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The Difference between HIV and Syphilis Prevalence and Incidence Cases: Results from a Cohort Study in Nanjing, China, 2008–2010

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Abstract

The available estimates of incidence and prevalence of syphilis among MSM in the Mainland China are high. We used Respondent Driven Sampling to recruit MSM in the study population. The participants were followed up to monitor the incidence and change of risk behaviors. A face-to-face interview was used to collect information about high-risk behaviors, demographics and recreational drug use. To test the difference between prevalent and incident cases, two nested matched case control studies were carried out. The cases were the HIV or syphilis positives found at baseline and during follow-up. We used density sampling to sample six controls for each case.

Our results indicate that compared to incident cases, prevalent cases had higher proportion of reported UAI for both HIV and syphilis. Regression analysis indicated that UAI was the main risk factor among HIV prevalent cases but not in HIV incident cases. These differences could possibly be explained by the implementation of the risk reduction interventions. Syphilis was not a risk factor or HIV prevalent cases but were highly associated with HIV incident cases. Tailored interventions addressing UAI and other risk factors can help to reduce the prevalence and incidence of HIV and syphilis.

Introduction

The rates of HIV incidence among men who have sex with men (MSM) in the Mainland China remain unacceptably high. It is estimated that about 32.5% of new HIV infections were attributable to male-to-male sex in China during 2009 with an increase of 12.2% since 2007 [1, 2]. Urban areas have documented higher HIV prevalence in the recent years and harbor intense epidemic characterized by factors that lead to initiation as well as persistence

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of high-risk behavior[3]. Similarly, there is high prevalence of syphilis reported in the recent years among Chinese urban areas. [4, 5]

The risk behaviors and socio-demographic characteristics of MSM depends on the length of their practice of gay sex.[5] With the incidence of current or recent syphilis among MSM in the Mainland China at approximately 17 per 100 person years,[6] and the prevalence of prolonged infections at around 22.4%, [7] it is important to understand how these acute or chronic disease states are impacted by several risk behaviors. Understanding the pathways of high-risk behavior and STDs in MSM helps in guiding evidence based prevention efforts. [8]

Studies that have examined factors affecting the link between high-risk behaviors namely, unprotected anal intercourse (UAI) and unprotected virginal intercourse (UVI)) on the sexually transmitted diseases (STDs) have primarily focused on heterosexual populations in Mainland China and other developing countries. [9, 10] The pathways between high-risk behavior (UAI and UVI) and syphilis in MSM of China, however, are not well understood. In this study, we examined the association between high-risk behavior and syphilis in MSM, and the pathways involved. We hypothesized that there would be difference between prevalent and incident cases of syphilis/HIV, and their associations with high-risk behavior (UAI and UVI) and socio-demographics might be attributable to knowledge and attitudes about high-risk behavior. By comparing the prevalent and incident cases, we can identify whether the participants changed their behaviors over a period of time and whether such change may have influenced the course of HIV/syphilis epidemic.

Methods

Our study employed Respondent-driver-sampling (RDS) to recruit participants, through the 10 seeds based on the feedback from non-government organizations [11][11][11][11] in Nanjing. The cruising areas are the places/areas where MSM go to find casual sex partners. Through these areas, the seeds recruited MSM from bars, bathhouses/spas, restrooms/parks and the Internet. After being interviewed, each participant was asked to recruit up to three other MSM, using a numbered coupon. All recruits were asked to present their recruitment coupons. The original seeds were different in terms of income, age, occupation, and cruising areas.. After each participant was interviewed, a pack of lubricant and condoms were given as primary incentive. For each person recruited (up to three), they received a prepaid phone card as secondary incentive. The inclusion criteria for our study were these: they must have had oral and/or anal sex with men in the past 12 months, must be currently living in Nanjing and must have been older than 18 years, and must not have participated in other similar studies within the past 3 months.

Measures

A face-to-face interview was used to collect information from participants. UAI was defined as lack of consistent and universal use (Not always using) a condom during anal sex with male partners during the past six months. UVI was defined as lack of consistent and universal use a condom during vaginal sex during the past six months with all female partners. Assessment of knowledge regarding HIV was based on answers to basic questions

related to HIV (correctly answered at least 6 of the 8 related questions), and coverage of HIV preventive services was defined as the proportion of population who received at least one of the six listed intervention services in the past year (condoms, lubricant, peer education, sexually transmitted diseases (STDs) diagnosis or treatment, HIV counseling or testing, and AIDS/STDs-related materials/pamphlets). Having multiple sexual partners was defined as having more than two male partners within the past 6 months. Regular sexual partners were defined as those who had a steady sexual relationship with their partners, while casual sexual partners were defined as occasional sexual partners.

Information was collected regarding details on recruitment of participants, demographic characteristics, knowledge about HIV, attitudes about HIV preventive services, recent sexual behaviors, recreational drug use, and STDs-related symptoms and signs. Higher education was defined as attend Junior college or higher. The study was conducted at the Clinic of the Jiangsu Provincial Center for Disease Control and Prevention in Nanjing. Information about characteristics of the population, their knowledge about HIV, attitudes regarding HIV preventive services, recent sexual behavior, and STDs-related symptoms and signs were also collected.

Follow up (Cohort)

After the baseline survey, all the sero-negative participants were followed up at 6 months, 12 months and 18 months after the first survey. To encourage the participation, incentives worth $16 were provided to each participant at each follow up visit. The retention rate was defined as participation in successive rounds compared to the initial round (Positive cases were removed from the denominator). For example, the retention rate for syphilis cohort at the second round was calculated as the number participants who attended the second round divided by the number of non-HIV positive and non-syphilis positive participants in the first round.

The detailed intervention method is reported in detail an earlier paper. [12] The intervention was implemented at each round, and had two components (basic package and individual specified intervention strategies). In basic package, we provided knowledge about ways to reduce specific risk behaviors, including number of sexual partners during the past six months, sexual practices, patterns of condom use, alcohol and/or drug use affecting sexual activity, STDs, and HIV. In personalized risk reduction counseling, based on risk behaviors and sero-testing results of the participant, tallied intervention, included but not limited psychological counseling, STDs treatment services and skills for providing results to sexual partners were offered to the participants.

Nested Matched Case Control Studies (1:6)

In order to distinguish the difference between prevalent and incident cases, two nested matched case control studies were carried out. The nested studies were two: one for prevalent cases and another for incident cases. In our study, prevalent cases were defined as the HIV/syphilis cases identified as baseline while incidence cases were defined as the baseline case-free participants who developed HIV or syphilis in the follow-up period. The cases were defined as the HIV or syphilis cases found at baseline and newly found HIV or

syphilis cases respectively. Density sampling was used to select six controls for each case, matched on sampling time. “Matching on sampling time” means six controls are sampled from the persisting population at risk at the same time around the case is identified.[13] For example, when a HIV case was detected, successive 6 non-HIV positive participants were matched to this case, thus making all of them sampled from the same amount of person-time at risk (and thus called density or at-risk sampling).[14] In the event of another HIV case detected among 6 people, the control will the seventh person and successive six participants would be matched to new case.

Case ascertainment

We have described the serologic measures in detail elsewhere.[15] In brief, before the interview, 5 ml of blood was drawn from each consenting participant for testing for HIV and syphilis. HIV antibodies were screened using a rapid test (Acon Biotech Co., Ltd) by using whole blood. Early studies conducted in China had already employed this test with success. [16]. If the result was positive, a western blot (HIVBLOT 2.2, Genelabs Diagnostics, Singapore) was performed to confirm HIV antibody positivity. Syphilis antibodies were screened using Rapid Plasma Reagin (RPR, Wantai Biopharmacy Co., Ltd)) and confirmed by Treponema Pallidum Particle Agglutination Assay (TPPA, (Wantai Biopharmacy Co., Ltd)). Syphilis positivity was defined as “current” when both TPPA and RPR were positive.

Age, income, occupation, cruising areas, marital status, and residence were expected to be potential confounders of the relationship between high-risk behavior and disease status.[4–6, 8, 11, 17]

Statistical Methods

Double entry of data was performed and the 2 data sets were compared (Epi Data for Windows; The Epi Data Association Odense, Denmark), and logic check was used for data cleaning. Respondent Driven Sampling Analysis Tool (RDSAT) version 5.6 (available free online, http://www.respondentdrivensampling.org) was used to estimate the population adjusted point estimate and 95% confidence intervals. HIV and syphilis incidence was estimated by using the number of sero-conversions within the follow-up period as the numerator and the total person-year (PY) of the cohort exposure to the risk of HIV and syphilis transmission as the denominator. For those with seroconversions for both (HIV and syphilis), half of the follow-up duration (between the 2 visits) was used as their contribution to the total person time at risk of exposure. Also, Chi-square test was used to compare the differences between prevalence cases and incidences cases for HIV and syphilis.

Two types of analysis were done in the case-control studies; one, with HIV prevalent cases and another with incident cases. Conditional Logistic regression model was used to identify the factors (unadjusted) correlated to HIV in these two case-control analyses; in addition, we also adjusted for age (continuous, in age), marital status (Single, Married or Divorced or Widowed), residence permit (Nanjing, Other cities in Jiangsu provinces, or other provinces).

The Statistical Analysis System was used for data analysis (SAS 9.1 for Windows; SAS Institute Inc., NC). Due to the small sample size, in order to improve the power of the study, statistical significance was defined by P value 0.10 and 0.15 respectively[18].

Ethical statement

The Ethics Committee of Jiangsu Provincial Center approved the study process and content on behalf of Disease Prevention and Control (JSCDC). Signed informed consent was obtained from each of the participants prior to the interviews, blood collection and intervention at each round of the surveys. Each participant had the right and voluntary decision to decline or to withdraw from this survey at any time freely.

Results

The survey was conducted in May and June of 2008. Overall, 430 participants (33.1% (427) of the 1,289 distributed coupons were returned, and 420 of them attended the survey) were enrolled at the baseline through ten initial 10 seeds of the initial recruitment. The crude HIV and syphilis prevalence rates at baseline were 4.7% (20/430) and 11.6% (50/430) respectively, and the adjusted HIV and syphilis prevalence rates were 6.6% (95% CI 3.0–10.4) and 12.6% (95% CI 8.1–18.3) respectively.

Figure 1 shows recruitment of MSM by RDS, number of HIV/syphilis seroconversions, retention rates, and loss-to-follow-up during each follow-up (syphilis cohort). The retention rate at 6 months was 72.5%, 65.8% at 12 months, and 51.2% at 18 months. HIV incidence rate at 6 months, 12 months and 18 months were 5.2 (95% CI 2.1–10.1), 3.8 (95% CI 1.2–8.8), 1.1 (95% CI 0.03–6.1) per 100 person-years, respectively, while overall HIV incidence was 3.6 (95% CI 1.9–6.2) per 100 person-years (Table 1). Table 1 also provides the incidence rate of syphilis. HIV incidence continuously decreased during the entire follow-up period, while there was a decreasing trend of syphilis incidence rate from baseline to the 12-month follow-up, but not between 12 and 18 months, suggesting waning of syphilis incidence.(Figure 2)

We compared the information of HIV/Syphilis prevalent and incident cases in our study (Table 2), indicating that there is no significant difference between HIV and syphilis prevalent and incident cases with respect to age distribution, marital status, residence and knowledge. However, compared with HIV and syphilis incidence, greater proportion of prevalent cases engaged in UAI (80.0% VS 40.2% for HIV, 74.0% VS 47.1%). Also, compared to incident cases, more HIV prevalent cases engaged in insertive anal sex, and less engaged in both insertive and receptive anal sex. However, these differences not seen between syphilis incident and prevalent cases. As shown in table 2, about three quarter of the first sexual partners of syphilis incident cases were male, while this was less than half for prevalent cases of syphilis.

Both univariate and multivariate analysis indicated that UAI is a major risk factor for HIV prevalent cases (Crude OR: 2.54; 95%CI 0.78–8.27, Adjusted OR: 2.50, with 95%CI:0. 72–8.65), but not for HIV incident cases (Table 3). In addition, the results show that syphilis is highly correlated with HIV incident cases but not with HIV prevalent cases. For the HIV prevalent cases, before adjustment, it was seen that the propensity for HIV infection was higher with advance in the age of the participants engaged in first sexual intercourse (OR=1.25; 95%CI: 1.07–1.49), however, after adjustment, the result was reversed (OR=0.84, 95%CI: 0.69–1.03).

Discussion

This study provides the prevalence and incidence rates of HIV and syphilis in a major urban area of Mainland China in addition to understanding determinants of differences between prevalent and incident cases. Overall, HIV and syphilis incidence rate were decreased during the study period, although no such consistency in decrease was observed for incidence rate of syphilis. The decreasing incidence of the HIV and syphilis rate may be explained by the success of the risk-reduction and counseling program. The results indicate inconsistency was seen only between 12 and 18 months, which may be due to random error as only two cases of incident syphilis cases were found during 6 to 12 months and only three during 12 to 18 months of follow-up.

We found that compared to HIV incident cases, prevalent cases had significantly higher proportion of reported UAI rate and similar results were found between prevalent and incident cases of syphilis. This study also reports that UAI was significantly related to HIV prevalent cases but not with incident cases. These differences could be explained by the risk reduction interventions employed in the study. In another study in the same cohort, we found that reported UAI significantly decreased during the study period in addition to decrease in reported UAI with casual and regular partners in the past six months.[19] These results can partially explain why UAI was related to HIV prevalent cases, but not with HIV incident cases. Nonetheless, this does not undermine the role of UAI as a major risk factor for HIV infection although risk reduction programs might have decreased the proportion of participants with this risk behavior. [20, 21] Also, it is possible that participants may underreport the risk behaviors due to the issue of social desirability. This can lead to misclassification of the exposure; however, this misclassification tends to be non-differential as the participants reported their risk behaviors before they got the testing results of HIV and syphilis. Behavioral disinhibition, also known as risk compensation [22] might be another possibility to be considered in intervention related studies. [23, 24] We did not find any evidence from this study regarding this and as cannot not rule out the probability of behavioral discrimination being present in the study. The change of the behaviors of participants may also partially explain the change of the HIV and syphilis incidence rate during the study period. Another important finding is that syphilis was not a risk factor or HIV prevalent cases but was highly associated with HIV incident cases. All these results indicate that even after the implementation of risk-reduction counseling, the treatment of syphilis and other STDs are even more important for prevent HIV infection.

The strengths of the study include use of RDS to access members of the otherwise hard-to-reach populations in a demographically diverse sample, and the use of biological markers of HIV and syphilis infection. A follow-up study monitored the incidence as well as change of risk behaviors of the participants. There are some limitations in our study. One major limitation is the small sample size. In our study, we only have 20 HIV prevalent cases, 13 HIV incident cases, 50 syphilis prevalent cases and 17 syphilis incident cases. Since we only have small number of cases, we had less power to test the difference between them, and we could not adjust for too many potential confounders during the data analysis and this might have resulted in residual confounding in our study. It is possible that such a bias ensues when stratification has exceeded the limits of the data.[25] The estimates of exposure-

disease association move further away from the null as more variables are added to the stratification or regression model. [25] This may explain despite adjustment and using conditional logistic regression, the ORs for partners at pub increased from 4.36 to 17.87. Higher loss-to-follow-up is another major challenge of our study. By the end of the study period, about half of the participants were lost-to-follow-up, and this may cause selection bias only if the loss to follow-up was related to the outcome in our study.

As reported at elsewhere[21], several methods were used to minimize the bias. We used four specially trained interviewers to conduct the face-to-face interviews while two professionals helped in quality check of each questionnaire after each interview.

Based on our data, we infer that during the study period, the burden of HIV and syphilis was decreased. However, the incidence rates of both diseases are higher compared to other parts of the world. Also, UAI is an important risk factor to tackle to reduce the burden of HIV prevalence in MSM. Hence, tailored intervention methods can be implemented to address risk behaviors of MSM including the testing and treatment of STDs.

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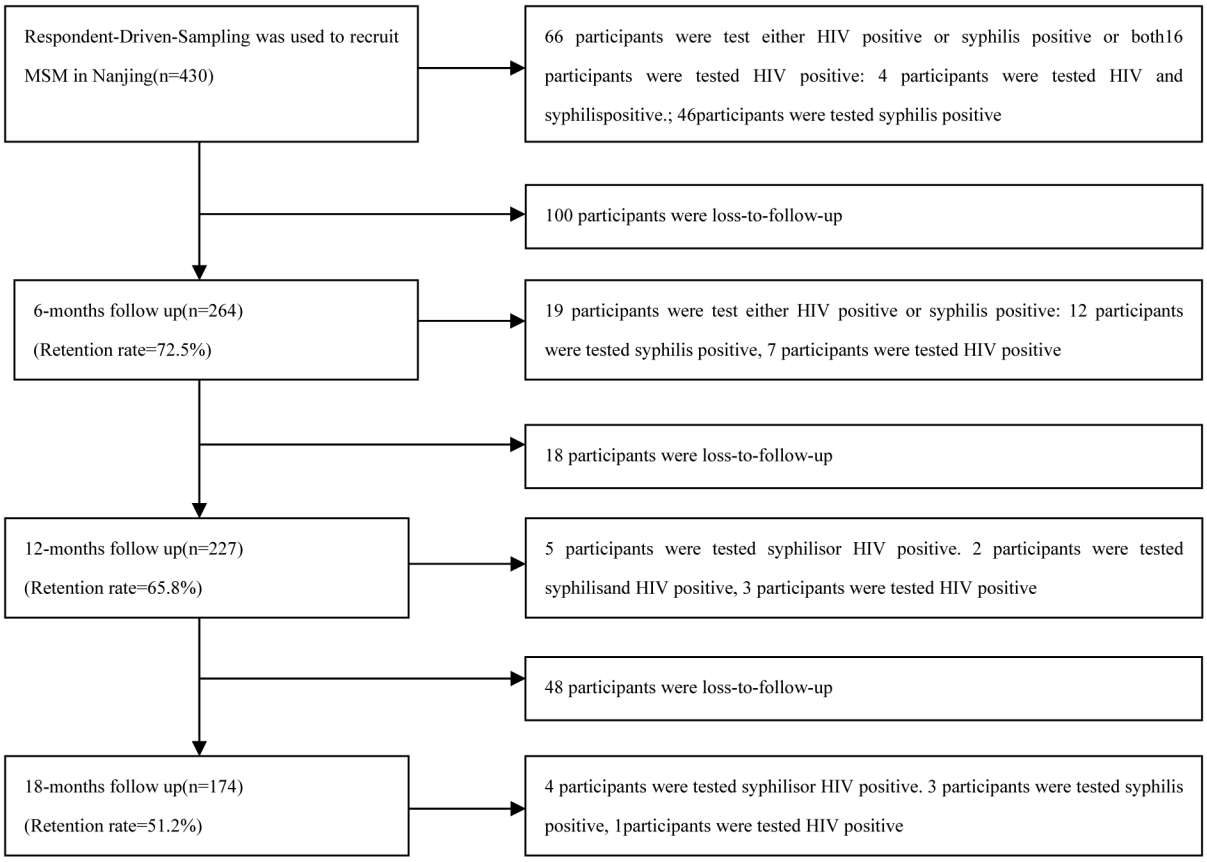

Figure 1.
Enrollment, follow-up, and outcome of the participants in Nanjing, China, 2008–2010

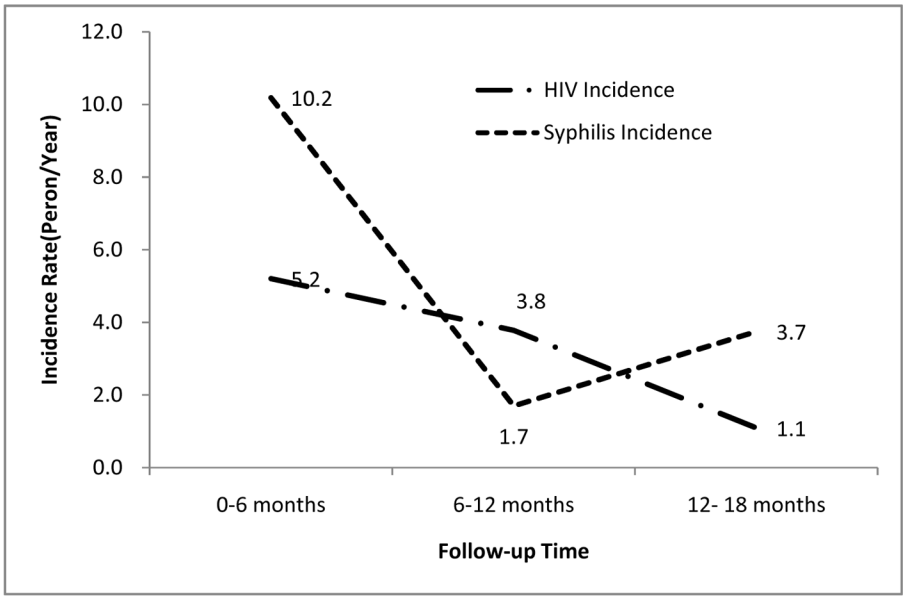

Figure 2.

The trend of incidence rate of HIV and Syphilis of the participants in the cohort among MSM in Nanjing, China, 2008–2010

Table 1

The incidence rate of HIV and Syphilis of the participants in a cohort among MSM in Nanjing, China, 2008–2010

Variables	0–6 months			6–12 months			12–18 months			Cumulative incidence		
	Person Years	**Number of cases**	**Incidence (95%CI)**	**Person Years**	**Number of cases**	**Incidence**	**Person Years**	**Number of cases**	**Incidence**	**Person Years**	**Number of cases**	**Incidence**
HIV	134.5	7.0	5.2(1.4,9.1)	132.4	5.0	3.8(0.5,7.1)	91.7	1.0	1.1(0.0,3.2)	358.6	13.0	3.6(1.6,5.6)
Syphilis	117.8	12.0	10.2(4.4,15.9)	117.1	2.0	1.7(0.0,4.1)	80.0	3.0	3.7(0.0,8.0)	315.6	17.0	5.4(2.8,7.9)

Table 2

Demographic, services coverage, attitude and risk behaviors for HIV and syphilis prevalence and incidence case from a cohort study among MSM in Nanjing, China, 2008–2010

	HIV			Syphilis		
	Baseline(N=20)	**Incidence cases(N=13)**	**P-value**	**Baseline(N=50)**	**Incidence cases(N=17)**	**P- value**
Age			0.92			0.36
20–29	50.0%(10)	53.8%(7)		36.0%(18)	52.9%(9)	
30–39	20.0%(4)	23.1%(3)		34.0%(17)	17.6%(3)	
40 and above	30.0%(6)	23.1%(3)		30.0%(15)	29,4%(5)	
Marital status			0.98			0.71
Single	60.0%(12)	61.5%(8)		48%(24)	58.8%(10)	
Married	30.0%(6)	30.8%(4)		42.0%(21)	35.3%(6)	
Divorced or Widowed	10.0%(2)	7.7%(1)		10%(5)	5.9%(1)	
Residence			0.19			0.82
Nanjing	30.0%(6)	53.8%(7)		44.0%(22)	35.3%(6)	
Other cities in Jiangsu	45.0%(9)	15.4%(2)		26.0%(13)	29.4%(5)	
Other provinces	25.0%(5)	30.8%(4)		30.0%(15)	35.3%(6)	
Knowledge coverage	80.0%(16)	92.3%(12)	0.33	90.0%(45)	94.1%(12)	0.61
Main reason for using condom is prevent HIV	90.0%(18)	100.0%(13)	0.51	76.0%(38)	64.7%(11)	0.36
Whether feel that in the coming year the chance of HIV infection is almost zero	40.0%(8)	46.2%(6)	0.14[b]	42.0%(21)	52.9%(9)	0.65
Gender of the first partner is male	55.0%(11)	53.8%(7)	0.95	46.0%(23)	76.5%(13)	0.03[a]
Whether had anal sex with man in the past six months	90.0%(18)	76.9%(10)	0.36	96.0%(48)	82.4%(14)	0.06[a]
Receipt or insert anal sex(Mainly)			0.02[a]			0.82
Receptive	16.7%(3)	10%(1)		37.5%(18)	46.7%(7)	
Insertive	44.4%(8)	0.0%(0)		22.9%(11)	20.0%(3)	
Both	38.9%(7)	90%(9)		39.6%(91)	33.3%(5)	
Whether had sex with regular sexual partner in the past six months.	72.2%(13)	70.0(7)	0.62	52.1%(25)	71.4(10)	0.20
UAI	80.0%(16)	46.2%(6)	0.05[a]	74.0%(37)	47.1%(8)	0.04[a]
UAI with regular partners	69.2%(9)	85.7%(6)	0.61	65.8%(25)	40.0%(4)	0.14[b]

	HIV			Syphilis		
	Baseline(N=20)	**Incidence cases(N=13)**	**P-value**	**Baseline(N=50)**	**Incidence cases(N=17)**	**P- value**
UAI with casual partners	84.6%(11)	0.0%(0)	<0.01[a]	76.0%(19)	50.0%(5)	0.13[b]
Syphilis (HIV for syphilis)	25.0%(5)	23.1(3)	0.62	8.0%(4)	0.0%(0)	0.23
UVI	25.0%(5)	15.4%(2)	0.42	20.0%(10)	11.8%(2)	0.44
Number of partners in the past six months (More than two)	50.0%(10)	30.8%(4)	0.23	46.0%(23)	47.1%(8)	0.94

Note:

[a] for P-value<0.10,

[b] for 0.10<P-value<0.15

Table 3

Predictors of HIV prevalence cases and HIV incidence cases in a cohort study among MSM in Nanjing, China, 2008–2010.

Variables	HIV Prevalence cases				HIV Incidence cases			
	Crude		Adjusted*		Crude		Adjusted*	
	Point estimate and 95% CI	P- value	Point estimate and 95% CI	P- value	Point estimate and 95% CI	P- value	Point estimate and 95% CI	P- value
UAI	2.54 (0.78, 8.27)	0.12[b]	2.50 (0.72,8.65)	0.15[b]	0.91 (0.29, 2.85)	0.87	1.18 (0.35,4.00	0.79
Syphilis	1.66(0.48, 5.76)	0.43	1.05 (0.25, 4.38)	0.95	5.21(10.31, 26.35)	0.046[a]	6.22 (1.02 37.91)	0.048[a]
Venue								
Internet	*Reference*							
Pub	3.32(0.78,14.04)	0.10[b]	2.67(0.58,12.29)	0.21	4.36(0.80,23.62)	0.09[a]	17.87(1.24,256.5)	0.03[a]
bathhouse	3.34(1.06,10.54)	0.04[a]	1.11(0.20, 6.26)	0.90	1.03(0.190,5.60)	0.97	1.214(0.10,15.20)	0.88
other	0.88(0.10,7.81)	0.91	0.46(0.04, 5.14)	0.53	2.39(0.22,26.28)	0.48	2.89 (0.21,39.05)	0.42
Age at first intercourse sex	1.26(1.07, 1.49)	0.01[a]	0.84(0.69, 1.03)	0.09[a]	0.96(0.84, 1.10)	0.56	0.86(0.66,1.13)	0.29
Knowledge	0.50(0.14, 1.68)	0.26	0.50(0.12, 2.12)	0.35	0.50(0.05, 4.81)	0.55	0.5(0.03,13.18)	0.78
STI symptoms	0.44(0.17, 1.14)	0.09[a]	0.48(0.14, 1.56)	0.22	0.79(0.19, 3.30)	0.74	1.49(0.15, 15.35)	0.74

Note:

[a] means P-value<0.10,

[b] means 0.10<P-value<0.15

* means the models were adjusted for age (less than 20, 20–29, 30–39, 40 and above), marital status (Single, married, and Divorced or Widowed), residence permit(Nanjing, other cities in Jiangsu and other provinces)