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Feasibility of RDS, Effectiveness of Risk-Reduction-Counseling and Testing,
and Factors Associated with Loss-to-Follow-Up in an Intervention Study for
Men Who Have Sex with Men in Nanjing

A dissertation submitted in partial satisfaction of the
requirements for the degree Doctor of Philosophy
in Epidemiology

By

Weiming Tang

2014



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ABSTRACT OF THE DISSERTATION

Feasibility of RDS, Effectiveness of Risk-Reduction-Counseling and Testing,
and Factors Associated with Loss-to-Follow-Up in an Intervention Study for
Men Who Have Sex with Men in Nanjing

By

Weiming Tang

Doctor of Philosophy in Epidemiology

University of California, Los Angeles, 2014

Professor Roger Detels, Chair

Background: Respondent-driven-sampling (RDS) has been recognized as a method for sampling from most hard-to-reach populations. Meanwhile, loss to follow up of the participants in follow up studies usually reduces the validity of the association measured in observational studies, and this problem cannot be overcome through data analysis.

Methods: In a cross sectional study in Nanjing city of Jiangsu province of China, 430 MSM were recruited including 9 seeds in 14 weeks of study period using RDS. Information

regarding socio-demographic characteristics and sexual risk behavior were collected and testing was done for HIV and syphilis. Duration, completion, participant characteristics and the equilibrium of key factors were used for assessing feasibility of RDS. All the HIV negative participants were followed up at 6, 12 and 18 months to evaluate behavioral changes after counseling to reduce risk behaviors. Logistic regression was performed to identify the factors correlated with loss to follow up.

Results: In the study sample, adjusted HIV and syphilis prevalence were 6.6% and 14.6% respectively, whereas HIV incidence was 5.2 per 100 person-years. The incidence was 3.8 during six to 12 months, and 1.1 during 12 to 18 months. Although there was a tendency for recruitment within the same self-identified group, considerable cross-group recruitment was also seen. During the study period, the reported unprotected anal intercourse (UAI) significantly decreased from 60.9% to 42.9%. The proportion of participants who had one or no partner significantly increased from 40.9% to 48.0%. The study also found that some risk behaviors decreased between baseline and 12 months, followed by a slight increase between 12 and 18 months. In addition, loss to follow up for the MSM study in Nanjing was associated with younger age, small social network, lower education, and non-official residence in Jiangsu.

Conclusion: RDS was found to be a potential efficient and feasible sampling method for recruiting a diverse sample of MSM in a reasonable time. Reductions in UAI can be achieved through counseling and testing, but may wane over time. The factors correlated

with loss-to-follow-up found in of our study may be helpful to increase the retention rate of future cohort studies.

The dissertation of Weiming Tang is approved.

Li Li

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2014

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Biographical sketch

Weiming Tang received the Bachelor of Medicine in Preventive Medicine from Nanjing Medical University in 2007 and the Master of Science in Epidemiology and Biostatistics from Nanjing Medical University in 2010. He was awarded the Chinese Outstanding student cadre at 2005.

Chapter.1. Background, Hypothesis and Study Design of the Original Study

I. Background.

HIV/AIDS epidemic among MSM is a complex and serious issue. There are several reasons for this: first sex between men occurs in every culture and society, although its extent and public acknowledgement vary from place to place. Second, in terms of HIV, sex between men is significant because it can involve anal sex, which when unprotected carries a very high risk. Third, at least 5-10% of HIV infections worldwide are estimated to occur through sex between men, though this number varies considerably between countries and regions. Fourth, MSM may also have sex with women, if infected they can transmit the virus to their female partners or wives. Finally yet importantly, although sex between men is often associated with a discrete HIV epidemic, it should also be regarded as linked to the epidemic in the general population.

Since the first several AIDS cases were reported in early 1980s, people started to think HIV/AIDS as homosexual related disease. At the beginning of the epidemic, homosexual or bisexual men accounted for 727 of the first 1,000 reported cases in USA[1].

In China, the nature of the HIV epidemic has shifted from being primarily driven by drug injection to now occurring through sexual transmission. Although the HIV/AIDS epidemic in China not started from MSM[2], the epidemic in this population has become more and more

serious. In China, the proportion of cases resulting from sexual transmission increased from 33.1% in 2006 to 76.3% in 2011, among this increasing, homosexual transmission played an important role[3]. By the end of 2009, about 8.6% of HIV infections were estimated to occur through sex between men. More seriously, 29.4% of the newly infection were due to homosexual behaviors at the same year in China, an increase of 12.2% since 2007 [4,5].

The higher prevalence of HIV among MSM in many metropolises also reflected this issue[6-9], The prevalence increased in Shenzhen from 0.9% in 2002 to 2.7% in 2005 [3], and from 0.4% in 2004 to 6.5% in 2007 in Beijing [6,7]. In Chongqing, the first large sample survey revealed that HIV prevalence was 10.4% in 2006, which increased to 16.7% in 2008 [8,9].

To learn the HIV and syphilis prevalence among Chinese MSM further, several meta-analyses were conducted recently [10-12]. For example, Gao et al conducted a meta-analysis at 2009, and reported that a a pooled HIV prevalence of 2.5% and a pooled syphilis prevalence of 9.1%[10]; Li et al reported a HIV prevalence ranged from 3.2% to 15.8%[11]; and Chow et al reported an overall HIV prevalence of 5.3% and an overall syphilis prevalence of 4.7%[12].

Meanwhile, the larger number of MSM in China will make this issue even complex. No one knows how many people are living with HIV/AIDS in China, no one knows the exact

number of MSM also. According to one estimation[4], 2-4% of adult males once had sex with the other males in China. Based on the estimation of Chinese MOH, there are about 4.1 million MSM among the sexual activity persons at 15-49 years old[13]. Also, according to another estimation[14], there are about 30 million homosexuals in China, while two third of them are gays. If about 5% of them get HIV infection, it will triple the number of current estimated people living with HIV/AIDS (PLHA) in China, which is about 780,000[3]. Due to all of these, the expanding epidemic among MSM in China was thought to be the gravest of challenges regarding transmission of HIV[15].

To understand HIV/STD epidemic among MSM throughout the country, to explore effective models, and to fully implement interventions targeting MSM at the operational level, many surveillances or surveys were conducted in China in the past several years, including a National Comprehensive HIV Prevention and Care Pilot Program among MSM (2008-2009). In 2008, National Comprehensive HIV Prevention and Care Pilot Program among MSM was conducted in 61 cities across mainland China[16]. The objectives of the study were to estimate the prevalence of HIV and syphilis among MSM, to estimate the geographic distributions of the two epidemics, and to understand their behavioral risk patterns. Respondent Driven Sampling (RDS) was used for recruitment in 10 of these cities, including Nanjing. The study found out that Jiangsu Province (Nanjing is the capital of Jiangsu) is one of the places that has the most serious HIV and syphilis epidemic among MSM in China. The label figures show us the overall epidemic of HIV and syphilis in China.

The secondary data that will be used in our studies are based on the National Comprehensive HIV Prevention and Care Pilot Program among MSM in Nanjing. Nanjing is the capital of Jiangsu province in eastern China, one of the largest economic zones of China. With an urban population of over seven million (2011, the overall population is about 8.5 million), Nanjing is the second-largest commercial centre in the East China region after Shanghai. Figure 1 shows the location of Nanjing.

In 2009, a study conducted in Nanjing estimated that Nanjing is the home for about 25,000 MSM[17]. In addition, under the influence of economic development, Nanjing already became one of the most active-zones for MSM. Many MSM traveled to Nanjing each year, which enlarges the overall pool of MSM.

At the Nanjing counseling centre, 430 MSM were recruited, and all of them accepted a face-to-face interview, which included demographic information, HIV related knowledge, social network size, and behavioral information. Blood was collected from all the participants for HIV and syphilis testing. In order to study the HIV and syphilis incidence, all the HIV sero-negative participants were encouraged to participate in the following follow up study, and they were followed up for 18 months. Behavioral interventions were offered in the form of counseling sessions about preventing acquisition of HIV and syphilis; also, condom promotion strategies were included in the intervention.

II. Rationale for the study

The studies in this dissertation were based on secondary data from the Nanjing cohort study among MSM. In 2008, in order to know the HIV and syphilis prevalence and incidence, as part of the national survey, RDS methods were used to recruit MSM by the Jiangsu Provincial Center for Disease Prevention and Control. Also, two parallel cohorts measuring HIV and syphilis incidence over 18 months through 6-month follow-up visits were conducted [18,19]. In addition, to intervention control the transmission of HIV and syphilis, risk-reduction counseling and HIV/syphilis testing strategies were implemented.

In the original study, signed informed consent was obtained from each of the participants prior to interview. Each of the participants had the ability to decline or to withdraw from the survey. Also blood collection and intervention were implemented at each round of the surveys. The questionnaires and written consent document of the original study were separately kept in locked cupboards at the study sites, and unauthorized persons could not access them. The Ethics Committee at Jiangsu Provincial Center for Disease Prevention and Control approved the study process and content.

Our studies will use the existing data from the original study. Our studies should not be subjected to data security because no names of the participants were included in the data set; also, no link to the identification number or contact information for the participants was included in the data set.

As one of the original researchers of the original study, I observed every process of the study, including study design, seed recruitment, data collection, and data management. Thus, I know the strengths and limitations of the original study.

By using existing data, our studies have several strengths. First, by using the existing data, our studies nearly have no cost. Also we can save much time, for no time is needed for the data collection, except data coding and data editing. Second, we can enhance the utility of the original data, by ensuring that data with an unused research potential are archived in a way that make it possible to find and use the data in the future.

III. Hypothesis

- 1). RDS increases our ability to reach hard-to-reach MSM population in Nanjing, and the strategy yields a diverse sample.
- 2). Risk-reduction Counseling and HIV/Syphilis Testing is a potential effective strategy to reduce risk behavior of MSM at each follow-up round of the cohort.
- 3). The loss-to-follow-up in the cohort could be correlated with some characteristics or behaviors of the participants at the baseline, and we could enhance the adherence of between cohorts by identifying these issues.

IV. Objective

The objectives of the original study were to estimate the prevalence and incidence rates of

HIV and syphilis among MSM in Nanjing, to understand their behavioral risk patterns, and to evaluate the factors correlated with UAI among MSM in Nanjing.

Meanwhile, different from the original study design, the unique objectives of our study include the following several points:

- 1). To evaluate the feasibility of RDS for recruiting MSM in Nanjing, China,
- 2). To evaluate the effectiveness of risk-reduction counseling and HIV/syphilis testing,
- 3). To identify the predictors that correlate with consistent/non-consistent participation in the cohort study.

Specific Aims:

- 1). To test the feasibility of RDS by comparing the study sample size to designated sample size, to evaluate whether the program reached the designated sample size; using an equilibrium distribution system to evaluate the stability of the sample collection;
- 2). To evaluate the joint recruitment (detail definition will be given in the definition of the variables part) between different patterns of MSM by testing the homophily of the participants; to evaluate the diversity of the samples by testing the homophily as well as the differences between the RDS-adjusted proportion of the interested variables and the equilibrium proportion of the variables.
- 3). To evaluate the effectiveness of RDS by testing the relations between the sample size,

Deff, standard error, $V(RDS, \hat{P}_A)$ and $V(SRS, \hat{P}_A)$;

To evaluate the effectiveness of Risk-reduction Counseling and HIV/STD testing by analyzing the trend of the risk behaviors of the participants, and the trend of the HIV/syphilis incidence;

4). To identify the predictors for consistent participation in the cohort study, in order to enhance the adherence of the participants in future studies.

V. Materials and Methods

1 Materials and Methods of the original study

1.1 Study Design and Selection of subjects

1.1.1 Defining the source population:

The source population of the original study is those MSM who were 18 years old or older and lived in Nanjing during the previous six months of the study period, and had sex (oral or anal) with other men in the past 12 months. Also, they should not have participated in any similar studies conducted in other cities in the past three months.

1.1.2 Sample recruitment

In the year 2008 between the months of May and August, a cross-sectional study was conducted using RDS as the sampling strategy for recruiting MSM in Nanjing city, China.

The sampling began with a set of initial participants (“seeds”) recruited with the help of MSM community-based organizations, operators of bars and bathhouses/spas and from

restrooms/parks or internet. Nine individual seeds who were different from each other in terms of income, age, occupation and “cruising area” (venues for meeting sexual partners), were recruited. These seeds initiated the expanding chain of referrals, whereby respondents from each link in the chain or “wave” referred other respondents to form the subsequent waves of referral. It has been shown that using RDS any member of a hard-to-reach community can be reached theoretically by using six separate waves (principle of “six degrees of separation”). In this study, each seed initially recruited three other MSM from their social networks for behavioral evaluation and serological testing, using uniquely numbered coupons to allow tracking of the recruitment process. Each respondent received a gift (containing lubricant and condoms) worth 4.50 USD approximately to compensate for his time. Three recruitment coupons (Maximum 3 coupons were given to the participants, when sample size reached 350, the coupon numbers were reduced to 2 or one, and no coupon was handed out when sample size reached 420) were also given to them to be passed on to their acquaintances. If at least one new participant was recruited with a coupon, the respondent making the referral with that coupon received an additional gift (prepaid phone card) worth 4.50 USD approximately as a token of appreciation of his effort. Residence (Hukou) , education level, marital status, syphilis sero-status, sexual orientation and cruising area were used to monitor whether RDS had reached equilibrium or not.

1.1.3 Procedures of the original study (The figure 3 shows the process of the original study also)

A) When a participant came in for the survey, he was asked to show his coupon. Then, the coupon was verified as valid and had not been used before. After the verification, the registers recorded the incoming coupon / study ID in the study log book under the survey day's date.

B) At the registration room, two volunteers were invited to conduct de-duplication (if visible characteristics are noted, record in study log book).

C) If the participants agreed proceed to screening for eligibility, they were explained what the survey entailed.

D) The participants were screened for eligibility. If the participants were not eligible, then the staff worked as registers will record "not eligible" in the study log book. If eligible, he was proceeded to consent, then contact information was collected for future contact.

E) Registers reviewed the consent form with the participant and asked him to answer all questions. All participants verbally stated that they understood and agreed to all of the items contained in the consent in order to enroll in the survey. After signed by the participants, the consent forms were saved in the appropriate space and a study ID number was assigned to the participant.

F) Once the consent form was completed, we introduced the participant how to collect the

biological specimen. In addition, all specimen submission forms were completed and study ID was recorded on the specimen and forms. HIV was tested by rapid test method (Produced by Acon Biotech Co., Ltd, lot 200803973/WB. If the screening result was positive, it was confirmed by Western blot later). Then, the participants were introduced to the interviewer who escorted him to a private room.

G) Once the participants arrived at the private room, they were given a face-to-face interview. Once the interview was completed, the questionnaires were reviewed to ensure that all of the questions had been answered, and there was no logistic conflict. In addition, we ensured that the coupon numbers were recorded on the questionnaire.

H) If subject agreed to recruit three of his peers, three numbered coupons were provided to him, and the interviewer explained the recruitment processes. Later, the three coupon numbers were recorded in the study log book.

I) Upon completion of the interview and collection of the biological specimen, the testing results were told to the participants in a private counseling room, and intervention was offered based on their risk behaviors.

J) The monitor tables and questionnaires were returned to the registration room. The questionnaires were checked for completeness and consistency. If any errors were found at this stage, the participants were re-asked the questions, and corrected answers were put

on the questionnaires. Then condoms / lube were provided to the participants as the primary incentive.

K) Secondary incentive was given to the participants when they successfully recruited another MSM.

1.1.2 Follow-up(Cohort)

After the first survey, all of the participants (except those who were HIV-positive, who were referred to HIV/AIDS care programs) were encouraged to attend the surveys conducted at 6, 12 and 18 months after baseline. Gifts worth US \$16 were provided as incentive for each follow-up visit to encourage them to participate. 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 the third round was calculated as the number of participants who attended the third round divided by the number of HIV-negative participants in the first round minus the number of HIV-positive participants in the second round. The following figure (figure 3) gives us the design features for the follow up.

1.1.3 Intervention

Testing and risk-reduction counseling was implemented for each participant at each round. The results of the HIV and syphilis testing were matched to individual records after they were obtained from Jiangsu CDC, China. After completing the questionnaire, the

participants were invited to a separate room for risk-reduction counseling with one of the two counselors who had previous experience in HIV voluntary counseling and testing at the Jiangsu CDC. The counselors spent five to ten minutes reading the responses to the questionnaire for the interviewee to understand his risk behaviors. They obtained more specific information by asking additional questions. Subsequently, the counselor conducted a detailed counseling session with the participant stressing the implications of his risk behaviors. The counselor answered all the participants' questions. The intervention was completed by providing knowledge about ways to reduce specific risk behaviors, including number of sexual partners, sexual practices (anal, oral, vaginal intercourse), patterns of condom use, alcohol and/or drug use affecting sexual activity, STDs, HIV, exchange of sex for money, and assumptions about partners' risk behaviors. Each participant received free condoms and lubricant, and all HIV-positive participants were referred for standard treatment at the Nanjing Second Hospital.

1.1.4 Serologic measures

Five ml of venous blood was collected from each subject for HIV and syphilis testing. HIV antibodies were screened using a rapid test (Acon Biotech Co., Ltd, lot 200803973/WB). If the screening result was positive, it was confirmed by Western blot (HIVBLOT 2.2, Genelabs Diagnostics, Singapore, lot AE8039). Syphilis antibodies were screened using Rapid Plasma Reagin (RPR; Beijing WanTai Biological Pharmacy Enterprise Co., Ltd., lot N20080404) test and confirmed with Treponema Pallidum Particle Agglutination assay (TPPA; Livzon Group Reagent Factory, Guangdong, China, lot VN80803). Syphilis

positivity was deemed “current” when both TPPA and RPR assays were positive.

2. Eligibility criteria

Inclusion criteria:

- 1) Male (Biologic);
- 2) Having sex with men (oral and/or anal) within the past year;
- 3) 18 years or older;
- 4) Had not participated in a similar survey within the past three months;
- 5) Had a valid referral coupon.
- 6) Was willing to participate in the survey.

3. Sample size for survey

This part summarizes the sample size and power estimation process for the original study in details. In the original study, we used $Deff=2.0$, for a detection of a 10% decrease in high risk sexual behavior, and we set power =0.80, $\alpha=0.05$, based on the following formula, we got the required sample size was 460. The estimation process was based on the following formula and assumptions:

$$n = Deff \cdot \frac{[(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}) \cdot \sqrt{P_{A,1}(1-P_{A,1}) + P_{A,2}(1-P_{A,2})}]^2}{(P_{A,2} - P_{A,1})^2}$$

In this formula:

$Deff$ = design effect of 2.0 (recommendations vary from 1.25 to 2.0, therefore 2.0 was conservative);

$P_{A,1}$ = the estimated proportion of sexual risk behavior at baseline (we used proportion of MSM having two or more partners as the proxy for sexual risk behavior and used 0.7 as the value for this according to recent surveys in China. This proportion had also been used for projecting the “at risk” sizes among MSM population of China);

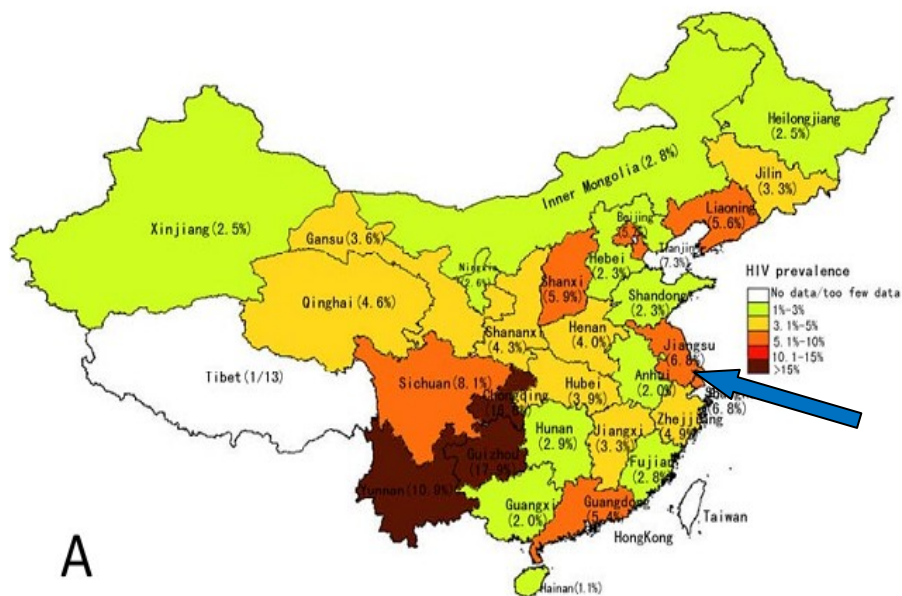
$P_{A,2}$ = the estimated proportion of sexual risk behavior at some different time after the baseline survey, so that $(P_2 - P_1)$ was assumed as the magnitude of change we wanted to be able to detect (we assumed $P_{A,2} = 0.8$ based on the rationale that we wished to be able to detect a 10% change in the proportion of MSM with having two or more partners);

$Z_{1-\frac{\alpha}{2}}$ = the z-score corresponding to desired confidence level (we used the 95% confidence level and corresponding two-sided z-score);

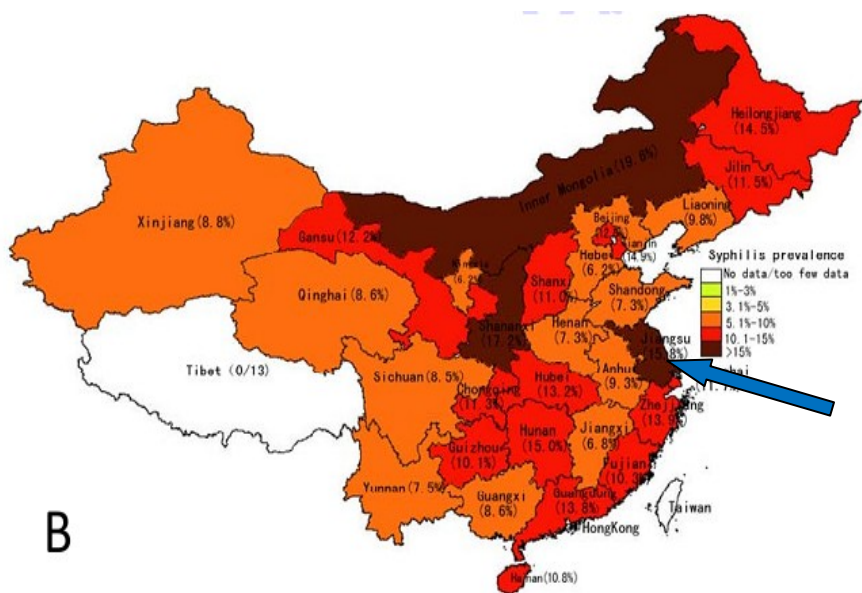
$Z_{1-\beta}$ = the z-score corresponding to the desired power (we used 80% power and the corresponding two-sided z-score)

The above parameters produced a required sample size of 460 participants per survey year, so, the estimated sample size for this study was 460. However, only 430 MSM attended the baseline survey.

VI. Figures



A



B

(These two pictures adapted from Dr. Wu's article)

Figure 1 The Overall HIV (A) and syphilis (B) Epidemic in China

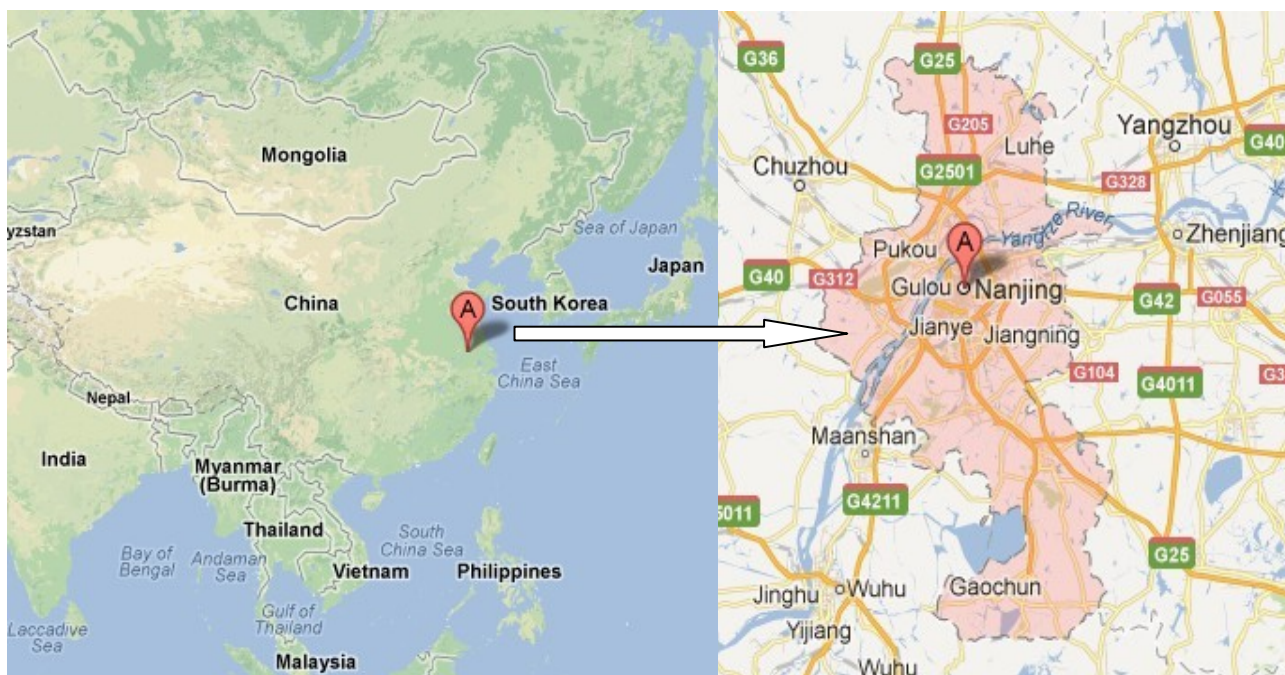


Figure 2, the location of the study.

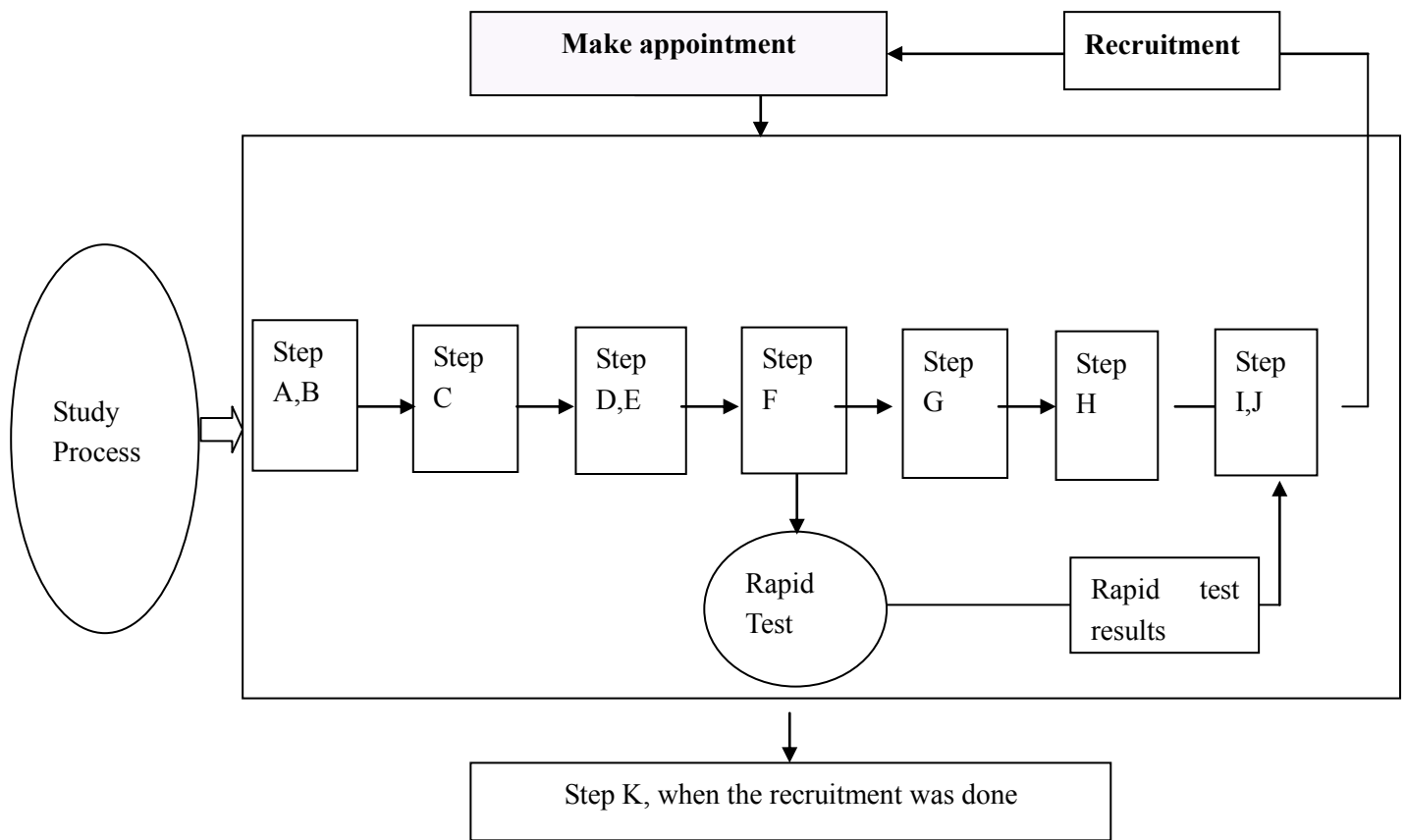
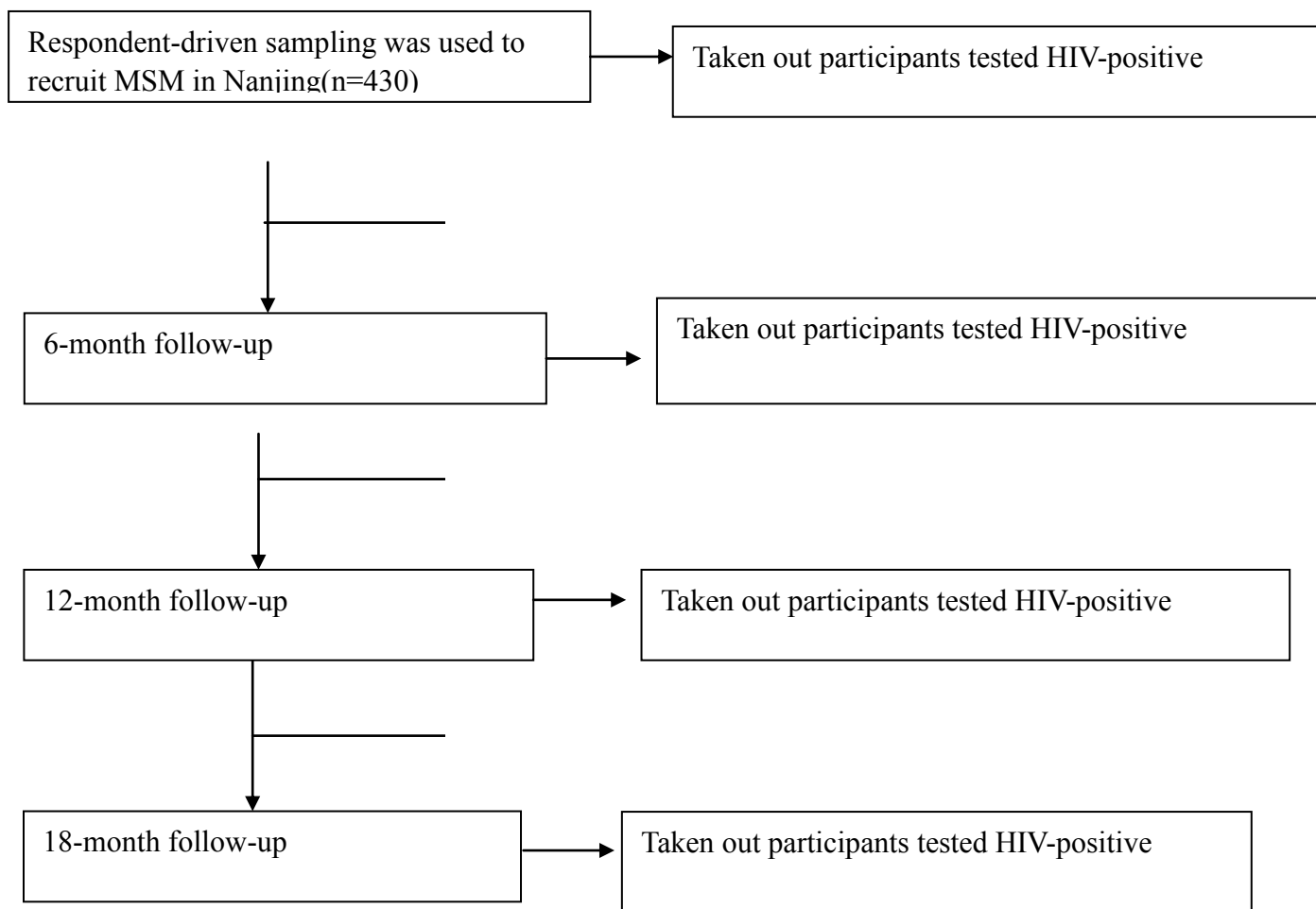


Figure 3 The Study Process of the Original Study



This trial profile describes recruitment of MSM by RDS, and includes enrollment during each follow-up.

Figure 4 Enrollment, follow-up of the participants in Nanjing, China, 2008-2010

Chapter 2. Feasibility of RDS on recruiting a diverse sample of Men Who Have Sex with Men: Observation from Nanjing, China

I. Abstract

Background: Respondent-driven-sampling (RDS) has been recognized as a method for sampling from most hard-to-reach populations like commercial sex workers, drug users and men who have sex with men. However, the feasibility of this sampling strategy in terms of recruiting a diverse spectrum of these hidden populations has not been understood well yet in developing countries.

Methods: In a cross sectional study in Nanjing city of Jiangsu province of China, 430 MSM were recruited including 9 seeds in 14 weeks of study period using RDS. Information regarding socio-demographic characteristics and sexual risk behavior were collected and testing was done for HIV and syphilis. Duration, completion, participant characteristics and the equilibrium of key factors were used for assessing feasibility of RDS. Homophily of key variables, socio-demographic distribution and social network size were used as the indicators of diversity.

Results: In the study sample, adjusted HIV and syphilis prevalence were 6.6% and 14.6% respectively. Although there was a tendency for recruitment within the same self-identified group (homosexuals recruited 60.0% homosexuals), considerable cross-group recruitment (bisexuals recruited 52.3% homosexuals) was also seen. Homophily of the self-identified

sexual orientations was 0.111 for homosexuals. Upon completion of the recruitment process, participant characteristics and the equilibrium of key factors indicated that RDS could be feasible for sampling MSM in Nanjing. Participants recruited by RDS were found to be diverse after assessing the homophily of key variables in successive waves of recruitment, the proportion of characteristics after reaching equilibrium and the social network size. The observed design effects were nearly the same or even better than the theoretical design effect of 2.

Conclusion: RDS was found to be an potential efficient and feasible sampling method for recruiting a diverse sample of MSM in a reasonable time.

Keywords

Respondent-driven-sampling, Feasibility, Men who have sex with men, HIV, China

II. Introduction

While conducting a research involving hard-to-reach populations, such as injecting drug users (IDUs), commercial sex workers (CSWs) or men who have sex with men (MSM), ensuring the representativeness of the study sample is a big challenge. In the past two decades, many strategies have been used to recruit diverse samples from these hidden population groups, but generalizability of the study results always remained an issue and selection bias was always a probability. These recruitment methods included time-location

sampling, snowballing and targeted sampling. However, most of these methods only provided limited coverage and could only claim pooled representation of the target populations [20]. To deal with these problems, Heckathorn DD introduced respondent-driven sampling (RDS) in 1994, while studying HIV-related risk behaviors among IDUs residing in the eastern part of United States [21].

In the past few years, RDS has been widely used in many countries to recruit hard-to-reach populations and to conduct large-scale HIV serologic and behavioral surveys [22]. It has also been recognized and adopted by public health researchers as a promising alternative method for sampling from most-at-risk populations [22-26]. RDS is a variant of the chain-referral methodology, which requires that the population of interest be internally well-connected through social networks [26]. The advantage of RDS method include its uses a mathematical model to compensate for the non-representativeness by keeping track of the recruitment process and using probabilistic weights. While sampling from a hidden population from which recruitment of a random sample is not feasible otherwise, the initially selected participants (“Seeds”) in RDS need not be random to have a somewhat representative sample as long as the seeds belong to target population. With the continuation of the recruitment process in RDS, the distribution of the characteristics of the sample stabilizes gradually and this condition is termed as “reaching the equilibrium” [27,28]. These frameworks of RDS help in minimizing the sampling biases found commonly in chain referral sampling [21,27]. However, the feasibility of RDS remained unclear.

MSM population is probably playing a significant role in the HIV epidemic of China where like other countries in Asia, HIV sero-positivity level is rising among MSM. Nanjing, a metropolitan city, located in one of the largest economic zone of China and having a population of approximately 8 million (according to 2010 census) is no exception. HIV percentage positivity among the participating MSM in Nanjing has increased from none detected in 2003 to 5.8% in 2007 [29]. “Money boy” is a group of male who provide commercial sexual services to other male in different parts of China and some other countries. In Nanjing, commercial sex with money boys is very common among MSM population, especially among young males [30,31].

Several studies have been conducted to assess whether RDS is a feasible strategy to recruit samples from hidden populations. However, most of these studies either did not evaluate the efficiency of RDS in terms of reaching a diverse spectrum of hard-to-reach populations or didnot address design effect (Deff) and sample size issues. These limitations called for this study among the MSM population of Nanjing, a large metropolitan city of China, with the aims of assessing the feasibility of RDS for reaching this hard-to-reach population, whether the strategy yields a diverse sample and whether it reaches the designed sample size and design effect.

III. Methods

Study Design and Sampling Methods

In the year 2008 between the months of May and August, a cross-sectional study was conducted using RDS as the sampling strategy for recruiting MSM in Nanjing city of China. The sampling began with a set of initial participants (“seeds”) recruited with the help of MSM community-based organizations, operators of bars and bathhouses/spas and from restrooms/parks or internet. 9 individual seeds who were different from each other in terms of income, age, occupation and “cruising area” (venues for meeting sexual partners), were thus recruited. These seeds initiated the expanding chain of referrals, whereby respondents from each link in the chain or “wave” referred other respondents to form the subsequent waves of referral [27]. It has been shown that using RDS any member of a hard-to-reach community can be reached theoretically by using six separate waves (principle of “six degrees of separation”) [20]. In this study, each seed initially recruited three other MSM from their social networks for behavioral evaluation and serological testing, using uniquely numbered coupons to allow tracking of the recruitment process. Each respondent received a gift (containing lubricant and condoms) worth 4.50 USD approximately to compensate for his time contribution. Three recruitment coupons were also given to them to be passed on to their acquaintances. If at least one new participant was recruited with a coupon, the respondent making the referral with that coupon received an additional gift (prepaid phone card) worth 4.50 USD approximately as a token of appreciation of his effort. Official residency, education level, marital status, syphilis sero-status, sexual orientation and cruising area these six key factors were used to monitor whether RDS had reached equilibrium or not.

Homophily is a statistic that describes the mixing patterns in networks and the probability of an HIV-positive individual successfully referring another HIV-positive individual from a population. Homophily can be negative or positive (ranging from -1 to +1), depending on whether an individual preferentially contacts or avoids someone with the same given characteristic [32-35]. It has been shown that when homophily is zero for all groups, the estimated population proportion (EPP) for the target population is identical to the actual sample population proportions (SPE) [32-36].

To attain the distribution of the sample characteristics, equilibrium distributions were set at the statistical software RDSAT (software for statistical analysis of data from sample recruited by RDS) to fall within 2% of the sample distribution [21,27,28]. Social network size was defined as the number of MSM in the city known (familiar with face, name/nickname, had contact information, and could get in touch with him in the next month) to the participant. The design effect was determined by the ratio of the actual variance under the used sampling method and the variance computed under the assumption of simple random sampling [36].

The study was conducted at the clinic for sexually transmitted infections (STI) of the Center for Disease Control and Prevention of Jiangsu Province (JSCDC) between May and August, 2008. Eligibility criteria for the participants were: 1) male; 2) having sex with men (oral and/or anal) within the past year; 3) 18 years or older; 4) had not participated in a similar survey within the past three months and 5) had a valid referral coupon.

Measures

Data measures

Duration of survey, completion of the recruitment process using RDS, characteristics of the seeds and their recruits and the equilibrium of the key factors were used as the parameters for the evaluation of the feasibility of RDS. While doing this design effects (Deff) of selected variables were also determined. Homophily of key variables, the proportional distribution of selected demographic variables and the social network size were the indicators to assess the diversity of RDS.

During data collection, the process of distribution of the referral coupons was kept restricted to control exponential sample growth. The number of distributed coupons was reduced from three to two and then to one after the sample size reached 350, and no more coupons were distributed after the sample size reached 420.

Face-to-face interviews with a structured questionnaire were conducted to collect information on recruitment patterns, demographics, HIV knowledge, coverage of HIV prevention services, recent sexual behavior and drug use, and STI-related symptoms.

Demographic information included age (less than 20, 20-29, 30-39, 40-49, and over 50 years old), marital status (single, married and divorced/widowed), occupation (15 occupational categories that included most recognized occupations), education level (illiterate, elementary school, junior high school; senior high school, technical secondary school and junior college/college degree/higher), residency (official resident of Jiangsu

province or other provinces) and family income in Yuan (less than 2,000, 2001-3000, 3001-4000, 4001-5000, and more than 5000; 1 USD= approximately 6.05 Yuan).

Self-identified sexual orientations were classified as undecided, only homosexual, mainly heterosexual and bisexual. Equilibrium distributions were assessed based on sexual orientation, being single, official residency for Nanjing, college degree or higher education, proportion of syphilis sero-positive cases and recruiting sexual partners online.

Homophilies were also calculated for self-identified sexual orientation and proportion of syphilis cases.

Serologic measures

Five ml of venous blood was collected from each subject for HIV and syphilis testing. HIV antibodies were screened using a rapid test (Acon Biotech Co., Ltd, lot 200803973/WB). If the screening result was positive, it was confirmed by Western blot (HIVBLOT 2.2, Genelabs Diagnostics, Singapore, lot AE8039). Syphilis antibodies were screened using Rapid Plasma Reagin (RPR; Beijing WanTai Biological Pharmacy Enterprise Co., Ltd., lot N20080404) test and confirmed with Treponema Pallidum Particle Agglutination assay (TPPA; Livzon Group Reagent Factory, Guangdong, China, lot VN80803). Syphilis positivity was deemed “current” when both TPPA and RPR assays were positive.

Sample size and design effect (Deff)

Using Deff=2.0, for the detection of a 10% increase in high risk sexual behavior with 80%

power and 95% confidence level, the required sample size for this study was calculated to be 460. The detailed sample size estimation process has been described in Appendix A. In our study, 430 participants were recruited during 14 weeks of study period, including the nine seeds. The Deff for being HIV-negative was 2.48, syphilis-negative 1.87, engaged in unprotected anal sex 2.20, only homosexual 1.85, and having college degree or higher education 2.95. The detailed estimation process for standard error (se), variance using RDS and observed Deff has been described in Appendix B.

Ethical approval

The study was approved by the Ethics Committee of Jiangsu Provincial Center for Disease Prevention and Control.

Data Analyses

Respondent Driven Sampling Analysis Tool (RDSAT), version 5.6 (available free online <http://www.respondentdrivensampling.org>) was initially used to calculate the population adjusted point estimate, 95% confidence interval and level of homophily. RDS uses network information to account for potential sources of bias in the sample and provides mathematical methods for adjusting estimates based on these biases [37]. Hence the data gathered using RDS methods in this study were analyzed with RDSAT using network sizes as the weight to adjust for the potential sampling biases. We also used STATA 10.0 to calculate the equilibrium and Deff.

IV. Results

Among the 430 participants recruited in this study with the help of the 9 seeds, 20 were HIV positive, with crude prevalence of 4.6% and adjusted prevalence of 6.6% (adjusted by RDSAT, based on the weight of network sizes). The characteristics of the 9 seeds for this study are presented in Table 1.

Feasibility

Among the 455 respondents who visited the study site and provided consent, 25 did not have a valid recruitment coupon and were excluded from the study. Data from the other 430, including the 9 seeds, were collected over a period of 14 weeks (between 5th May and 1st August, 2008). The survey office was open six days a week from 8:30 am to 5:00 pm and two to four interviewers were present at the site during this period. The average number of completed interviews was 30.71 (minimum=2, maximum=64) per week. The wait time for being interviewed and seen by the clinicians was less than 20 minutes and the average time that a participant spent at the survey site was about 45 minutes

Figure 1 shows the recruitment flow of the participants (level of enrollment) as the survey progressed toward the targeted sample size. As the process of recruitment progressed beyond the 5th week, the percentage of participants coming to the survey site started to decrease. When the number of recruited subjects reached 350, we gradually reduced the number of recruitment coupons given to participants from 3 to 2 and then to 1 while the coupon validity was shortened from 15 to 10 days. After the recruitment of 420 subjects, no

more coupons were distributed. By the end of 14th week, the survey reached the sample size of 430.

To see how coupons were distributed by the participants within their social networks, participants were asked about their relationship with the person who gave them the coupon. 41.6% received coupons from a close friend, 3.0% from a sexual partner more than six months ago and 13.3% from a sexual partner within the past six months. Only 3.7% reported receiving one from a stranger. The majority (90.2%) of participants reported that their primary reason for accepting a coupon and coming to the clinic site was to be tested and treated for HIV/STIs. Only 0.3% reported coming only for the incentive.

An equilibrium distribution system was used to evaluate whether the recruitment met the design needs. The rate of syphilis reached equilibrium by the fifth wave. Equilibrium distribution for being self-identified homosexual, single and resident of Nanjing were all reached by the seventh wave while usually meeting sexual partners on the internet and having a college degree or higher education were reached by the tenth wave.

Diversity

56.5% of the participants found their sexual partners on the internet, 15.8% at pubs, discos, tearooms or clubs; 15.8% at spas, bathhouses, saunas or massage centers; 4.4% in parks and public restrooms while 7.4% found them somewhere else.

Figure 2 shows the branching patterns of the path of maximum recruitment (88 recruits, 8 waves), which began with one self-identified homosexual seed. The figure also shows the cross distributions of sexual orientations among different chains.

The homophily of the self-identified sexual orientations was 0.111 for only homosexuals (n=242), indicating that only homosexuals were probably socially insular and preferentially recruited other self-identified homosexuals more (59.7%) than MSM of other orientations (40.3%). Bisexuals (n=167) demonstrated a homophily of -0.012 and mainly heterosexuals (n=10) demonstrated a homophily of 0.236.

Table 2 shows the RDS estimates for the proportion of syphilis cases among participants. MSM infected with syphilis (n=54) demonstrated a homophily of 0.077 while those who were syphilis-negative (n=376) demonstrated a homophily of 0.251. Although only 14.6% of the population was syphilis-positive, they recruited 21.2% other syphilis cases and 78.8% syphilis-negatives. While 85.4% of the population was syphilis-negative, they recruited 89.1% syphilis-negative and 10.9% positive participants. However, cross-recruitment was substantial (19.2%), implying that recruitment chains did not become trapped within a single group, but instead crossed lines. This contributed toward a strong convergence between the sample composition (12.6% syphilis cases) and the equilibrium sample composition (12.1% syphilis cases). It also indicated that homophily and estimated network size both were potentially important factors for the referral process. Table 2 also shows that the unadjusted and adjusted rates were not significantly different

(P value=0.45). Average network size was found to be 6.9 and 5.6 for syphilis negative and positive participants respectively.

The recruitment patterns according to self-identified sexual orientation indicated mixing of different orientations amongst participants (Table 3). However, there was a tendency for recruitment within a group, along with considerable cross-group recruitment. Overall, homosexuals recruited 60.0% only homosexuals, 1.2% mainly heterosexuals, 36.8% bisexuals. Bisexuals recruited 40.5% bisexuals, 52.3% only homosexuals. There was a strong convergence between the sample composition (56.8% only homosexuals, 2.4% mainly heterosexuals, 38.2% bisexuals) and the equilibrium sample composition (56.7% only homosexuals, 2.6% mainly heterosexuals, 38.1% bisexuals).

Homophily for self-identified sexual orientation was 0.111 in cases of only homosexuals, 0.236 for mainly heterosexuals and -0.012 for bisexuals. Mainly heterosexuals had a larger network size (9.3) compared to only homosexuals (7.0) and bisexuals (6.2). When the equilibrium distribution was reached, the proportions of self-identified sexual orientations were 56.4% only homosexual, 38.8% bisexual, 2.2% mainly heterosexual.

At equilibrium, 11.4% were aged less than 20 years, 58.6% belonged to 20-30 years, 17.9% 30-40 years, 10.2% 40-50 years, and 1.9% over 50. Equilibrium proportions for the average monthly income in Yuan were 31.8% under 1,000, 24.0% 1,000-2,000, and 12.8% over 4,000.

The final sampling shows the results for social network sizes. The proportions of social network sizes were 27.4% under six (adjusted proportion 67.4%, 95% CI 62.1-72.7), 6.0% 6-10 (adjusted proportion 20.1%, 95% CI 16.2-24.0), 25.8% 11-20 (adjusted proportion 9.6%, 95% CI 7.7-11.7), and 20.1% over 20 (adjusted proportion 2.8%, 95% CI 2.1-3.6). The average social network size was 20, the median was 10, the maximum was 400, and the minimum was one. The average social network sizes were 24 for homosexuals, 16 for heterosexuals, 16 for heterosexuals.

Table 4 shows the sample size and design effects of certain variables.

V. Discussion

Our study began with nine seeds, recruited a sample of total 430 eligible participants, and observed the crude and adjusted HIV prevalence of 4.6% and 6.6% respectively. The unadjusted prevalence was nearly the same as observed in a study in 2007, using non-probability sampling (convenience sampling) techniques, with HIV prevalence of 4.7% [38].

The recruitment period lasted over 14 weeks, with a maximum wave of 14 and recruited participants with varying self-identified sexual orientations who looked for partners in varying venues. The nine seeds for our study were selected non-randomly, based on their differing sexual orientations, cruising areas and ages. However, the findings of our study

suggested that using RDS with a small number of seeds recruited from non-random, well-defined venues, successful recruitment of participants from a broader spectrum was feasible. This reflected the Markov theory that biases introduced into a chain referral sample by the non-random selection of an individual (seed) are weakened with each recruitment wave and are ultimately eliminated [39,40]. As recruitment continued, the participants were gradually distant from the seeds.

We found that the majority of the participants were recruited by someone in their own personal social network (96.3%). The majority (90%) responded because they wanted to be tested and treated (if required) for HIV, syphilis and HCV. We accept that the diversity demonstrated in our study did not ensure representativeness, due to the fact that there was always a higher likelihood for selection of more concerned and compliant participants.

The variables of interest reached equilibrium and a relatively small number of waves were needed to yield sufficient sociometric depth to attain an equilibrium distribution. To reach the equilibrium of self-identified sexual orientation, marital status, residency, proportion of syphilis-positives and education levels, we needed to enroll seven, seven, six, seven, five, and ten waves, respectively.

We used homophily scores to analyze the performance of RDS in recruiting diverse samples. Homophily, an index to evaluate whether the study sample from RDS could obtain a diverse sample [25,32], demonstrated that RDS was an effective method to reach

a diverse sample. The cross-recruitment and the related homophily implied that self-identified heterosexual MSM were not closely linked with the MSM networks of other orientations, possibly because most MSM who identified themselves as heterosexuals were money boys. The cross-recruitment among others was substantial, as homophily of them were close to zero, instead of to be too extreme (close to -1 or 1). This implies that recruitment chains did not become trapped within a single group, but instead, crossed group lines. This also meant that although the seeds were limited in some particular characteristics, the entire sample was not trapped within a particular group and we were successful in recruiting a diverse study population.

The distribution of the social network sizes of the participants changed significantly when we adjusted the crude distribution for the sizes of the social networks. Participants with strong network ties with other MSM were demonstrated by the large average social network sizes calculated according to sexual orientation. This might have indicated that social networks were important for distribution of the recruitment coupons and for continuation of recruitment. Therefore, social networks might be a very good medium for propagating HIV and STI prevention programs. The heterosexuals had the largest social network sizes, perhaps because most were money boys (about 6.7% of the participants reported that they were money boys).

Our study was initially designed to have a sample size of 460 but only 430 were actually recruited. However, we found that the backed calculated sample size for several interested

variables were less or equal to 430, which demonstrated that the recruited sample size had met the needs.

We also recognized that our study data have many limitations. First, there was a possibility for information bias, especially recall bias, since many participants may be already diagnosed for STDs or had some STDs symptoms when they were recruited. Secondly, although RDS was feasible in studies of IDUs, FSWs and MSM in terms of recruitment efficiency in the past [27], the data we collected were hard to analyze using conventional statistical software, particularly for univariate and bivariate analyses. We used RDSAT 5.6, which is a software designed specifically for analysis of data collected through RDS. An RDS sample without proper adjustment is nothing more than a very good snowball sample (not a representative sample). However, there might still be potential for bias due to over-sampling participants with large personal networks. In addition, in our study, only 427 (33.1%) of the 1289 coupons distributed were returned, which may introduce selection bias at baseline. The invited participants were came to the STI clinic of Jiangsu CDC for HIV/STDs testing, which may introduce potential selection bias since a big part of the participants were afraid that their statuses were revealed, this could be one reason for the lower return rate of coupons that were distributed. Another potential reason lead to the lower return percentage of distributed coupons is that each coupon was given an expired day, and some potential participants may could not schedule the appointment within the valid period, and did not attend the survey.

To control and reduce the effects of some of those problems, we used the following methods. Four interviewers were trained for the interview to minimize interviewer bias while conducting the face-to-face interviews. We also appointed two persons to check for completion of questionnaires after each interview to minimize errors and inconsistencies. If any error was detected, it was corrected before the participant left the survey site. We believe that due to hidden character of MSM, RDS was the optimal sampling method for our objectives. Further, we used the most advanced methods to adjust the collected data.

VI. Conclusion

This was the first time RDS was used for sampling MSM in Jiangsu Province. Even through the representative of our study may be questionable, and may have had lots of bias, we still found that RDS among MSM in Nanjing was feasible, and RDS could be a potential effective strategy to achieve a diverse sample of MSM. Our study could be a potential guide for other cities in Jiangsu Province and other areas of China to use RDS to gather data from hard to reach populations, like MSM, for serologic and behavior surveillance in future.

VII. Tables

Table 1. Seed characteristics and success of recruitment using RDS

Seed ID	Main venue for meeting partners	Age	Network size	Self-identified sexual orientation	Maximum number of waves	Maximum number of recruits (excepting seeds)	Percent of total participants recruited
A	Bathhouses/spas	44	100	Only Homosexual	6	13	3.1
B	Internet	26	50	Only Homosexual	8	87	20.7
C	Internet	28	35	Only Homosexual	9	65	15.4
D	Restrooms/parks	24	10	Bisexual	3	11	2.6
E	Bathhouses/spas	38	20	Bisexual	13	73	17.3
F	Restrooms/parks	39	2	Only Homosexual	0	0	0.0
G	Bars	41	100	Bisexual	11	86	20.4
H	Bars	32	60	Only Homosexual	11	83	19.7
I	Internet	35	50	Only Homosexual	1	3	0.7

Table 2. Characteristics of the estimation process using RDS, regarding syphilis serostatus

Participants giving referral coupons	Syphilis status of subsequent recruit	
	Infected	Uninfected
Syphilis-positive participants		
Recruitment count	11	41
Recruitment proportion	21.2%	78.8%
Syphilis-negative participants		
Recruitment count	40	328
Recruitment proportion	10.9%	89.1%
Estimated network size	5.6	6.9
Sample proportion, P_s	12.6%	87.4%
RDS-adjusted proportion, P	14.6%	85.4%
t-test for ($P_s - P$)	0.29 ($p=0.45$)	
Equilibrium proportion, P_e	12.1%	87.9%
Absolute discrepancy between P_s and P_e	0.5%	
Standard error of P	2.8%	2.8%
RDS-weight	1.159	0.977
Homophily	0.077	0.251

Table 3. Sexual orientations of the participants

Sexual orientation of person giving referral coupon	The identified sexual status of recruiter				Total
	Only Homosexuals	Mainly Heterosexuals	Bisexual	Undecided	
Only Homosexuals	153 60%	3 1.2%	94 36.8%	5 2%	255 100.0%
Mainly Heterosexuals	1 12.5%	2 25%	5 67.5%	0 0.0%	8 100.0%
Bisexuals	80 52.3%	5 3.3%	62 40.5%	6 3.9%	153 100.0%
Other	5 100%	0 0.0%	0 0.0%	0 0.0%	5 100.0%
Total	239	10	161	11	421
Sample proportion	56.8%	2.4%	38.2%	2.6%	100.0%
Equilibrium proportion	56.7%	2.6%	38.1%	2.6%	100.0%
RDS-adjusted proportion, P	54.7%	1.8%	41.0%	2.5%	100.0%
Standard error of P	0.033	0.008	0.031	0.007	
Homophily	0.111	0.236	-0.012	-1.0	
Estimated network size	7.0	9.3	6.2	7.1	

Table 4. Estimated design effects of certain variables

Study description		Study results				Estimated sample size
N/real sample size	Characteristic	\hat{P}_A	$\hat{V}(\text{RDS}, \hat{P}_A)$	$\hat{V}(\text{SDS}, \hat{P}_A)$	$\hat{Deff}(\hat{P}_A)$	
430	HIV+	0.066	0.00036	0.00014	2.48	425
430	Syphilis+	0.146	0.00062	0.00029	1.87	376
430	Unprotected anal sex	0.705	0.00107	0.00048	2.20	428
430	Homosexual	0.548	0.00107	0.00058	1.85	429
430	College degree or higher	0.583	0.00167	0.00056	2.95	430

Note: the formula for estimation are presented in Appendix B

VIII. Figures

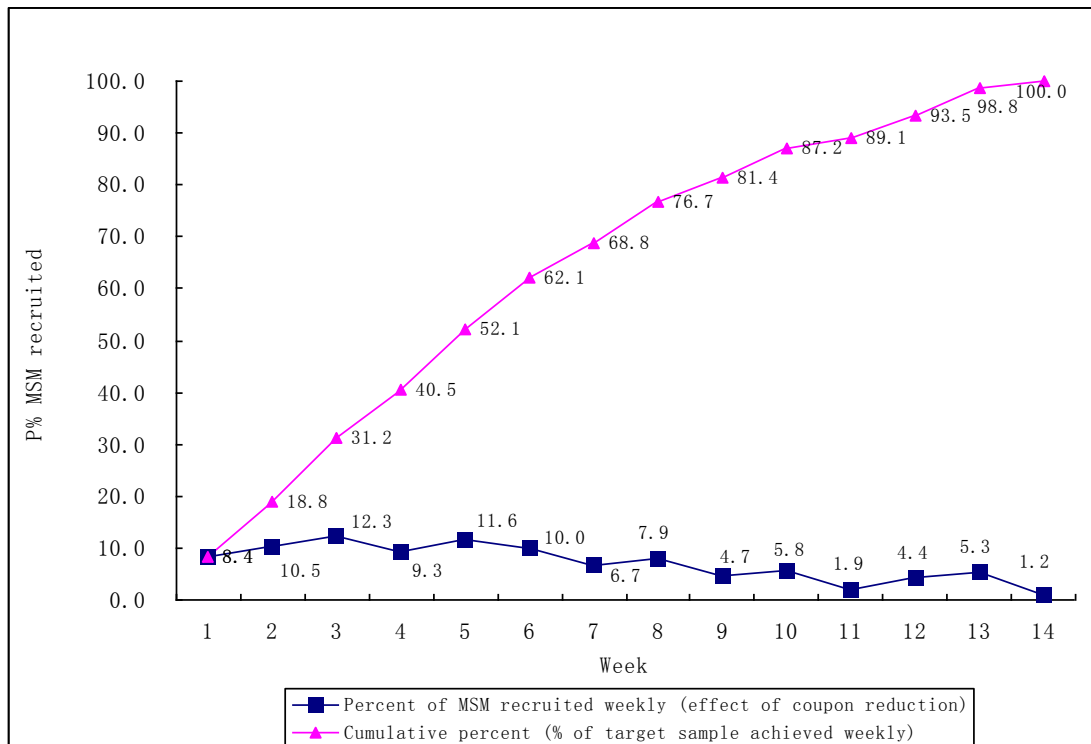


Figure 1. Flow of study participants over the course of 14 weeks, Nanjing, China, 2008.

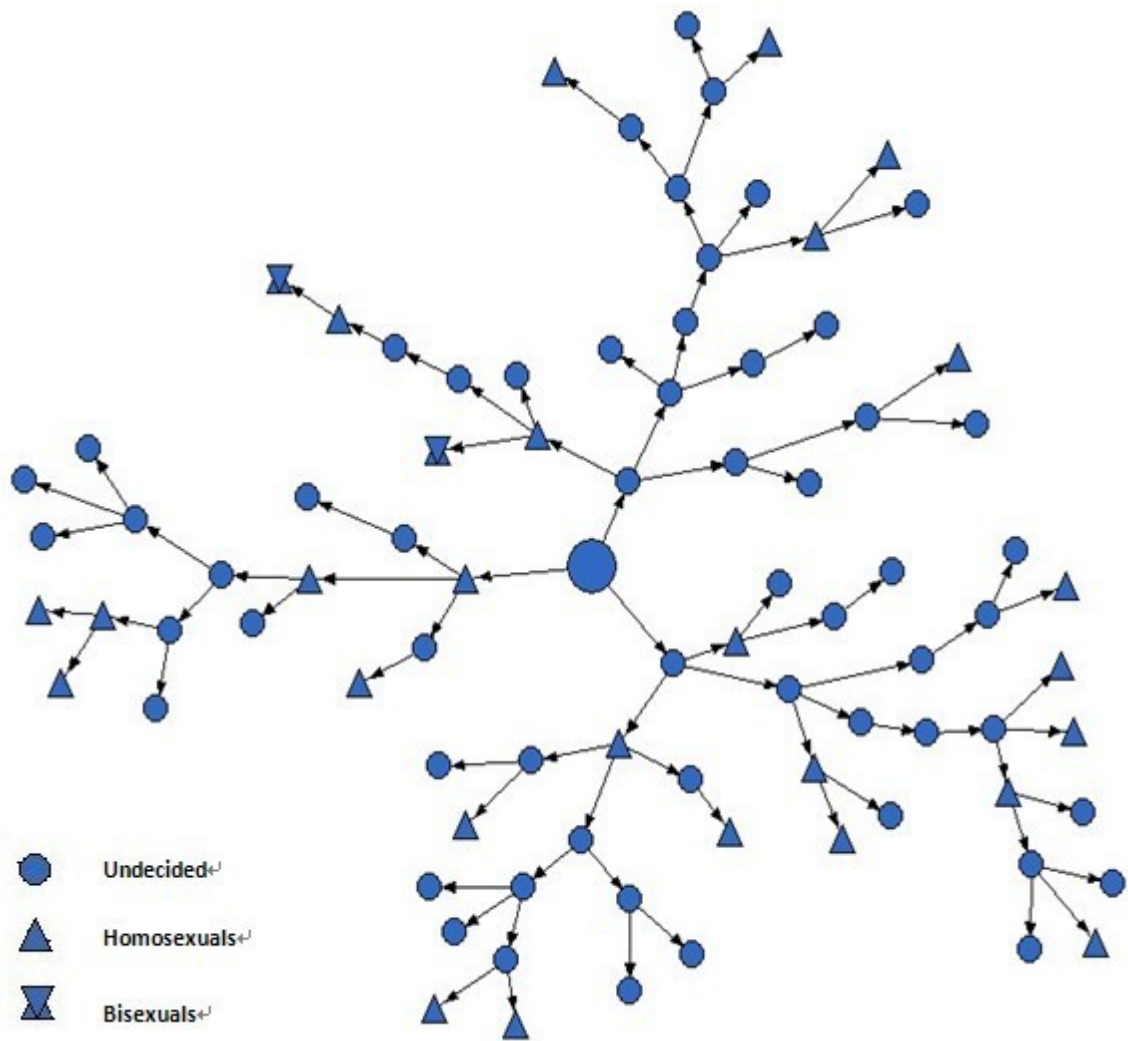


Figure 2. Branching patterns (NetDraw) recruited by most effective seed

Chapter.3: HIV Risk-Reduction Counseling and Testing on Behavior Change of MSM: Results from a Cohort Study in Nanjing, China

I. Abstract

Background: HIV and AIDS incidence in China is high among men who have sex with men (MSM) and ours was one of few studies in China to evaluate the role of HIV risk reduction counseling and testing.

Method: Respondent-driven sampling (RDS) was used to recruit 430 MSM. Participants were followed up at 6, 12 and 18 months to evaluate behavioral changes after counseling to reduce risk behaviors.

Results: At baseline, HIV prevalence was 4.7%, whereas HIV incidence was 5.2 per 100 person-years. The incidence was 3.8 during six to 12 months, and 1.1 during 12 to 18 months. During the study period, the reported unprotected anal intercourse (UAI) significantly decreased from 60.9% to 42.9%. The proportion of participants who had one or no partner significantly increased from 40.9% to 48.0%. The study also found that some risk behaviors decreased between baseline and 12 months, followed by a slight increase between 12 and 18 months.

Conclusion: Reductions in UAI can be achieved through counseling and testing, but may wane over time. Future programs should consider HIV risk-reduction counseling and testing for interventions among MSM in China.

Key words: HIV, sexually transmitted diseases, risk behavior, behavior change, risk reduction counseling, HIV testing, men who have sex with men (MSM), China

II. Introduction

The proportion of HIV infections and AIDS cases is increasing among men who have sex with men (MSM) in China [41-47]. It is estimated that among all the cases, new HIV infections among MSM increased from 12.2% in 2007 to 32.5% and 29.4% in 2009 and 2011 [15,48]. The number of MSM living in China is approximately 2-8 million [49], with data from several major urban areas showing a rapid increase in prevalence of HIV among them. For example, the prevalence increased in Shenzhen from 0.9% in 2002 to 2.7% in 2005 [50], from 0.4% in 2004 to 6.5% in 2007 in Beijing [6,7], and from 10.4% in 2006 to 16.7% in 2008 in Chongqing [8,9]. The HIV epidemic among MSM poses a serious threat to the general population, as MSM may also have unprotected sex with women [51-53]. This trend underscores the need for implementation and evaluation of interventions to prevent the spread of HIV infection from and within this risk group.

In an extensive meta-analysis of interventions for MSM, the authors concluded that individual-level behavioral interventions are effective if done in a short span of time[54]. This review also suggested that interventions are most successful when efforts are incorporated to promote personal management skills for MSM [54]. It has also been documented that targeted interventions including reducing alcohol, drug use, risk sexual behaviors and other environmental risk factors can be useful in addressing the epidemic among MSM [55-57].

Among several potential intervention models to reduce risk behaviors, the transtheoretical model (TTM) of behavior change has shown promising evidence [58] for smoking cessation[59], reduced alcohol use [60,61] and risk sexual behaviors reduction[62,63]. This model uses past behavior and behavioral intentions to assess willingness to make changes [64]. The five stages of TTM are pre-contemplation,

contemplation, preparation, action, and maintenance [65]. Each stage is necessary before the participants can successfully move to the next stage, and the stages cannot be rushed or skipped [65].

Using TTM as a theoretical guide, HIV risk reduction counseling sessions can be tailored to encourage behavior changes among participants. Counseling sessions are recognized as an important strategy to reduce the risk of HIV spread in high-risk groups [66-68]. They are thought to be most effective when they are planned as a collaborative process involving the members of the targeted group [69]. The counseling sessions play a significant role in imparting HIV prevention education, and can clear up misconceptions and misinformation regarding HIV. It is possible that some participants will be concerned about revealing their personal behaviors in the presence of other participants. Therefore, one-on-one HIV risk reduction counseling sessions provide an opportunity for participants to discuss sexual information and risky behaviors in private. The sessions play a role in preparing participants to positively contribute towards reducing their risk for HIV and other sexually transmitted diseases (STDs) [15]. However, few studies have examined the role of counseling in reducing the risk behavior of MSM in China[70].

In 2008, a nationwide study of MSM was conducted in 62 cities across mainland China. The objective of the study was to estimate the prevalence of HIV and syphilis among MSM and understand their behavioral risk patterns.

Respondent-driven-sampling (RDS) was used for sampling in 10 of these cities, including Nanjing. At the Nanjing counseling centre, we assessed the efficacy of behavioral interventions offered in the form of counseling sessions about preventing acquisition of HIV and syphilis. The study explored risk behaviors and determinants of HIV/syphilis acquisition at baseline in Nanjing, China, and assessed the effectiveness of a counseling session in reducing risk behavior at each follow-up round.

III. Materials and Methods

Recruitment

Our study employed respondent-driven-sampling[71]to recruit participants, using 10 seeds selected by non-governmental organizations (NGO) for MSM in Nanjing [45]. 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 with numbered coupons. All recruits were asked to present their recruitment coupons. The original seeds were different in terms of income, age, occupation, and cruising areas. Cruising areas are the venues where MSM look for casual sex partners. Each participant received a packet of lubricant and condoms after being interviewed, and was given a prepaid phone card for each person recruited (up to three). The inclusion criteria for our study were having oral and/or anal sex with a man in the past 12 months, currently living in Nanjing, being at least 18 years old.

Behavioral Measures

A face-to-face interview collected information from participants. In this study, unprotected anal intercourse (UAI) was defined as lack of consistent use of condoms during anal sex with male partners during the past six months. Unprotected vaginal intercourse (UVI) was defined as lack of consistent use of condoms during vaginal sex during the past six months with all female partners. Information was collected regarding details on recruitment patterns of participants, demographic characteristics, knowledge and attitudes about HIV, preventive services, recent sexual behaviors, recreational drug use, and STD-related symptoms and signs. Higher education was defined as having attended junior college or higher. The survey was conducted at the clinic of the Jiangsu Provincial Center for Disease Control and Prevention in Nanjing. All the participants were offered free HIV/syphilis testing.

Intervention

HIV risk-reduction counseling and testing was implemented for each participant at each round. The results of the HIV and syphilis testing were matched to individual records after they were obtained from Jiangsu CDC, China. After completing the questionnaire, the participants were invited to a separate room for risk-reduction counseling with one of the two counselors who had previous experience in HIV voluntary counseling and testing at the Jiangsu CDC. The counselors spent five to ten minutes reading the responses to the questionnaire for the interviewee to understand his risk behaviors. They obtained more specific information by asking additional questions. Subsequently, the counselor conducted a detailed counseling session with the participant stressing the implications of his risk behaviors. The counselor answered all the participants' questions. The intervention was completed by providing knowledge about ways to reduce specific risk behaviors, including number of sexual partners during the past six months, sexual practices (anal, oral, vaginal intercourse), patterns of condom use, alcohol and/or drug use affecting sexual activity, STDs, HIV, exchange of sex for money, and assumptions about partners' risk behaviors. Each participant received free condoms and lubricant, and all HIV-positive participants were referred for standard treatment at the Nanjing Second Hospital.

Follow-up(Cohort)

After the first survey, all of the participants (except those who were HIV-positive, who were referred to HIV/AIDS care programs) were encouraged to attend the surveys conducted at 6, 12 and 18 months after baseline. Gifts worth US \$16 were provided as incentive for each follow-up visit to encourage them to participate. The retention rate was defined as participation in successive rounds compared to the initial round (positive participants were removed from the denominator). For example, the retention rate for the third round was calculated as the number of participants who attended the third round divided by the number of HIV-negative participants in the first round minus

the number of HIV-positive participants in the second round.

HIV incidence was estimated by using the number of sero-conversions within each follow-up period as the numerator and the cohort's total person-year exposures to the risk of HIV transmission within each follow-up period as the denominator. For those who sero-converted, half of the follow-up duration (between two follow-ups) was used as their contribution to the total person time at risk of exposure. The Poisson method was used to estimate the confidence interval of the incidence rates.

Serologic Measures

We have described the serologic measures in detail elsewhere [70]. In brief, before the interview, 5 ml of blood was drawn from each consenting participant to be tested for HIV and syphilis. HIV antibodies were screened using a rapid test (Acon Biotech Co. Ltd). Early studies conducted in China had already successfully used this test [72]. If the result was positive, a western blot was performed to confirm HIV antibody positivity. Syphilis antibodies were screened using Rapid Plasma Reagin (RPR) and confirmed by Treponema Pallidum Particle Agglutination Assay (TPPA). Syphilis positivity was defined as "current" when both TPPA and RPR were positive.

Data Analysis

Data were double-entered using EpiData 3.0 [73]. Logic checking was used to clean the data. We used the Respondent Driven Sampling Analysis Tool (RDSAT) version 5.6 [74] to calculate the population adjusted point estimates and 95% confidence intervals of HIV and syphilis at baseline. The RDSAT model was adjusted for social network size and recruitment patterns. Netdraw version 2.119 [75], a program for visualizing social networks graphic distributions, was used to define the recruitment chains of RDS. Generally, the nodes in the graph reflect the participants, while the arrows reflect the recruitment relationship (the participants at the head of the arrows

were recruited by the participants at the end of the arrow). Each seed had a separate chain. Trend analysis was used to assess trends in behavior changes over time for the follow-up. Trend analysis and basic description analysis were conducted using Statistical Analysis Software version 9.1 [76], and the threshold for statistical significance was set at P value less than 0.05. To test the efficacy of HIV risk-reduction counseling and testing, sensitivity analysis was conducted in this study. In the sensitivity analysis, we removed the prevalent participants and incident participants initially from the baseline and the calculated person years at each subsequent follow-up, and analyzed only HIV negative during the whole follow up period.

Possible effect of loss to follow-up was assessed further by assuming that those who dropped out were different from those who stayed in the study, and that those people did not change their behavior even after dropping out. To estimate this effect, we repeated the analysis by imputing the prior values from last visit for those who were lost to follow-up.

Ethic Statement

Signed informed consent was obtained from each of the participants prior to interview, blood collection and intervention at each round of the surveys. Each of the participants had the ability to decline or withdraw from this survey. The questionnaires and written consent document were separately kept in locked cupboards at the study sites, and unrelated persons could not access on them. The study process and content were approved by the Ethics Committee at Jiangsu Provincial Center for Disease Prevention and Control.

IV. Results

The study was conducted between May 2008 and January 2010. Four hundred and thirty participants (including the 10 seeds) completed the first survey. Only 33.1% (427) of the 1,289 distributed coupons were returned. Table 1 presents the demographic characteristics of the participants. About 70.2% of the participants were 21 to 35 years old, about 28.9% (124 participants) were students, but only 18.8% were married. Two-thirds had higher education.

At the baseline survey, crude HIV and syphilis prevalence rates were 4.7% and 11.9%. 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 the recruitment networks at the baseline survey and the waves and networks of participants, as well as the distribution of HIV-positive participants among all the participants. Convergence was reached between the sample composition (4.7% with HIV) and the equilibrium sample composition (4.9% with HIV) (Table 2). Table 2 also demonstrates that the network size (average 30.4) for HIV-positive participants was much larger than for HIV-negative participants (average 19.8).

Figure 2 shows recruitment of MSM by RDS, number of HIV-seropositive participants, retention rates, and loss-to-follow-up during each follow-up. The retention rate at six months was 69.0%, 62.2% at 12 months, and 44.6% at 18 months. There were 20, 7, 5 and one HIV-positive participant(s) at baseline, six months, 12 months and 18 months, with an HIV incidence rate at each round of 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 3, Figure 3).

At baseline, 40.9% of participants reported that they had no more than one male

partner (either regular or casual) in the past six months, which increased to about 48.0% by the end of the study (P-value for trend 0.03; Table 4). Also, 60.9% of the participants reported UAI in the past six months at baseline, which decreased to 42.9% by the end of the study (P-value for trend <0.001). The results were statistically significant for increased sexual encounters with regular partners and decreased sexual encounters with casual partners (P-values for trend 0.02 and <0.001). Table 3 explains the results of sensitivity analysis, which imply similar results as compared to inclusion of HIV positive participants as mentioned above. Figure 4 presents the trend of UAI among regular and casual partners, and the percentage who also had sex with women. The percentage engaging in UAI with regular and casual partners decreased between baseline and 12-months; however, it increased between 12 and 18 months. There was not much change in the proportion of MSM having sex with women and UVI. The greatest decreases in risk behaviors were observed between baseline and the initial six months.

We tested whether the results would change after accounting for loss to follow-up by imputation, by assuming those who dropped out did not change their risk behaviors. The results are provided in Table 5, which indicates that even after imputation, the decrease in UAI among participants was significantly reduced from 60.9% to 46.2% (P-value for trend <0.001), and engaging in UAI with regular and casual partners significantly decreased from 73.7% and 52.6% to 57.4% and 38.9%, respectively. The trend analysis with imputation indicated decreased risk behaviors between baseline and 12 months, but an increase between 12 and 18 months.

We further tested whether the participants who attended both baseline and all the follow up surveys changed their behaviors during the study period. Overall, there are 177 meet this definition. Among these 177 participants, UAI was significantly reduced from 60.5% to 42.9% (P-value for trend <0.001), and engaging in UAI with regular and

casual partners significantly decreased from 72.5% and 55.9% to 53.7% and 37.3%, respectively. Significantly decreasing was also observed for had anal sex with a man in the past six months, paid for sex in the past six months, had anal sex with a man in the past six months.

V. Discussion and Conclusions

Overall, our study found that reported UAI significantly decreased, from 60.9% to 42.9%, during the study period. Further, UAI with casual and regular partners in the past six months was significant reduced by 15.3% and 20.0% respectively. By taking those participants who attended both baseline and all the follow up surveys, significant behavior change for UAI was also observed. Similar results for UAI were documented in an randomized control trial by Chun Hao in China in 2008 [70]. Comparing with other studies used risk-reduction counseling as intervention strategies among MSM, the results of our study were similar to the findings of the EXPLORE randomized controlled study (our study followed the similar intervention protocol as this study), which found an overall 20.5% UAI reduction in the intervention group[55]. Also, compared to one study conducted in Auckland, New Zealand[77], our study found much higher UAI reduction rate; however, these reductions were lower than one study conducted in San Francisco, USA[78]. Also, this is the first exploration of whether reductions in UAI occur in MSM who undergo private HIV risk reduction counseling in China. This is also the first cohort study examining risk reduction behaviors in MSM in China.

The results of our study also showed that the proportion of participants who reported no partner in the past six months significantly increased. To our knowledge, this is the first time that HIV risk reduction counseling was tested in China as an intervention for reducing numbers of sexual partners. In addition, our study demonstrated that the proportion reporting sex with regular partners in the past six

months increased, while the proportion reporting sex with casual partner decreased. There was a decreasing trend of some risk behaviors from baseline to the 12-month follow-up, but not between 12 and 18 months, suggesting waning effectiveness of counseling and testing.

The underlying transtheoretical model of behavior change may explain some of the failure in achieving complete reduction of risk behaviors. According to this theory, there are five stages for behavior change, including pre-contemplation, contemplation, preparation, action, and maintenance. Achieving change in behavior is arduous, as each stage is necessary before moving on to the next. These stages cannot be hurried or skipped [79]. This process can take a long time and may involve cycling back through earlier stages before moving on to the next stage.

The wane of some behaviors in our study may be the potential results of this, even we did not the levels of the behavior change for each participants[80-82]. It is also possible that during the follow-up period, negative reinforcement of risky behavior occurred, which we were unable to identify [71]. It might be contended that the results are due to HIV positive participants, which may have higher risk behavior. However, the results of sensitivity analysis indicated that results did not change much despite including of HIV positive participants supporting the conclusion that the behavior changes of the participants could be due to the intervention and testing.

There are other important results from this study. The crude HIV and syphilis prevalence at baseline were 4.7% and 11.9%, respectively. These Prevalence was lower than estimates from other cities in China [7,8]. The HIV and syphilis prevalence and incidence in Nanjing (overall 3.6 per 100 person-years during the entire follow-up) call for planning intervention programs targeting MSM in Nanjing. Reduction of HIV incidence rates in Nanjing during the follow-up period (from 5.2 per 100 person-years

to 1.1 per 100 person-years) supported the hypothesis that risk behaviors of the participants changed during the study period..

The strengths of the study include its use of RDS to access members of the otherwise hard-to-reach populations in a demographically diverse sample[71]. This is the main difference between our study and some previous studies. Convenience sampling (or targeted sampling), and time-space sampling are the main sampling strategies that were used by the earlier studies [55,83-85]. However, these methods often fail to let the researchers make accurate estimates about a hidden population[86]. Also, a report released by WHO demonstrated that standard sampling and estimation techniques do not have the ability to monitor the behavior and HIV sero-prevalence of at-risk subpopulations, such as MSM [87]. RDS was designed address this problem even in the studies with lower response rate and high loss to follow up. By combining of these two methods (RDS and standard HIV risk-reduction-counseling and testing), the study aids in updating current knowledge about the effectiveness of HIV risk-reduction-counseling and testing. In addition, this is the first time in China that follow-up study is done using RDS for initial recruitment and hence important to report in addition to exploring further whether further studies demonstrate the success of HIV risk-reduction and counseling in China.

The use of biological markers of HIV and syphilis infection is also a potential strength of our study. A follow-up study monitored the change of risk behaviors of the participants. Also, compared with other studies, including several studies targeted at MSM [23-26,[77,88,89], longer intervention and follow up time is another important strength of our study. Besides these, all the HIV sero-positive participants were referred to the standard care and treatment program running by Chinese CDC. All diagnosed persons with syphilis were referred and treated at the STD clinic at our study site.

The major limitations of our study were the low response rate and high rate of loss to follow-up. The loss to follow up, in the initial period from baseline to 6 months might bias the results, which in turn may potentially affect the validity of our results. However, this is possible only if the loss to follow up was differential (the loss to follow up was associated with exposure and outcome)[90]. It might be possible that those who were lost to follow up might have higher HIV incidence rate or UAI rate than those consistently participated, in which case the loss to follow-up might have overestimated the association that we measured. However, it is more likely that it is not associated outcome of interest as the participants migrated out of the study due to their temporary engagement in Nanjing due to their occupation or otherwise (52.8% from baseline to 6 months), in which case, the loss to follow-up is non-differential and hence may or may not underestimate the results. Without additional information, we cannot conclusively predict the direction of the bias nor can this bias be adjusted in conventional analysis. Future studies might provide more evidence regarding the behavior of MSM population and how their loss to follow-up might affect the hypothesis of interest.

There are several potential reasons for the higher lost to follow up rate. First, about one-fifth of the participants were students who graduated from university and subsequently moved away from Nanjing during the study period, and were not accessible. The number of students at the end of the study was only 30, compared to 124 students at the beginning of follow-up. Second, lack of adequate funding limited our ability to continue to trace the participants for further follow-up. Frequent migration between different cities makes tracking of participants a challenging task (among the 127 participants who were lost to follow-up at the six months follow-up, 67 had already moved to other cities and could not be reached) [91].

We performed imputation analysis to explore the sensitivity of results to loss to follow-up by assuming that the participants lost to follow-up continued the same behaviors as in the immediate previous round of follow-up. This strategy assumes that there was no effect of the intervention on behavior change among those lost to follow-up, and thus biases the results towards the null; in addition, the HIV and syphilis incidence were higher among those who lost to follow up. Behaviors were self-reported and were thus subject to desirability bias. However, the drop in HIV and syphilis incidence suggests that the reported changes were real.

Another limitation of our study was that only 427 (33.1%) of the 1289 coupons distributed were returned. Even though the low response rate is common in such studies and is consistent with other RDS surveys [92,93], the low response rate may result in limiting generalizability to MSM population. The participants who attended the survey may be different from those who unwilling to come. Also, we could not address this by data analysis as no information was available regarding those who refused.

The absence of a suitable cohort of control participants is a limitation for our study. It is possible that sources of information other than counseling might be available, such as national media campaigns or learning from friends. We also could not evaluate the impact of this program on risk behaviors because we lacked a control group who did not receive counseling and testing. We therefore advice caution for making causal inference from our study, as we could not rule out the other probabilities that lead to the behavior change of the participants. Randomization is the gold standard and our inability to have such comfort is another limitation of our study due to which uncontrolled confounders might have affected our results. We have included all the known confounders; however, might have missed out those not identified by prior literature or based on our contextual knowledge regarding their role in possible causal

association. Besides these, the participants recruited in our study may be more compliant, since the main reason for them to attend the study was to get test. The HIV and syphilis incidence and prevalence of the participants in our study could be lower than they in the source population. However, the HIV prevalence reported in our study was similar with the findings of a cross-sectional study conducted in Nanjing in 2007.

We used certain methods to minimize the bias. Four specially trained interviewers used a standardized protocol consistently throughout the study. Well-trained CDC staff conducted the interviews and interventions. Quality assurance was enhanced by having two separate workers check each questionnaire carefully. We analyzed loss to follow-up by performing imputation analysis when assuming that there were no significant changes in behavior after loss to follow-up. We further analyzed only those participants who attended both baseline and all follow up surveys to test whether behaviors were changed among them.

Despite the limitations, our study suggests that HIV/STD risk-reduction counseling and testing is an effective method to reduce the risk behaviors of MSM and prevent new HIV/STDs in the short term, but may require continued intervention to assure maintenance. In addition, the higher HIV/syphilis prevalence and incidences in our study call for more surveillance programs to monitor the future HIV/syphilis epidemic as well as the risk behaviors of MSM in Nanjing. It is important to screen all the MSM for syphilis and ensure treatment to affected persons irrespective of risk reduction interventions.

VI. Tables

Table 1. Demographic characteristics of MSM at baseline in Nanjing, China, 2008 (n=430)

	Sample (n)	Crude %	Adjusted % (95%CI)		Sample (n)	Crude %	Adjusted % (95%CI)
Age				Education level			
≤20 years	49	11.4	11.5 (7.9, 15.9)	<i>Illiterate or elementary school</i>	5	1.2	0.7(0.1, 1.9)
21-35 years	302	70.2	59.5 (62.5, 75.5)	<i>Junior high school</i>	38	8.8	15.5(9.3, 21.1)
36-50 years	71	16.5	16.6 (11.2, 22.8)	<i>Senior high school or technical secondary school</i>	99	23.0	25.4(20.3, 31.4)
51 or older	8	1.9	2.4 (0.5, 5.2)	<i>Junior college or higher</i>	288	70.0	58.3(50.3, 66.4)
Marital status				Residence			
<i>Single, divorced or widowed</i>	349	81.2	73.0(65.6, 80.0)	<i>Nanjing</i>	251	58.4	47.9(41.5,54.9)
<i>Married</i>	81	18.8	27.0(20.0, 34.4)	<i>Not in Nanjing</i>	179	41.6	52.1(45.1, 58.5)
Occupation				Monthly income (RMB)			
<i>Student</i>	124	28.9	18.5(12.0,22.2)	<i>≤2000</i>	137	31.8	25.4(18.7, 31.2)
<i>Worker</i>	22	5.0	8.4(5.0,15.0)	<i>2001 - 4000</i>	189	44	48.1(42.3, 55.7)
<i>Staff</i>	89	20.7	26.7(20.3,32.5)	<i>4001 and above</i>	104	24.2	26.5(20.5, 32.3)

Table 2. Reported rates and status of HIV testing among MSM, in Nanjing, China, 2008 (n=420 *)

Variables	HIV status of participants	
	HIV-positive	HIV-negative
Number of participants recruited by HIV-positive participants (%)	2 (12.5%)	14 (87.5%)
Number of participants recruited by HIV-negative participants (%)	18 (4.5%)	386 (95.5%)
Estimated network sizes	30.4	19.8
Sample proportion, P_s	0.04	1.0
Equilibrium proportion, P_e	0.04	1.0
RDS-adjusted proportion, P	0.07	0.9
Absolute discrepancy between P_s and P_e	0.002	
Standard error of P	0.02	0.02
RDS-weight	1.4	1.0
Homophily	0.06	0.3

*When analyzing the total distribution of recruitment between HIV-positive and -negative participants, the RDSAT dropped the 10 seeds from the analysis automatically, since the seeds were selected by researchers, not recruited by participants.

Table 3, 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	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	132.4	5.0	3.8	91.7	1.0	1.1	358.6	13.0	3.6
Syphilis	117.8	12.0	10.2	117.1	2.0	1.7	80.0	3.0	3.7	315.6	17.0	5.4

Table 4. The trend of HIV-related knowledge and reported risk behaviors of the participants in Nanjing, China, 2008-2010.

Variables	Trend analysis					Sensitivity analysis				
	Baseline (N=430)	six months (N=283)	12 months (N=249)	18 months (N=177)	P for trend	Baseline (N=397)	six months (N=270)	12 months (N=243)	18 months (N=176)	P for trend
Knowledge	90.2%	95.8%	94.8%	94.9%	0.01*	91.0%	95.9%	95.0%	94.9%	0.04*
One or no partner	40.9%	47.7%	52.4%	48.0%	0.03*	41.5%	48.1%	52.1%	47.7%	0.06
UAI (unprotected anal sex)	60.9%	49.1%	39.9%	42.9%	<0.001*	59.5%	49.6%	40.1%	42.6%	<0.001*
UVI (unprotected vaginal sex)	17.2%	12.7%	14.9%	13.6%	0.4	17.0%	12.2%	14.5%	13.1%	0.3
Had anal sex with a man in the past six months	88.1%	90.1%	81.8%	85.1%	0.03*	88.0%	90.0%	83.8%	85.1%	0.2
Paid for sex in the past six months	5.3%	3.5%	2.8%	1.1%	0.09	5.7%	3.7%	2.9%	1.1%	0.06
Was paid by another man to have sex in the past six months	6.3%	1.1%	0.8%	0.0%	<0.001*	6.3%	1.1%	0.8%	0.0%	<0.001*
Had sex with women in the past 6 months	24.7%	19.4%	19.0%	20.3%	0.2	24.8%	19.3%	18.2%	19.9%	0.2
Had sex with regular partner in the past six months	66.2%	73.3%	78.2%	73.3%	0.02*	65.1%	73.3%	78.3%	73.2%	0.006*
UAI with regular partner in the past 6 months	73.7%	56.1%	47.7%	53.7%	<0.001*	72.9%	56.2%	47.0%	53.3%	<0.001*
Had sex with casual partner in the past six months	66.8%	62.4%	47.6%	57.8%	<0.001*	66.8%	62.1%	47.8%	58.2%	<0.001*

UAI with casual partner in the past six months	52.6%	41.5%	31.1%	37.3%	0.001*	51.1%	43.0%	31.5%	37.3%	0.007*
Last sexual partner for anal sex was a regular partner	54.1%	62.4%	68.0%	64.7%	0.005*	54.3%	62.1%	68.0%	64.4%	0.008*

* Significant differences between groups

Table 5. The trend of HIV-related knowledge and reported risk behaviors after imputation in Nanjing, China, 2008-2010

Variables	Baseline (N=430)	six month (N=410)	12 months (N=403)	18 months (N=398)	P for trend
Knowledge	90.2%	93.7%	93.8%	94.0%	0.1
One or no partner	40.9%	45.4%	47.9%	46.2%	0.2
UAI (unprotected anal sex)	60.9%	50.2%	45.9%	46.2%	<0.001 [*]
UVI (unprotected vaginal sex)	17.2%	15.4%	16.4%	16.3%	0.9
Had anal sex with a man in the past 6 months	88.1%	89.3%	86.1%	84.8%	0.2
Paid for sex in the past six months	5.3%	3.6%	3.1%	2.3%	0.2
Was paid by others to have sex in the past six months	6.3%	5.6%	5.4%	5.5%	0.9
Had sex with women in the past six months	24.7%	23.7%	22.6%	23.1%	0.2
Had sex with regular partner in the past six months	66.2%	69.7%	72.9%	71.2%	0.2
UAI with regular partner in the past 6 months	73.7%	58.8%	53.7%	57.4%	<0.001 [*]
Had sex with casual partner in the past six months	66.8%	64.2%	56.2%	61.1%	0.02 [*]
UAI with casual partner in the past six months	52.6%	41.3%	38.0%	38.9%	0.005 [*]
Last sexual partner for anal sex was a regular partner	54.1%	67.9%	61.7%	60.8%	0.2

^{*} Significant differences between groups

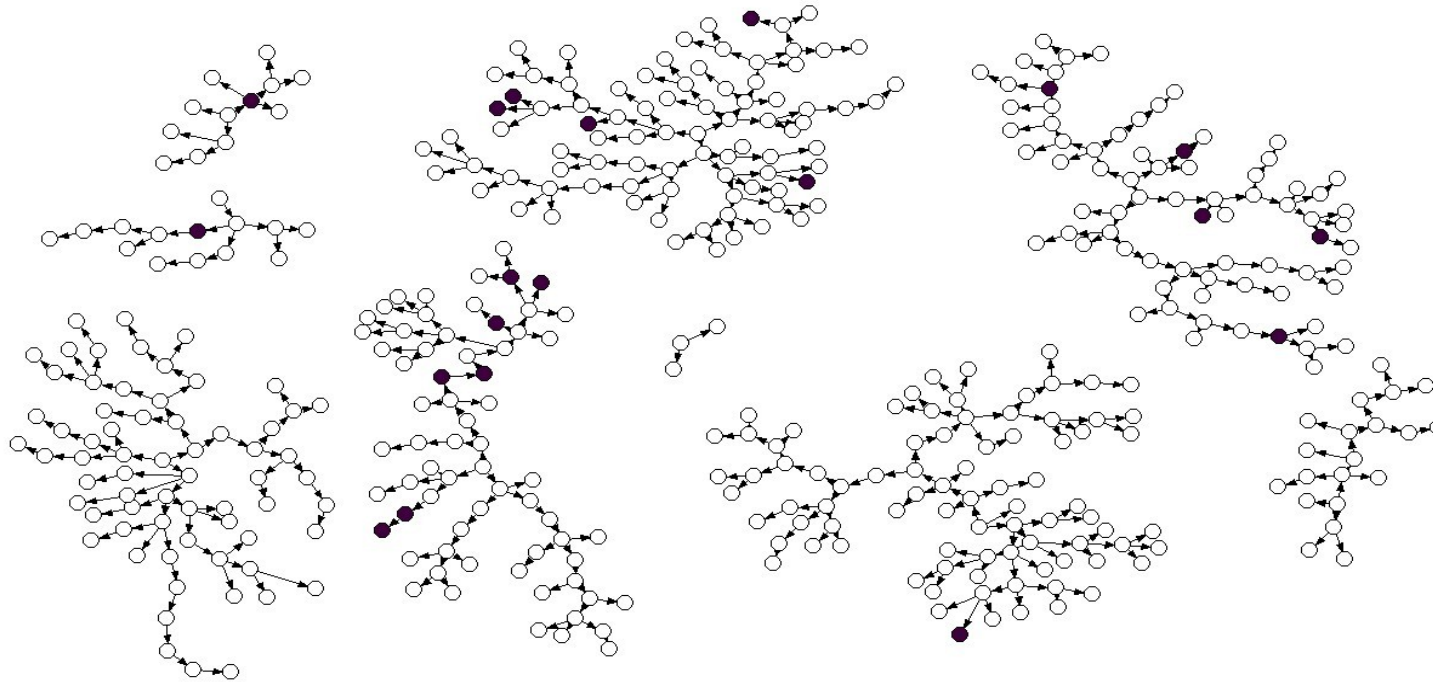
Table 6. The trend of HIV-related knowledge and reported risk behaviors of the participants in Nanjing, China, 2008-2010.

Variables	Trend analysis [§]				
	Baseline (N=177)	six months (N=177)	12 months (N=177)	18 months (N=177)	P for trend
Knowledge	92.7%	95.8%	93.2%	94.9%	0.56
One or no partner	46.3%	48.2%	54.8%	48.0%	0.40
UAI	60.5%	48.8%	36.2%	42.9%	<0.001 [*]
UVI	15.3%	13.7%	15.8%	13.6%	0.91
Had anal sex with a man in the past six months	88.1%	88.1%	78.4%	85.1%	0.04 [*]
Paid for sex in the past six months	7.1%	1.8%	3.4%	1.1%	0.01 [*]
Was paid by another man to have sex in the past six months	0.6%	1.2%	1.1%	0.0%	0.54
Had sex with women in the past 6 months	20.3%	19.0%	20.3%	20.3%	0.99
Had sex with regular partner in the past six months	69.9%	70.9%	79.9%	73.3%	0.22
UAI with regular partner in the past 6 months	72.5%	56.2%	45.9%	53.7%	<0.001 [*]
Had sex with casual partner in the past six months	65.4%	64.2%	46.0%	57.8%	<0.001 [*]
UAI with casual partner in the past six months	55.9%	42.1%	28.6%	37.3%	0.004 [*]
Last sexual partner for anal sex was a regular partner	56.4%	59.5%	69.8%	64.7%	0.09

^{*} Significant differences between groups

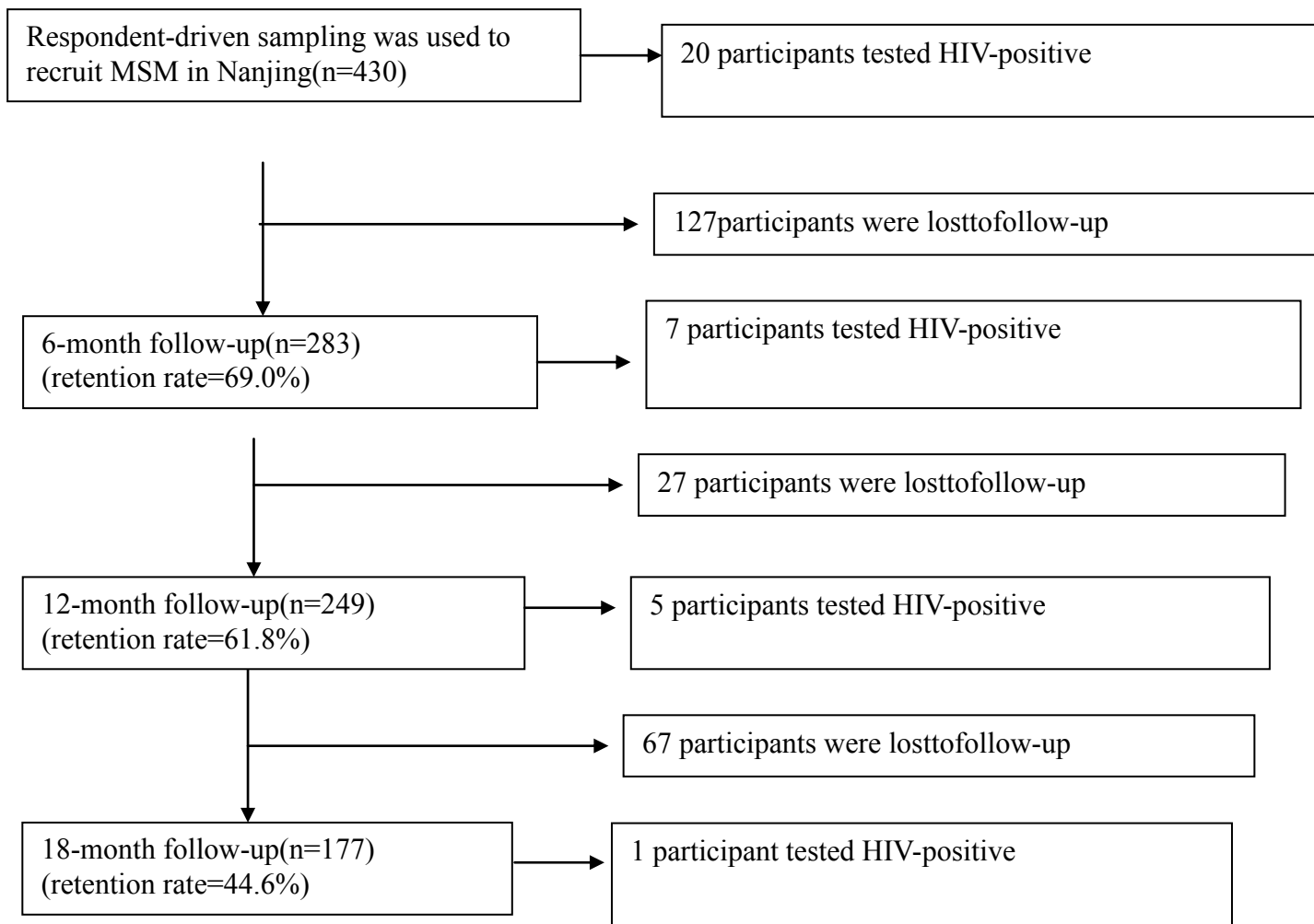
[§] The behaviors of the 177 participants who attended both baseline and all the follow up surveys

VII. Figures



Black circles represent HIV-positive and white circles represent HIV-negative participants. One seed who did not recruit any other participants and was dropped from this figure.

Figure 1. Respondent-driving sampling for cross-recruitment of MSM who were HIV-positive or negative in Nanjing, China, 2008 (N=430)



This trial profile describes recruitment of MSM by RDS, and includes enrollment, number of HIV-seropositive participants, retention, and loss to follow-up during each follow-up.

Figure 2. Enrollment, follow-up, and outcome of the participants in Nanjing, China, 2008-2010

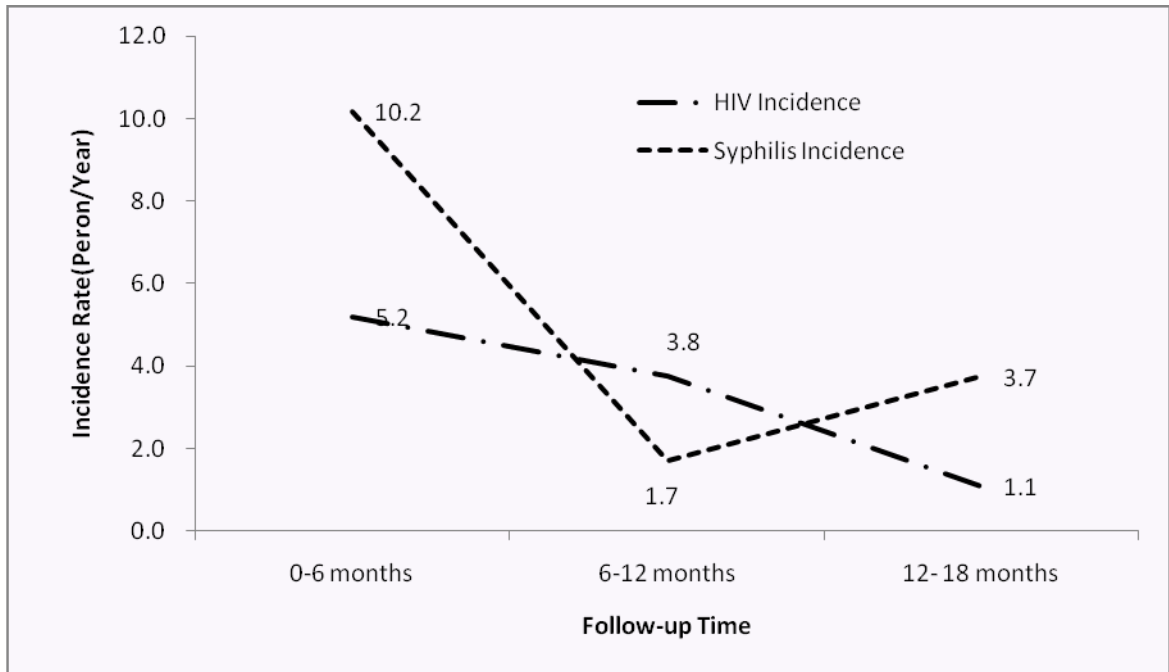


Figure 3. The trend of HIV and Syphilis among MSM in Nanjing, China, 2008-2010

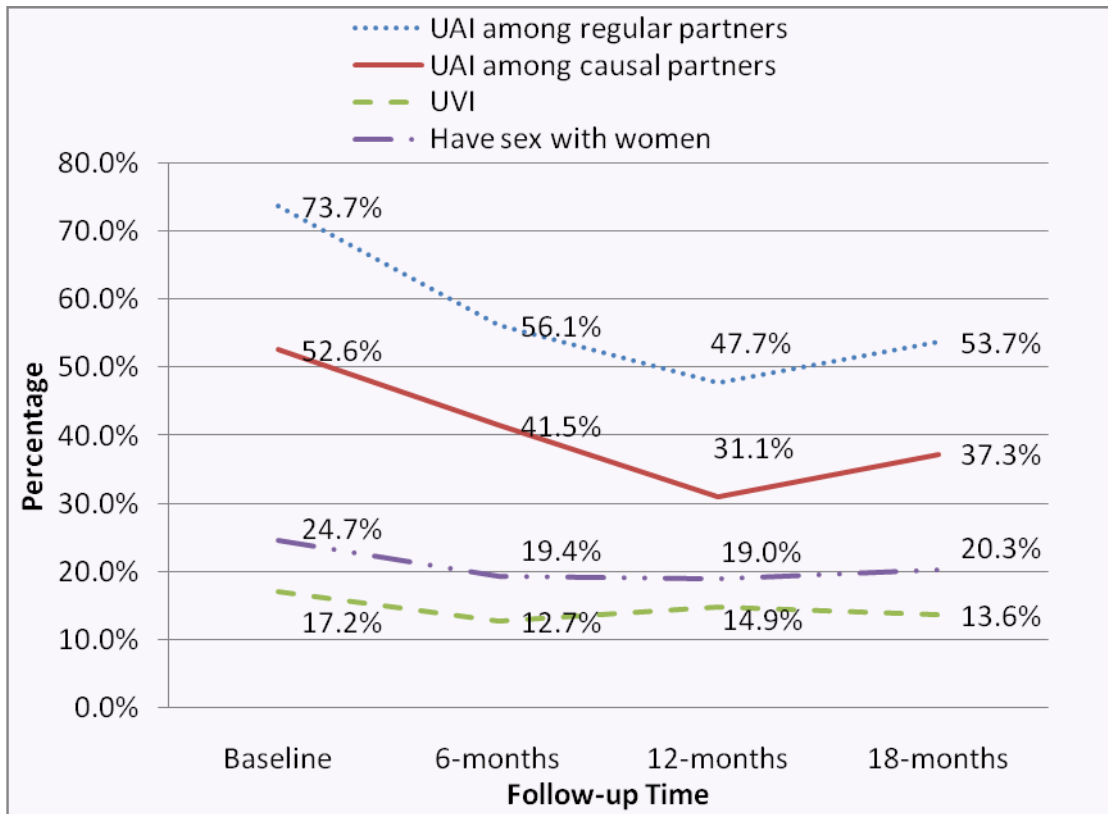


Figure 4. The trend of UAI among regular and casual partners and UVI with women in Nanjing, China, 2008-2010

Chapter 4 Factors Associated with Loss-to-Follow-Up in a Cohort Study in Nanjing, China

I. Abstract

Background: Non-adherence or loss to follow up of the participants in follow up studies usually reduces the validity of the association measured in observational studies, and this problem cannot be overcome through data analysis processes.

Methods: RDS was used to recruit participants, for an intervention that all the HIV negative participants were encouraged to attend the follow up surveys, and logistic regression was performed to identify the factors correlated with loss to follow up.

Results: Loss to follow up for the MSM study in Nanjing was associated with younger age, small social network, lower education, and non-official residence in Jiangsu.

Conclusion: The findings of this study may be helpful to increase the retention rate of future cohort studies, thereby reducing the potential bias introduced by loss to follow up.

II. Introduction

In order to measure the incidence of a disease or to evaluate the effectiveness of an intervention method, follow up studies (either random clinical trial or cohort) are usually used [90,94]. One key issue in these kinds of studies is the non-adherence or

the loss to follow up of the participants.

The loss to follow up may cause those who stayed in the study to be different from those who dropped out, which not only introduces bias, but also reduces the precision and power of the study by lowering the number of participants for analysis[95,96].

Previous studies have demonstrated that the differential loss to follow up usually reduces the validity of the association measured in observational studies, and this problem cannot be overcome through data analysis processes[97-99]. These problems are particularly serious for follow up studies that are conducted among hard to reach populations, e.g. men who have sex with men (MSM) [100].

Sensitivity analysis can be used to estimate the magnitude of the bias caused by loss to follow up on the effect/association measures, and it can also be used to assess the degree of uncertainty of the study results[101,102]. However, the bias that is introduced by loss to follow up is a complex problem, and sensitivity analysis can only deal with a small part of the problem. In addition, sensitivity analysis is usually based on strong assumptions which often cannot be tested, but depend on reports in the literature. Sensitivity analysis produces a range of values that could result from different levels of bias due to drop out, non-compliance or missing values. By using sensitivity analysis, the researchers are able to back calculate and estimate the range within which the true effect/association measure lies.

Since the bias that is introduced by loss to follow up cannot be controlled in the data analysis process, prevention of loss to follow up by use of an appropriate study design, sample selection and follow up strategies is important. Thus, to identify factors correlated with loss to follow up in follow up studies would help us to improve the design of future studies employing more effective follow up strategies, which could reduce the bias due to the loss to follow up. In addition, by testing the relationship between loss to follow up and different variables, we could adjust the potential bias caused by loss to follow up in sensitivity analysis.

The objective of the study reported herein was to identify the factors associated with loss to follow up in an intervention study conducted among MSM in China, in order to provide guidelines for future studies, which could increase their retention rate and reduce the bias caused by loss to follow up.

III. Methods

To identify the predictors for loss to follow up, an integrated behavioral and serologic intervention study targeted at MSM was conducted in Nanjing, China.

Study Design and Sampling Methods

Detailed methods of our study are described elsewhere[103,104]. In brief, respondent-driven sampling (RDS) was used to recruit participants who were eligible

(reporting having had oral and/or anal sex with men during the past 12 months, aged 18 years or older, and who had not participated in a similar survey within the past 3 months). Overall, 10 seeds who were diverse in terms of income, age, occupation, and “cruising areas” were select to initiate the recruitment. All the interviews and biological samples were obtained at the STD clinic of the Jiangsu Provincial Center for Disease Control in Nanjing.

Demographic and behavioral Measures

Face-to-face interviews were used to collect information (demographic and behavioral measures) from the study population. In our study, social network size was defined on the basis of the reported number of MSMs the participants knew (knew the person’s face and name/nickname, had his contact information and could get in touch with him within the next month). If the participants had any of the following signs or symptoms: burning pain when urinating, genital discharge, and ulcer/sores on penis/anus, they were considered to have a sexually transmitted infection (STI).

After the baseline survey, all the HIV negative participants were encouraged to attend the follow up surveys conducted at 6, 12 and 18 months. All HIV positive participants who tested sero-positive at baseline and at each follow up round were introduced to the national free treatment programs and were no longer followed in the cohort. In our study, the participants who met either of the following situations were defined as meeting the criteria for consistent participation: 1) the participants who attended

baseline survey remained HIV sero-negative and attended all the three following visits;

2), the participants who sero-converted to HIV during the follow up period.

Non-consistent participation or loss to follow up status was assigned to the participants if they did not complete one or more of the follow up visits. The participants who tested syphilis positive but remained HIV negative were continued to be followed in our study.

Cruising areas/venues, knowledge, and coverage of HIV preventive services have been reported previously[103,104].In brief, cruising areas/venues were categorized as conventional venues (specifically, gay bars, parks, massage parlors, spas, saunas, and the internet) or non-conventional venues (specifically, meeting partners on campuses, introduced by friends, etc.).

Serologic Measures

5.0 ml of blood was drawn from each participant for HIV and syphilis testing. Initial screening of the subjects for the presence of HIV antibodies was done using a rapid test (Acon Biotech Co. Ltd). Positive results were confirmed by Western blot (HIVBLOT 2.2, Genelabs Diagnostics, Singapore). The subjects were screened for syphilis antibodies with the Rapid Plasma Reagin test (RPR) (Beijing Wantai Biological Pharmacy Enterprise Co. Ltd) and confirmed by the Treponema Pallidum Particle Agglutination assay (TPPA; Livzon Group Reagent Factory). Syphilis positivity was defined as “current” when both TPPA and RPR were positive. The HIV

and syphilis results were given to the participants after the interviews.

A signed informed consent was obtained from each participant prior to the interview and blood collection. The survey protocol was approved by the Institutional Review Board of the Jiangsu Provincial Center for Disease Control and Prevention (JSCDC).

Intervention

HIV risk-reduction counseling and testing was implemented for each participant at each round. After completing the questionnaire, the participants were invited to a separate room for risk-reduction counseling with one of the two counselors who had previous experience in HIV voluntary counseling and testing at the Jiangsu CDC. The counselor conducted a detailed counseling session with the participant stressing the implications of his risk behaviors. The counselor answered all the participants' questions. The intervention was completed by providing knowledge about ways to reduce specific risk behaviors, including number of sexual partners during the past six months, sexual practices (anal, oral, vaginal intercourse), patterns of condom use, alcohol and/or drug use affecting sexual activity, STDs, HIV, exchange of sex for money, and assumptions about partners' risk behaviors.

Statistical Methods

Data were double-entered using EpiData 3.0[73]. Logic checking was used to clean the data by using Microsoft Excel. SAS statistical analysis software version 9.1 [76]

was used to describe the demographic and sexual behaviors for participants who were defined as lost to follow up and consistent participation, respectively. To determine the predictors for lost to follow up, we used logistic regression to perform univariate analysis (odds ratio, 95% confidence intervals (CI), followed by the multivariate analysis, with the status of participation (lost to follow up) as the dependent variable. Independent variables were age, cruising venue/area, marital status, official residency status, education, income, occupation, sexual orientation, unprotected anal sex (UAI), unprotected vaginal sex (UVI), HIV knowledge, engagement of HIV preventive services, STI-related symptoms and signs, social network size, and syphilis. Variables with a P-value of less than 0.3 in univariate analysis were included in the multivariate analysis.

IV. Results

Overall, 430 participants, including 20 sero-positive participants, attended the baseline survey which was conducted during May to August in 2008. After the baseline survey, the 410 sero-negative participants were invited and encouraged to participate in the intervention study. During the 18 months follow up, a total of 221 (53.9%) participants missed one or more follow up visits. In our study, thirteen participants sero-converted to HIV positive during the follow up period.

Table 1 represents the demographic characteristics, behaviors, STI signs or

symptoms and syphilis prevalence for the participants who were lost to follow up and for the participants who consistently participated in the follow up surveys.

About three-fifths (61.2%) of the participants were aged between 20 and 29 and three quarters of them had never married (76.1%). Among the baseline sero-negative participants, approximately 60% were official residents of Nanjing, 68% attended college or above, 25% had a monthly income less than 1,000 Chinese Yuan (1 US Dollar=6.10 Chinese Yuan). About 58% of the participants usually meet their casual partner online and about 30% of them were students. Only about 13% of them had not received any kind of HIV prevention service in the past year.

In addition, about 60% of the baseline HIV sero-negative men reported that they had engaged in UAI in the past 6 months, and about 17% of them had engaged in UVI in the past 6 months (Table 1). About 25% of the participants reported that they had STI signs or symptoms in the past year.

Among the 410 sero-negative participants at baseline, 46 MSM were positive for syphilis, with an overall prevalence of 11.2% (10.4% among the participants who missed one or more visits, and 12.2% among the participants who missed no visits.

Participants who attended all the follow-up visits were different from those who were lost to follow up, as evident from the non-overlapping 95% CIs presented in Table 1.

Univariate analysis (Table 2) indicated that compared to internet, loss to follow up was positively correlated with meeting casual partners in pubs, discos, tearooms, or clubs, with OR of 2.57 (95%CI 1.39-4.74). In addition, participants who were single or married had a significantly higher chance of missing visits, compared with those who were widowed or divorced, with ORs of 5.05 (95%CI 1.64-15.55) and 3.48 (95%CI 1.06-11.40) respectively. Compared to self-identified homosexual participations, bisexual participants were more likely to miss one or more visits (OR=1.78, 95%CI 1.20-2.66). Being the official residents of other cities in Jiangsu (OR=2.08, 95%CI 1.25-3.46), or other provinces in China (OR=3.97, 95%CI 2.26-6.98) also had higher chance to miss one or more visits, compared to the participants who were residents of Nanjing. Also, only having attended high school or less was positively associated with loss to follow up (OR=1.65, 95%CI 1.08-2.53), compared with attended college or higher. With lower social network size was also associated with loss to follow up (OR=1.64, 95% CI 1.09-2.47).

Table 2 also indicates that age was negatively associated with loss to follow up (OR=0.93, 95%CI 0.90- 0.95), younger participants were more likely to be lost to follow up.

In multivariate analysis (Table 2) model, being the official resident of another province of China (OR=2.50, 95%CI 1.30-4.76), having a small social network size (OR=2.49,

95%CI 1.32-4.71), and less education (OR=2.01, 95%CI 1.10-3.66) were still positively associated with missing one more visits. Younger age was also positive associated with loss to follow up in our study.

Meeting partners at bathhouse and at park, being single, being official residents of other cities of Jiangsu Province and being bisexual were not found to be significantly associated with loss to follow up after controlling for the other variables.

V. Discussion

Almost 54% of the baseline HIV sero-negative participants missed one or more visits during the 18 months follow up period. This missing visit rate was much higher than among many other cohort studies targeted at MSM[105,106], which had similar definition of loss to follow up with our study. This high loss to follow up rate might have biased the results of the parent study, if the loss to follow up was differential (if the loss to follow up was influenced by both exposure and outcome).

Being official residents of the other provinces of China was positively associated with the loss to follow up. In recent years, under the influence of social and economic development, MSM in China have become more active. To protect themselves, they often travel to different cities to looking for casual or regular partners, but they usually only stay a short time at one place[107]. Such migration may increase the percentage of loss to follow up. This finding was also observed by two clinic cohorts conducted in

other populations, which demonstrate that immigration is positively associated with loss to follow up[108,109]. However, to our knowledge, no previous that conducted among MSM has tested the relationship between the two variables before. Meanwhile, such migration is considered to be related to other related variables, like age and education, while such variables were also highly correlated with loss to follow up.

The results of our study also found that being married or single was associated with missing visits. Possible explanations for this phenomenon were that the life of single MSM may still not be stable, and they were more likely to travel to different cities to find different casual partners. Married MSM be more likely to worry about the disclosure to their sexual orientation by their female partners.

Both univariate and multivariate analysis indicated that age was correlated with the loss to follow up, with the increasing of age, the odds for missing visits decreased. This finding is similar to findings of a cohort study conducted among children[110] and another following hospital outpatients[111]. Both studies report that the loss to follow up was associated with younger age. One study conducted among MSM in San Francisco also demonstrated that younger age participants have lower retention rates[55].

Our study also found that small social network size was positively associated with missing visits. There are several potential reasons for this. First, the density of the

social networks of MSM appears associated with patterns of sexual behavior, and the participants who had larger social network size tend to have more sexual partners[112]. These patterns may potentially increase their potential risk and concern about HIV infection and their willingness to seek health care[113], which in turn may increase their retention rate. Secondly, a large social network size provides a stronger social support structure [114], which may increase their willingness to seek health care. In addition, RDS, which was based on the social network of the participants, was used for participants sampling at baseline of our study. The recruiters and the recruited were usually in the same social network, the participants who have small social network size might receive less encouragement from the other participants in their social network size, but were also less likely to be recruited through RDS.

The study also showed that having less education was positively associated with loss to follow up. This finding is similar to a longitudinal study on adherence to antiretroviral therapy in Switzerland, which indicated that lower education was an independent predictor of poor adherence[115]. This result was also similar to the finding of the Multicenter AIDS Cohort Study (MACS) and one cohort study conducted in China[100,116]. One possible explanation for this situation is that the participants who received less education may have a poor understanding of health and disease, and generally are poor health practitioners.

Different from the findings of a previous study[55], our study found that UAI and UVI were not associated with the missing visits. These findings indicated that the participants who dropped out of our study had similar UAI and UVI behaviors as those who stayed in the study. This assumes that they continued the same behavior. Similar results were also found for other variables like syphilis, and reporting STI signs or symptoms. Therefore, greater concern among with those with higher risk behaviors is unlikely.

The strict definition of loss to follow up or missing visits could be one potential strength of our study, since it could reduce the possibility of misclassification of the outcome. In our study, if any participants were lost to follow up at first, and came back for the later visits, they were still counted as not consistent participated in our study.

As we discussed before[103], as a cross-sectional study at baseline, our study had several limitations. First, information bias, particularly desirability and recall bias may be present. Second, the lower response rate (427 (33%) of the 1289 coupons distributed were returned) may introduce potential information bias in our study. Even though the low response rate is common in such studies and is consistent with other RDS surveys [92,93], the low response rate may result in limiting generalizability to MSM population. The participants who attended the survey may be different from those who unwilling to come. Also, we could not address this by data analysis as no information was available regarding those who refused. In addition, the

non-compliance in a study is usually related to many unpredictable factors, and there may exist many unknown or unmeasured confounders, which may again bias our results. Due to the sample size issue, we could not put too many variables in the final model, thus there may still have been some measured but uncontrolled confounders, as well as unmeasured confounders.

Despite these limitations, we conclude that loss to follow up for this MSM intervention study in Nanjing was associated with younger age, small social network, lower education, and non-official residence in Jiangsu. Most importantly, the loss to follow up was not correlated with variables, like UAI and UVI. These findings will be helpful for future cohort studies. We can use these findings to evaluate the probability of loss to follow up for each participant, and implement more intensive strategies to encourage the participants who have higher likelihood of loss to follow up to stay in the study. We can also use the associations detected in our study for conducting sensitivity analysis. Thus, the findings of this study may be helpful to increase the retention rate of future cohort studies, thereby reducing the potential bias introduced by loss to follow up.

VI. Tables

Table 1, Demographic characteristics, behaviors, STI signs or symptoms and syphilis prevalence of the participants (N=410).

Variable		Loss to follow up (n=221)			Consistent participation (n=189)			Overall	
		Frequency	Percent	95% CI	Frequency	Percent	95% CI	Frequency	Percent
Age	<i>Less than 20</i>	23	10.4	6.4,14.5	1	0.5	0.0,1.6	24	5.8
	<i>20-29</i>	146	66.1	59.8,72.4	105	55.6	48.4,62.7	251	61.2
	<i>30-39</i>	38	17.2	12.2,22.2	45	23.8	17.7,29.9	83	20.2
	<i>40-49</i>	13	5.9	2.8,9.0	29	15.3	10.2,20.5	42	10.2
	<i>50 or above</i>	1	0.4	0.0,1.3	9	4.8	1.7,7.8	10	2.4
Marital status	<i>Single</i>	179	81.0	75.8,86.2	133	70.4	63.8,76.9	312	76.1
	<i>Married</i>	38	17.2	12.2,22.2	41	21.7	15.8,27.6	79	19.3
	<i>Divorced or Widowed</i>	4	1.81	0.0,3.6	15	7.9	4.0,11.8	19	4.6
Hukou	<i>Nanjing</i>	107	48.4	41.8,55.1	137	72.5	66.1,78.9	244	59.5
	<i>Other cities in Jiangsu</i>	52	23.5	17.9,29.2	32	16.9	11.5,22.3	84	20.5
	<i>Other provinces</i>	62	28.0	22.1,34.0	20	10.58	6.2,15.0	82	20.0
Education	<i>High school or below</i>	81	36.6	30.2,43.0	49	25.9	19.6,32.2	130	31.7
	<i>College or above</i>	140	63.4	57.0,69.8	140	74.1	67.8,80.4	280	68.3
Income	<i>Less than 1000</i>	59	30.9	24.3,37.5	43	26.4	19.5,33.2	102	24.9

	<i>1000-4000</i>	109	57.1	50.0,64.2	97	59.5	51.9,67.1	206	50.2
	<i>4000 or above</i>	23	12.0	7.4,16.7	23	14.1	8.7,19.5	46	11.2
Cruisingvenue	<i>Internet</i>	121	54.8	48.1,61.4	115	60.8	53.8,67.9	236	57.6
	<i>Pub, Disco, Tearoom, or Club</i>	46	20.8	15.4,26.2	17	9.0	4.9,13.1	63	15.4
	<i>Spa or bathhouse, Sauna</i>	29	13.1	8.6,17.6	32	16.9	11.5,22.3	61	14.9
	<i>Park, Public Restroom, or Public Lawn</i>	8	3.6	1.1,6.1	11	5.8	2.4,9.2	19	4.6
	<i>Other</i>	17	7.7	4.2,11.2	14	7.4	3.6,11.2	31	7.6
Student	<i>Yes</i>	66	29.9	23.79,36.0	55	29.1	22.6,35.6	121	29.5
	<i>No</i>	155	70.1	64.0,76.2	134	70.9	64.4,77.4	289	70.5
Coverage	<i>Yes</i>	189	85.5	80.8,90.2	168	88.9	84.4,93.4	357	87.1
	<i>No</i>	32	14.5	9.8,19.2	21	11.1	6.6,15.6	53	12.9
UAI	<i>Yes</i>	130	58.8	52.3,65.4	116	61.4	54.4,68.4	246	60.0
	<i>No</i>	91	41.2	34.6,47.7	73	38.6	31.6,45.3	164	40.0
UVI	<i>Yes</i>	39	17.6	12.6,22.7	30	15.9	10.6,21.1	69	16.8
	<i>No</i>	182	82.4	77.3,87.4	159	84.1	78.9,89.4	341	83.2
Have STIsigns or symptoms	<i>Yes</i>	53	24.0	18.3,29.7	48	25.4	19.1,31.7	101	24.6
	<i>No</i>	168	76.0	70.3,81.7	141	74.6	68.3,80.9	309	75.4
Syphilis	<i>Yes</i>	23	10.4	6.4,14.5	23	12.2	7.5,16.9	46	11.2
	<i>No</i>	198	89.6	85.5,93.6	166	87.8	83.1,92.5	364	88.8

Table 2 Factors Associated with for loss-to-follow-up among MSM in Nanjing, China, 2008

(N=410)

Variable		Crude		Adjusted	
		OR (95%CI)	<i>P-value</i>	OR (95%CI)	<i>P-value</i>
Age		0.93(0.90,0.95)	<0.001	0.90(0.86,0.94)	<0.001
Cruisingvenue	<i>Internet</i>	<i>Ref</i>		<i>Ref</i>	
	<i>Pub, Disco, Tearoom, or Club</i>	2.57 (1.39, 4.74)	0.001	2.02(0.98, 4.19)	0.061
	<i>Spa or bathhouse, Sauna</i>	0.86(0.49,1.51)	0.28	1.42(0.62,3.21)	0.92
	<i>Park, Public Restroom, or Public Lawn</i>	0.69(0.27,1.78)	0.21	1.12(0.36,3.47)	0.56
	<i>Other</i>	1.15(0.54,2.45)	0.92	2.05(0.86,4.88)	0.33
Marital Status	<i>Divorced or Widowed</i>	<i>Ref</i>		<i>Ref</i>	
	<i>Single</i>	5.05(1.64, 15.55)	0.002	2.11(0.50, 8.81)	0.55
	<i>Married</i>	3.48 (1.06, 11.40)	0.047	2.53(0.64,10.01)	0.20
Official resident (Hukou)	<i>Nanjing</i>	<i>Ref</i>		<i>Ref</i>	
	<i>Other cities in Jiangsu</i>	2.08(1.25,3.46)	0.005	1.50(0.85,2.65)	0.86
	<i>Other provinces</i>	3.97(2.26,6.98)	<0.001	2.49(1.32,4.71)	0.027
Education	<i>College or above</i>	<i>Ref</i>		<i>Ref</i>	
	<i>High school or below</i>	1.65(1.08,2.53)	0.021	2.01(1.10,3.66)	0.022
Income	<i>4000 or above</i>	<i>Ref</i>			
	<i>Less than 1000</i>	1.37(0.68, 2.76))	0.32		
	<i>1000-4000</i>	1.12(0.59, 2.13)	0.85		
Student	<i>Yes</i>	<i>Ref</i>			
	<i>No</i>	1.04(0.68,1.59)	0.86		
Sexual Orientation	<i>Homosexual</i>	<i>Ref</i>		<i>Ref</i>	
	<i>Bisexual</i>	1.78(1.20,2.66)	0.004	1.34(0.85,2.12)	0.21
UAI	<i>No</i>	<i>Ref</i>			
	<i>Yes</i>	0.90(0.61,1.33)	0.60		
UVI	<i>No</i>	<i>Ref</i>			

	<i>Yes</i>	1.14(0.68,1.92)	0.63		
Have STI signs or symptoms	<i>Yes</i>	<i>Ref</i>			
	<i>No</i>	1.08(0.69,1.69)	0.74		
Coverage of HIV/STI related service	<i>No</i>	<i>Ref</i>			
	<i>Yes</i>	0.74(0.41,1.33)	0.31		
Knowledge	<i>No</i>	<i>Ref</i>			
	<i>Yes</i>	0.83(0.42,1.64)	0.60		
Social Network Size	<i>10 or larger</i>	<i>Ref</i>		<i>Ref</i>	
	<i>Less than 10</i>	1.64(1.09,2.47)	0.018	1.75(1.09,2.80)	0.021
Syphilis	<i>Yes</i>	<i>Ref</i>			
	<i>No</i>	1.19(0.65, 2.20)	0.57		

Appendix

Appendix A

Appendix A summarizes the relations between the sample size, Deff, standard error,

variance using RDS= $V(RDS, \hat{P}_A)$ and variance while using simple random

sampling= $V(SRS, \hat{P}_A)$, based on the calculation formula provided by Matthew J. Salganik and U.S. Department of Health and Human Service [25-27]:

$$n = deff \cdot \frac{[(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}) \cdot \sqrt{P_{A,1}(1-P_{A,1}) + P_{A,2}(1-P_{A,2})}]^2}{(P_{A,2} - P_{A,1})^2}$$

Before we began this survey, the sample size estimation was based on equation 1, and the estimated sample size was 460, while the estimated design effect was 2. However, only 430 MSM were actually recruited, raising the concern whether the sample size met the requirements or not. To evaluate this, we used the following:

First, we designed $V(RDS, \hat{P}_A)$ and $V(SRS, \hat{P}_A)$ to be determined using the formula below:

$$V(RDS, \hat{P}_A) = deff \cdot \frac{P_A(1-P_A)}{n}$$

$$V(SRS, \hat{P}_A) = \frac{P_A(1-P_A)}{n}$$

Next we calculated $V(SRS, \hat{P}_A)$ for different variables and after analysis in RDSAT 5.6, we calculated the confidence intervals of the target variables, standards errors (se) and

$$V(RDS, \hat{P}_A) \text{ using formula: } n = deff \cdot \frac{P_A(1-P_A)}{(se(\hat{P}_A))^2} \text{ and } V(RDS, \hat{P}_A) = deff \cdot \frac{P_A(1-P_A)}{n}$$

$$deff(\hat{P}_A) = \frac{V(RDS, \hat{P}_A)}{V(SDS, \hat{P}_A)}$$

Finally, we used formula: and obtained the final Deff, and compared the estimated Deff and the observed Deff[25-27].

Using HIV positivity as an example, $V(SRS, \hat{P}_A)$, with the formulation of

$$V(SRS, \hat{P}_A) = \frac{0.066 * (1 - 0.066)}{430} = 0.00014$$

. Using RDSAT 5.6, we obtained the HIV positivity rate = 6.6%, its 95% confidence intervals being (2.9%, 10.3%), se=0.137,

$$V(RDS, \hat{P}_A) = 0.00036 \text{ and the final observed } deff(\hat{P}_A) = 2.48.$$

Appendix B Questionnaire

Instructions: 1. Mark \surd in the box before on the appropriate answer. 2. Mark only one box per question unless otherwise indicated.

A. ID

A04 ID: (stick bar code here)

A11 Coupon Number:

B. Demographic information

B01 Birth year:

B02 Marital status: Single Married Living with a significant other (but not married)

Divorced or Widowed

B03 Hukou (residence permit):

Guangzhou (Go to B04) Other district in Guangdong Province

Other province (_____Province)

B031 How long have you resided in Guangzhou:

<3 months 3~6 months 7~12 months Longer than 1 year ~ 2 years

Longer than 2 years

B04 Nationality: Han Other (The _____ Nationality)

B05 Education level: Illiterate Elementary school Junior high school

Senior high school or technical secondary school

Junior college or higher

B06 Occupation:

Student Teacher Nurserymaid Restaurant Commercial attendant

Doctor, nurse or pharmacist Worker Migrant worker

Farmer Herdsman Fisherman Government worker Retired Housewife or

unemployed Other _____

B061 Monthly income:

0 ≤1000 RMB 1001-2000 RMB 2001-3000 RMB 3001-4000 RMB

>4000 RMB

B07 Sexual orientation

Homosexual Heterosexual Bisexual not sure

Refuse to answer

A06 Where do you usually go to meet your partners?

Pub, Disco, Tearoom, or Club Spa or bathhouse, Sauna, Foot Massage or Body

Massage Park, Public Restroom, or Public Lawn Internet Other

Refuse to answer

B08 (Only RDS) In this city, how many MSM do you know? (You know the person's face and name/nickname, have his contact info, and could get in touch with him within the next month)

Number _____ Refuse to answer

B09 (Only RDS) What's the relationship between you and the man who gave the coupon to you?

Former partner (over 6 months ago) Partner in the past 6 months

Good friend Common friend Acquaintance Stranger

Refuse to answer

B10 The main reason why you came here:

Test, to know your HIV status For the money Forced to come

Persuaded to come To learn more about AIDS

Contribute to the prevention of AIDS Refuse to answer

C. Knowledge and attitude

C01 Can a healthy looking person have HIV? Yes No Don't know

C02 A person can get HIV by using infected blood or blood product. Yes No Don't know

C03 A person can get HIV by sharing needles with someone who is infected. Yes No

Don't know

C04 HIV can be avoided by using condoms each time correctly. Yes No Don't know

C05 HIV can be avoided by having sex with only one uninfected partner. Yes No

Don't know

C06 A baby can get HIV from his/her mother. Yes No Don't know

C07 A person can get HIV by sharing a meal with someone who is infected. Yes No

Don't know

C08 A person can get HIV from mosquito bites. Yes No Don't know

C09 Have you had an HIV test during the past 12 months? Yes No (Go to J 01) Don't know

C10 Do you know the result of your previous test? (You needn't tell me the result) YesNo

J. Access to HIV prevention services

In the past one year, did you receive the following services?

J01 condom Yes No

J02 lubricant Yes No

J03 Peer education Yes No

J04 STD diagnosis or treatment Yes No

J05 HIV counseling or testing Yes No

J06 AIDS/STD Materials (pamphlets, etc) Yes No

J07 How do you get your information about HIV? (Multiple choices)

TV Radio Newspaper Book Friend Doctor

Counseling (Including telephone counseling) Free pamphlet etc. Ad column

Internet School Other

D. Sex behavior with men

D01 How old were you when you had your first insertive sexual intercourse? Yrs Refuse to answer

D02 What was the gender of your first partner: Male (Go to D04) FemaleRefuse to answer

D03 How old were you when you had your first sexual intercourse with another man?
Yrs Refuse to answer

D04 In the past 6 months, have you had anal sex with any man?

Yes No (Go to G01) Refuse to answer

D05 How many different male partners have you had sex with in the past 6 years? Number

Don't remember Refuse to answer

D06 Did you use a condom with your last male partner when having anal sex? Yes

No Refuse to answer

D07 In the past 6 months, what frequency did you use a condom with your male partners when having anal sex?

never occasionally every time Refuse to answer

E. F. Commercial sex with men

E01 Have you bought sex with a man in the past 6 months?

Yes No (Go to F01) Refuse to answer

E02 How many men have you bought sex from in the past 6 months?

Number Don't remember Refuse to answer

E03 Did you use a condom with your partner the last time you had anal sex?

Yes No Refuse to answer

E04 How often do you use condoms when you have anal sex?

never occasionally every time Refuse to answer

F01 Have you sold sex to any men in the past 6 months?

Yes No (Go to G01) Refuse to answer

F02 How many different male sex partners did you sell sex to in the past 6 months?

Number Don't remember Refuse to answer

F03 Did you use a condom with your male partner when having anal sex last time?

Yes No Refuse to answer

F04 In the past 6 months, what frequency did you use a condom with your male partners when having anal sex?

never occasionally every time Refuse to answer

G. Sex with female

G01 Have you had sex with a female in the past 6 months?

Yes No (Go to H01) Refuse to answer

G02 How many different females have you had sex with in the past 6 months?

Number Don't remember Refuse to answer

G03 Did you use a condom the last time you had sex with a female partner?

Yes No Refuse to answer

G0 In the past 6 months, how frequently did you use a condom with your female partners?

never occasionally every time Refuse to answer

H. Drug use

H01 Have you ever tried drugs? Yes No (Go to I01) Refuse to answer

H02 Have you injected drugs in the past 6 months? Yes No (Go to I01) Refuse to answer

H03 Did you share needles with others the last time you injected? Yes No Refuse to answer

H04 Over the past 6 months, how frequently have you shared needles with others while

injecting?

never occasionally every time Refuse to answer

I. STD defining signs and symptoms and treatment

During the past year:

I01 Have you had any of following signs or symptoms: burning pain when urinating, genital discharge, ulcer/sores on penis/anus ? Yes No(Finish the interview)

Refuse to answer

I02 When you had the signs or symptoms, how did you treat them? (Please choose all appropriate answers)

treated at STD clinic treated in a comprehensive hospital treated in a private clinic
bought medications myself did nothing other Refuse to answer

The end of the questionnaire, thank you very much for you cooperation.

A01 investigation site: _____ province (autonomous regions、 municipalities)

_____ city _____ district (town)

A02 investigation target: MSM

A03 Regional code of investigation site: : □□□□□□

A05 date: □□□□year□□month□□day

A07 Blood collecting: Yes No

A12 Did you attend the first investigation (the second/third investigation must fill in)

No Yes, the first investigation ID: _____ (based on the registration form)

A13 Did you attend the second investigation (the third investigation must fill in)

No Yes, the second investigation ID: _____ (based on the registration form)

A08 HIV-Ab testing results:

A081 first screening test: HIV-Ab positive (Go to A082) HIV-Ab negative

A0811 Was counseling available after the screening test?

Yes (date: □□□□year□□month□□day) No

A082 result of second screening testing HIV-Ab positive HIV-Ab negative

A0821 Was counseling available after the screening test?

Yes (date: □□□□year□□month□□day) No

A083 Repeat ELISA result: HIV-Ab positive HIV-Ab negative

A0831 Was counseling available after the screening test?

Yes (date: □□□□year□□month□□day) No

A084 WB confirmatory testing result:

HIV-Ab positive HIV-Ab negative HIV-Ab indeterminate

A0841 Were you notified of the test result? Yes (date: □□□□year□□month□□day) No

A09 Syphilis testing result

A091 screening test (RPR/TRUST): positive negative

A092 confirmatory (TPPA): positive negative

A10 HCV:

A101 screening test (ELISA-1): positive negative

A102 repeat test(ELISA-2): positive (S/CO \geq 3.8) positive (S/CO $<$ 3.8)

negative

A103 confirmatory test (RIBA): positive negative indeterminate

investigator Signature: _____

principal signature: _____

supervisor signature: : _____

Appendix C Papers

1, Published or accepted manuscripts during study at UCLA

Published

1. Haitao Yang, **Weiming Tang (Co-first author)** et al. Worsening epidemic of HIV and Syphilis among Men Who Have Sex with Men in Jiangsu, China: A tale of two cities. (submitted to CID, Accepted).
2. Jiannan Xing, Ying Li, **Weiming Tang** et al. The emerging HIV/AIDS epidemic among older adults in China: from 2005 to 2012 (submitted to CID, Accepted).
3. **Weiming Tang**, Tanmay Mahapatra, Jinkou Zhao. Prejudice, Stigma and Social Discrimination: Perceived Barriers in HIV Prevention and Control among Men Who Have Sex with Men in China. *Epidemiology: Open Access*.
4. **Weiming Tang** et al. HIV, STIs Prevalence among FSW and the Factors Correlated with CT and NG: Effective intervention strategies were called. *Plos One* no.1 (2014)
5. **Weiming Tang**, Tanmay Mahapatra, Xiping Huan, et al. Feasibility of recruiting a diverse sample of Men Who Have Sex with Men: Observation from Nanjing, China. (*PloS one* 8, no. 11 (2013): e77645.).
6. Xiping Huan, **Weiming Tang (Co-first-author)**, Giridhara R Babu. Risk-reduction Counseling and HIV/STD testing on Behavior Change of MSM: Results from a Cohort Study in Nanjing, China (*PloS one* 8, no. 7 (2013): e69740).
7. Yongze Li, Junjie Xu, Kathleen Reilly, Jianming Zhang, Hongyi Wei, Yongjun Jiang, Wenqing Geng, **Weiming Tang**, Hong Shang Prevalence of HIV and syphilis infection among high school and college student MSM in China: A systematic review and meta-analysis (*PloS one* 8, no. 7 (2013): e69137).
8. **Weiming Tang**, Xiping Huan, Tanmay Mahapatra et al. 2013. Factors Associated with Unprotected Anal Intercourse Among Men Who Have Sex with Men: Results from a Respondent Driven

Sampling Survey in Nanjing, China, 2008 (AIDS and Behavior, DOI 10.1007/s10461-013-0413-4).

9. XipingHuan, Chun Hao, Hongjing Yan, Wenhui Guan, Xiaoqin Xu, Haitao Yang, Na Wang, Min Zhang, **Weimin Tang** et al. High Prevalence of HIV and Syphilis Among Men Who Have Sex With Men Recruited by Respondent-Driven Sampling in a City in Eastern China.(Asia Pac J Public Health. 2013 Mar 27)
10. Chun Hao, Hongjing Yan, Haitao Yang, XipingHuan, Hongjing Yan, Wenhui Guan, XiaoqinXu, Min Zhang, **Weiming Tang**, et al. 2011. The incidence of syphilis, HIV and HCV and associated factors in a cohort of men who have sex with men in Nanjing, China. Sex Transm Infect
11. Chun Hao, Hongjing Yan, Haitao Yang, XipingHuan, Hongjing Yan, Wenhui Guan, XiaoqinXu, Min Zhang, **Weiming Tang** et al.. 2012. A Randomized Controlled Trial to Evaluate the Relative Efficacy of Enhanced Versus Standard Voluntary Counseling and Testing on Promoting Condom Use among Men Who Have Sex with Men in China. AIDS and behavior.
12. Hongling Bai, XipingHuan, **Weiming Tang** et al. 2012. A survey of HIV infection and related high-risk factors among men who have sex with men in Suzhou, Jiangsu, China. Journal of Biomedical Research.
13. Mahapatra, Tanmay; Mahapatra, Sanchita; R Babu, Giridhara; **Weiming Tang** et al. Cholera Outbreaks in South & South-East Asia: A Descriptive Analysis, 2003-2012. (Accepted, Japanese Journal of Infectious Diseases).
14. Junjie XU, **Weiming Tang (co-first author)**. The factors correlated with HIV infection among TB patients. (Accepted, PLOS ONE).
15. Xiaoyan Liu, Chao Hao, Hui Jiang, Lin Sun, Jian-BoZhou, Yue-PingYin, **WeimingTang** et al. Syphilis and its correlates among heterosexual males attending sexually transmitted infection clinics – observation from a multicity cohort in Jiangsu Province, China. (Accepted, PLOS ONE).
16. Na Han, Shouling Wu, Peixun Zhang, Xiaofeng Yin, Yuhui Kou, **Weiming Tang** et al. Vitamin D Deficiency and Its Correlation with Bone Mineral Density among Coal Miners. (submitted to Plos One, Accepted).

2, Submitted and under review manuscripts during study at UCLA

17. **Weiming Tang**, Lu Wang, Xiayan Zhang et al. Pre-exposure prophylaxis: A right way to go or a long way to go? (Submitted, under review).
18. **Weiming Tang**, Giridhara R Babu, Jianjun Li et al. The Difference between HIV and Syphilis Prevalence and Incidence Cases: Results from a Cohort Study in Nanjing, China, 2008-2010 (Submitted, under review).
19. Aritra Das, **Weiming Tang (Corresponding author)**, et al. Predictors of HIV and Syphilis of Men Who Have Sex with Men in China. (submitted to International Journal of AIDs and STD, under review).
20. Gengfeng Fu, Haiyang Hu, **Weiming Tang** et al. SiRNA against KIR3DL1 is the potential gene therapeutic agent in HIV-1 infection. (submitted to Viral immunology, under review).
21. Lu Wang, **Weiming Tang (Co-first author)** et al. The HIV, Syphilis and HCV Epidemic among Female Sex Workers in China: Results from a Serial Cross-sectional Study between 2008 and 2012. (Submitted to Plos Medicine, under review).
22. Furu Wang, **Weiming Tang (Co-first author)** et al. Hospital work environmental radiation and the risk of different kind of cancers among Physicians in Jiangsu, China: Results from a 61 years follow up study. (Submitted to AJE, under review).
23. **Weiming Tang** et al. The Epidemic of HIV, Syphilis, Chlamydia and Gonorrhea, and the Correlates of Sexual Transmitted Infectious among Men who Have Sex with Men in Jiangsu, China, 2009. (Submitted to STD, under review).
24. Weiming Tang (**Corresponding author**) et al. The Prevalence and factors correlated with non-communicable diseases among rural residents (aged 15 or more) in Shijiazhuang, Hebei, China. (Submitted to PLOS One, under review).

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