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HIV incidence among men who have **PEN** sex with men in Beijing: a prospective cohort study

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ABSTRACT

Objectives: (1) To assess the HIV incidence rate among men who have sex with men (MSM) in a large cohort study in Beijing, China and (2) to identify sociodemographic and behavioural risk factors of HIV seroconversion among MSM in Beijing, China. Design: A prospective cohort study.

Setting: Baseline and follow-up visits were conducted among MSM in Beijing, China.

Participants: A cohort of 797 HIV-seronegative MSM was recruited from August to December 2009, with follow-up occurring after 6 and 12 months.

Primary and secondary outcome measures:

At baseline and follow-up visits, participants reported sociodemographic and sexual behaviour information, and were tested for HIV, herpes simplex virus-2 (HSV-2) and syphilis with whole blood specimens. Cox regression analysis was used to identify factors associated with HIV seroconversion.

Results: Most study participants (86.8%) were retained by the 12-month follow-up. The HIV, HSV-2 and syphilis incidence rates were 8.09 (95% CI 6.92 to 9.26), 5.92 (95% CI 5.44 to 6.40) and 8.06 (95% CI 7.56 to 8.56) cases per 100 person-years, respectively. HIV seroconversion was significantly associated with being <25 years old, having <12 years of education, having >1 male sex partner in the past 6 months, and being syphilis positive or HSV-2 positive.

Conclusions: The HIV incidence among MSM in Beijing is serious. Interventions and treatment of sexually transmitted diseases (STD) should be combined with HIV control and prevention measures among MSM.

BACKGROUND

It is estimated that 780 000 persons were living with HIV/AIDS (PLWHA) in China by the end of 2011, and that homosexual transmission is accounting for a greater proportion of HIV infections. Men who have sex with men (MSM) as a proportion of PLWHA in China rose from 7.3% in 2005, to 11% in 2007 and 17.4% in 2011.1 Of China's 48 000

ARTICLE SUMMARY

Article focus

- In China, homosexual transmission has now become a major mode of HIV transmission. However, HIV incidence among Chinese men who have sex with men (MSM) remains poorly understood.
- To date, findings from the sparse handful of Chinese MSM cohort studies have been limited by small sample sizes, short-term follow-up or heavy loss to follow-up.

Key messages

- The present cohort study was conducted to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up.
- This study provides empirical HIV seroincidence data relevant for HIV prevention and intervention planning strategies among MSM in China.

Strengths and limitations of this study

Evidence-based studies among Chinese MSM are urgently needed to provide scientific decisions for the prevention and control of HIV transmission.

new HIV infections in 2011, 29.4% were attributed to homosexual transmission.¹ Hence, the HIV epidemic in China is still on the rise and spreading among MSM.

Although many cross-sectional studies have reported on HIV prevalence among MSM in China, data on HIV incidence rates among this subpopulation remain limited. Among the only three MSM cohort studies which have been conducted thus far in China, HIV incidence rates ranged between 2.6 and 5.4 cases per 100 person-years.^{2–4} Unfortunately, two of these studies were characterised by small sample sizes, short-term follow-up or heavy loss to follow-up. The most recent cohort study was only able to recruit 218 eligible MSM participants, 44% of whom were

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lost to follow-up.⁴ In response, the present cohort study was designed to follow-up a large number of MSM participants over an extended time period with minimal loss to follow-up. To better guide HIV prevention and intervention programmes among MSM in China, this study focuses on two key objectives: (1) assess the HIV, herpes simplex virus-2 (HSV-2) and syphilis incidence rates among MSM in Beijing, China and (2) identify sociodemographic and behavioural risk factors of HIV seroconversion among MSM in Beijing, China.

METHODS

Study design and participant recruitment

This prospective cohort study was conducted in Beijing, the capital of China. Participants were recruited using three methods. First, study participants were recruited directly through website advertisements by a nongovernmental AIDS volunteer group (http://www. hivolunt.net). Second, peer recruiters were hired and trained to distribute flyers with study-related information at MSM-frequented venues (eg, MSM clubs, bars, parks and bathhouses). Third, study participants were encouraged to refer their peers to enrol in the study. Prospective study participants then came to a Beijing study clinic that was easily accessible via various transportation routes. Baseline participant inclusion criteria included ≥18 years old, male individual, had anal or oral sex with another male in the past 6 months, and provided written informed consent with their actual name or nickname. Baseline participant exclusion criteria were HIV-seropositive status, lack of contact information and planned relocation away from Beijing within the next year. A total of 962 participants were screened during administration of the baseline survey from August to December 2009, of whom 61 were HIV positive, 36 could not provide contact information, 56 planned to relocate away from Beijing within the next year and 12 refused to participate in follow-up visits; thus, a total of 797 eligible participants were enrolled into the cohort study, each of whom was assigned a unique and confidential study identification code.

Study participants were followed up for 1 year, with follow-up visits occurring at 6 and 12 months. At each study visit (ie, baseline, 6-month follow-up and 12-month follow-up), trained health professionals conducted one-on-one questionnaire-based interviews with eligible participants in a private room of the study clinic. After interviews were completed, confidential HIV voluntary counselling and testing (VCT) was conducted, followed by a clinical sexually transmitted diseases (STD) examination by experienced physicians. Venipuncture blood samples were collected from each participant and tested for HIV, syphilis and HSV-2. To ensure confidentiality, each participant was required to provide their preassigned identification code to receive their test results, which became available after 1 week. All participants who tested positive for HSV-2 and syphilis were referred to an

STD clinic or hospital for appropriate treatment. After each completed study visit, participants received 50 RMB (approximately US\$7.40), 12 free condoms and one free lubricant. At completion of the baseline and 6-month follow-up visits, each participant was asked to return for a follow-up evaluation after 6 months. The study was approved by the Institutional Review Boards of the National Center for AIDS/STD Control and Prevention of the China Center for Disease Control and Prevention.

Questionnaire measures

Sociodemographic measures included participant age, ethnicity, education, marital status, Beijing permanent residency status, income and housing status. Behavioural measures included self-identified sexual orientation, sought male sex partners on the internet, sought male sex partners in bathhouse/public washroom/park, had HIV tested in the past year, participated in HIV intervention programme in the past year, number of MSM social contacts, number of male sex partners in the past 6 months, had commercial sex (ie, bought or sold sex) with male partners in the past 6 months, had unprotected anal sex with regular or casual male partners in the past 6 months, had sex with female partners in the past 6 months, had STD syndrome in the past 6 months, bought condom/lubricant in the past 6 months and used illicit drugs in the past 6 months.

Laboratory tests

Blood samples were tested for HIV, HSV-2 and syphilis infections. The HIV infection status was determined with an ELISA (InTec Products Company, Xiamen, China) screening and an HIV-1/2 western blot confirmation (HIV Blot 2.2 WBTM, Genelabs Diagnostics, Singapore). HSV-2 infection status was determined using ELISA (Trinity Laboratories, San Antonio, TX, USA). Syphilis infection status was determined with a rapid plasma reagin (RPR) test (Shanghai Rongsheng, Shanghai, China) and a confirmation of positive tests by the Treponema pallidum particle assay (TPPA) test (Fujirebio Inc, Tokyo, Japan).

Statistical analysis

Questionnaire-based data and biological testing results were recorded, double checked and compared with EpiData software (EpiData 3.0 for windows; The EpiData Association, Odense, Denmark). After corrections, data were then converted and analysed using statistical analysis system (SAS V.9.1 for windows; SAS Institute Inc, Cary, North Carolina, USA). To identify correlates of time to HIV seroconversion, the Cox regression model was used in univariate and multiple regression analyses. Statistically significant variables in univariate analyses were then entered simultaneously into a multiple Cox regression model. The assumed time of seroconversion was the half-way time point between the participant's last negative HIV test and first positive HIV test. Statistical significance was defined as p value <0.05 (two tailed).

RESULTS

Baseline characters of the participants

Of the 797 participants, 448 were recruited by peer referral, 173 were recruited via the internet and 158 were recruited through outreach. The median age was 28 years; 92.6% belonged to the Han ethnic group; and 51.9% graduated from high school or above. Beijing permanent residents accounted for 18.7%; the median monthly income was US\$294; 61.7% were single, 17.7% were married and 15.7% were cohabiting with male or female sex partners; 67.6% identified as homosexual, and 32.4% identified as heterosexual or bisexual. The median age of sexual debut was 20 years old and the median age of homosexual sexual debut was 25 years old; 65.8% and 34.2% experienced their sexual debut with another male and female, respectively.

Regarding behaviours in the past 6 months among study participants, the median number of male sex partners was 2; 6% bought or sold sex with male sex partners; 23.7% had unprotected anal sex with regular male sex partners; 12.9% had unprotected anal sex with casual male sex partners; 17.7% had sex with female sex partners; 11.8% had unprotected sex with female sex partners; and 1% used illicit drugs. Experience of an STD syndrome in the past year was reported by 17.2% of participants. Baseline prevalence of syphilis and HSV-2 was 16.4% and 4.6%, respectively. Descriptive results are shown in table 1.

Cohort retention and contact information

Of the 797 participants, 96.5% (769/797) were retained in the cohort at the 6-month follow-up, and 86.8% (692/797) were retained at the 12-month follow-up. Participants were contacted for their 6-month and 12-month follow-up visits by cell phone calls (1792), short text messages (2179) and QQ (Tencent Inc, Beijing, China) or MSN online social networking software (1369) (Web Messenger, Microsoft Cooperation, USA) (table 2). Of the 692 participants retained in the cohort at the 12 month follow-up, 393 were followed up by cell phone calls, 121 by short text messages, 136 by QQ/MSN (Tencent QQ/Mobile Social Network) social

Factors	Ν	Per cent
Overall	797	100
Age (median, years)	28	100
Ethnicity	20	
Han	738	92.6
Minority	59	7.4
Education		
Less than high school	383	48.1
High school and above	414	51.9
Beijing permanent resident	149	18.7
Monthly income (median, US\$)	294	
Marital status in the past 3 months		
Single	492	61.7
Married	141	17.7
Cohabiting with male or female sex partner	125	15.7
Separated or divorced or widowed	39	4.9
Sexual orientation		
Homosexual	539	67.6
Heterosexual or bisexual	258	32.4
Age of sexual debut (median, years)	20	
Age of homosexual debut (median, years)	25	
Partner of sexual debut		
Male	524	65.8
Female	273	34.2
Number of male sex partners in the past 6 months (median)	2	
Bought or sold sex with male sex partners in the past 6 months	48	6.0
Had unprotected anal sex with regular male sex partners in the past 6 months	189	23.7
Had unprotected anal sex with casual male partners in the past 6 months	103	12.9
Had sex with female sex partners in the past 6 months	141	17.7
Had unprotected sex with female sex partners in the past 6 months	94	11.8
Used illicit drugs in the past 6 months	8	1.0
Had STD syndrome in the past year	137	17.2
Syphilis positive	131	16.4
HSV-2 positive	37	4.6

Table 2 Contact patterns and times for cohort follow-up study								
Follow-u	Cell phone call	Short text message	QQ/MSN	Peer contact	Email	Landline telephone	Total	
6 months	884	1075	665	87	31	5	2747	
12months	908	1104	704	93	43	2	2854	
Total (%)	1792 (32.0)	2179 (38.9)	1369 (24.4)	180 (3.2)	74 (1.3)	7 (0.1)	5601 (100.0)	
QQ, Tencent QQ; MSN, Mobile Social Network.								

networking software and 29 by peer contacts. There was no difference of sexual behaviours among subjects by the method of follow-up.

Incidence of HIV, syphilis and HSV-2 and factors predicting HIV seroconversion

Among the 797 participants who were seronegative for HIV at baseline, 48 HIV seroconversions were observed over 592.98 person-years of observation, resulting in an incidence rate of 8.09 cases per 100 person-years (95% CI 6.92 to 9.26). Among the 666 participants who were seronegative for syphilis at baseline, 30 syphilis seroconversions were observed over 506.06 person-years of observation, resulting in an incidence rate of 5.92 cases per 100 person-years (95% CI 5.44 to 6.40). Among the 760 participants who were seronegative for HSV-2 at baseline, 46 HSV-2 seroconversions were observed over 570.61 person-years of observation, resulting in an incidence rate of 8.06 per 100 person-years (95% CI 7.56 to 8.56).

Univariate and multivariate Cox regression analyses indicated that younger age, less education, having multiple male sex partners in the past 6 months, syphilis infection and HSV-2 infection were significantly associated with time to HIV seroconversion (table 3). Results of the univariate and multivariate Cox regression analyses are shown in table 3.

DISCUSSION

The first objective of this large cohort study was to assess the HIV incidence rate among MSM in Beijing, China. Results indicate that the HIV incidence rate among MSM has increased dramatically. Using the Bureau of Epidemiology (BED) capture enzyme immunoassay (BED-CEIA), previous cross-sectional studies among MSM in Beijing have estimated HIV incidence at 2.9% in 2005 and 3.6% in 2006.5 (Essentially, the BED assay calculates anti-HIV IgG relative to total IgG and is based on the principle that the ratio of anti-HIV IgG to total IgG increases with time shortly after HIV infection. This method enables cross-sectional serosurveys to estimate HIV-1 incidence and distinguish recent infections from long-term infections.) Previous prospective cohort studies conducted among MSM in Beijing found that the incidence rate increased from 2.6 cases per 100 person-years in 2007 to 3.4 cases per 100 person-years in 2008.² ⁶ However, our large cohort study conducted from 2009 to 2010 shows that the HIV incidence rate among Beijing MSM has now increased to 8.09 cases per 100 person-years, an extremely high rate compared with other cities in both China and around the world.²⁻⁴ 7-9 Explanations for the exceptionally high and steady rise in HIV incidence among Beijing MSM are not entirely clear, but one possibility may be that Beijing's relatively vibrant MSM culture facilitates greater disassortative

			Incidence rate (per 100				
Factors	No. of seroconversions	Person-years	person years)	HR (95% CI)	p Value	Adjusted HR (95% CI)	p Value
Total	48	592.98	8.09	·			
Age (years)							
>25	24	389.31	6.16	1.00		1.00	
≤25	24	203.67	11.78	1.96 (1.11 to 3.45)	0.0198	2.59 (1.41 to 4.75)	0.0021
Ethnicity							
Minorities	2	43.32	4.62	1.00			
Han	46	549.66	8.37	1.79 (0.44 to 7.39)	0.4191		
Years of educ	ation						
>12	16	317.66	5.04	1.00		1.00	
≤12	32	275.31	11.62	2.68 (1.43 to 5.02)	0.0021	2.12 (1.12 to 4.03)	0.0213
Married/cohab	iting with female sex	partner					
No	36	401.14	8.97	1.00			
Yes	12	191.84	6.26	0.70 (0.36 to 1.34)	0.2822		

Table 3 Continued

Factors	No. of	David and 110 and 1	Incidence rate (per 100 person		p	Adjusted HR	p
Factors	seroconversions	Person-years	years)	HR (95% CI)	Value	(95% CI)	Value
	inent resident	404.00	0.54	4.00			
No	41	481.63	8.51	1.00	0 45 40		
Yes	7 (10 ⁽¹⁾)	111.34	6.29	0.74 (0.33 to 1.64)	0.4542		
Monthly incor		200 AE	0.04	1 00			
≤440 >440	32 16	388.45 204.52	8.24 7.82	1.00 0.94 (0.52 to 1.71)	0.8365		
Sexual orienta		204.52	1.02	0.94 (0.52 (0 1.71)	0.0305		
Sexual Offeria	10	194.52		1.00			
Heterosexual		104.02		1.00			
bisexual							
biooxuu	38	398.45	9.54	1.84 (0.92 to 3.69)	0.0871		
Homosexual		000.10	0.01		0.0071		
	sex partners on the in	ternet					
No	19	255.49	7.44	1.00			
Yes	29	337.48	8.59	1.16 (0.65 to 2.06)	0.6227		
Sought male	sex partners in bathho			- (
No	32	442.51	7.23	1.00			
Yes	16	150.46	10.63	1.48 (0.81 to 2.70)	0.1994		
Had HIV test	in the past year			, , , , , , , , , , , , , , , , , , ,			
No	23	269.11	8.55	1.00			
Yes	25	323.87	7.72	0.89 (0.50 to 1.56)	0.6789		
Participated in	n an HIV intervention	programme in th	e past year				
No	7	92.43	7.57	1.00			
Yes	41	500.55	8.19	1.08 (0.48 to 2.40)	0.8555		
	SM social contacts						
≤10	30	348.52	8.61	1.00			
>10	18	244.46	7.36	0.86 (0.48 to 1.54)	0.6056		
	ale sex partners in P6						
≤1	9	218.23	4.12	1.00		1.00	
>1		374.75	10.41	2.54 (1.23 to 5.24)	0.0117	2.52 (1.20 to 5.32)	0.015
	ted anal sex with mal		0.00	1 00			
No	30	361.94	8.29	1.00	0.0400		
Yes	18 Siel eeu witte mede in D	231.04	7.79	0.94 (0.52 to 1.69)	0.8469		
No	cial sex with male in P 46	569.25	8.08	1.00			
Yes	40 2			1.00 1.06 (0.26 to 4.38)	0.9314		
	ex partners in P6M	23.73	8.43	1.00 (0.20 10 4.30)	0.9314		
No	40	481.90	8.30	1.00			
Yes	8	111.08	7.20	0.87 (0.41 to 1.86)	0.7249		
	ted sex with female p		7.20	0.07 (0.41 10 1.00)	0.7243		
No	43	520.92	8.25	1.00			
Yes	5	72.06	6.94	0.84 (0.33 to 2.13)	0.7152		
	drome in P6M			(5.00 10 2.10)			
No	38	512.54	7.41	1.00			
Yes	10	80.43	12.43	1.69 (0.84 to 3.40)	0.1388		
	om/lubricant in P6M			, , , , , , , , , , , , , , , , , , , ,			
No	26	321.90	8.08	1.00			
Yes	22	271.08	8.12	1.00 (0.57 to 1.77)	0.9891		
Syphilis positi	ive						
No	34	502.95	6.76	1.00		1.00	
Yes	14	90.02	15.55	2.35 (1.26 to 4.38)	0.0072	2.28 (1.19 to 4.34)	0.0126
HSV-2 positiv	re			· · ·			
No	39	533.50	7.31	1.00		1.00	
Yes	9	59.48	15.13	2.07 (1.00 to 4.27)	0.0497	4.01 (1.61 to 9.97)	0.0029

sexual mixing between MSM groups, which in turn can increase HIV background prevalence. Previous crosssectional studies conducted among MSM in Beijing showed increasing HIV prevalence among this population, from 0.4% in 2004, 4.6% in 2005 to 5.8% in 2006¹⁰ and 6.3% in 2009. The high HIV incidence rate and prevalence among MSM in Beijing indicate that the epidemic in this group is extremely serious and that effective intervention services are urgently needed.

Owing to prevailing social stigma against MSM and MSM-associated behaviours in China and worldwide, and conventional recruitment cohort follow-up approaches with MSM remains challenging. Using multiple methods of recruitment and follow-up contact, we were able to retain 86.8% of all 797 participants after 12 months. This is the first large cohort study in China to evaluate the retention rate for a prospective cohort of MSM. Based on previous cohort studies among injection drug users and MSM,¹¹⁻¹⁵ the following protocols were implemented in order to ensure greater participant retention: (1) an explicit cohort retention plan was written and adhered to throughout the study; (2) peer MSM staff were hired to contact participants; (3) all participants were asked to provide at least two different means of contact and (4) participants had the flexibility of choosing cell phone calls, short text messages and/or QQ/MSN internet social networking platforms as the means by which the study staff contacted them.

Many epidemiological studies have found that HIV infection is strongly associated with HSV-2 and syphilis.¹⁶ In this study, we found that HSV-2 incidence was high among MSM and that HSV-2 infection also increased the risk of HIV acquisition. It has been reported that the persistence of HIV-1 receptor-positive cells after HSV-2 reactivation is a potential mechanism for increased risk of HIV-1 acquisition.¹⁷ However, HSV-2-based HIV intervention studies continue to be disappointing, and the mechanisms of association between HSV-2 and HIV infection require further study.¹⁸

International studies have shown that younger MSM are at higher risk of HIV infection,⁹ ¹⁹ ²⁰ minor geographic variations notwithstanding. Results from this study are consistent with such studies, and may be partly explained by China's changing social norms concerning homosexuality, brought about by the rapid economic and social development of the past 30 years. In traditional culture in China, MSM were severely socially marginalised and stigmatised. Virtually all MSM faced strong social pressure to hide their sexual orientation, and most of them eventually married. Today, China's social environment is gradually becoming less stigmatising for MSM, whereby younger MSM are more active in homosexuality than older MSM. Older MSM are also more likely to be married. Furthermore, our previous study conducted in the same area showed that younger MSM were more likely to use the internet for sex seeking than older MSM,²¹ implying that younger MSM were likelier to have more casual sex partners and face higher risk.

Meanwhile, these study results also imply that intervention and prevention should be focused on MSM with lower education and multiple male sex partners.

Our study has several limitations. The study subjects were recruited using non-random sampling methods that could have led to selection bias. Although the cohort retention was high, HIV, HSV-2 and syphilis incidence rates may have been significantly different among those lost to follow-up. This may have led to overestimation or underestimation of the true incidence. However, our baseline analyses indicated that demographic and behavioural characteristics were similar between those lost to follow-up and those retained in the cohort.

In conclusion, this cohort study was able to maintain a high retention rate and demonstrate that HIV incidence is extremely high among MSM in Beijing. Such findings indicate that the HIV epidemic among MSM in Beijing is more serious than previously expected and is rapidly intensifying. Given the synergistic relationship between STD and HIV infection, interventions for high-risk behaviours and treatment and management for STDs should be combined with HIV control and prevention initiatives among MSM in China. We believe data from this study will help guide future research towards innovative STD/ HIV interventions for MSM in China, and mobilise government, public health and non-governmental communities to control the rapid transmission of HIV and STDs among Chinese MSM. Comprehensive actions are urgently needed and the time is now.

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Contributors DL, SL and YL was involved in study design and data collection, manuscript writing. YG, MY, XY, QL, SJ, ZZ, ZZ, Li, GJ and DX was involved in study design, data collection and manuscript writing. SWP, YR, FL and YS was involved in study design, data collection, data interpretation and manuscript writing. QL and YR was involved in data analysis. FL and YS was involved in principal investigation. The paper has been reviewed by biostatistician, LY, PhD, Vanderbilt Institute for Global Health and Departments of Pediatrics, Biostatistics, and Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee 37203, USA. The paper has been edited by SWP, The School of Population and Public Health University of British Columbia, Vancouver, BC, Canada.

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Competing interests None.

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HIV incidence among MSM in China

Data sharing statement Supplementary data are available by contacting Dongliang Li, Idl66@126.com.

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