High HIV Incidence among Men Who Have Sex with Men in Eight Chinese Cities: Results from a Trial

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Key point:

Through evaluating the HIV incidence among a cohort of MSM nested in an RCT, we found an extremely high HIV incidence among Chinese MSM, especially among bisexual MSMs. Our finding is calling for more effective HIV prevention strategies.
Abstract

**Background.** In China, while the overall HIV prevalence has been decreasing within key populations, the epidemic among men who have sex with men (MSM) is still on the rise. This study aims to assess the HIV incidence rate and identify driving forces of HIV seroconversion among MSM in a closed cohort.

**Methods.** This study is a secondary analysis of a large trial of HIV testing promotion among Chinese MSM in 2016-2017. Sexual behaviors, HIV testing activities, and HIV serostatus were measured at baseline and follow-ups every three months. HIV seroconversion in this study was defined as the self-report HIV-positive test result. Participants who reported testing for HIV at least twice during different follow-up periods were included. Subgroup analysis and Cox regression were used to examine the correlates with HIV seroconversion.

**Results.** Overall, 347 participants were included in this study, with a mean age of 25.3±6.1, and 71.2% migrants. The socio-demographic characteristics of the included participants were similar to the rest participants in the trial (n=1034). 7.2% (25/347) of participants seroconverted during the study period, resulting in an incidence rate of 15.56/100 person-years. In subgroup analysis, the HIV incidence rate was higher among migrants than non-migrants (IRR=1.26, 95% CI, 0.47-3.87). In the time-dependent cox-regression model, bisexual MSM had a higher risk of contracting HIV than gay men (Adjusted HR=2.19, 95%CI: 1.02-4.72).

**Conclusion.** Our findings suggest a high HIV incidence rate among Chinese MSM. Further expansion of pre-exposure prophylaxis and other effective HIV prevention interventions are urgently needed.
Background

HIV incidence among men who have sex with men (MSM) remains high and is still increasing in many low- and middle-income countries [1]. In China, compared to other key populations in which new HIV infections has been decreasing, MSM are currently the only group in which HIV continues to rise (HIV prevalence has increased from 5.73% to 7.75% between 2010-2014) [2]. Empirical studies mainly reported HIV prevalence or incidence rather than incidence rate. A meta-analysis of HIV prevalence among student MSM showed an increasing prevalence from 3.0% to 6.8% between 2003-2010 [3]. The prevalence was also found to have stark geographic disparities among different regions in China [4, 5], with higher in metropolis cities than in small cities [2]. In 2011, data from a meta-analytic study estimated HIV incidence among Chinese MSM to be 3.5% for cohort and 6.7% for cross-sectional studies [6]. In 2014, one cohort study observed a HIV incidence rate as high as 13.59/100 PY in a city of Jiangsu province [7]. Still, limited HIV incidence rates reports among MSM are insufficient to reveal the latest drastic increase of HIV epidemic.

Typically, the HIV incidence rate calculation requires a cohort of MSM with health facilities attendance or biological sample collections to determine their HIV status. However, due to the nature of this sensitive population, the typical approach may underestimate the incidence rate by excluding MSM who did not attend healthcare facilities and did not want to give biological samples.

To increase the generalizability of the HIV incidence rate estimation among MSM, in this study, we used self-report HIV test result to assess the HIV incidence rate in a large closed cohort study in China. We also verified the self-reported testing results by asking the participants sending back their tested results through the photographs. We further identified subgroups of MSM who had a higher risk of HIV seroconversion and its correlates.
Methods

Study design and study population

This study is a secondary analysis of a stepped-wedge randomized control trial (NCT02796963) focusing on using crowdsourcing to promote HIV testing among Chinese MSM. The detailed information about this trial has been described in elsewhere [8]. In brief, participants were recruited through Blued (the largest gay social networking app in China) in July 2016 from eight cities in China (Guangzhou, Jiangmen, Shenzhen, and Zhuhai in Guangdong Province; Jinan, Jining, Qingdao and Yantai in Shandong Province) (Clinical Trials ID: NCT02796963). Eligibility criteria including: (1) being born biologically as male, (2) being age 16 years or older, (3) having anal sex with a man at least once during lifetime, (4) never tested positive for HIV, (5) not testing for HIV within the past 3 months, and (6) currently living or planning to live in one of the eight cities for 12 months after the enrollment.

The order of receiving intervention was randomly assigned to the four cities of each province. Then cities having the same order of intervention were paired [9]. Participants in each paired-city received a 3-month intervention in a random assigned order. All participants were followed at 3-month intervals for 12 months. In each follow-up survey, participants were asked their HIV testing experience and the testing result in the last 3 months. HIV seroconversion in this study was defined as self-report HIV-positive test result. Participants were also encouraged to return a photo of HIV test result to our research team via WeChat (a Chinese messaging and social media mobile application). Any participant who reported a positive test result was then connected to local CDC for confirmatory testing and was no longer eligible for subsequent follow-up surveys. In this secondary analysis, to ensure that participants were HIV negative at the beginning and had at least one additional HIV test over follow-up, we only included those participants who had reported to have tested HIV at least twice during the study period and calculated their HIV incidence rate.
Measures

Sociodemographic characteristics were assessed at baseline and included age, education level, annual income, marital status, and migrant status. Migrant status was defined as the participant’s current city’s *hukou* status (*hukou* is the household registration system in China, which is also used to provide social services including public healthcare and education) [10]. The *hukou* status is assigned to citizens based on the place they were born and is difficult to change [11]. We also collected data about sexual orientation, early sexual debut, and sexual orientation disclosure to people other than sexual partners at the baseline survey. We defined early sexual debut as having had first anal sex at or before the age of 16 given the average age of sexual debut among adolescents, and the cultural context among MSM in China [12, 13]. In each follow-up survey, we asked the participants about their sexual activities with men and women, condom use, HIV testing, and syphilis test in the last three months. Bisexual behavior was defined as men who have had sex with at least one man and at least one woman in the last three months.

Statistical Analysis

Descriptive analysis was used to describe the sociodemographic characteristics and baseline sexual behaviors of the eligible participants. In this HIV incidence calculation, the total person-time was initially calculated by assuming all the HIV seroconversion happened at the mid-point between the last HIV negative test result and the HIV positive result in the follow-up period. For those participants who had HIV seroconversion during the study, their follow-up periods were determined as the periods between their first HIV-negative tests and their first HIV-positive tests. Otherwise, the follow-up periods were the time between their first HIV-negative tests and their last HIV-negative tests.

Considering the representativeness of the included participants for the overall sample in the closed cohort, we conducted a sensitivity analysis that re-calculated the incidence rate by using inverse sampling probability weighting [14]. We used a propensity score to model the
probability of each participant being included from the trial, by logistic regression. Covariates included in this logistic regression were age, education, geographic location (city), sex orientation, disclosure, ever tested for HIV, ever had sex with female, multiple male sex partner, multiple female sex partner, and bisexual behavior in the last 3 months. These covariates were identified by possible confounders from literature [15, 16].

To identify the geography location differences, we calculated the incidence rate separately for Guangdong and Shandong province. We also conducted sub-analysis on HIV incidence rate among participants with different characteristics, including migrant status, whether or not had an early sexual debut, and whether had their sexual orientation disclosure to others. Cox regression model with time-varying covariates was used to examine the correlation between the time-dependent variables of condom use, multiple male sexual partners, multiple female sexual partners), bisexual behavior, and HIV seroconversion, while fixed variables being age, education, income, and the order of intervention.

Statistical analyses were conducted using SAS 9.4 (Cary, NC). The estimated effect sizes were reported as hazard ratio (HR) with 95% confidence intervals (CIs) and p values. Statistical significance was based on p-value <0.05.

**Ethical Statement**

Ethical approval was obtained from the ethics review committees at the Guangdong Provincial Center for Skin Diseases and STI Control (Guangzhou, China), University of North Carolina at Chapel Hill (Chapel Hill, North Carolina), the University of California, San Francisco (San Francisco, California), and Rutgers University (Piscataway, New Jersey) before the study launched.
Results

Sociodemographic Characteristics and Behaviors

Overall, 1381 participants were enrolled into the stepped-wedged randomized controlled trial, among which 1219 participants attended at least one follow-up survey, and 755 reported at least one HIV test during the study period (Figure 1). In this analysis, we included 347 eligible participants for this analysis whose first HIV testing was negative and at least tested twice during the study period. 132 of men submitted verified HIV testing results reports. There was 93.9% concordance between self-report and photo-verification [17].

More than half of the MSM were less than 25 years old (56.8%), had a college degree or beyond (66.6%), were migrant (71.2%), and had disclosed their sexual orientation to others (68.0%). Importantly, most of them had their sexual debut above 16 years old (94.5%). Of the included 347 MSM, more than half of the MSM had condomless sex (52.3%) and over a third had multiple male partners (32.3%) in the last three months at baseline (Table 1).

Table 1 also showed the sociodemographic characteristics among the included MSM and the not-included participants. Demographics and behaviors were similar between the included MSM and not-included participants, except whether they had bisexual behavior and multiple male partners in the last three months at baseline. Included MSM had higher proportion of men who had bisexual behavior (5.8%) than not-included MSM (3.3%). Similarly, included MSM had higher proportion of men who had multiple male partners (32.3) than not-included MSM (24.0%). The sociodemographic characteristics and sexual behaviors were also compared between the included MSM and those who only tested HIV once during the study period (Supplement 1). Significant difference was only found between these men in whether had multiple male partners.
**HIV Incidence**

Among 1219 participants who have finished at least one follow-up survey, 99 participants reported had a positive HIV test result, including 50 from Guangdong province and 49 from Shandong province [17]. Among 755 participants who had at least one HIV test over the study period, including baseline and follow-up surveys, the cumulative HIV positive rate was 13.1% [17]. During the study period, 25 HIV seroconversions were reported among those 347 eligible participants over 12 months, corresponding to an incidence proportion of 7.2% and an incidence rate (IR) of 15.56 per 100 person-years (PY), ranged from 15.17 to 15.97 per 100 PY (Table 2). After adjusted by inverse sampling probability weight, the overall HIV incidence rate was 17.21 per 100 PY, ranged 16.75-17.70 per 100 PY (Table 2).

Table 3 shows the HIV incidence rate among different subgroups of men. The incidence rate was 17.28 (95% CI, 16.87-17.72) per 100 PY in four cities of Guangdong province and 15.56 (13.46-14.19) per 100 PY in four cities of Shandong province, respectively. The HIV incidence was significant higher in Guangdong province than in Shandong, which echoed with the previous study regarding the geographic differences in HIV incidence [18]. Comparing with the incidence rate among participants who had sexual debut above 16 years old (IR=15.17, 95% CI, 10.08-22.83), the incidence rate among those who had sexual debut under 16 was higher (IR=22.22, 95% CI, 5.56-88.85). The incidence rate among migrants (IR=16.56, 95% CI, 10.56-25.96) was also higher than people who were not migrant (IR=13.08, 95% CI, 5.88-29.11). In terms of sexual orientation disclosure to people other than sexual partners, the incidence rate was higher among those who have not disclosed (IR=19.51, 95% CI, 10.50-32.26) (Table 3). However, due to the sample size issue, none of results are significantly different from each other.
Correlates of HIV seroconversion

After adjusting for age, education, income and the assigned group, the results of Cox regression model indicated that having bisexual behaviors in the last 3 months was associated with a higher risk of HIV infection (Adjusted HR = 2.19, 95% CI, 1.02-4.72). In addition, having multiple female partners in the last three months was also associated with an increased risk of HIV infection (Adjusted HR = 4.63, 95% CI, 1.45-14.76) (Table 4).

Discussion

Incidence rate is a critical measure that suggested by UNAIDS to better track the progress towards ending AIDS [19]. Data on HIV incidence among the key population like MSM often limited to clinic-based cohorts, which omitted those men who never visit health facilities. This study estimated the HIV incidence rate among MSM by expanding the included MSM outside the clinics. The use of inverse sampling probability weighting increased the generalizability of this incidence rate estimation. We found an overall significantly high incidence rate among MSM, particularly among those who were migrant or had bisexual behaviors.

The observed high HIV incidence rate indicated that the high burden of ongoing HIV transmission among MSM remained in the study regions. This high HIV incidence rate is consistent with previous Chinese researches [17, 20], and higher than incidence rates from Thailand [21], Peru [22], and other high-income countries [23, 24]. This HIV incidence rate among MSM is comparable to Kenya (12.5/100PY) [25]. The observed high HIV incidence may be related to low condom use [15], low pre-exposure prophylaxis (PrEP) uptake [26], high rates of sexually transmitted diseases co-infection [27], and network factors [28] known to amplify HIV transmission. To address the concern of selection bias that rising from people who reported to have tested HIV at least twice during the study period may be different from the rest of the sample in the cohort study, we conducted a sensitivity analysis to adjust the
incidence rate using inverse sampling probability weighting. After the adjustment, we found a comparable HIV incidence rate with initial high HIV incidence rate. Moreover, due to the HIV-related stigma, people would be more likely to report negative results than positive results, which could yield an underestimate HIV incidence rate in this study. This high HIV incidence suggests that HIV prevention strategies such as PrEP should be incorporated into Chinese HIV prevention guidelines and practices to slow down HIV transmission.

We found that migrant MSM were more likely to HIV seroconvert. Although migrant participants constituted less than one-third of the sample size (28.8%), the HIV seroconversion of migrant MSM was much higher than non-migrants (19 in migrants vs. 6 in non-migrants). Unsurprisingly, this high HIV seroconversion rate contributed to a high incidence rate among migrant MSM, though the difference between migrant and non-migrant was not statistically significant (Incidence Rate Ratio (IRR)=1.26, 95% CI 0.47-3.87), which could due to the limited number of seroconversions observed. Extensive studies have indicated migrant MSM were more likely to engage in risk sexual behaviors [29], had sexual transmitted infectious [30], less access to sexual health services [31], and had high incidence of HIV [32]. Thus, specially attention should be given to these migrant MSM, who may have more obstacles in HIV prevention compared to residents as these previous studies indicated.

Our analysis also indicated that bisexual behavior was associated with the risk of HIV infection among the study MSM. Having sex with women may facilitate the HIV transmission to general population, given the high HIV incidence rate that we found among these MSM. Previous researches have suggested that men who have sex with men and women (MSMW) could be the integral bridge and spread the disease across communities through their socio-sexual networks [28]. Given MSMW are less likely to disclose their sexual orientation to their female partners, be exposed to HIV prevention interventions, and lack of social support [33], their vulnerability of acquiring HIV may increase compared to men who only have sex with men. Though facilitating condom use and increasing HIV testing may still be the main focus
in HIV prevention, researchers and health educators may need to explore a better approach to reach the MSMW while considering the different characteristics between MSMW and men who only have sex with men.

This study has several limitations. First, the HIV test results were based on self-report in the follow-up survey. However, it is unlikely that participants would self-reported as HIV positive when they are uninfected, under a high anticipated HIV stigma. Additionally, we verified the accuracy of these self-report results by asking the participants to send their testing result photos. We found a very high agreement with the HIV testing results with the returned photo results on our platform in this stepped-wedge randomized control study, with the high sensitivity and specificity of the blood-based HIV testing kits that were distributed to the participants for self-testing [17]. Second, participants for this study was recruited through Blued, which may only reveal the HIV incidence situation among MSM who use online social media. Third, the included participants could have higher risk of HIV (higher proportion of multiple partners and bisexual behaviors), which may introduce selection bias. However, the HIV incidence results adjusted by the inverse probability weighting were comparable with the unadjusted results. More importantly, we found that most risk behavioral factors were similar between the included MSM and the overall MSM participants, which could reduce the concern of the selection bias.

**Conclusion**

Through expanding the included MSM with self-report HIV testing results, we found a high HIV incidence rate among MSM in China. This high HIV incidence rate indicates the high ongoing HIV transmission among MSM, calling for special attention on migrants and people who had bisexual behavior, as well as the implementation of more effective HIV prevention strategies (i.e., PrEP). Promoting condom use and HIV testing with sexual health education may still be the top priorities in controlling the epidemic among MSM, while clearly understand the driving force of this high incidence is urgent.
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Conflict of Interest

All authors: No reported conflicts.

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### Baseline sociodemographic and behavioral characters among included MSM (who tested HIV at least twice) and the excluded MSM, 2016-2017, China (N=1381)

| Baseline characteristics | Included MSM (N=347) | Excluded MSM (N=1034) | P value
|--------------------------|----------------------|-----------------------|---------|
| Age                      |                      |                       | 0.90    |
| 16-25                    | 197 (56.8)           | 583 (56.4)            |         |
| >25                      | 150 (43.2)           | 451 (43.6)            |         |
| Marital status           |                      |                       | 0.47    |
| Never married            | 306 (88.2)           | 888 (85.9)            |         |
| Married                  | 41 (11.8)            | 146 (14.1)            |         |
| Highest Education        |                      |                       | 0.78    |
| High school or below     | 116 (33.4)           | 367 (35.5)            |         |
| College or beyond        | 231 (66.6)           | 667 (64.5)            |         |
| Annual income (US$)      |                      |                       | 0.56    |
| <3000                    | 73 (21.0)            | 212 (20.5)            |         |
| 3000-6000                | 73 (21.0)            | 226 (21.9)            |         |
| 6001-9500                | 118 (34.0)           | 316 (30.6)            |         |
| >9500                    | 83 (23.9)            | 280 (27.1)            |         |
| Province                 |                      |                       | 0.36    |
| Guangdong               | 178 (51.3)           | 501 (48.5)            |         |
| Shandong                 | 169 (48.7)           | 533 (51.5)            |         |
| Migrant status           |                      |                       | 0.20    |
| No                       | 100 (28.8)           | 336 (32.5)            |         |
| Yes                      | 247 (71.2)           | 698 (67.5)            |         |
| Age of anal sexual debut |                      |                       | 0.82    |
| <16                      | 19 (5.5)             | 60 (5.8)              |         |
| >=16                     | 328 (94.5)           | 974 (94.2)            |         |
| Disclosure\(^2\)        |                      |                       | 0.18    |
| No                       | 111 (35.0)           | 372 (36.0)            |         |
| Yes                      | 236 (68.0)           | 662 (64.0)            |         |
| Condomless sex\(^3\)    |                      |                       | 0.18    |
| No                       | 104 (30.0)           | 272 (26.3)            |         |

\(^1\) Chi-square test; \(^2\) Based on interview; \(^3\) Based on self-report.
|                                  | Yes            | No            |
|----------------------------------|----------------|---------------|
| Bisexual behavior$^3$            | 243 (70.0)     | 762 (73.7)    |
| Yes                              | 327 (94.2)     | 1000 (96.7)   |
| No                               | 20 (5.8)       | 34 (3.3)      |
| Multiple male partners$^3$       |                |               |
| Yes                              | 235 (67.7)     | 786 (76.0)    |
| No                               | 112 (32.3)     | 248 (24.0)    |
| Multiple female partners$^3$     |                |               |
| Yes                              | 344 (99.1)     | 1032 (99.8)   |
| No                               | 3 (0.9)        | 2 (0.2)       |

1 P-value for Chi-square test / Fisher-exact test
2 Disclosure of sexual orientation to people other than their sexual partners
3 In the last three months
Table 2. Overall HIV seroconversion and incidence rate among MSM with and without inverse sampling probability weighting, China, 2016-2017 (N=347)

|                                      | Without inverse sampling probability weight | With inverse sampling probability weight |
|--------------------------------------|--------------------------------------------|-----------------------------------------|
| Number of seroconverted cases        | 25                                         | 27                                      |
| Personal year estimated              | 160.63 (156.50, 164.75)                    | 159.00 (155.00, 164.00)                 |
| Incidence rate estimated\(^1\)       | 15.56 (15.17, 15.97)                       | 17.21 (16.75, 17.70)                    |

\(^1\) Per 100 person-years
Table 3. HIV incidence rate among participant with different characters, China (N=347)

| Province      | HIV seroconversion | IR\(^1\) (95% CI) | IRR (95% CI) | P value |
|---------------|--------------------|--------------------|--------------|---------|
| Guangdong     | 14                 | 17.28 (10.23-29.18)| 1.25 (0.53-3.04) | 0.29    |
| Shandong      | 11                 | 13.81 (7.65-24.94) |              |         |
| Migrant status|                    |                    |              |         |
| Yes           | 19                 | 16.56 (10.56-25.96)| 1.26 (0.47-3.87) | 0.32    |
| No            | 6                  | 13.08 (5.88-29.11) |              |         |
| Age of anal sexual debut |          |                    |              |         |
| <16           | 2                  | 22.22 (5.56-88.85) | 1.46 (0.17-5.93) | 0.29    |
| >=16          | 23                 | 15.17 (10.08-22.83)|              |         |
| Disclosure\(^2\) |                |                    |              |         |
| Yes           | 15                 | 13.71 (8.27-22.75) | 0.07 (0.30-1.75) | 0.20    |
| No            | 10                 | 19.51 (10.50-32.26)|              |         |

Abbreviations: IR, incidence rate; IRR, incidence rate ratio; CI, confidence interval.

\(^1\) Per 100 person-years

\(^2\) Disclosure of sexual orientation to people other than their sexual partners
Table 4. Behavioral factors of HIV seroconversion as time-dependent covariates in cox regression model, 2016-2017 (N=347)

|                                | HR  | 95% CI       | Adjusted HR\(^1\) | 95% CI       |
|--------------------------------|-----|--------------|--------------------|--------------|
| **Condomless sex**             |     |              |                    |              |
| No                             | Ref | Ref          |                    |              |
| Yes                            | 0.75| 0.42-1.34    | 0.72               | 0.40-1.28    |
| **Bisexual behavior**          |     |              |                    |              |
| No                             | Ref | Ref          |                    |              |
| Yes                            | 2.19*| 1.04-4.59   | 2.19*              | 1.02-4.72    |
| **Multiple male sexual partners** |    |              |                    |              |
| No                             | Ref | Ref          |                    |              |
| Yes                            | 1.36| 0.82-2.26    | 1.32               | 0.81-2.17    |
| **Multiple female sexual partners** |    |              |                    |              |
| No                             | Ref | Ref          |                    |              |
| Yes                            | 4.17*| 1.52-11.44  | 4.63*              | 1.45-14.76   |

Abbreviations: HR, hazard ratio; CI, confidence interval.

\(^1\) Adjusted HR adjusting for age, education, income, and the order of intervention.

\(* p<0.05\)
Figure 1. Data extraction process and HIV seroconversion, 2016-2017, China
Figure 1

1381
Enrolled in the cohort

755 (54.7%)
At least one HIV test during study period

347 (46.0%)
HIV negative for the first testing result

25 (7.2%)
HIV seroconversion