-related services, despite the global importance of this vulnerable population (Chow, et al., 2012; Huang et al., 2012).

As important as the objective influences from political and institutional viewpoints, subjective factors experienced within key populations themselves are also pertinent or researchers to assess problems related to the utilization of HIV care services. Through 2014, a number of quantitative studies have been published to address issues related to HIV care utilization (Ankiersztein-Bartczak et al., 2014; Cooley et al., 2014b; Irvin et al., 2014; Yan et al., 2014). However, qualitative studies which could have in-depth examination of this phenomena and guide building intervention theories, are not published in higher impact journals and are less well known to the HIV research community, and in some ways are more limited in their research scope than are larger epidemiological and clinical studies.

Some qualitative studies have reported a variety of factors associated with suboptimal utilization of HIV care services among both Chinese and international high-risk populations, predominantly among PWID, CSWs, and blood donors (da Silva et al., 2014; Garland et al., 2011; Miller, Hennessy, Wendell, Webber, & Schoenbaum, 1996; Y. Song, et al., 2011; Stekler & Golden, 2009; Surratt, O'Grady, Kurtz, Buttram, & Levi-Minzi, 2014; Vissers, Voeten, Nagelkerke, Habbema, & de Vlas, 2008). Findings



suggested that: individual socio-demographic characteristics were possible factors associated with lower HIV testing behaviors (e.g., younger age, currently unmarried, lower educational level) (Miller, et al., 1996); structural factors (e.g., exposed location of the testing, inconvenience, confidentiality disclosure, high cost, lack of counseling provision) were associated with access and discontinued utilization of HIV care (Stekler & Golden, 2009). HIV-related stigma and discrimination were other important factors influencing people's ability to link to and actively engage in HIV testing and treatment (Rotheram-Borus, et al., 2006). Lack of HIV knowledge, low HIV awareness and low HIV risk perception were also determinants of low HIV testing and linkage to HIV care (Miller, et al., 1996; Y. Song, et al., 2011; Vissers, et al., 2008). However, there is a paucity of such studies conducted among MSM, including Chinese MSM.

Linking HIV positive patients to care and sustaining high levels of engagement represent challenges in the early stages of the HIV care cascade, and is essential for reliable viral load suppression and reduction in HIV/AIDS related mortalities (Bangsberg et al., 2000; Biadgilign, Deribew, Amberbir, & Deribe, 2009; Paterson et al., 2000). Because Chinese MSM represent the key population in terms of emerging and future HIV risk in China (Lau, et al., 2011), there is an urgent need to have an incisive assessment of the existing problems that influence the linkage to, and engagement in HIV care among this subgroup.

To our knowledge, our study was one of the very few studies to comprehensively assess both barriers to and facilitators of linkage to and engagement in HIV care among Chinese MSM using qualitative research methodology (Wei et al., 2013). Additionally, we will quantitatively characterize the participants and present the qualitative findings.

Our findings would provide data relevant for potential policy decisions and intervention implementations specifically to foster linkage to HIV care and subsequent adherence.

### Significance of Aim 3

Helping people to know their HIV infection status and enhancing linkage to and engagement in HIV care are necessary, but not sufficient features for all treatment-as-prevention approaches to be effective (D. Li, et al., 2012). Long-term success in HIV/AIDS control also entails further efforts in strengthening timely initiation of ART, with high rates of retention and adherence (Y. Zhang et al., 2012). Despite the fact that China has launched the National Free Antiretroviral Treatment Program and reached a notable reduction in HIV/AIDS mortality among its participants (Y. Zhang, et al., 2012), the benefits of the program are not optimized due to two reasons—delayed ART initiation and attrition during the treatment program (Zhu et al., 2012). A study by Zhang and colleagues reported that among a cohort of 214,714 people with laboratory confirmed HIV infection alive in 2009 and living in mainland China, only 88,185 (41%) initiated ART and remained active; even among a restricted subset of 153,806 who met national free ART criteria, the treatment-active patients only represented 61% of that eligible subset (F. Zhang et al., 2011). Results from another study evaluating 106,542 HIV-infected patients receiving ART in China from January 1, 2003 to 31 December, 2010 showed that the cumulative probability of attrition was 9% at 12 months, 13% at 18 months, 16 at 24 month and 24% at 60 months (Zhu, et al., 2012). Preliminary results of an ongoing study by our collaborators in Beijing CDC also suggest that, as a result of late

ART initiation and poor retention, among all estimated HIV positive MSM in Beijing who were on ART, only 8% had clinically defined low viral load of less than 500 copies/mL in 2011 (unpublished model). If this gap in coverage of services in the care cascade cannot be bridged in a timely fashion, it will inhibit success both in slowing disease pathogenesis and also in stemming the spread of the virus (Starks et al., 2008).

Evidence shows that timely CD4+ cell count testing after HIV diagnosis is a crucial monitoring step to determine whether the infected patients should receive ART (Y. Zhang et al., 2011). In high income countries, most have adopted policies to offer ART to all HIV infected persons regardless of CD4 count (Cuzin, Delpierre, Yazdanpanah, & Lert, 2011; Hsu et al., 2014; Thompson et al., 2010), which was based on the proven efficacy that ART could reduce HIV-related morbidity and mortality (Hsu, et al., 2014; Jain & Deeks, 2010; Muessig, et al., 2012). However, some studies indicate possible increases in patient loss to follow-up associated with very early initiation of ART that may offset the positive clinical outcome from earlier ART (Clouse et al., 2013; Horne, Cooper, Gellaitry, Date, & Fisher, 2007). Controversies also remain on whether CD4-based or earlier initiation of ART could reduce or prevent sexual transmission of HIV-1 among HIV-infected MSM (Muessig, et al., 2012), because, in part, published studies were predominantly conducted among heterosexual individuals.

Although promising as a prevention and intervention tool, MSM themselves are often reluctant to receive ART due to a variety of socioeconomic, structural, and personal reasons (Rodriguez-Arenas et al., 2006). In China, there are several possible explanations for the concerns among MSM to actively access HIV care and receive ART. First, the HIV epidemic among Chinese MSM is more recent compared with the epidemics in other

key populations in China. Although different prevention-oriented intervention programs exist in China for MSM, ART is relatively new and therefore unfamiliar to many (L. Zhang, D. Zhang, et al., 2013). Second, because of social taboo and cultural discrimination against HIV-infected MSM, this subgroup endures a double stigma (homosexuality and HIV) when seeking HIV care and treatment (Feng, Wu, & Detels, 2010; Grossman, 1991; Mahajan et al., 2008). Third, as also observed in other high-risk groups, concerns over side-effects, the psychological burden of lifelong drug adherence, and concomitant financial costs are also factors impeding HIV-infected MSM in China from initiating ART (Dou et al., 2010; Johnson, Dilworth, Taylor, & Neilands, 2011; X. Wang & Wu, 2007).

To our best knowledge, no observational studies have assessed factors that play a role in ART initiation among HIV-infected MSM in China. Our study was designed to comprehensively describe and quantify important correlates regarding ART initiation in this specific subgroup. Among all factors to be evaluated with ART initiation, we specifically hypothesized that MSM with Beijing ‘Hukou’ are more likely to use ART than those without Beijing ‘Hukou’, because ‘Hukou’ is of distinct feature in Chinese residential system which has a profound impact on the rights of residents to use local medical and social services, including HIV treatment. Lack of Hukou, or legal residency, inhibits access to medical and social services. We sought outcomes from our study that would guide targeted and prioritized resource distributions to effectively mobilize HIV positive MSM to initiate ART.

## CHAPTER III

### DATA AND METHODOLOGY

#### Aim 1

##### Data sources

The China-MP3 study conducted in Beijing, China, was a community-based intervention project that aimed to pilot test the feasibility, acceptability and initial efficacy of a multi-component testing-and-linkage-to-care intervention packages among MSM in China. This intervention planned to target 50,000 MSM and estimated that 6000 of them could be recruited for expanded HIV testing, based on results of a pilot study conducted in 2009, in which 3000 MSM were tested.

MSM participants were invited for participation in the China-MP3 study through short message interventions via cell phones, advertising on a gay-oriented website, and peer referral. Eligibility criteria included: (1) men or transgender women who reported having anal sex with at least one man during the past three months; (2) 18 years of age or older; (3) lived in Beijing; (4) willing to provide biological sample for HIV testing; and (5) willing to answer general health questions and questions related to sexual behaviors. In addition to the abovementioned criteria, I further restricted the analytical sample to those who were unaware of their HIV status, or tested negative from the last test. The

actual number tested was 3760 from about 46,000 MSM (8%) contacted via text messaging or email. After excluding 172 participants due to repeated testing (126), previous positive result (30), not MSM (5), no blood drawn (5), invalid identification (ID) card or documents (4) and questionnaire lost (2), a total of 3,588 of participants (95.4%) were included as the analytic sample.

#### Dependent variable (Outcome)

HIV infection status was the main outcome variable, which was recorded in a binary format (yes vs. no). An enzyme-linked immunosorbent assay (ELISA, Wantai Biological Medicine Company, Beijing, China) was used as a screening test for HIV-1 antibody, and a positive sample was confirmed by HIV-1/2 Western blot (HIV Blot 2.2 WB; Genelabs Diagnostics, Singapore).

#### Independent variable (Exposure)

The history of HIV testing is the exposure variable. It was ascertained using an interviewer-administered questionnaire, and recorded in continuous format ('how many times in your life have you ever taken HIV testing?'). In data analysis, three formats of the exposure variable were employed to explore the association with HIV infection. First, a dichotomous variable (tester vs. non-tester) was used. Most of the published literature has used this conventional categorization method for HIV testing, and our results based on dichotomous categorization were comparable to findings from other studies (Ohl & Perencevich, 2011; Phillips, et al., 2013; Straub, et al., 2011). Second, a categorical format of the HIV testing based on quintile was also used to assess different frequency range and its association with HIV risk. Third, continuous format of the exposure

variable was also used to explore the dose response relationship between prior HIV testing frequency and HIV infection using restricted cubic spline method.

### Covariates

Covariates that were described and/or analyzed in our aim 1 include: age, ethnicity, current marital status, education, employment status, health insurance status, monthly income, Beijing residency (Hukou), frequency of alcohol use, alcohol use before sex, drug use/injection, age of sex debut, number of years of sexual activity (age minus age of sex debut), number of male or female sexual partners during different timeframe, practice of insertive or receptive anal sex with either HIV- or HIV+ male partners, sex with female partners, condom use during any sort of sexual practice, perception of HIV risk, reasons for not taking an HIV testing, and reasons for active HIV testing.

### Data analysis and methodology

To present the distribution of general socio-demographic characteristics of the studied population, conventional descriptive statistics were presented. First, frequencies and column percentages were calculated for each group of the categorical variables; means with standard deviations or medians with interquartile ranges were calculated for continuous variables.

To describe the factors for mobilizing HIV testing, and the reasons for not having HIV testing among the studied population, frequency of each identified reason with the corresponding percentage was calculated; then a rank index was assigned to each of the responses based on the frequencies and percentages calculated for the order.

Bivariate analyses were conducted to examine the significance of the association of each included covariate with HIV infection status. Specifically: (1) uncorrected Chi-squared test was performed to assess the significance of the association between each categorical variable and HIV infection status. Fisher's exact test was performed for categorical variable with expected cell counts less than 5 observations; (2) Student's t-test was conducted to compare the mean of the continuous variable between the 'HIV-positive' and 'HIV-negative'; or the non-parametric test (Wilcoxon Mann-Whitney test) was performed to compare the medians. *P*-value at the significance level of 0.05 (two-sided) was also calculated and reported.

I also explored factors that might be associated with HIV testing history, assessing the significance of the association between any pre-specified covariate and HIV testing (ever tested for HIV vs. never tested for HIV). Three methods were used to construct the multivariable models: (1) selection of the confounders was based on a priori knowledge and proposed mechanism, followed by use of directed acyclic graphs (DAGs) (Hernan, Hernandez-Diaz, Werler, & Mitchell, 2002) of the relationships among exposure, outcome, and relevant covariates to guide what covariates were finally included in the model; (2) a propensity score summarizing information from all potential confounders and other important factors that may contribute to the selection bias was created and adjusted in the final model; and (3) the adjustment of confounders in (1) and the propensity score simultaneously. In the study, I did not identify any potential effect modifier for the analysis based on prior knowledge.



## Model building

Logistic regression is the best fit for the main analyses because (1) odds ratios (OR) were our main interested measures of association; (2) the main outcome was of binary nature; (3) data were collected from across-sectional survey. Overall, three multivariable models will be explored.

After selection of covariates and evaluation based on DAG, they were fitted into an unconditional logistic regression model, with HIV infection status as the main outcome, HIV testing history as the main exposure, and the remaining variables as confounders or effect modifiers to adjust for. This is considered the full DAG model (model A). The model B would be the model adjusting for the propensity score. Model C would be adjusting for covariates in model A and propensity score simultaneously. Since the China-MP3 had confirmed 455 HIV cases, according to the ‘rule of thumb’ of 10-15 cases for one covariate to be retained in the model, over-fitting was not a concern for this multivariable analysis; no further modeling building strategy was applied.

Pearson correlation coefficient was computed to assess potential collinearity between variables prior to model fitting. Presence of substantial multicollinearity may inflate the standard errors of the beta-parameter estimates in the regression model, and may reduce power of the test associated with beta-parameter estimates (e.g., Wald statistic) (Harrel, 2001).

In addition, to address non-linear relationships and to avoid biased or distorted exposure-response relationship and the loss of statistical power and precision,(Filardo, Hamilton, Hamman, Ng, & Grayburn, 2007; Fleisher, 1996; Royston, Altman, &

Sauerbrei, 2006) restricted cubic spline method with the independent variable originally recorded in continuous format was applied to examine the dose-response relationship between HIV testing frequency and risk of contracting HIV. Specifically, the frequency of HIV testing against the probability of HIV infection will be plotted to visually inspect the dose-response pattern, then number of knots at specific locations will be specified using relevant Stata® programming commands.

## Aim 2

### Description of focus group discussions

Focus group discussions (FGD) were a preparatory component of the China-MP3 Project that was used to develop protocols for HIV risk reduction, ART adherence and short message service (SMS) interventions. For the FGD, peer referral strategy was used to recruit participants who were 18 years of age or older, self-reported MSM or transgender women, self-reported current residence in Beijing and were willing to share detailed information about feelings, thoughts, and experiences related to HIV care utilization. Subjects with cognitive impairment, gross psychotic or emotional impairments were excluded after evaluation by clinical staff, as they were deemed incapable of providing contribution to the FGDs. A total of six FGD were held in Beijing, with 10-12 participants in each group. Participants included both HIV-positive and HIV-negative MSM. Two groups were exclusively HIV negative MSM (MSM who had HIV testing with negative result upon enrollment, and one MSM who never had HIV testing);

four groups were exclusively HIV-positive MSM (MSM who had taken ART and MSM who had never taken ART). All FGDs lasted for about two hours, were led by trained facilitator, and were recorded on digital devices. A trained observer/assistant was also assigned to each group to monitor the process in terms of time and discussion relevance, document key points under each pre-specified themes, take notes of any spontaneous conversation and reactions, catch non-verbal expressions of participants and provide instant feedback to the facilitator. All participants were required to sign an institutional review board (IRB) consent form prior to participation. After the FGD were completed, all information from the audio recordings was transcribed verbatim and paper-based notes were organized. Both were translated into English in Microsoft Word® document by a certified translator. All transcripts were also reviewed, edited, and confirmed by bilingual investigators from the research team. Identifying information such as participants' names and national ID number had been removed to protect confidentiality.

#### Qualitative data analysis procedure

This study focused on issues of linkage to and engagement in HIV care among HIV infected MSM. Hence, we only analyzed transcribed data produced by the subset of four HIV-positive FGDs, and specifically gathered responses from twelve questions that ascertained aspects related to linkage to and engagement in HIV care.

For the first step, original transcripts were read carefully in full by three individual research team members (YL, HZQ and RA), and independently summarized into four pre-specified categories, including (a) barriers of linkage to and engagement in HIV care; (b) strategies that would promote linkage to and engagement in HIV treatment; (c)

recommendations to improve experience of HIV care utilization; and, (d) important notes/other. For the identification of emerging sub-themes, we merged and reviewed these summaries without consideration of the four pre-specified categories, and grouped them by creating two main themes: barriers to and facilitators of linkage to and engagement in HIV care. Then, each summary under either the ‘barriers’ or ‘facilitators’ main themes was examined again; where the summaries reflecting similar aspects, they were additionally coded to form an emerging sub-theme.

In step 2, after the emerging sub-themes were established from step 1, we further characterized them based on the following two steps. First, two standardized MS Excel<sup>®</sup> sheets were established to itemize all sub-themes from ‘barriers’ and ‘facilitators’, respectively. Second, for each sub-theme, we referred to the original transcripts to locate the responses, as direct quotes, from the specific participants who gave the responses and abstracted them into the Excel sheet under that specific sub-theme. Participants’ corresponding study IDs and group number were also recorded. This information was linked to participants’ intake form to abstract participants’ age, marital status, educational level, occupation, Beijing residency status, years of living in Beijing, housing status and current treatment status.

In step three, we conducted quality assurance, in which we had a separate researcher (X.J.Z.) from the China-MP3 Project collaborative clinic to independently perform step 1-2, following the same procedures as described above. Then, all discrepancies between two independent reviewers, were examined carefully and discussed until all discrepancies were resolved. Lastly, the final work from two reviewers was reconciled and synthesized for final summarization and interpretation.

## Aim 3

### Study description

Aim 3 was to examine factors associated with ART initiation among HIV-positive MSM in Beijing, China. A cross-sectional study was conducted between 2010 and 2011 to assess the association of male circumcision with HIV infection and HPV infection among 1,155 Chinese MSM in Beijing. Among all participants, there were 290 confirmed HIV-positive MSM, where 242 were previously diagnosed with HIV and 48 were newly infected. And after further excluding 4 participants without data on ART initiation, our study only used 238 prevalent HIV-positive MSM from this study to further explore any potential socio-demographic, behavioral and clinical characteristics that are associated with ART initiation. In the meantime, reasons for not initiating ART and particular concerns for ART initiation were described.

### Study variables and measurement

The main outcome variable is ART initiation, which was ascertained by asking HIV positive MSM ‘Have you already initiated ART?’ The response was originally recorded in a dichotomous format as ‘yes’ (coded as ‘1’) and no (coded as ‘0’), and was used without further grouping in the data analysis.

Other covariates analyzed in descriptive, bivariate, or multivariable analyses included: age, age of sexual debut, years of sexual activity, ethnicity, marital status, education, occupation, Beijing Hukou, year of living in Beijing, alcohol use, illicit drug

use, sexual orientation, ever had sex with female, number of female sexual partners, anal role and unprotected sex with male sexual partners, oral sex with male sexual partners, number of lifetime male sexual partners, male partner concurrency, sexual violence, sex trade, syphilis serostatus, HPV infection, history of STIs, ever had CD4 test and latest CD4 count, any clinical symptoms of AIDS, current health status, and reasons for not initiating ART. Measurement of the abovementioned variables was based on the questionnaire of the original project (Hu et al., 2013).

#### Data collection and management

Upon enrollment, all participants were referred to one of the participating hospitals and/or CDC clinics in Beijing to have blood specimens drawn for testing HIV, HPV and syphilis. To ascertain HIV infection status, Enzyme-linked immunosorbent assay (ELISA, Wantai Biological Medicine Company, Beijing, China) was used for HIV-1 screening. Positive samples were confirmed by HIV-1/2 Western blot (HIV Blot 2.2 WB™; Genelabs Diagnostics, Singapore). Syphilis serostatus was determined by using a rapid plasma regain (RPR) test confirmed by a Passive Particle Agglutination Test for Detection of Antibodies to *pallidum* (TP-ELISA, Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., China). HPV testing was performed by trained physician by collecting genital samples by rotating a saline water moistened nylon flocked swab in the penile skin and anal cavity for about 2 minutes, then keeping the swab in 3mL of sample transport medium for Tellgenplex™ HPV DNA Test (Tellgen Life Science, Shanghai, China)(Gao et al., 2010).

For other variables, a questionnaire was administered by trained interviewers to all participants to collect data on socio-demographic characteristics, behavioral risk factors, STD history and all aspects related to ART initiation in a self-report fashion. The questionnaire was first designed in English and then translated to Mandarin Chinese with validation by a certified translator and the principal investigator of the project to avoid discrepancies. All collected data were checked and cleaned by colleagues in the China CDC and the Vanderbilt Institute of Global Health, and recorded in appropriate format for further data analyses.

### Data analysis

To describe the socio-demographic characteristics of the study population, descriptive statistics were presented for all participants, as well as subgroups based on CD4 counts (CD4+ cells  $<350/\mu\text{L}$  vs. CD4  $\geq 350/\mu\text{L}$ ), as China ART guideline recommends treatment initiation for all HIV infected patients with CD4 count less than  $350/\mu\text{L}$ . Specifically, continuous variables were presented as means with standard deviations or medians with interquartile ranges based on the normality test results; frequencies and column percentages were calculated for categorical variables.

The reasons and concerns for not initiating ART were described and presented in a bar graph, with frequency and percentage noted for each response. Then, they were prioritized based on the frequency of response.

To examine the significance of the association between ART initiation and each of the selected socio-demographic, behavioral and clinical characteristics: Student's t-test was used for comparing the mean. Wilcoxon Mann-Whitney test was used for comparing

the median of the continuous variables, based on the normality test. Uncorrected Chi-squared tests was conducted for categorical variables, and specifically, Fisher's exact test was used for categorical variables with cell counts less than 5. All analyses using the above tests were presented with two-sided *P*-values at the significance level of 0.05 for judging the statistical significance of the association.

Socio-demographic characteristics and high risk behaviors with *P*-values less than 0.2 in the bivariate analyses were selected for further multivariable analyses of the association with ART initiation. Specifically, each factor was evaluated using the DAG gold standard change-in-estimate method. Logistic regression was used for the multivariable analyses. Since we had limited case (MSM who initiated ART) in our study, we aimed to keep a minimum sufficient set of confounders to adjust for in the model to avoid model inflation. Thus, the backward elimination strategy was used according to the DAG gold-standard change-in-estimate procedure to determine the covariates finally retained in the model (Weng, Hsueh, Messam, & Hertz-Picciotto, 2009). Specifically, for every round of elimination, one covariate that causes the smallest change in OR will be removed, if the change of the OR is less than 10% compared to the OR from the full DAG model:

$$\Delta OR = |OR_i - OR_{DAG}| / OR_{DAG}$$

Where  $OR_i$  is the odds ratio obtained during the  $i^{\text{th}}$  round of elimination, and the  $OR_{DAG}$  is the odds ratio of the full DAG model. The procedure was terminated if no additional removal of the covariate would result in 10% or bigger change of the  $\Delta OR$ .



Pearson correlation coefficient was also computed to assess potential collinearity between variables in the final model.

## CHAPTER IV

# REPEAT HIV TESTING IS ASSOCIATED WITH A LOWER LIKELIHOOD OF HIV INFECTION AMONG CHINESE MEN WHO HAVE SEX WITH MEN: A MULTIVARIABLE ANALYSIS WITH PROPENSITY SCORE ADJUSTMENT

### **Abstract**

Objective: To assess the impact of prior HIV testing engagement on odds of HIV among Chinese men who have sex with men (MSM)

Design: Cross-sectional study

Methods: MSM were recruited from local community via text messages and peer-referral. HIV serostatus was ascertained by lab test upon enrollment. Demographic and behavioral factors were assessed by questionnaire interview. Associations of prior HIV testing experience with odds of HIV infection were assessed through multivariable logistic regression analysis with propensity score adjustment and the modeling of restricted cubic splines.

Results: Among 3,588 participants included for the analyses, HIV prevalence was 12.7% (455/3,588); 70.8 % (2,534/3,588) reported ever tested for HIV prior to the study. Compared to MSM who never tested for HIV in the past, those who ever tested had a

41% reduction in the odds of being HIV-infected (adjusted odds ratio [aOR], 0.59; 95% confidence interval [CI]: 0.48, 0.74). Higher HIV testing frequency categories were associated with a decreasing trend in the likelihood of being infected with HIV, all when compared with no prior HIV testing as the reference (>6 tests [aOR: 0.27; 95% CI: 0.18, 0.41]; 4-6 [aOR: 0.55; 95% CI: 0.39, 0.78]; 2-3 [aOR: 0.61; 95% CI: 0.45, 0.82]; *P* for trend < 0.001). A multivariable-adjusted model with restricted cubic splines of HIV testing frequency shows that higher HIV testing frequency was associated with decreased HIV risk.

**Conclusions:** Strengthening HIV testing intervention is likely to reduce HIV risk among Chinese MSM. Further randomized controlled trials and longitudinal studies are needed to confirm this conclusion based on cross-sectional associations.

**Keywords:** HIV; testing; men who have sex with men; HIV care continuum; prevention intervention; China

## **Introduction**

The introduction and scale-up of modern antiretroviral therapy (ART) has led to a substantial reduction in AIDS-related morbidity and mortality (Cohen, et al., 2011; Layer et al., 2014; MacCarthy et al., 2015). Long-term success of ART as a strategy for HIV control through achieving viral suppression among seropositive persons depends upon substantially increased engagement of vulnerable persons and decreased attrition in multiple stages of care, including HIV testing, linkage to care, engagement in care, and initiation of and adherence to ART (Burns et al., 2014; Burns, et al., 2010; L. W. Chang

et al., 2013; Forsyth & Valdiserri, 2012; Gardner, et al., 2011; Hull, Wu, & Montaner, 2012; Kurth, Celum, Baeten, Vermund, & Wasserheit, 2011; McNairy, Cohen, & El-Sadr, 2013; Nachega et al., 2014; Vermund & Hayes, 2013a; Vermund et al., 2013). The HIV care cascade has been recently emphasized to tackle HIV epidemics (Hull, et al., 2012; MacCarthy, et al., 2015; Van Beckhoven et al., 2014), where HIV testing to determine HIV serostatus is the entry point and a key step to glean the documented health advantages of timely health services and the benefits of early ART (Layer, et al., 2014; South et al., 2013; Zhao et al., 2015; Zou, et al., 2012). Moreover, individuals who are aware of their HIV status may be less likely to engage in high-risk behaviors. Reduced risky behaviors, in combination with ART, can reduce the likelihood of HIV transmission (Cohen, et al., 2011; Cooley et al., 2014a; Marks, Crepaz, & Janssen, 2006; Marks, Crepaz, Senterfitt, & Janssen, 2005).

The HIV epidemic in China has gone through three major waves in the past three decades: first among injection drug users, then among plasma donors, and now through both heterosexual and homosexual transmissions. While HIV prevalence remains at <1% among female sex workers (Z. Yang, Su, Peng, & Wu, 2013), it is >5% among men who have sex with men (MSM) in many Chinese cities (Wu, et al., 2013b). A recent mathematical model predicted that if there is no change in prevention intervention coverage, HIV prevalence will increase from 7.8% in 2010 to 21.4% by 2020 among MSM in Beijing, the capital city of China (Lou et al., 2014).

Despite the high HIV risk among Chinese MSM, the HIV testing rate in this population is low. It is estimated that only 13%-47% MSM have ever been tested for HIV (Crepaz, et al., 2009; Zou, et al., 2012). To cope with the increasing HIV epidemic and

suboptimal HIV testing engagement, the Chinese government and community-based organizations (CBO) have taken steps to strengthen HIV testing by increasing free voluntary counseling and testing (VCT) provisions and extending outreach to Chinese MSM. In the U.S., national guidelines recommend at least annual HIV testing among all MSM, while those at especially elevated risk are recommended to test every three to six months (Das, et al., 2010; Granich, et al., 2009; L. Zhang, Chow, & Wilson, 2012). However, Chinese policies focus on expanded coverage, not specifying recommended testing frequencies (Zhao, et al., 2015). According to Chinese guidelines, HIV testing is recommended every six months for high-risk MSM, but the extent to which people adhere to this guideline is unknown. Among MSM in other countries, being tested for HIV has been associated with knowing your last sexual partner's HIV status, having fewer causal sex partners (Mannheimer et al., 2014; Phillips, et al., 2013; Straub, et al., 2011; Wilson, Hoare, Regan, & Law, 2009), and a lower risk of being diagnosed as HIV positive (Phillips, et al., 2013). Thus, routine HIV testing among Chinese MSM might reduce the risk of HIV in this at-risk population.

Numerous quantitative studies have assessed the correlates of HIV testing among Chinese MSM.(X. Li et al., 2014b; Yan, Yang, et al., 2015; L. Zhang, Y. Xiao, et al., 2013; Zhao, et al., 2015). However, there has been no hypothesis-driven study examining the association between HIV testing and HIV risk among MSM in China. Using the baseline data from a NIH-funded randomized clinical trial of HIV test and linkage-to-care (TLC) interventions among MSM in Beijing, we tested the hypothesis that prior HIV testing reduces the risk of HIV infection among Chinese MSM.

## Methods

### Study setting and population

We conducted this TLC trial in Beijing, China, including Phase I expanded HIV testing among MSM with unknown HIV serostatus and Phase II randomized clinical trial of linkage-to-care interventions among men who were diagnosed with HIV infection in Phase I. Data for this analysis are from the Phase I, which was completed from March 2013-March 2014. The inclusion criteria for participation were: men, age 18 years or older, self-reported sex with men or transgender women in the last 12 months, living in Beijing, and able and willing to provide written informed consent. The study protocol was reviewed and approved by the institutional review boards of Vanderbilt University, and the National Center for AIDS/STD Control and Prevention (NCAIDS) of China Center for Disease Control and Prevention.

### Data collection

An interviewer-administered questionnaire was used to collect relevant information on the following: (1) socio-demographics (age, ethnicity, marital status, education, employment, income, legal residence, length of living in the city and health insurance coverage); (2) high risk behaviors (alcohol consumption, illicit drug use, age of first sex, number of male and female sex partners, practices of insertive and receptive sex with men, sex history with women, self-reported HIV risk perception); and (3) factors related to HIV testing (prior HIV testing experience and perceived barriers/facilitators related to HIV testing uptake).

The primary exposure variable of interest for the analysis was prior HIV testing. Participants were asked how many times they had been tested for HIV prior to the HIV test they received as a participant in the study. In measuring the outcome variable (HIV infection status), participants were directed to have blood drawn for rapid HIV testing prior to completing the questionnaire. Participants who had negative results were informed immediately after the interview. For those with positive rapid test results, blood samples were delivered for further laboratory confirmatory testing, and participants were informed of the results within two weeks. All test results were entered into the database and linked to the completed questionnaire with a unique study identity number.

#### Laboratory test

We used the ELISA (HIV ELISA testing kit 1, Zhuhai Livzon Diagnostics Inc., China) as the initial confirmatory HIV antibody test for persons with a positive rapid HIV test. The biological specimen was also tested twice, using the aforementioned ELISA kit and a second ELISA kit (HIV ELISA testing kit 2, Beijing Wantai Biological Pharmacy Enterprise Co. Ltd., China), if the first ELISA screening was positive. We used the Western blot test (HIV Blot 2.2 WB; MP Biomedicals Co, Ltd., China) for final confirmation of a positive result from either or both of the ELISA tests.

#### Statistical analysis

We used self-reported frequency of prior HIV testing to categorize participants into 'ever tested' or 'never tested' for HIV. We used descriptive statistics, including proportions for categorical variables and the median with interquartile ranges (IQR) for continuous variables to describe the sample. All socio-demographic and behavioral

characteristics were then compared between men who ever tested with men who never tested for HIV, and MSM with and without HIV infection. Chi-square tests were used to compare categorical variables, while Wilcoxon rank-sum tests were used for continuous variables. For the perceived barriers and facilitators of HIV testing, percentages were calculated for each item.

Bivariate and multivariable logistic regression models were performed to assess the association between prior HIV testing and HIV infection. We used directed acyclic graphs (DAG) to evaluate and select potential confounders to adjust for in the multivariable model. In the model, we adjusted for age, education, marital status, health insurance coverage, drug use, alcohol use before sex, age of first sex, years of sexual activity with men, unprotected anal sex with men, lifetime number of male partners, lifetime number of female partners, and HIV risk perception. Besides categorizing subjects as ever and never tested for HIV, we also categorized participant into five groups based on the quintile of HIV testing frequency. Lastly, we treated the prior HIV testing as a continuous exposure and applied restricted cubic spline with four knots to fit the non-linear association between HIV testing frequency and HIV risk (Alvarez-Uria, Pakam, Midde, & Naik, 2014; Harrell, 2001).

Systematic differences in baseline characteristics might exist between exposed and non-exposed groups; thus, estimation of the exposure effect could be biased due to confounding variables having an unbalanced distribution (Austin, 2011; Tran et al., 2012). For instance, those who frequently engage in high-risk behaviors tend to be ‘worried’ and use HIV testing more frequently. As a consequence, unadjusted comparisons might show that more HIV testing is less protective against HIV infection, or even associated with an



increased likelihood of being HIV-infected. On the contrary, the “worried well” may falsely overestimate the preventive effect of HIV testing. To minimize pre-existing differences of the sample characteristics and yield unbiased estimates (Linden & Adams, 2010), we used propensity score methods to perform propensity score-adjustment in addition to conventional multivariable adjustment. A propensity score is defined as the conditional probability of being ever tested for HIV given a series of variables that summarized information across potential confounders (B. Lu, 2005; Rotheram-Borus, et al., 2006; Tran, Nguyen, Do, Nguyen, & Maher, 2014). Therefore, a logistic regression model was used to estimate the propensity for dichotomous HIV testing exposure (Tran, et al., 2014). An ordinal logistic regression model was used to generate the propensity score for the 5-category HIV testing groups. In our study, we estimated a propensity score with socio-demographic and high-risk behavioral characteristics that were considered to be associated with HIV testing and HIV risk based on *a priori* evidence. These variables included: age, education, marital status, employment, income, registered Beijing household residence ( or “*Hukou*”), health insurance coverage, year of living in Beijing, alcohol use before sex, illicit drug use in the past three months, year of sexual activities, age of first sex, lifetime number of male sex partners, unprotected sex with men in the past three months, sex with HIV-positive men in the past three months, commercial sex with men in the past three months, lifetime number of female sex partners, and HIV risk perception.

We applied three multivariable models to evaluate associations. *Model A* adjusted for DAG-identified *a priori* confounders; *Model B* adjusted for the propensity score; *Model C* adjusted for both *a priori* confounders and the propensity score simultaneously.

In our multivariable logistic regression model with the restricted cubic spline of HIV testing frequency, we only adjusted for *a priori* confounders. All statistical analyses were performed using Stata 12.0™ (StataCorp LP, College Station, Texas, USA).

## Results

### Population characteristics by HIV infection and prior testing status

Of the 3,760 recruited participants, 172 were excluded from our analyses due to duplicate testing results (126); confirmed HIV serostatus prior to the study (30); not MSM (5); blood sample not collected (5); invalid identification number (4); and questionnaire lost (2). Thus, 3,588 MSM (95.4%) were included in our analyses. In this population, the age ranged from 16 to 75 (median 28), 94% were of Han ethnicity, 15% were married with women, 72% at least a college education, 82% were employed, 25% were registered Beijing residents (Beijing ‘*Hukou*’), and 61% were medically insured.

In this sample, the HIV prevalence was 12.7%. Compared with HIV-negative MSM, HIV-positive MSM were more likely to be unemployed or retired (7.5% vs. 4.7%;  $P<0.001$ ), junior middle school-educated (13.0% vs. 9.7%;  $P=0.04$ ), drinkers of alcohol before sex in the past three months (25.9% vs. 19.8%;  $P=0.002$ ), users of illicit drugs in the past three months (34.7% vs. 26.5%;  $P<0.001$ ), have  $\geq 10$  male partners in their lifetime (56.5% vs. 48.4%;  $P<0.001$ ), have unprotected receptive sex with men in past three months (36.0% vs. 18.2%;  $P<0.001$ ), have sex with HIV-positive men (4.0% vs.

2.4%;  $P=0.04$ ), and have high HIV risk perception (72.1% vs. 36.2%;  $P<0.001$ ). HIV-positive men were less likely to be married to a woman (84.5% vs. 88.3%;  $P=0.03$ ), have health insurance (51.0% vs. 62.6%;  $P<0.001$ ), have Beijing “Hukou” (14.5% vs. 26.3%;  $P<0.001$ ), have lived longer in Beijing (median years, 4 vs. 5;  $P<0.001$ ), have had unprotected sex with a women in past three months (3.7% vs. 7.0%;  $P=0.008$ ) and ever tested for HIV (63.5% vs. 71.7%;  $P<0.001$ ) (Table 1).

Prior to study participation, 71% of our studied participants reported ever testing for HIV in their lifetime. Being an MSM who had ever tested for HIV was associated with being older (median years, 29 vs. 26;  $P<0.001$ ), married to a women (16.1% vs. 12.4%;  $P=0.005$ ), employed (85.6% vs. 74.9%;  $P<0.001$ ), having a higher monthly income (median, 5000 vs. 4000 Chinese Yuan;  $P<0.001$ ), having lived longer in Beijing (median years, 6 vs. 4;  $P<0.001$ ), drinking alcohol before sex in the past three months (22.2% vs. 16.7%;  $P<0.001$ ), using illicit drugs in the past three months (28.7% vs. 24.7%;  $P=0.01$ ), having more years of sexual activity (median years, 8 vs. 5;  $P<0.001$ ), and have  $\geq 10$  male sexual partners in lifetime (57.7% vs. 30.0%;  $P<0.001$ ). Notably, men who had unprotected receptive sex in past three months were less likely to test for HIV (19.4% vs. 23.0%;  $P=0.02$ ) (Table 1).

#### Association of prior HIV testing experience with HIV infection

Table 2 presents the association between different HIV testing categories and their associations with HIV infection in both bivariate and multivariable logistic regression analyses. Results from three multivariable models were similar in magnitude and consistent in directionality. Models that adjusted for both *a priori* potential confounders

and propensity score simultaneously suggested the strongest associations. Having ever tested for HIV was associated 30%-40% reduction in the likelihood of being newly diagnosed with HIV (e.g., Model C, adjusted odds ratio [aOR]: 0.59; 95% confidence interval [CI]: 0.48, 0.74). For quintile-based HIV testing frequency, higher HIV testing frequency categories were associated with a decreasing trend in the likelihood of being infected with HIV, all when compared with no prior HIV testing as the reference (e.g., Model C, >6 tests [aOR: 0.27; 95% CI: 0.18, 0.41]; 4-6 [aOR: 0.55; 95% CI: 0.39, 0.78]; 2-3 [aOR: 0.61; 95% CI: 0.45, 0.82]; *P* for trend<0.001).

Figure 1 depicts the non-linear contribution of prior HIV testing frequency to the likelihood of being diagnosed with HIV. Results from the multivariable-adjusted model with restricted cubic spline of HIV testing frequency shows that higher HIV testing frequency was associated with decreased HIV risk. However, our estimates were not dependable at the right-sided tail of the curve due to sparse data and insufficient statistical power; we truncated the graph for lifetime HIV testing frequency at >20 times. Specifically, for HIV testing frequency below 5, the frequency-OR curve slope decreased more drastically, while the steepness of the slope was weakened above this threshold.

#### Perceived barriers and facilitators for HIV testing

Figure 2 presents the reasons for not taking HIV testing previously. Among 1,054 MSM who never tested for HIV, the top three barriers to HIV testing were: “perceived low risk of HIV infection” (39.6%), “fear of being HIV-positive” (20.0%), and “not knowing where to get tested” (15.1%). Factors that were considered to have the potential to mobilize HIV testing were illustrated in Figure 3. Among all 3,588 participants, the

three most commonly identified facilitators were: “anonymity in taking HIV testing” (23.9%), “confidentiality of test results” (21.9%), and “rapid test” (18.4%).

## **Discussion**

Our study assessed the association between prior repeat HIV testing experience and HIV risk among Chinese MSM. This study confirmed the projection of our prior mathematical model that the HIV epidemic continues to rise rapidly among Chinese MSM; and frequent HIV testing can reduce HIV risk by possibly achieving higher awareness and more exposure to HIV interventions among Chinese MSM (Lou, et al., 2014).

The robustness of the HIV epidemic in global MSM populations remains a huge public health concern (Beyrer, et al., 2013; Beyrer, Sullivan, et al., 2012). China has an estimated 1.4 billion populations in 2015, over 19% of the global total. If 2-5% of adult men have a male-to-male sexual preference, as has been reported in many other nations, between 10 to 25 million Chinese men (denominator of 514 million men ages 15-64 years) may be at higher risk of HIV due to unprotected receptive anal intercourse. This is vast population at risk, representing, too, many bisexuals and some persons who inject drugs who can transmit beyond the gay and bisexual community. In our Beijing urban study, we observed a HIV prevalence of 12.7%, which was substantially higher than the latest national estimate (7.3%) (van Griensven, de Lind van Wijngaarden, Baral, & Grulich, 2009b), and similar to the findings documented in recent studies among Chinese MSM in other metropolitan areas (12.4%-14.5%) (Bai, Xu, et al., 2014a; Long et al.,

2014b; Q. Q. Wang et al., 2014b; Y. Zeng et al., 2014). Consistent with findings in previous studies (D. Li et al., 2010; H. Mao et al., 2014; X. Wang et al., 2014; Y. Zeng, et al., 2014; X. Zhang et al., 2013), we found familiar risk factors among HIV-positive MSM such as younger age of sex debut, lower educational level, never have been married to a woman, being a transient resident, more lifetime male sexual partners, ever having engaged in unprotected anal sex, and drug use and alcohol use before sex.

Higher HIV prevalence among MSM in large Chinese cities such as Beijing is to be expected. Compared with small cities, large cities are less vulnerable to traditional taboos that suppress male-to-male sexual activity, large urban sexual networks are more complex and anonymous, and more venues exist for men to seek sexual partners. These factors likely contribute to higher HIV risk and the likelihood of transmitting the virus. Large Chinese cities attract numerous internal migrants to seek better job opportunities and better living condition, including MSM migrants. Large numbers of single men may increase the possibility of spreading HIV when combined with high-risk behaviors such as male-male sexual activity or sexual contact with sex workers (H. Mao, et al., 2014). Medical care services are more available and accessible than in small cities, including HIV testing. Therefore, more HIV diagnoses may contribute to the observed high HIV prevalence in large cities, though well done surveys can overcome biased ascertainment.

In China, HIV testing is mainly sponsored by government through self-initiated free VCT and provider-initiated testing and counseling (PITC). Despite the success of free VCT, many MSM never used this service or failed to return for periodical testing due to lack of confidentiality in identity and results, long wait-times, and stigma associated with the testing (Han et al., 2014; Wei et al., 2014). Most of our participants thought

“anonymity”, “confidentiality of the test results” or “rapid HIV testing” would facilitate their testing activities, while “not knowing where to test” and “perceived low risk of HIV infection” were two of the top three barriers for testing. This situation implied that some “innovative” testing provisions such as the community-initiated home-based counseling and testing (HBCT) should also be legalized and expanded to involve more MSM to periodically test for HIV.

About 71% of our studied participants ever tested for HIV in their lifetime prior to the survey, which is comparable to previous studies conducted in Beijing (Y. Song, et al., 2011; Zhao, et al., 2015) Despite the seemingly high testing rate, it is important to mention that nearly 71% of them had been sexually active with men for more than 5 years, but only 21% tested 5 times or more, while 48% previously tested once or never. Moreover, by study design, all HIV-infected MSM in our analyses were unaware of their HIV seropositive status prior to our study. Given the ever-growing HIV epidemics and dynamic nature of MSM, those undiagnosed persons were more likely to be infectious to partners than seropositive men who knew their status and were taking preventive precautions and/or were taking ART that reduced transmission risk. Further efforts are still needed to expand HIV testing coverage and encourage periodical testing.

Some significant predictors of HIV testing are worthy of note. We found MSM who were married were more likely to test for HIV, also noted by Han et al. (Han, et al., 2014) It is possible that the responsibility for their wives or family members motivates men to take an HIV test and take precautions if they are infected. Campaigns and intervention programs aiming to enhance HIV testing should incorporate educational sessions to raise

their consciousness in protecting one's significant others, including oneself, especially among unmarried MSM.

Other studies have found that younger age was associated with higher HIV testing rates (Bai, Xu, et al., 2014a; X. Li, et al., 2014b). A possible explanation is that younger men visit MSM venues (e.g., gay bars, bathhouses) more frequently and would be more likely to expose to venue-based VCT (Bai, Xu, et al., 2014a). However, consistent with Chow et al. (Chow, et al., 2013), we found younger MSM were less likely to ever test for HIV. This could be reflected by what we observed in our data that student MSM were significantly more likely to be non-testers (7.6% vs. 18.5%;  $P < 0.001$ ), though this may be more due to younger age than to student status (L. Zhang et al., 2012). HIV prevalence is higher among student MSM than in general population in China, as would be expected (Z. Yang, Jin, Dong, Zhang, & Qiu, 2013). Student MSM could be more vulnerable to HIV stigma, peer discrimination and have low HIV risk perception (Z. Yang, Jin, et al., 2013), which results in underutilization of HIV testing. It is essential to promote HIV testing among youth as well as the vulnerable subgroup of youth who are students.

The duration of living in a city is also an indicator of HIV testing uptake among Chinese MSM (X. Li, et al., 2014b). We found those who lived for fewer years in Beijing tended to have no prior testing experience. MSM with less income were also less likely to ever test for HIV. This subgroup may overlap with those without Beijing "Hukou" and largely consists of migrants. Studies in Beijing showed that migrant population were low in socio-economic status and were limited in knowledge of HIV and benefit of timely HIV diagnosis (Y. Song, et al., 2011; B. Wang, Li, Stanton, Liu, & Jiang, 2013).



Intervention thus should also focus on these special transient residents to increase frequency of HIV testing.

The HPTN 043 trial showed that community-based voluntary counselling and testing led to borderline significant reduction on HIV-incidence among all participants (RR, 0.86; 95% CI, 0.73-1.02;  $p=0.082$ ) (Coates et al., 2014). Nonetheless, our study confirmed findings from previous studies among Chinese MSM that “ever-testers” had a lower likelihood of being HIV-infected than non-testers (Bai, Xu, et al., 2014a; X. Li, et al., 2014b; X. Wang, et al., 2014; Zhao, et al., 2015), and found a strong signal that higher lifetime HIV testing frequency was associated with a lower risk of HIV infection among Chinese MSM. It is plausible that, compared to non-testers and occasional testers, frequent MSM testers are exposed more to doctors, healthcare workers, peer MSM or channels with HIV/AIDS education and information for the participation in MSM-friendly intervention programs. During this process, they might be able to gain more knowledge on appropriate HIV prevention and enhance HIV awareness (Straub, et al., 2011). Therefore, frequent testers might be more attentive to take precautions (e.g., use condoms and refrain from other high-risk behaviors such as substance use before sex, group sex and commercial sex), which lowers their HIV risk. Alternatively, frequent testers may be better informed to begin with, and therefore have a greater likelihood to get regular testing and benefit from the concomitant counseling or knowledge learned. In spite of the lack of rigor in study design as a randomized control trial, we consider our findings carry the merit of large sample size and propensity score method to minimize pre-existing selection bias. Our propensity score analysis might suggest the former possibility (testing reducing risk), but we cannot rule out the latter (testing as a marker of

better education/lower risk). It may be difficult to elucidate the temporal relationship between high HIV awareness/perception and frequent testing utilization. Nonetheless, we are encouraged that our study suggests that HIV testing may be both an entry point into the HIV care continuum, and also a potential intervention tool for reducing HIV risk. In either case, strengthening of frequent HIV testing for MSM must be a continuing effort to identify men in need of care, as well as a motivator to initiate and sustain lower HIV risk behavior (Weinhardt, Carey, Johnson, & Bickham, 1999; Williams-Roberts, Chang, Losina, Freedberg, & Walensky, 2010).

Findings in this study provided epidemiologic evidence to encourage frequent HIV testing guidelines establishment for Chinese MSM. All the strategies that we used helped increase testing: SMS messaging, gay-oriented web site outreach, and peer referrals. Intervention trial and longitudinal designs can help strengthen the evidence that selected strategies to promote HIV testing can help reduce HIV risk among Chinese MSM.

**Table 1. Demographic and behavioral characteristics of men who have sex with men in Beijing, China, 2013 (N=3,588)**

Characteristics	Total (N=3,588) n (%)*	HIV testing history			HIV infection		
		Ever tested (N=2,534) n (%)	Never tested (N=1,054) n (%)	<i>P</i> -value	HIV-positive (N=455) n (%)	HIV-negative (N=3,133) n (%)	<i>P</i> -value
		<hr/>					
<b>Age (year)</b>				<0.001			0.37
Median, IQR	28, (24-33)	29, (25-34)	26, (23-30)		28, (24-32)	28, (24-33)	
<b>Ethnicity</b>				0.34			0.28
Han	3,361 (93.7)	2,380 (93.9)	981 (93.1)		421 (92.5)	2,940 (93.8)	
Other	227 (6.3)	154 (6.1)	73 (6.9)		34 (7.5)	193 (6.2)	
<b>Marital status</b>				0.005			0.03
Currently unmarried	3,049 (85.0)	2,126 (83.9)	923 (87.6)		402 (88.3)	2,647 (84.5)	
Currently married	539 (15.0)	408 (16.1)	131 (12.4)		53 (11.7)	486 (15.5)	
<b>Education (year)</b>				0.23			0.04
College and above (>12)	2,579 (71.9)	1,799 (71.0)	780 (74.0)		330 (72.5)	2,249 (71.8)	
Senior high (10-12)	593 (16.5)	438 (17.3)	155 (14.7)		59 (13.0)	534 (17.0)	
Junior middle school (7-9)	362 (10.1)	260 (10.3)	102 (9.7)		59 (13.0)	303 (9.7)	
Primary school or lower(<=6)	54 (1.5)	37 (1.4)	17 (1.6)		7 (1.5)	47 (1.5)	
<b>Employment</b>				<0.001			<0.001

Employed	2,960 (82.5)	2,170 (85.6)	790 (74.9)	377 (82.9)	2,583 (82.4)	
Unemployed/retired	182 (5.1)	123 (4.9)	59 (5.6)	34 (7.5)	148 (4.7)	
Student	388 (10.8)	193 (7.6)	195 (18.5)	29 (6.4)	359 (11.5)	
Other	58 (1.6)	48 (1.9)	10 (1.0)	15 (3.2)	43 (1.4)	
<b>Monthly income (Chinese yuan; k=1,000)</b>				<0.001		0.91
Median, IQR	5k, (3k-8k)	5k (3k-9k)	4k (2k-6k)	5k (3k-8k)	5k (3k-8k)	
<b>Health insurance</b>				0.36		<0.001
No	1,395 (38.9)	973 (38.4)	422 (40.0)	223 (49.0)	1,172 (37.4)	
Yes	2,193 (61.1)	1,561 (61.6)	632 (60.0)	232 (51.0)	1,961 (62.6)	
<b>Beijing “Hukou”</b>				0.60		<0.001
No	2,699 (75.2)	1,900 (75.0)	799 (75.8)	389 (85.5)	2,310 (73.7)	
Yes	889 (24.8)	634 (25.0)	255 (24.2)	66 (14.5)	823 (26.3)	
<b>Year of living in Beijing</b>				<0.001		<0.001
Median, IQR	5, (2-10)	6, (3-11)	4, (2-8)	4, (2-8)	5, (3-10)	
<b>Alcohol use (past 3 months)</b>				0.002		0.12
Never	1,574 (43.9)	1,075 (42.4)	599 (47.3)	203 (44.6)	1,371 (43.8)	
Once a month	1,108 (30.9)	779 (30.7)	329 (31.2)	121 (26.6)	987 (31.5)	
2-4 times a month	594 (16.5)	436 (17.2)	158 (15.0)	90 (19.1)	507 (16.2)	
≥ twice a week	312 (8.7)	244 (9.7)	68 (6.5)	44 (9.7)	268 (8.5)	
<b>Alcohol use before sex (past 3 months)</b>				<0.001		0.002

No	2,850 (79.4)	1,972 (77.8)	878 (83.3)	337 (74.1)	2,513 (80.2)	
Yes	738 (20.6)	562 (22.2)	176 (16.7)	118 (25.9)	620 (19.8)	
<b>Drug use (past 3 months)</b>				0.01		<0.001
No	2,600 (72.5)	1,806 (71.3)	794 (75.3)	297 (65.3)	2,303 (73.5)	
Yes	988 (27.5)	728 (28.7)	260 (24.7)	158 (34.7)	830 (26.5)	
<b>Age of sex debut</b>				0.33		0.06
Median, IQR	20, (18-23)	20, (18-23)	20, (18-23)	20, (18-22)	20, (18-23)	
<b>Year of sexual activity</b>				<0.001		0.52
Median, IQR	7, (4-12)	8, (5-13)	5, (2-9)	8, (5-12)	7, (4-12)	
<b>Lifetime number of male sexual partners</b>				<0.001		<0.001
<10	1,815 (50.6)	1,075 (42.4)	740 (70.2)	198 (43.5)	1,617 (51.6)	
≥10	1,773 (49.4)	1,459 (57.6)	314 (29.8)	257 (56.5)	1,516 (48.4)	
<b>Unprotected insertive sex with men (past 3 months)</b>				0.85		0.22
No	2,801 (78.1)	1,976 (78.0)	825 (78.3)	345 (75.8)	2,456 (78.4)	
Yes	787 (21.9)	558 (22.0)	229 (21.7)	110 (24.2)	677 (21.6)	
<b>Unprotected receptive sex with men (past 3 months)</b>				0.02		<0.001
No	2,855 (79.6)	2,043 (80.6)	812 (77.0)	291 (64.0)	2,546 (81.8)	
Yes	733 (20.4)	491 (19.4)	242 (23.0)	164 (36.0)	569 (18.2)	
<b>Commercial sex with men (past 3 months)</b>				0.30		0.95

No	3,487 (97.2)	2,458 (97.0)	1,029 (97.6)	442 (97.1)	3,045 (97.2)	
Yes	101 (2.8)	76 (3.0)	25 (2.3)	13 (2.9)	88 (2.8)	
<b>Sex with HIV positive men (past 3 months)</b>						0.10
No	3,496 (97.4)	2,462 (97.2)	1,034 (98.1)	437 (96.0)	3,059 (97.6)	
Yes	92 (2.6)	72 (2.8)	20 (1.9)	18 (4.0)	74 (2.4)	
<b>Unprotected sex with women (past 3 months)</b>						0.95
No	3,351 (93.4)	2,367 (93.4)	984 (93.4)	438 (96.3)	2,913 (93.0)	
Yes	237 (6.6)	167 (6.6)	70 (6.6)	17 (3.7)	220 (7.0)	
<b>Lifetime number of female sex partners</b>						0.10
0	2,169 (60.5)	1,510 (59.6)	659 (62.5)	277 (60.9)	1,892 (60.4)	
≥1	1,419 (39.5)	1,024 (40.4)	395 (37.5)	178 (39.1)	1,241 (39.6)	
<b>Perception of HIV risk</b>						0.11
Low or very low	2,126 (59.3)	1,523 (60.1)	603 (57.2)	127 (27.9)	1,999 (63.8)	
High or very high	1,462 (40.7)	1,011 (39.9)	451 (42.8)	328 (72.1)	1,134 (36.2)	
<b>HIV infection</b>						<0.001
No	3,133 (87.3)	2,245 (88.6)	888 (84.3)	-	-	
Yes	455 (12.7)	289 (11.4)	166 (15.7)	-	-	
<b>HIV testing</b>						-
Ever	1,054 (29.4)	-	-	166 (36.5)	888 (28.3)	
Never	2,534 (70.6)	-	-	289 (63.5)	2,245 (71.7)	

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IQR, interquartile range; “*Hukou*”, registered household residence

**Table 2. Logistic regression analyses of the association between prior HIV testing and risk HIV infection among Chinese MSM (N=3,588)**

HIV testing	% of HIV+ (n/N)	Unadjusted odds ratio (95% CI)	Adjusted odds ratio (95% CI)		
			Model A <sup>a</sup>	Model B <sup>b</sup>	Model C <sup>c</sup>
<i>Overall</i>					
Never tested	15.8 (166/1,054)	1.0	1.0	1.0	1.0
Ever tested	11.4 (289/2,534)	0.69 (0.56,0.84)	0.68 (0.55,0.85)	0.62 (0.49,0.77)	0.59 (0.48,0.74)
<i>Quintile-based frequency range (times of HIV testing taken prior to current survey)</i>					
0	15.8 (166/1,054)	1.0	1.0	1.0	1.0
1	15.4 (103/668)	0.97 (0.75,1.27)	0.94 (0.71,1.25)	0.86(0.66,1.13)	0.84 (0.63,1.11)
2-3	12.4 (88/709)	0.75 (0.57,1.00)	0.71 (0.53,0.96)	0.65 (0.49,0.86)	0.61 (0.45,0.82)
4-6	10.7 (60/558)	0.64 (0.47,0.88)	0.67 (0.48,0.94)	0.54 (0.39,0.75)	0.55 (0.39,0.78)
>6	6.3 (38/599)	0.36 (0.25,0.52)	0.33 (0.22,0.48)	0.31 (0.21,0.46)	0.27 (0.18,0.41)
<i>P for trend</i>	<0.001	-	-	-	-

NOTE: CI, confidence interval

<sup>a</sup> Adjusted for *a priori* confounders: age, education, marital status, health insurance, drug use, alcohol use before sex, age of sex debut, years of sexual activity with men, unprotected anal sex with men, lifetime male partners, lifetime female partners, HIV risk perception

<sup>b</sup> Adjusted for the propensity score. The propensity score is derived using the following variables: age, education, marital status, employment, income, Beijing legal residence (*Hukou*), health insurance, years of living in Beijing, alcohol use before sex in the past 3 months, drug use in the past 3 months, years of sexual activities, age of first sex, No. of lifetime male sex partners, ever had unprotected sex with men in the past 3 months, ever had sex with HIV-positive men in the past 3 months, ever had commercial sex with male in the past 3 months, No. of lifetime female sex partners and HIV risk perception

<sup>c</sup> Adjusted for the *a priori* confounders and the propensity score.



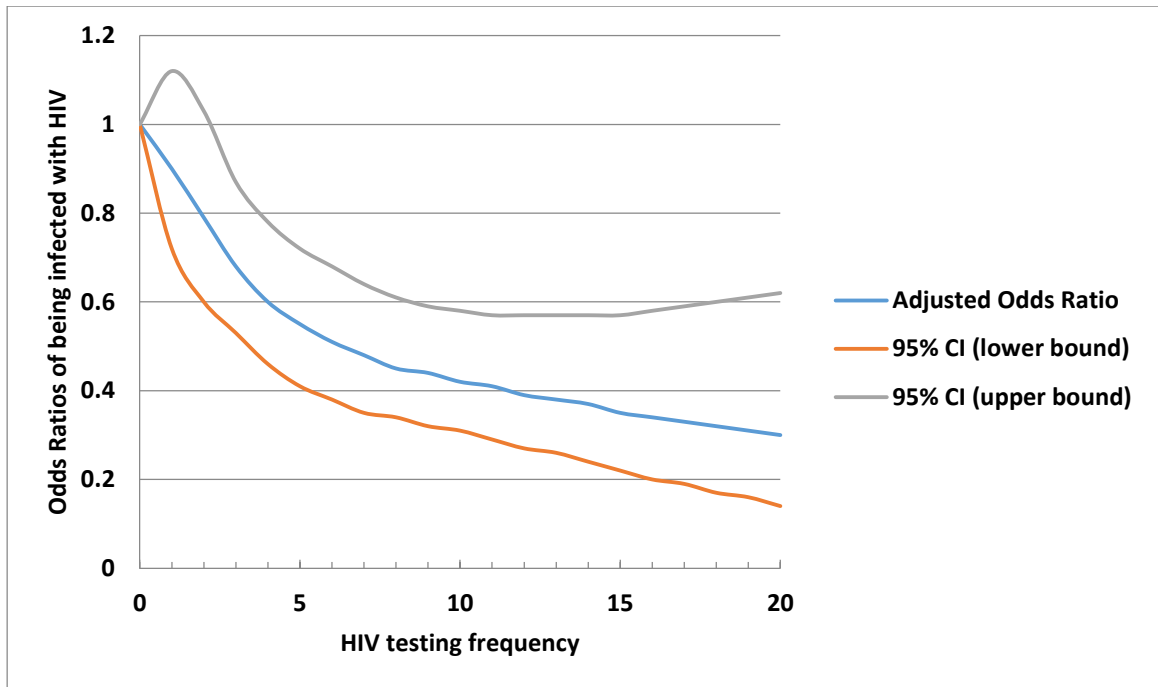
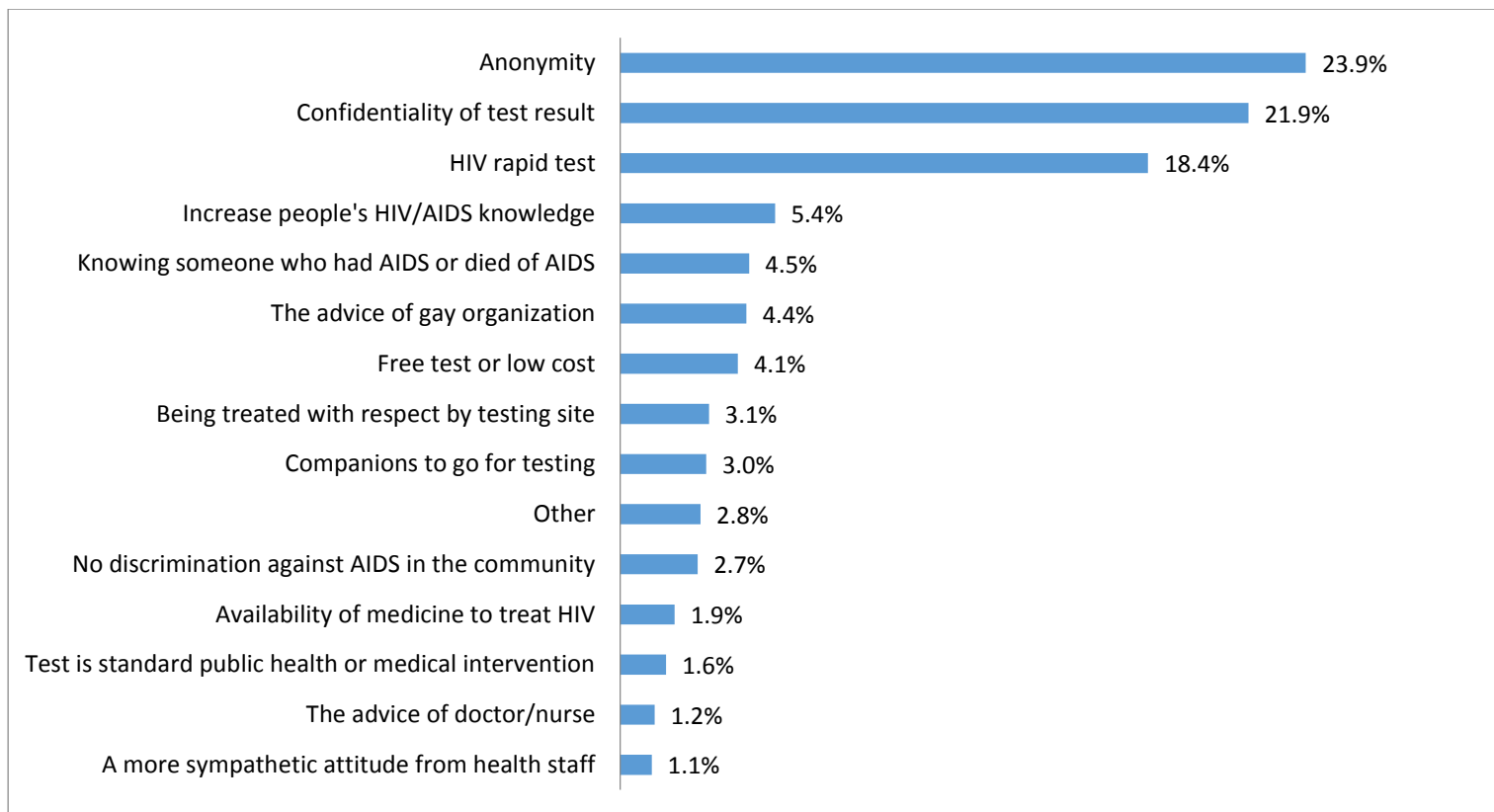
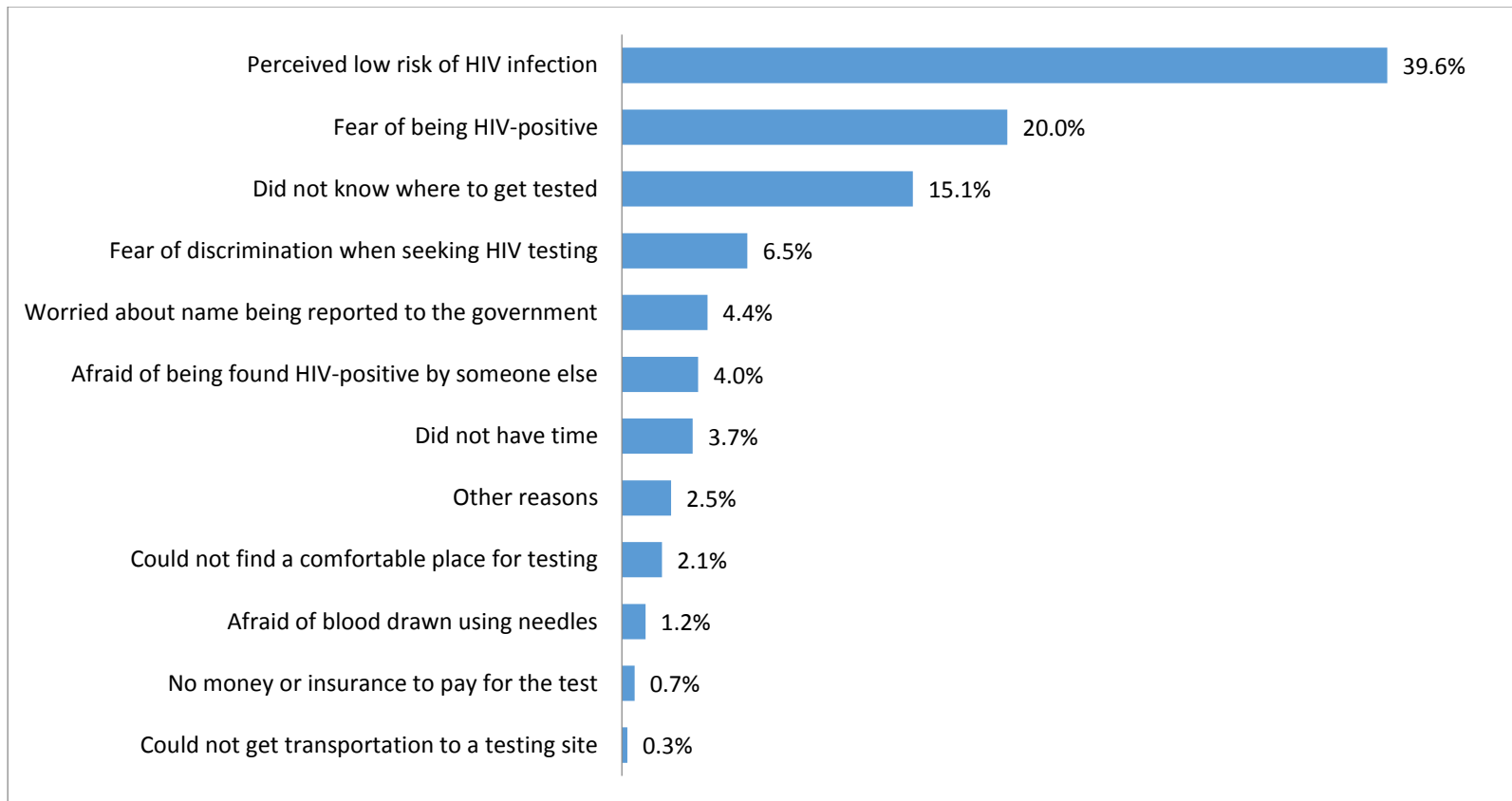


Figure 2. Association between frequency of prior HIV testing and odds ratios of being infected with HIV (N=3,588)



**Figure 3. Perceived facilitators for enhancing HIV testing among men who have sex with men in Beijing, China (N=3588)**



**Figure 4. Barriers to test for HIV identified by men who have sex with men who never tested for HIV in Beijing, China (N=1,054)**

## CHAPTER V

### BARRIERS AND FACILITATORS OF LINKAGE TO AND ENGAGEMENT IN HIV CARE: A QUALITATIVE STUDY AMONG HIV-POSITIVE MEN WHO HAVE SEX WITH MEN IN CHINA

#### **Abstract**

Introduction: Linking and engaging HIV-positive patients in care is the key bridging step to glean the documented health advantages of antiretroviral therapy (ART). In China, HIV transmission among men who have sex with men (MSM) is surging drastically, yet many HIV-infected MSM were unlikely to utilize HIV care services. To prepare for intervention development to promote linkage-to-care among this high-risk subgroup, we conducted a qualitative study to address the research gap.

Methods: Four focus groups were held among HIV-positive MSM in Beijing, China, to ascertain knowledge, beliefs, attitudes, and practices related to HIV care utilization. Each focus group discussion lasted for approximately 2 hours. A trained facilitator led each focus group using a semi-structured discussion guide, with a note-taker assisting the facilitator during the process. All discussions were digitally recorded and transcribed verbatim. Transcripts were reviewed, analyzed and reconciled to form several emerging subthemes denoting barriers and facilitators related to linkage to and engagement in HIV care.

Results: Major barriers to linkage to HIV care documented in this study included: (1) Perceived discrimination from health care workers; (2) Lack of guidance and follow-up; (3) Time or location inconvenience; (4) Privacy disclosure concerns; (5) Psychological burden of committing to HIV care; and (6) Treatment concerns. Five major sub-themes emerged from discussions on the facilitators of linking to care. These facilitators were: (1) Peer referral and accompaniment; (2) Free HIV care; (3) Advocacy from HIV-positive MSM counselors; (4) Extended involvement for linking MSM to care; and (5) Standardization of HIV care.

Conclusions: An understanding of the barriers and facilitators which may impact the access to HIV care is essential for future intervention design. Findings from our study provide policy suggestions for how to bolster current HIV prevention intervention efforts to enhance linkage to HIV care among Chinese MSM.

Keywords: HIV; men who have sex with men; China; HIV care continuum; linkage to care; barriers; facilitators

## **Introduction**

The advancement and expansion of point-of-care HIV testing has increased the diagnosis of people living with HIV (PLHIV) (C. L. Cook, Lutz, Young, Hall, & Stacciarini, 2015). Identification of HIV-positive individuals is necessary for entering HIV care (the HIV care continuum) and achieving viral suppression with antiretroviral therapy (ART) (Cohen & Gay, 2010; Gardner, et al., 2011; Vallecillo, Mojal, Torrens, & Muga, 2014). Nonetheless, the success of ART depends on the optimal transition through

several intermediate stages of the HIV care continuum (also referred to as the HIV care cascade) (Kilmarx & Mutasa-Apollo, 2013; Tobias, Cunningham, Cunningham, & Pounds, 2007), where challenges are particularly evident in the early phase of linking newly diagnosed individuals to care and keeping them engaged in care long-term (Biadgilign, et al., 2009; Paterson, et al., 2000; van Zyl, Brown, & Pahl, 2015).

There were an estimated 780,000 people in 2011 living with HIV in China (Crepaz, et al., 2009). The uptrend of HIV incidence and prevalence among Chinese men who have sex with men (MSM) has spiked the overall incidence of HIV in this country (van Griensven, et al., 2009b). In China, HIV care is centralized and linkage to care can be tracked from the first CD4+ test after a confirmed HIV diagnosis (Yan, et al., 2014). Among 4,063 newly diagnosed HIV-positive Chinese MSM, 21% did not have their HIV status confirmed and 34% (1,025/3,024) did not have a CD4+, i.e., were never linked to care (D. Zhang et al., 2014). Since 2003, the establishment and scale-up of the “Four Free and One Care”(free ARV drugs, free prevention of mother-to-child transmission, free voluntary counseling and testing, free schooling for children orphaned by AIDS, and care to people living with HIV/AIDS) policy (Shao, 2006) in China has been one of the major intervention and prevention strategies to treat infected individuals and contain HIV transmission among high risk subgroups, such as female commercial sex workers (FSW), persons who inject drugs (PWID), illegal plasma donors, and MSM (Chow, et al., 2012; Y. Song, et al., 2011). However, when this policy was established, MSM did not receive adequate attention from the government commensurate with the focus on other key populations (e.g., plasma donors, PWID, FSW); thus MSM-friendly programs were late in development, without a clear risk reduction strategy and HIV-related service

provision policy. Thus, HIV-positive MSM had low utilization of HIV-related services despite their high risk (Chow, et al., 2012; Huang, et al., 2012).

Studies have suggested certain socio-demographic characteristics (e.g., being younger, single, or less educated)(Miller, et al., 1996) are associated with lower HIV care utilization rates. Some structural barriers (e.g., exposed location of care, inconvenience, confidentiality disclosure, high cost, and lack of in-time counseling provision) might delay access to and discontinue HIV care utilization (Stekler & Golden, 2009). The presence of HIV-related stigma and discrimination have also been important factors influencing people's willingness to link to HIV care and treatment (Rotheram-Borus, et al., 2006). However, very few studies have been conducted to assess the factors associated with linkage to care among HIV-positive MSM in China (H. H. Li, Holroyd, Li, & Lau, 2015). Therefore, whether or not these factors are applicable to HIV-positive Chinese MSM regarding linkage to care, and how to facilitate access to care in the presence of these barriers, is poorly understood.

In China, there is a lack of qualitative studies conducted to explore these issues. The purpose of this qualitative study was to ascertain the knowledge, beliefs, attitudes, and practices among Chinese MSM to inform the design, content and adaptation of the intervention programs for the improvement of linkage-to-care among HIV-positive MSM in China.

## Methods

### Participant Recruitment

In 2011, we conducted focus groups with MSM in Beijing, China. The Chaoyang Chinese AIDS Volunteer Group (CCAVG), a community-based gay-friendly organization in Beijing, recruited eligible participants. We used a peer-referral snowball strategy to recruit additional participants. Eligible participants were 18 years of age or older, self-reported MSM, a resident of Beijing, capable of giving consent, and consenting to complete the survey and answer questions during a focus group. CCAVG and medical staff from China CDC further excluded persons with a cognitive, speech or auditory impairment after evaluation. The research protocol was reviewed and approved by institutional review boards of Vanderbilt University and the National Center for STD/AIDS Control and Prevention (NCAIDS) at China Center for Disease Control and Prevention (China CDC).

### Data Collection

Six focus group discussions (FGD) were conducted, including four among HIV-positive (11,10,10 and 9 participants in each positive group, respectively) and two among HIV-negative or status-unknown MSM (10 participants in each negative group with 4 status-unknown participant in negative group #2). Given our goal was to identify the barriers to and facilitators of linkage to HIV care among HIV-positive Chinese MSM, we analyzed qualitative data from focus groups with HIV-positive MSM only.



Prior to the focus groups (FG), a self-administered questionnaire was used to collect information on participants' age, marital status, education, occupation, and registered Beijing residence ('Hukou') status for background description. A trained facilitator led each group using a semi-structured discussion guide, in a confidential and convenient location in MSM community in Beijing. A note-taker was also assigned to each FG to monitor the group process and assist the facilitator when needed. For the groups with seropositive MSM, focus group questions covered items related to HIV testing experience prior to diagnosis, and obstacles experienced during linkage to HIV care after diagnosis, and suggestions for better facilitate the utilization of HIV care and subsequent engagement. All focus groups lasted approximately two hours, and all conversations and discussions were audio recorded on two digital recording devices. Digital recordings were transcribed verbatim in Mandarin. The notes and transcripts were then translated to English, embedded with the original language (Mandarin) as a reference for maintained meaning. (<http://globalhealth.vanderbilt.edu/research/mp3/>)

### Data Analysis

We used descriptive statistics to summarize quantitative, self-report data. Specifically, frequencies and percentages summarized participants' age, marital status, education, occupation, and Beijing residence ('Hukou').

First, the research team iteratively reviewed all transcripts in English (Y.L., R.A., and H.Z.Q.) and in Mandarin (Y.L. and H.Z.Q.). We applied four pre-specified themes to these data: (1) barriers to linkage to HIV care, (2) strategies to promote link-to-care, (3) specific recommendation for improving linkage to and engagement in HIV care, and (4)

other comments that may help guide intervention development but were not overlapped with previous thematic areas. Then, two investigators (Y.L. and X.J.Z.) independently reviewed all participant statements within these four categories, and merged similar statements to produce emergent sub-themes. Reviewer discrepancies were discussed until agreement was reached. We have used representative quotes to characterize and interpret each sub-theme below (Biadgilign, et al., 2009; Green & Thorogood, 2004; Strauss & Corbin, 1998; Wagner et al., 2011).

## **Results**

### Participant characteristics

The socio-demographic characteristics of the HIV-positive participants are shown in Table 1. Forty MSM participated in one of our HIV-positive focus groups. The median age was 29 years with interquartile range (IQR) from 26 to 33.5 years. Most participants self-reported that they were unmarried (single or divorced; 90%), had at least a college education (80%), were employed (92.5%) and did not have Beijing “Hukou” (80%).

### Barriers to linkage to HIV care

Major barriers to linkage to HIV care documented in this study included: (1) Perceived discrimination from health care workers; (2) Lack of guidance and follow-up; (3) Time or location inconvenience; (4) Privacy disclosure concerns; (5) Psychological burden of committing to HIV care; and (6) Treatment concerns.(Table 2)

### Discrimination from healthcare workers

A common reason for not seeking HIV care after diagnosis noted by our participants was their perceptions of discriminatory attitudes from healthcare providers. Participants complained about the unprofessionalism of some healthcare workers observed during their conversations. For example, the use of unfriendly tone/ words, indifference, distrust, and prejudice were all noted. These negative expressions heightened respondents' anger and anxiety, and decreased their motivation to use HIV care services.

*“The first time I came here, I found that she [healthcare worker] was very cold to me. She even joked [about] my homosexuality and HIV-positive status with another co-worker when they were having lunch, laughing out loud like I was something special animal. She wanted to force me to fill [out] some questionnaires. I felt angry and [I] didn't fill them [out]. My point is, if they treat you like this, you will be unwilling to use any care service or go to appointments at the recommended intervals.” (29-year-old, single, currently employed, non-Beijing resident)*

### Lack of guidance or follow-up

Participants talked about experiences after HIV diagnosis, and identified two reasons for disrupted linkage to care once diagnosed. Some healthcare providers never provided post-testing guidance, such as where they could avail themselves of the CD4+ cell count test, viral load tests, psychological counseling services, and procedures applying for free ART if they were eligible. In addition, many healthcare workers were

said to have failed to explain the importance of these services to patients. Those unaware of such services would just walk out of the clinic without taking further action. For example, one participant said:

*“That doctor in the hospital, she didn’t give me an explanation from [a] medical perspective. I didn’t know [they] had to test [my] CD4 and virus load, etc. I had the test in a first-class hospital, and I knew I had [a] lab-confirmed positive result, but they didn’t guide me through the available HIV care services. They just asked me to test again to confirm, on purpose just to charge me more money. I did not know why. As a result, everything was delayed.” (43-year-old, single, currently unemployed, legal Beijing resident)*

In addition, most participants complained they had never been contacted by healthcare providers to discuss their health conditions, the availability of care, or their progress while in care, which made them feel abandoned, discouraged, and want to give up on seeking care. For instance, one participant said:

*“I had my HIV testing in Ditan Hospital. After it was confirmed, they just called me to go to pick up a diagnosis report and provided me with several options for post-diagnosis care. But after that, I have never received a call from them. I was so upset because I thought they gave up on me. I lost hope and did not know what to do next. Those doctors should have at least given me a call to follow-up on my status.” (30-year-old, single, currently employed, non-Beijing resident)*

### Time or location inconvenience

Most participants worked from early morning to late afternoon, Monday through Friday, which usually conflicted with the office hours of CDC clinics and hospitals where HIV care was available. Participants said they were unwilling to leave work for HIV care because of the sensitivity of this issue as an excuse to ask for leave, and the potential loss of work compensation.

*“I think the HIV care provision is very limited in time flexibility. Usually, they are not held on weekends, and we have to go to work on weekdays. We all have jobs, and [the] boss will not allow you to ask for leave every now and then to see doctors.” (26-year-old, single, currently employed, non-Beijing resident)*

The inaccessibility of HIV care hospitals involved spending time traveling, and was a major perceived barrier to patients’ actively linking to care.

*“If you live far away from the hospital, you need to get up very early to go to a counseling session or have [a] CD4+ test. And often it is [a] workday, which are very inconvenient. So you may choose not to go if you feel it is not necessary.” (29-year-old, single, currently employed, legal Beijing resident)*

### Privacy disclosure

Another commonly discussed barrier to linking to care by our participants was the fear of disclosing one’s HIV and homosexuality status. The potential embarrassment of meeting non-gay acquaintance such as colleagues, friends and family members in the hospitals, and the concern that their records of seeking HIV care and their gay identity

would be documented and reported to the government or linked to future healthcare plans, influenced decisions to avoid the available HIV care services.

*“I know many residents in Beijing don't like to go to the CDC in their own district for fear of being recognized [by] their friends, [a] family member, colleagues or sexual partners. They are just reluctant to go there. ” (41-year-old, married, currently employed, legal Beijing resident)*

*“In almost all hospitals, the doctors will keep all the reports and details. Although I know this is their routine work, I am still uncomfortable and afraid that this sensitive information will be disclosed to the government, my health insurance company, or my employer. You know, this disease and gay experience are a shame! Maybe I am worrying too much, but that’s a major reason I avoid seeking HIV care if I feel I don’t need it.” (23-year-old, single, currently employed, non-Beijing resident)*

#### Psychological burden of commitment to care

Being committed to HIV care, once initiated, was considered to have a long-term influence on one’s lifestyle and require making sacrifices. Despite the benefits of HIV care, several participants thought they would endure a lifetime of pessimism, stigmatization, and suffer from psychological burden as a result of repeatedly frequenting HIV care facilities and being treated as sick individuals for the rest of their life. Hence, they would rather avoid getting involved in care from day one. For example, one participant said:

*“I met one person who thought this disease was no big deal. He wanted to be alive without going to [the] hospital continuously as a ‘sick’ person. Compared to the suffering from the psychological burden of linking to and engaging in the care for the remainder of his life, he said he would rather choose to live another 4-5 years happily instead of a miserable 20-30 years.” (43-year-old, single, currently unemployed, legal Beijing resident)*

### Treatment concerns

HIV treatment affected decisions to use HIV care. Generally, participants voiced concerns about experiencing drug side-effects, having insufficient knowledge of the benefits of treatment, and taking medicines at inconvenient times that added to their uncertainty about linking to and engaging in care. For example, one participant said:

*“I am not sure whether the medicine will work. I don’t have much knowledge [about] that. But I heard from a friend saying he had been taking the drug for two years and always felt dizzy and could not work. And he also said it was too troublesome to take the pills regularly, and once you took it, you needed to take it all your life or drug resistance will develop...It sounds horrible to me. I would rather not use that care or take drugs until I am very sick.” (25-year-old, single, currently employed, non-Beijing resident)*

### Facilitators of linkage to care

Five major sub-themes emerged from discussions on the facilitators of linking to care. These facilitators were: (1) Peer referral and accompaniment; (2) Free HIV care; (3)

Advocacy from HIV-positive MSM counselors; (4) Extended involvement for linking MSM to care; and (5) Standardization of HIV care. (Table 2)

Peer referral and accompaniment

Many participants thought they would be more likely to initiate HIV care if a friend or partner introduced them to a hospital or a specific healthcare provider. Positive testimonies based on a peer's experience would build up their confidence and trust in those services.

*“Before taking the first step out, it is very essential to have an open communication with a friend who frequents a clinic or hospital and let him give you a suggestion as to which doctor is the best choice. If positive feedback [towards the hospital or doctor] is given repeatedly, I will be more willing to follow in his footsteps.” (19-year-old, single, student, legal Beijing resident)*

Having a companion (gay friend or intimate partner) would also be a great facilitator for those who were first-time HIV care seekers. Participants considered accompaniment as a tremendous source of emotional support and psychological comfort.

*“I think the role of an experienced companion is highly recommended for those newly infected with HIV [who are] deciding to seek HIV care. Your companion would be able to comfort you and explain further from his perspective based on what the doctor said. This is my experience. For me, I am not willing to go alone.” (24-year-old, single, currently employed, non-Beijing resident)*



### Free HIV care

Despite national policies that have instituted free HIV counseling services and antiretroviral drug provisions (for eligible individuals) in China, some routinely recommended HIV care services (e.g., CD4+ tests, viral load tests, sexually transmitted infections [STIs] tests) require expensive out-of-pocket costs. Almost all participants said the government-supported HIV care services facilitated their linkage to and engagement in HIV care. For instance, one participant said:

*“At least I think the tests [CD4+ cell and viral load check] before treatment are necessary and should be free. And the drugs should be made free to everyone who wants to initiate ART. Then I believe more people would be financially relieved and willing to be cared if all expenses of these services are financially covered by the government.” (25-year-old, single, currently employed, legal Beijing resident)*

### Advocate of HIV-positive MSM counselor

Participants thought post-diagnosis counseling was a strong determinant of receiving subsequent HIV care. They suggested hospitals and clinics should recruit and train volunteer HIV-positive MSM to deliver this counseling either in the hospital or in community settings. Participants said they would be more comfortable talking to a HIV-positive peer, and would be more willing to take suggestions from someone who is similar to themselves. For example, one participant said:

*“I think the counseling services should be carried out by a person who has been diagnosed as HIV-positive before and has had experience in HIV care. I think their words are more trustworthy. When I was a volunteer, I did psychological*

*counseling and they [the clients] trusted me very much. The first reason is that I've been alive for such a long time and they believe me very much. So they all went to care.”(43-year-old, single, currently unemployed, legal Beijing resident)*

*Extended involvement for linking MSM to care*

Despite healthcare providers failing to inform HIV-positive persons about available HIV care services, the major route of receiving such information is still from professionals. Participants suggested the government and relevant organizations should do a better job of communicating where, how, and why to initiate and engage in HIV care. Participant ideas included giving lectures, disseminating booklets, and playing video tutorials in some MSM-frequented venues to increase exposure of MSM to such information.

*“Most infected guys generally have no idea about it. This is due to insufficient publicity. If you meet some good guy, he can give you some useful information. My point is, why not publicize those services in some places that we regularly visit? Invite some professional to give a talk or pass down a flyer with detailed information. I believe this will improve the situation greatly.”(29-year-old, single, currently employed, non-Beijing resident)*

Participants also endorsed electronic communication platforms to promote HIV care services. Participants suggested leveraging short message service text messaging via cell phones, e-mail, and use of QQ (an instant message chatting tool in China). In the meantime, some participants expressed concerns about the sensitive words being used in these messages. For example, one participants said:

*“Of course it is helpful [to receive messages]. HIV positive friends [would] be glad to receive these messages through QQ groups. At least I like it. It is also helpful to send emails periodically. This [would] raise their awareness [of] HIV care and function as a reminder. But do not use words like ‘HIV’ or ‘gay’ or others words of this kind in the conversation.” (34-year-old, single, currently employed, non-Beijing resident)*

*“Targeting us through email or other chatting tools is okay, but I personally prefer short messages sent to my smartphone because I am not always logged on QQ or my email account, but I can always take a glance at my phone and notice such information. But be aware of the words used, because someone may stand around you. Basically all these channels would be efficient [to facilitate linking people to HIV care].” (32-year-old, single, currently employed, legal Beijing resident)*

### Standardization of HIV care

Participants suggested the government should establish a national guideline for all participating clinics and hospitals across the country to standardize HIV care vis-à-vis services provision, operational management, and training of healthcare providers. A comprehensive regulation and an authoritative monitoring system for the execution of the guidelines would not only greatly strengthen patients’ confidence in care, but facilitate access to consistently high quality care, without geographic constraints in terms of quality variation.

*“I think that current HIV care should be standardized. I mean, in addition to the CD4 and viral load tests, counseling, and ART provision, more should be included. For example, test of renal function, the liver function, ultrasound, chest, hepatitis B and HCV should be all examined. I know these are just optional based on personal will, but they are important, too. The country should invest more to make them a standard part of HIV care.” (43-year-old, married, currently employed, legal Beijing resident)*

*“In my experience, HIV care varies from hospital to hospital in terms of wait time, logistics, and the quality of healthcare providers. My assumption is that there is no specific rule that applies to all these HIV care facilities. Well...this is understandable...but...I guess we [would] be more motivated and see it as convenient to go if the quality and operational efficiency is consistent among all these settings. So...I think a universal standard should be promoted by the government to ensure [that] changes.”(29-year-old, single, currently employed, non-Beijing resident)*

## **Discussion**

There is a substantial research need to update existing policies and design intervention programs that are able to meet patients’ expectations and better link PLHIV to care more efficiently and effectively. Yet, few studies employed qualitative study designs to examine the barriers and facilitators of the linkage to HIV/AIDS related services among HIV-positive MSM in China(Wei, et al., 2013).Hence, knowledge of

such intervening factors has remained limited. Our study explored the barriers to and facilitators of linking to HIV care reported by HIV-positive MSM in China, providing direction for future research and further validation. Consistent with studies (H. H. Li, et al., 2015; Ma, et al., 2012; Wei, et al., 2014), HIV-positive Chinese MSM reported barriers to care such as discrimination from healthcare providers, inaccessible HIV care facilities, lack of understanding what services are offered, concerns about privacy and disclosure, and negative attitudes towards HIV treatment. Facilitators of HIV care validated in our study included government support to compensate all HIV care costs, provision of comprehensive HIV care, and peer support/referral to care. In addition, participants in our study were concerned about drastic lifestyle change and lifetime stigma as a result of linking to and committing to care, which might impede their initiation of those services. In contrast, some innovative strategies were suggested to have the potential to attract more HIV-positive MSM to care, such as the use of peer counselors in regular HIV care sessions and e-communication tools for expanded inclusion coverage.

The stigma surrounding HIV/AIDS and homosexuality rooted in traditional Chinese social taboos and cultural isolation of MSM continue to play a crucial role in causing a series of negative emotions and feelings (Williams et al., 2005). This was perceived by our respondents to lower the willingness and motivation to receive HIV care services. Some participants in our study who interrupted their own HIV care emphasized their anger and disappointment in the prejudice and disrespect they perceived from healthcare workers. Previous studies also suggested that HIV/AIDS stigmatizing and discriminatory attitudes from healthcare providers hindered the utilization of HIV

prevention, care and treatment (X. Li, H. Lu, X. Ma, et al., 2012; Liao et al., 2014). It is important to conduct routine training and evaluation among all medical staff who provide HIV care in order to provide care through a positive and unprejudiced relationship with patients. In addition to the stigmatizing behaviors from healthcare professionals, our participants also anticipated the commitment to HIV care would raise their stress and label them with lifetime stigma. It is possible that, with the presence of this internalized stigma, individuals would tend to over-amplify perceived stigmatizing beliefs, heightening their concerns for experiencing discrimination, rejections, and indignities when engaged in HIV care (Golub & Gamarel, 2013). As a consequence, individuals may purposely sacrifice their objective interest just to avoid being associated with a stigmatized condition (Golub & Gamarel, 2013; Young, Nussbaum, & Monin, 2007), including linkage to and engagement in HIV care. These reports demonstrate the need to increase the availability of psychological counseling services and educational campaigns to equip MSM with stigma-coping skills and promulgate positive beliefs towards using HIV care services.

Despite successes of China's "Four Free and One Care" policy in reducing the HIV-related mortality and morbidity (Jia et al., 2013), no national regulations exist to guide the operation, management, monitoring, and evaluation of the quality of HIV care provision. The standardization of HIV care services was one of the facilitators deemed to have the capability to counter several personal, inter-personal, and structural barriers by our participants. As suggested in our focus groups, the government should enforce guidelines for all participating clinics and hospitals to abide to a strict standard with accommodation to patients' needs. These standardized guidelines would refer to

approaches for the introduction and description of HIV care service content, specified convenient times and timeframes for handling logistics and follow-up, the training of ethical and professional healthcare providers, fair cost and compensation rules, precise operational hours with weekend shift schedules, a toll-free hotline for collecting public feedback for improvement, and an internal mechanism for service and staff evaluation. With a standardized HIV care system, patients may be more motivated and reassured to use those services in the desirable volume.

Although it may take a long time to standardize HIV care across the country, some facilitators could be integrated into intervention programs in the short-term. The recruitment and training of volunteer HIV-positive MSM to assist healthcare providers in care settings or conduct active outreach within the MSM community would be a cost-effective and sustainable way to improve linkage to care among MSM. This is because communicating with a peer would lessen the anxieties of HIV-positive MSM who have not yet initiated care; and peer-initiated care might be carried out in MSM-friendly manner with flexible schedules in convenient locations (Yan, et al., 2014). Thus, this approach would address several barriers such as time or location inconvenience, stigma, and discrimination associated with traditional hospitals and clinics. In addition, the vast development of electronic technology (emails, short message service text messaging via cell phone, QQ, WeChat, Grindr, etc.) in past decade and its efficiency in communication has gain tremendous popularity among Chinese MSM (Nehl et al., 2013). Thus, we speculate that the better application of these tools could cost-effectively target more HIV-positive MSM for the dissemination of relevant information on care and

stigma management tips for improved linkage to and engagement in HIV-related services.

There are limitations in our study. First, FG were conducted among a small convenience sample in Beijing. Although we identified several important barriers to and facilitators of HIV care, these findings may not be generalized to other populations and may need further studies to validate. Second, our focus groups consisted of a mixed sample of HIV-positive MSM who had never initiated HIV care and who had experience in care. Thus, findings should be interpreted with caution. Third, the FG were mainly facilitator-driven, there could be a lack of interactive dynamics during the discussion among participants, which might somehow affect the richness of our findings. Despite these limitations, our study is one of very few qualitative studies exploring the barriers to and facilitators of utilizing of HIV care among Chinese MSM. Our findings provide policy guidance for future interventions.

In conclusion, we identified several important individual, healthcare provider, and structural-level factors that might determine how MSM may or may not be linked or engaged in HIV care. Our focus group participants also suggested some innovative strategies to improve HIV care utilization among MSM. Future efforts in sustaining HIV care among Chinese MSM lies in the close collaboration between the government, community-based organizations, HIV care provision facilities, and MSM themselves to create a more socially and culturally tolerant environment and a robust and comprehensive HIV care system.



**Table 3. Socio-demographic characteristics of HIV-positive men who have sex with men in Beijing, China (N=40)**

Characteristics		
	<u>N</u>	<u>%</u>
Median age in years (IQR*)	29 (26.0 -33.5)	
Marital status		
Currently married	4	10.0
Single or divorced	36	90.0
Education (year of schooling)		
College or above (>12)	32	80.0
High school (10-12)	6	15.0
Junior middle school or lower(<10)	2	5.0
Employment		
Employed	37	92.5
Student	1	2.5
Unemployed/ or retired	2	5.0
Beijing residence ( <i>Hukou</i> )		
Yes	8	20.0
No	32	80.0

\* IQR: interquartile range

**Table 4. Perceived barriers and facilitators for HIV testing among HIV-positive men who have sex with men in Beijing, China (N=40)**

Barriers	Facilitators
Perceived discrimination from healthcare workers	Peer referral and accompaniment
Lack of guidance or follow-up	Free HIV care
Time or location inconvenience	Advocacy of HIV-positive MSM counselors
Privacy and disclosure concerns	Extended involvement for linking MSM to care
Psychological burdens of commitment to long-term care	Standardization of quality HIV care
Treatment concerns	

## CHAPTER VI

### PREDICTORS OF ANTIRETROVIRAL THERAPY INITIATION: A CROSS-SECTIONAL STUDY AMONG CHINESE HIV-INFECTED MEN WHO HAVE SEX WITH MEN

#### **Abstract**

Introduction: Early antiretroviral therapy (ART) is crucial to achieve HIV viral suppression and reducing transmission. HIV-infected Chinese men who have sex with men (MSM) were less likely to initiate ART than other HIV-infected individuals. We assessed predictors of ART initiation among Chinese MSM.

Methods: In 2010-2011, a cross-sectional study was conducted among MSM in Beijing, China. We examined ART initiation within the subgroup who were diagnosed with HIV infection prior to participation in the survey. Logistic regression models were fitted to evaluate socio-demographic and behavioral factors associated with ART initiation. The eligibility criterion in the 2010/2011 national HIV treatment guidelines was CD4 cell count <350 cells/ $\mu$ L or World Health Organization (WHO) clinical stage III/IV.

Results: Of 238 eligible HIV-infected participants, the median duration of HIV infection was 15 months (range: 31 days-12 years); 62 (26.1%) had initiated ART. Among 103 men with CD4 counts <350 cells/ $\mu$ L, 38 (36.9%) initiated ART. Being married to a woman (adjusted odd ratios [aOR]: 2.50; 95% confidence interval [CI]: 1.07-5.87),

longer duration of HIV infection (aOR: 10.71; 95% CI: 3.66-31.32), and syphilis co-infection (aOR: 2.58; 95% CI: 1.04-6.37) were associated with a higher likelihood of ART initiation. Of 135 men with CD4 count  $\geq$ 350 cells/ $\mu$ L, 24 (18%) initiated ART. Being married to a woman (aOR: 4.21; 95% CI: 1.60-11.06), longer duration of HIV infection (aOR: 22.4; 95% CI: 2.79-180), older age (aOR: 1.26; 95% CI: 1.1-1.44), Beijing *Hukou* (aOR: 4.93; 95% CI: 1.25-9.33), presence of AIDS-like clinical symptoms (aOR: 3.97; 95% CI: 1.32-14.0), and history of sexually transmitted infections (aOR: 4.93; 95% CI: 1.25-9.43) were associated with ART initiation. Compared with men who did not initiated ART, those with ART were more likely to receive counseling on benefits of ART (96.8% vs. 66.4%,  $P=0<0.01$ ), HIV stigma coping strategy (75.8% vs. 65.9%,  $P=0.04$ ), mental health (66.1% vs. 52.9%,  $P=0.02$ ), and substance use (46.7% vs. 36.6%,  $P=0.04$ ).

Conclusions: We documented low rates of ART initiation among Chinese MSM. Policy changes for expanding ART eligibility and interventions to improve the continuum of HIV care are in progress in China. Impact evaluations can help assess continuing barriers to ART initiation among MSM.

Keywords: HIV, antiretroviral therapy; continuum of care; men who have sex with men; China

## Introduction

Antiretroviral therapy (ART) use among HIV-infected individuals is crucial for long-term success in reducing HIV transmission and disease progression (Gardner, et al., 2011; Mugavero, Amico, Horn, & Thompson, 2013). Early initiation of ART can suppress viral replication and reduce harmful immune activation, slowing pathogenesis, and stem the spread of the virus ('treatment-as-prevention') (Cohen, et al., 2011; Vermund & Hayes, 2013b). Mathematical modeling and observational studies suggested that the regions with higher ART coverage had reduced HIV transmission between regular and casual sexual partners, lower community viral load, and decreased HIV incidence (Das, et al., 2010; Fang et al., 2004; Tanser, Barnighausen, Grapsa, Zaidi, & Newell, 2013; Wood et al., 2009). The randomized clinical trial HPTN052 confirmed that early initiation of ART could significantly reduce sexual transmission of HIV among serodiscordant couples (Grinsztejn et al., 2014).

Despite these benefits of modern ART (Das, et al., 2010; Gardner, et al., 2011; Gill et al., 2010), many HIV-infected individuals in China are still not on ART (Zhu, et al., 2012). A 2011 study showed that only 41% (88,185/214,714) HIV-infected individuals had initiated ART (F. Zhang, et al., 2011), though the rate has been increasing steadily in the recent years. Chinese men who have sex with men (MSM) are less likely to start ART compared with other risk groups (Jiang et al., 2013).

HIV epidemic among Chinese MSM is the most robust in all high risk groups ("State Council AIDS Working Committee Office (SCAWCO):China 2012 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of

China; 2012.," ; Wu et al., 2013a; Zhou, et al., 2014). According to the latest national estimates, HIV prevalence among Chinese MSM uniquely represented a marked uptrend (7.3% in 2013 vs. 0.9% in 2003), while in other risk groups it either dropped or maintained at a low level ("State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2014.,")(State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2014.). Male-to-male transmission accounted for 21.4% of all new infections in 2013, with the fastest increasing rate among all risk groups ("State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2014.,")(State Council AIDS Working Committee Office (SCAWCO):China 2014 UNGASS Country Progress Report.Beijing, China: Ministry of Health of the People's Republic of China; 2014.). As Chinese MSM may marry a women due to social and family pressures (Chow, et al., 2013; He, et al., 2006a; Y. Ruan et al., 2011), HIV-infected MSM are also likely transmit the virus to their female sexual partner. Therefore, it is a crucial strategy for HIV prevention to expand ART coverage among Chinese MSM. However, there is little knowledge about ART initiation among Chinese MSM. A qualitative study suggested that Chinese MSM may not seek HIV care or initiate ART due to psychological, social, cultural and institutional barriers (Wei, et al., 2014). We conducted the first quantitative assessment of ART initiation and its predictors among Chinese HIV-infected MSM.

## Methods

### Study design and population

In 2010-2011, we conducted a cross-sectional study among Chinese MSM with a primary objective of assessing the association between male circumcision and HIV risk among MSM in Beijing, China. This study was described elsewhere (Hu, et al., 2013; Y. Liu et al., 2014a; Tao, et al., 2013a). In brief, participants were recruited from HIV/sexually transmitted disease (STD) clinics or the community, and through peer-referral; participants who were tested HIV positive from other studies in Beijing were also recruited. Eligibility criteria included: being a male, living in Beijing, self-reporting ever having sex with men, willingness to provide blood samples for HIV and syphilis serological tests and anal swab specimens for HPV testing, and willingness to provide written informed consent were eligible to participate in the study. All eligible participants were asked to complete a questionnaire interview, undertake genital examinations, and provide blood samples (Hu, et al., 2013). The study protocol was approved by the Institutional Review Boards of the National Center for AIDS/STD Control and Prevention of the Chinese Center for Disease Control and Prevention, and the Vanderbilt University School of Medicine.

### Data collection

Each participant completed a questionnaire on socio-demographic characteristics: age, ethnicity, marital status, education, occupation, registered household in Beijing (or Beijing *Hukou*), duration of living in Beijing, and sexual orientation. The questionnaire

also assessed behavioral risk factors: unprotected insertive or receptive anal sex, most recent CD4+ T-lymphocyte cell count (CD4+ count), and history of sexually transmitted diseases (STDs). Those who had been diagnosed with HIV infection prior to participation in this study were also asked about AIDS clinical symptoms, experiences of using ART and HIV care and counseling, such as substance use, mental health, stigma coping strategies, benefits of ART, and prevention of HIV transmission.

### Laboratory testing

Enzyme-linked immunosorbent assay (ELISA, Wantai Biological Medicine Company, Beijing, China) was used for HIV-1 screening. Positive samples were confirmed by HIV-1/2 Western blot (HIV Blot 2.2 WB™; Genelabs Diagnostics, Singapore). Syphilis serology was determined through rapid plasma reagin (RPR, Shanghai Kehua Biotechnology Ltd, China) and confirmed by *Treponema pallidum* Enzyme-linked immunosorbent assay (TP-ELISA, Beijing Wantai Biological Pharmacy Enterprise Co., Ltd, China)(Hu, et al., 2013).

### Statistical analysis

A significant portion of participants had been previously diagnosed with HIV infection, and were asked for ART initiation. Therefore, we performed a subgroup analysis among these participants to assess their ART initiation and its predictor variables.

We expressed descriptive statistics as proportions for categorical variables and as means and standard deviations, or medians and interquartile ranges for continuous variables, depending on the distribution of the variables. The socio-demographic, clinical,



and behavioral characteristics were compared between those who had initiated ART and who had not in the whole study sample and in subgroups by CD4 count of 350 cells/ $\mu$ L which was the cut point of ART eligibility in Chinese national guidelines during 2010 and 2011. We also examined WHO HIV clinical staging (III or IV) for dividing the subgroups. Continuous variables were compared with Wilcoxon rank-sum tests, and categorical variables were compared with the Chi-square or Fisher's exact tests. Proportions of MSM receiving HIV care counseling services comparing men who did and did not initiate ART were compared using Chi-square tests.

To further assess the strength and direction of the associations between selected predictors and ART initiation stratified by CD4+ count, variables moderately associated with ART initiation ( $P < 0.2$ ) in bivariable analyses were selected for multivariable logistic regression analyses. In the multivariable logistic regression models, variables with a  $P < 0.2$  in the bivariable logistic regression analyses were preliminarily fitted into each model, respectively, then a manual backward selection procedure was used to conclude the final multivariable models that only retained covariates significantly associated with the outcome ( $P < 0.05$ ). However, factors considered as *a priori* predictors or confounders based on prior evidence were forced to retain in the final models regardless of  $P$ -value (Blank et al., 2014). All statistical analyses were performed using Stata 12.0™ (StataCorp LP, College Station, Texas, USA).

## Results

### Characteristics of Study Population

Among 1,155 participants in the study, 290 were confirmed to be HIV positive (25.1%), including 48 men newly diagnosed upon enrolled in the current study and 242 previously diagnosed. The 48 newly diagnosed HIV cases were excluded in the analysis since they had had no opportunity to initiate ART upon the survey. Of the 242 previously diagnosed HIV-infected MSM, 4 had missing data on ART initiation, and therefore, 238 (98.3%) were included in this analysis.

The median age of these 238 men was 31 years (interquartile range [IQR], 26-37) and median duration from HIV diagnosis to participation in this survey was 15 months (IQR, 6-31). A majority of participants were Han ethnics (94.1%), were currently unmarried (71.4%) and employed (74.8%), had college education (53.8%), and had Beijing *Hukou* (61.8%).

Over a quarter (26.1%) men had started ART. Compared with those who had not initiated ART, men who had initiated ART were more likely ( $P<0.05$ ) to be older, be married to a woman, have Beijing *Hukou*, live longer in Beijing, have a longer duration of HIV-infection, experience adverse clinical symptoms, have a history of STDs, and be co-infected with syphilis. However, those who had initiated ART were less likely ( $P<0.05$ ) to be engaged in unprotected insertive or receptive anal sex (Table 1a).

Among 103 MSM with CD4+cell count (CD4 count) <350 cells/ $\mu$ L who met the eligibility criteria for Chinese free ART program during this survey, 36.7% initiated ART. Those who had initiated ART were more likely ( $P<0.05$ ) to be married to a woman, have longer duration of HIV-infection, and have syphilis co-infection, but were less likely ( $P<0.05$ ) to have unprotected insertive or receptive anal sex (Table 1b).

Of 135 MSM with CD4 count  $\geq 350$  cells/ $\mu$ L who did not meet the criteria, 17.8% initiated ART. Those who had initiated ART were more likely ( $P<0.05$ ) to be older, married to a woman, have Beijing *Hukou*, live longer in Beijing, have longer duration of HIV-infection, have ever had clinical symptoms, have a history of STDs, and have syphilis co-infection, but were less likely ( $p<0.05$ ) to have unprotected insertive or receptive anal sex (Table 1b).

#### Factors associated with ART initiation by CD4 count level

Table 2 shows the variables associated with ART initiation in both bivariable and multivariable logistic regression analyses. In the final multivariable logistic regression models, being married (adjusted odd ratio [aOR]: 2.50; 95% confidence interval [CI]: 1.07-5.87), longer duration of HIV infection (aOR: 10.7; 95% CI: 3.66-31.3), and syphilis co-infection (aOR: 2.58; 95% CI: 1.04-6.37) were associated with a higher likelihood of ART initiation among subgroup of CD4 count <350 cells/uL. Being married (aOR: 4.21; 95% CI: 1.60-1.06), longer duration of HIV infection (aOR: 22.42; 95% CI: 2.79-180.01), older age (aOR: 1.26; 95% CI: 1.1-1.44), Beijing *Hukou* (aOR: 4.93; 95% CI: 1.25-9.33), presence of AIDS-like clinical symptoms (aOR: 3.97; 95% CI: 1.32-14.0),

and prior STDs (aOR: 4.93; 95% CI: 1.25-9.43) were associated with a higher likelihood of ART initiation among subgroup of CD4 count  $\geq 350$  cells/uL.

#### HIV care counseling services received

The top three HIV care counselling received by the participants were HIV transmission prevention (78.6%), benefits of ART (66.4%), and HIV stigma coping strategy (65.6%). Other counseling topics included mental health (52.9%), nutrition (41.2%), substance abuse (36.6%), and birth control (25.6%) (Figure 1). MSM who initiated ART were more likely to receive counseling than those without ART on benefits of ART (96.8% vs. 66.4%,  $P < 0.01$ ), HIV stigma coping strategy (75.8% vs. 65.9%,  $P = 0.04$ ), substance use (46.7% vs. 36.6%,  $P = 0.04$ ), and mental health (66.1% vs. 52.9%,  $P = 0.02$ ). There was no statistically significant difference in receiving counseling on HIV transmission prevention, birth control, and nutrition between those who had or had not initiated ART.

### **Discussion**

To our knowledge, this is the first study on ART initiation and receipt of HIV care among Chinese MSM. In the study, we found older age and ever having adverse clinical symptoms were positively associated with ART initiation, and this is consistent with findings from other regions (Zala et al., 2008). Due to social and family pressure, some Chinese MSM are married with women or have female sexual partners (Tao, et al., 2013b). Our study showed that married MSM were more likely to start ART than unmarried MSM. Married men might have more sense of responsibility for the health of

themselves and their wives, and therefore have started ART; however, more research is needed to explore the reasons. Beijing *Hukou* and longer duration of living in Beijing were also positively associated with ART initiation. Migrant MSM, particularly recent migrants, might not know that free ART is for everyone, or where they could get it. It is suggested HIV intervention programs should give special emphasis among migrant MSM who account for the majority of MSM population in many large cities. In addition, Men who had initiated ART reported receiving more HIV care counseling services than those without ART, and therefore could get more health benefits from the counseling.

Our findings suggest considerations for the design of future intervention programs. The positive association between being married and ART initiation observed among both ART eligible and ineligible MSM (using criteria in place in 2010-2011) suggest that a built-in educational or psychological counseling session would be necessary for cultivating the sense of responsibility for spouses and family among married HIV-infected MSM, which might facilitate early ART initiation. Given that the longer time from HIV diagnosis to the survey and older age were positively associated with ART initiation, greater government and community efforts to target and engage men earlier and more intensively may be effective, alongside linking recently infected MSM to HIV care for ART initiation. The benefits of legal residence (Beijing *Hukou*) in accessing HIV care reflects both one's ability to use local medical services and social benefits, and also one's motivation and willingness in seeking these services. People without local residence might be more financially, physically, and/or emotionally burdened as compared to local residents. In our study, having Beijing *Hukou* played a crucial role in ART initiation among MSM who did not meet free ART criterion. In the meantime, those

who had longer duration living in Beijing demonstrated a higher likelihood of proactive ART initiation. Thus, our findings suggest the need for researching the sexual network and cooperating with local gay organizations with outreach to the migrant MSM who recently move to Beijing and/or are transiently working in Beijing.

China started its national free ART program in 2003 (F. Zhang et al., 2007). This program has significantly reduced mortality among HIV-infected individuals (F. Zhang et al., 2009; F. Zhang et al., 2008). However, our study showed that 26% of HIV-infected participants who had been infected with HIV for a median 15 months (IQR, 6-31) initiated ART, a lower rate that noted among other key populations at-risk in China (Luo et al., 2014; Muessig et al., 2014; Xing et al., 2013) and lower than among MSM in other countries (Ferro et al., 2015; Graham et al., 2013; Hidalgo-Tenorio et al., 2014; Paz-Bailey et al., 2014; Raymond et al., 2013). Men who met treatment criteria (36.7%) were more likely to initiate ART than those who did not (17.8%), but both were quite low.

Our study examined predictors of ART initiation among Chinese MSM. Previous surveys suggested considerable willingness to receive ART (Jiang, et al., 2013; Q. Zhang et al., 2014), yet this willingness seems not translating into uptake of ART, where studies revealed low ART use (Liao, et al., 2014; Rodriguez-Arenas, et al., 2006; Y. L. Wu et al., 2014; Wu, et al., 2013a). There are multiple reasons for low ART use. First, Chinese free ART program were originally developed to provide “Four Free and One Care” (free ARV drugs, free prevention of mother-to-child transmission, free voluntary counseling and testing, free schooling for children orphaned by AIDS, and care to people living with HIV/AIDS) to HIV-infected former plasma donors and persons who injected drugs and their family members. Chinese government has vigorously promoted ART use in these

populations (Choi, et al., 2006). In contrast, the promotion activities of ART use among HIV-infected MSM were sporadic prior to 2011, mainly through programs funded by international agencies such as Global Fund to Fight AIDS, Tuberculosis and Malaria and The Bill and Melinda Gates Foundation. HIV-infected MSM might not be aware that they can use the Chinese free ART program. Second, the HIV epidemic among Chinese MSM is more recent compared with those in other key populations. Although prevention-oriented intervention programs exist for Chinese MSM, ART is relatively new and therefore unfamiliar to many (L. Zhang, D. Zhang, et al., 2013). Third, the majority of HIV-infected MSM are generally young (<40 years), well educated, and living in large cities, so they are well accessible to HIV-related knowledge and information. They are concerned about side-effects of first-line generic ARVs in the Chinese free ART program and possible drug resistance due to failure in treatment adherence; they are concerned about no alternative drugs due to the limited number of available antiretroviral drugs (ARVs) in Chinese ART program (Dou, et al., 2010; Johnson, et al., 2011; X. Wang & Wu, 2007). Fourth, Chinese MSM face dual stigma of HIV and homosexuality, and they may encounter discrimination from the community and healthcare providers, which prevents them from seeking HIV care and treatment (Feng, et al., 2010; Grossman, 1991; Mahajan, et al., 2008). Last, the stricter eligibility criteria in earlier years might also exclude some MSM from treatment. China ART program relaxed its eligibility criteria to include all persons with CD4 counts <500 cells/ $\mu$ L in 2013. Actually in some cities, HIV-infected individuals can start ART immediately at diagnosis, the approach now prevalent in high income countries (Cuzin, et al., 2011; Hsu, et al., 2014; Thompson, et al., 2010).

We recognized the limitations of our study: (1) With a relatively small sample of HIV-infected Chinese MSM living in Beijing, findings may not represent very precise estimates or be generalizable to other settings; (2) Data on socio-demographic characteristics, risky behaviors, and some clinical factors were based on self-reporting, subjecting these data to recall and social desirability biases; (3) We did not record the exact time of ART initiation, which limited us from further assessing factors associated time from HIV diagnosis to ART initiation. However, this study investigated ART initiation in this marginalized population and will shed light on future observational and interventional studies.

In conclusion, HIV among Chinese MSM represents current and future HIV risk in China, and the strengthening of ART use among this subgroup plays an important role in ameliorating HIV care cascade in China. A more refined assessment of the associated factors with ART use and potential HIV risk compensation is imperative in a large cohort with longitudinal study design in order to shed light on appropriate strategy to enhance linkage to and engagement in HIV care.



**Table 5. Sociodemographic and behavioral characteristics of HIV-infected men who have sex with men in Beijing, China (N=238)**

Characteristics	Total (N=238), n (%)	Having initiated ART		P-value
		Yes (N=62), n (%)	No (N=176), n (%)	
Age in years; Median, IQR	31 (26-37)	36 (31-42)	30 (26-35)	<0.001
Ethnicity				0.69
Han	224 (94.1)	59 (95.2)	165 (93.7)	
Non-Han	13 (5.9)	3 (4.8)	6.3 (6.3)	
Marital status				<0.001
Currently unmarried	170 (71.4)	31 (50.0)	139 (79.0)	
Currently married	68 (28.6)	31 (50.0)	37 (21.0)	
Education (year of schooling)				0.78
College or above(>12)	128 (53.8)	31 (50.0)	97 (55.1)	
Senior high school(10-12)	69 (29.0)	18 (29.1)	51 (29.0)	
Junior high school(7-9)	34 (14.3)	11 (17.7)	23 (13.1)	
Primary school(<=6)	7 (2.9)	2 (3.2)	5 (2.8)	
Occupational status				0.27
Employed	178 (74.8)	47 (75.8)	131 (74.4)	
Non-employed/retired	34 (14.3)	12 (19.4)	22 (12.5)	
Student	10 (4.2)	1 (1.6)	9 (5.1)	
Other	16 (6.7)	2 (3.2)	14 (8.0)	
Had Beijing <i>Hukou</i>				0.003
No	91 (38.2)	14 (22.6)	77 (43.7)	
Yes	147 (61.8)	48 (77.4)	99 (56.3)	
Time living in Beijing (year)				0.008
<5	99 (41.6)	17 (27.4)	82 (46.6)	
>=5	139 (58.4)	45 (72.6)	94 (53.4)	

Time from HIV infection to survey (month)				0.001
<15	115 (48.3)	6 (9.7)	109 (61.9)	
>=15	123 (51.7)	56 (90.3)	67 (38.1)	
Self-report health condition				0.91
Very good/good	193 (81.1)	50 (80.6)	143 (81.3)	
Somewhat poor/very poor	45 (18.9)	12 (19.4)	33 (18.7)	
Ever had AIDS-like clinical symptoms <sup>&amp;</sup>				0.02
No	177 (74.4)	39 (62.9)	138 (78.4)	
Yes	61 (25.6)	23 (37.1)	38 (21.6)	
Had unprotected insertive anal sex with men in past 6 months				0.004
No	77 (71.3)	21 (95.5)	56 (65.1)	
Yes	31 (28.7)	1 (4.5)	30 (34.9)	
Had unprotected receptive anal sex with men in past 6 months				<0.001
No	86 (64.7)	27 (93.1)	59 (56.7)	
Yes	47 (35.3)	2 (6.9)	45 (43.6)	
Had multiple concurrent male partners in past 12 months				0.60
No	211 (90.9)	57 (93.4)	154 (90.1)	
Yes	21 (9.1)	4 (6.6)	17 (9.9)	
Had commercial sex in past 12 months				0.52
No	220 (94.4)	60 (96.8)	160 (93.6)	
Yes	13 (5.6)	2 (3.2)	11 (6.4)	
History of sexually transmitted diseases				0.003
No	100 (44.4)	17 (28.3)	83 (50.3)	
Yes	125 (55.6)	43 (71.7)	82 (49.7)	
Syphilis co-infection				0.003
No	93 (39.1)	15 (24.2)	78 (44.3)	

Yes	145 (60.9)	47 (75.8)	98 (55.7)
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Note: Sample size for each variable may reduce due to missing data; IQR: inter quartile range; Hukou means permanent legal residence vs. transient status with *Hukou* elsewhere in China.

& Ever had at least one of these adverse clinical symptoms in the past 6 months: severe weight loss (>10%), fever (>1 month, continuing or intermittent), chronic diarrhea (>1 month), severe bacterial infection (e.g. pneumonia), oral candidiasis, oral leukoplakia, tuberculosis other stage III or stage IV symptoms

**Table 6. Sociodemographic and behavioral characteristics of HIV-infected men who have sex with men by CD4+ cell count (<350 cells/ $\mu$ L eligible for free antiretroviral treatment at the time of the study) in Beijing, China (N=238)**

Characteristics	CD4 count <350 cells/ $\mu$ L			<i>P</i> -value	CD4 count $\geq$ 350 cells/ $\mu$ L			<i>P</i> -value
	Total (N=103), n (%)	Initiated ART (N=38), n (%)	Not initiated ART (N=65), n (%)		Total (N=135), n (%)	Initiated ART (N=24), n (%)	Not initiated ART (N=111), n (%)	
Age (year)				0.07				<0.001
Median, IQR	32 (27-38)	34 (29-39)	30 (26-36)		31 (26-37)	41 (35-45)	30 (25-34)	
Ethnicity				1.00				0.59
Han	95 (92.2)	35 (92.1)	60 (92.3)		129 (95.6)	24 (100.0)	105 (94.6)	
Non-Han	8 (7.8)	3 (7.9)	5 (7.7)		6 (4.4)	0 (0)	6 (5.4)	
Marital status				0.03				<0.001
Currently unmarried	68 (66.0)	20 (52.6)	48 (73.8)		102 (75.6)	11 (45.8)	91 (82.0)	
Currently married	35 (34.0)	18 (47.4)	17 (26.2)		33 (24.4)	13 (54.2)	20 (18.0)	
Education (year of schooling)				0.92				0.52
College or above(>12)	57 (55.3)	21 (55.2)	36 (55.4)		71 (52.6)	10 (41.7)	61 (55.0)	
Senior high school(10-12)	24 (23.3)	8 (21.1)	16 (24.6)		45 (33.3)	10 (41.7)	35 (31.5)	
Junior high school(7-9)	19 (18.5)	8 (21.1)	11 (16.9)		15 (11.1)	3 (12.5)	12 (10.8)	
Primary school( $\leq$ 6)	3 (2.9)	1 (2.6)	2 (3.1)		4 (3.0)	1 (4.1)	3 (2.7)	
Occupational status				0.87				0.39

Employed	81 (78.6)	31 (81.6)	50 (76.9)	97 (71.8)	16 (66.6)	81 (73.0)	
Non-employed/retired	15 (14.6)	5 (13.2)	10 (15.4)	19 (14.1)	7 (29.2)	12 (10.8)	
Student	2 (1.9)	1 (2.6)	1 (1.5)	8 (5.9)	0 (0)	8 (7.2)	
Other	5 (4.9)	1 (2.6)	4 (6.2)	11 (8.2)	1 (4.2)	10 (9.0)	
Had Beijing <i>Hukou</i>				0.19			<0.001
No	39 (37.9)	11 (28.9)	28 (43.1)	52 (38.5)	3 (12.5)	49 (44.1)	
Yes	64 (62.1)	27 (71.1)	37 (56.9)	83 (61.5)	21 (87.5)	62 (55.9)	
Time living in Beijing (year)				0.06			0.04
<5	45 (43.7)	12 (31.6)	33 (50.8)	54 (40.0)	5 (20.8)	49 (44.1)	
>=5	58 (56.3)	26 (68.4)	32 (49.2)	81 (60.0)	19 (79.2)	62 (55.9)	
Time from HIV infection to survey (month)				<0.001			<0.001
<15	46 (44.7)	5 (13.2)	41 (63.1)	69 (51.1)	1 (4.2)	68 (61.3)	
>=15	57 (55.3)	33 (86.8)	24 (36.9)	66 (48.9)	23 (95.8)	43 (38.7)	
Self-report health condition				1.00			0.53
Very good/good	77 (74.8)	28 (73.7)	49 (75.4)	116 (85.9)	22 (91.7)	94 (84.7)	
Somewhat poor/very poor	26 (25.4)	10 (26.3)	16 (24.6)	19 (14.1)	2 (8.3)	17 (15.3)	
Ever had AIDS-like clinical symptoms <sup>&amp;</sup>				0.35			0.02
No	77 (74.8)	26 (68.4)	51 (78.5)	100 (74.1)	13 (54.2)	87 (78.4)	
Yes	26 (25.2)	12 (31.6)	14 (21.5)	35 (25.9)	11 (45.8)	24 (21.6)	
Had unprotected insertive anal sex with men in past 6 months				0.02			0.25

No	34 (79.1)	14 (100)	20 (69.0)	43 (66.2)	7 (87.5)	36 (63.2)	
Yes	9 (20.9)	0 (0)	9 (31.0)	22 (33.8)	1 (12.5)	21 (36.8)	
Had unprotected receptive anal sex with men in past 6 months							0.04
No	43 (75.4)	16 (94.1)	27 (67.5)	43 (56.6)	11 (91.7)	32 (50.0)	
Yes	14 (24.6)	1 (5.9)	13 (32.5)	33 (43.4)	1 (8.3)	32 (50.0)	
Had multiple concurrent male partners in past 12 months							0.71
No	93 (93.0)	36 (94.7)	57 (91.9)	118 (89.4)	21 (91.3)	97 (89.0)	
Yes	7 (7.0)	2 (5.3)	5 (8.1)	14 (10.6)	2 (8.7)	12 (11.0)	
Had commercial sex in past 12 months							1.00
No	94 (94.0)	36 (94.7)	58 (93.6)	126 (94.7)	24 (100.0)	102 (93.6)	
Yes	6 (6.0)	2 (5.3)	4 (6.4)	7 (5.3)	0 (0)	7 (6.4)	
History of sexually transmitted diseases							0.30
No	43 (43.0)	13 (35.1)	30 (47.6)	57 (45.6)	4 (17.4)	53 (52.0)	
Yes	57 (57.0)	24 (64.9)	33 (52.4)	68 (54.4)	19 (82.6)	49 (48.0)	
Syphilis co-infection							0.03
No	39 (37.9)	9 (23.7)	30 (46.2)	54 (40.0)	6 (25.0)	48 (43.2)	
Yes	64 (62.1)	29 (76.3)	35 (53.8)	81 (60.0)	18 (75.0)	63 (56.8)	

Note: Sample size for each variable may reduce due to missing data; IQR: inter quartile range

*Hukou* means permanent legal residence vs. transient status with *Hukou* elsewhere in China.

& Ever had at least one of these adverse clinical symptoms in the past 6 months: severe weight loss (>10%), fever (>1 month, continuing or intermittent), chronic diarrhea (>1 month), severe bacterial infection (e.g. pneumonia), oral candidiasis, oral leukoplakia, tuberculosis other stage III or stage IV symptoms

**Table 7. Bivariable and multivariable logistic regression analyses of factors associated with initiation of antiretroviral therapy (ART) among HIV-infected men who have sex with men by CD4+ cell count (<350 cells/ $\mu$ L eligible for free ART at the time of the study) in Beijing, China (N=238)**

Factors	CD4 count <350 cells/ $\mu$ L (n=103)			CD4 count $\geq$ 350 cells/ $\mu$ L (n=135)		
	Initiated ART,% (n=38)	Crude OR (95% CI)	Adjusted OR (95% CI)	Initiated ART,% (n=24)	Crude OR (95% CI)	Adjusted OR (95% CI)
Age in years; Median (IQR)	34 (29-39)	1.04 (0.99,1.09)*	1.02 (0.96,1.09)	41 (35-45)	1.18 (1.10,1.27)***	1.26 (1.11,1.44)***
Marital status						
Currently unmarried	29.4	1.00	1.00	10.8	1.00	1.00
Currently married	51.4	2.54 (1.09,5.91)**	2.50 (1.07, 5.87)**	39.4	5.38 (2.11,13.73)***	4.21 (1.60,11.06)***
Had Beijing <i>Hukou</i>						
No	28.2	1.00	1.00	5.8	1.00	1.00
Yes	42.2	1.86 (0.79,4.37)*	2.02 (0.74,5.50)	25.3	5.53 (1.56,19.63)***	4.93 (1.25,19.33)**
Time living in Beijing (year)						
<5	26.7	1.00	1.00	9.3	1.00	1.00
$\geq$ 5	44.8	2.23 (0.96,5.17)*	1.91 (0.77, 4.75)	23.5	3.00 (1.05,8.61)**	1.98 (0.28,14.04)
Time from HIV infection to survey (month)						
<15	10.9	1.00	1.00	1.5	1.00	1.00
$\geq$ 15	57.9	11.28 (3.88,32.78)***	10.71(3.66,31.32)***	34.9	36.37(4.74,279.22)***	22.4(2.79,180.01)***



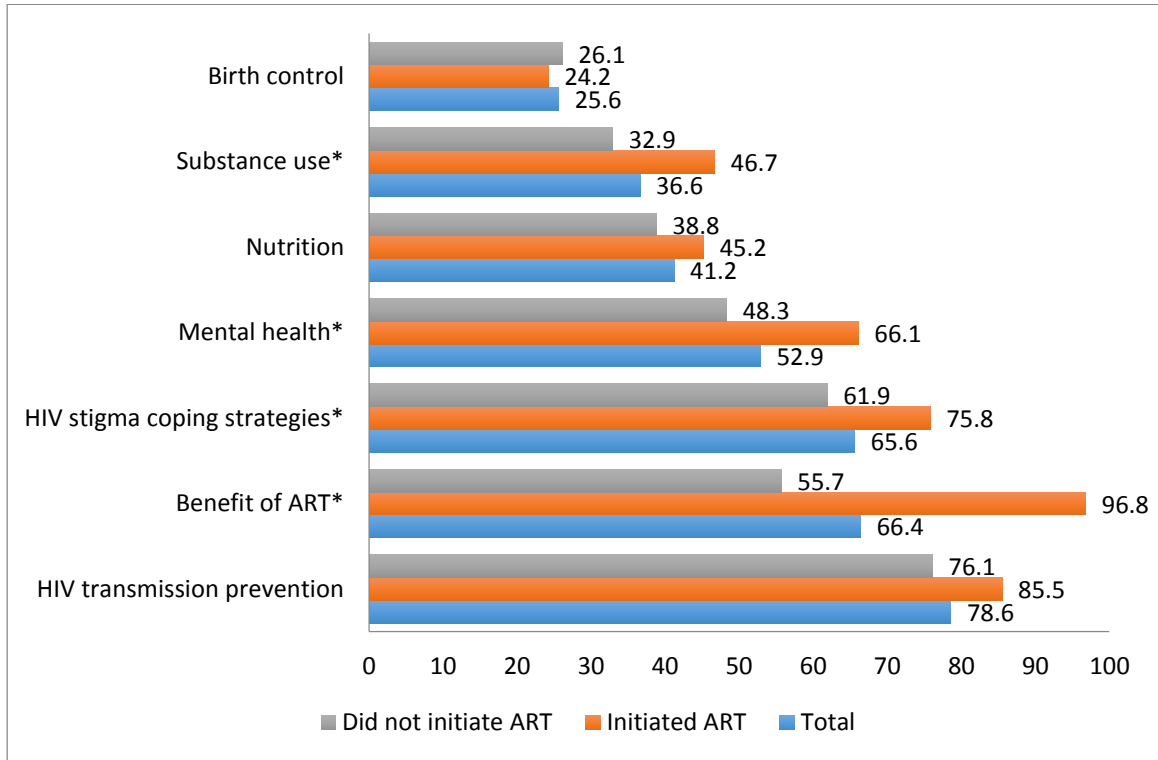
Ever had AIDS-like clinical symptoms <sup>&amp;</sup>							
No	33.8			13.0	1.00	1.00	
Yes	46.2	NS	NS	31.4	3.07 (1.22,7.71)**	3.97 (1.32,13.96)**	
Had unprotected insertive anal sex with men in past 6 months							
No	41.2	1.00	1.00	16.3			
Yes	0	-	-	4.6	NS	NS	
Had unprotected receptive anal sex with men in past 6 months							
No	37.2	1.00	1.00	25.6	1.00	1.00	
Yes	7.1	0.13 (0.02,1.09)*	0.22 (0.02,2.13)	3.0	0.09 (0.01,0.75)**	0.11 (0.01,1.40)	
History of sexually transmitted diseases							
No	30.2			7.0	1.00	1.00	
Yes	42.1	NS	NS	27.9	5.14 (1.63,16.16)***	4.93 (1.25,19.43)**	
Syphilis co-infection							
No	23.1	1.00	1.00	11.1	1.00	1.00	
Yes	45.3	2.76 (1.13,6.74)**	2.58 (1.04,6.37)**	22.2	2.29 (0.84,6.20)*	1.39 (0.41,4.72)	

IQR, inter quartile range; OR, odds ratio; CI, confidence interval; NS, not selected for logistic regression analyses because  $p > 0.2$  in Table 1b; *Hukou* means permanent legal residence vs. transient status with *Hukou* elsewhere in China.

& Ever had at least one of these clinical symptoms in the past 6 months: severe weight loss (>10%), fever (>1 month, continuing or intermittent), chronic diarrhea (>1 month), severe bacterial infection (e.g. pneumonia), oral candidiasis, oral leukoplakia, tuberculosis other stage III or stage IV symptoms

\* $p < 0.2$ , \*\* $p < 0.05$ , \*\*\* $p < 0.01$

**Figure 5. HIV care counseling services received among participants by ART initiation status**



\*  $P < 0.05$  for comparison between participants who had initiated ART and who had not.

## CHAPTER VII

### SYNOPSIS

In this dissertation research, I employed existing data from the China-MP3 project and the circumcision project, and used both quantitative and qualitative techniques to explore crucial elements of the HIV care continuum among Chinese MSM, including (1) prior HIV testing experience and its impact on current HIV risk; (2) barriers and facilitators of linkage to and engagement in HIV care; and (3) predictors of ART initiation. I also spent eight months in China helping gather these data with the research team.

HIV prevalence remains high among Chinese MSM, and it has been experiencing an upwards trend in the past decade. The robust HIV epidemic is even more evident among Chinese MSM residing in major metropolitan areas, where sexual network is more complex and more venues exist for MSM to seek sexual partners. Our study documented high HIV prevalence among Chinese MSM in Beijing (12.7% in Aim 1; 25.1% in Aim 3), which were substantially higher than the latest national estimate (7.6% in 2013). Some significant factors remain major contributors to the high HIV risk among this population, such as low educational attainment, being a non-local registered resident (no local 'Hukou'), being unmarried, younger age when first sex with men, higher number of lifetime male partners, ever had UAI and alcohol/drug use before sex.

Despite the high HIV prevalence, Chinese MSM are often not motivated to test for HIV as a result of personal, structural and cultural barriers. Our analysis showed that 71% of the studied participants ever tested for HIV at least once in their lifetime. However, the proportion of repeat testers was very low. As reported by our participants, some important reasons for never testing for HIV included ‘perceived low risk of HIV infection’, ‘fear of being diagnosed as HIV-positive’ and ‘not knowing where to test for HIV’. Our quantitative results also indicated several factors that were significantly associated with HIV testing uptake, such as older age, being married, being employed, having higher income, ever used alcohol or illicit drug before anal sex, younger age of first sex with men, having more lifetime male sexual partners, which were worth of consideration when designing targeted intervention to enhance HIV testing among Chinese MSM.

We conducted a hypothesis-driven study to test the hypothesis that prior HIV testing is associated with lower HIV risk among Chinese MSM. We found that MSM who ever tested for HIV had a reduced likelihood of being diagnosed as HIV positive than those who never had a test in the past. We also witnessed a signal that higher prior HIV testing frequency was associated with a lower HIV risk. One of the strengths of this study was to use propensity score methodology to compensate the pre-existing differences in baseline characteristics as a result of selection bias. With this technique, we were able to construct relatively comparable group in terms of exposure status (HIV testing) and tease out some extremes which may lead to over or underestimation of our measurement of association. These important findings imply the importance of repeat HIV testing as a possible intervention step, during which MSM may be able to access to potential HIV counseling

and get exposed to prevention information for the enhancement of HIV risk perception and awareness. As a result, frequent testers may be more likely to take precautions during anal sex and avoid high-risk behaviors (e.g., group sex, seeking casual partner), which may lower their risk of being infected with HIV. Our findings suggest that HIV testing may have an impact on lowering HIV risk. Ideally, confirmatory studies will validate our findings using longitudinal and trial design.

Linkage to and engagement in HIV care is a key bridging step following HIV diagnosis, and it is the necessary antecedent for receipt of the documented benefits of ART. In China, HIV care services have been expanded in the past decade under the influence of the ‘Four Free, One Care’ policy established in 2003. However, compared to other key populations (e.g., FSW, PWID), MSM did not draw adequate attention from the government until recent years when HIV epidemics among Chinese MSM became substantial. In the meantime, there is a lack of MSM-friendly programs that are designed specially to maximize the utilization of HIV care among this subgroup. There are also important personal and structural barriers impeding HIV-positive MSM’s access to care, which are poorly understood based on the current literature—the China-MP3 study and my thesis work addressed this research gap by assessing these determinants.

To specifically explore factors that play a role in linkage-to-care among Chinese MSM, we used data from FG to conduct qualitative data analyses to identify relevant barriers and facilitators. The fear of being stigmatized as a result of HIV and homosexuality and the subsequent perceived discrimination from healthcare workers still exert a great impact on HIV care utilization among Chinese MSM. Some structural barriers such as inconvenient of HIV care facilities, suboptimal management and service

provision, are also noted barriers. Concerns of privacy disclosure to friends and family and negative impact to life after commitment to care as well dampens the motivation to use HIV care. We also identify several facilitators that were endorsed by our participants, such as free HIV care, hiring peer MSM counselor for more comfortable HIV care sessions, enhance quality and comprehensiveness of HIV care services provision, and extend more venues to advertise HIV care to more MSM.

Our study sheds light on future intervention efforts to strengthen linkage to and engagement in HIV care among Chinese MSM. For example, (1) future prevention intervention and educational program should focus on increasing availability and accessibility of psychological counseling services to equip MSM with specific stigma coping skills and promulgate positive beliefs towards using HIV care services; (2) government should spend more resources in standardizing HIV care service provision in all participating hospitals and special clinics, including sensitivity training for health care workers; (3) recruiting and training HIV-positive MSM to facilitate HIV care service provision in both regular setting and community setting would be a cost-effective way to sustain a promising and continuing HIV care utilization; (4) the application of modern communication technology would be a powerful and convenient tool to target more MSM to disseminate information related to HIV care for the improvement of linkage-to-care.

After successfully linking and engaging HIV patients in care, timely initiation of ART is a critical step in HIV control in terms of slowing the pathogenesis and stemming the spread of virus. It is also a determining stage of achieving ultimate viral suppression. China launched the free ART program in 2003 and the guideline indicates those with CD4+ cell count less than 350 cells per microliter were eligible to receive ART for free.

From December 2013, the cutoff point was raised to 500 cells per microliter to comply with new WHO guidelines. Despite the friendly policy and practice, ART use is suboptimal among HIV-positive Chinese MSM. Some external factors may explain this situation, for example, (1) HIV epidemic among Chinese MSM is recent, and ART is relatively new and unfamiliar to many of Chinese MSM; (2) social taboo, cultural discrimination and dual stigma (HIV and homosexuality) result in Chinese MSM being reluctant to initiate ART; (3) the concern of side-effects, psychological burdens for life-long drug adherence, and concomitant financial costs are also factors influencing their motivation to use ART. In the meantime, there is a research need to understand what individual factors may play a role in ART initiation

Our study was assessed the socio-demographic, behavioral and clinical predictors of ART initiation among this subgroup. In the study, as we expected, we documented a low ART initiation prevalence among all study participants (26.1%) and an even lower proportion among participants who did not meet the national free ART criteria (17.8%). The proportion of ART initiation was slightly higher among participants who met the national free ART criteria (36.1%). We identified several important predictors of ART initiation among Chinese MSM, such as being married, longer duration of being HIV-positive, having legal Beijing residence, presence of AIDS-like symptoms, having history of STD and current syphilis co-infection. Participant who initiated ART also demonstrated significantly higher likelihood to be exposed to several HIV counseling topics, such as ART benefit, stigma coping strategies, substance use and mental health

These important ART initiation predictors provide implications for the design of future intervention. For example, Since MSM who were married were more likely to



initiate ART, intervention programs should emphasize educational campaign to cultivate the sense to protect family members or significant others as the motivation to initiate ART; MSM with longer duration of HIV infection demonstrated a higher likelihood of initiating ART, which implies future effort should be spent targeting newly infected individual and linking them to HIV care for ART initiation; having legal Beijing residence played an crucial role in ART initiation, and those without legal residence might be marginalized and refused in terms of ART provision, which suggested the need to specifically target migrants, transient workers and those who recently move to the city, and enhance their linkage to ART services.

In conclusion, efforts in maximizing HIV testing, linkage-to-care and ART initiation are three key stages of the continuum of HIV care and are essential for the ultimate viral suppression and successful control of HIV transmission. Findings from our study may further contribute to the existing HIV/AIDS prevention intervention efforts and provide guidance for future longitudinal, cohort studies and pragmatic clinical trials for the reinforcement of ‘test-and-treat’ and ‘treatment-as-prevention’ strategies among Chinese MSM.

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