# A comparison of respondent-driven and venue-based sampling of female sex workers in Liuzhou, China

Sharon S Weir,[1] M Giovanna Merli,[2] Jing Li,[3] Anisha D Gandhi,[1] William W Neely,[4] Jessie K Edwards,[1] Chirayath M Suchindran,[5] Gail E Henderson,[6] Xiang-Sheng Chen[3]

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[1]The Carolina Population Center and the Department of Epidemiology in the Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
[2]Sanford School of Public Policy, Duke Population Research Institute, and Duke Global Health Institute, Duke University, Durham, North Carolina, USA
[3]The National Center for STD Control and the Chinese Academy of Medical Sciences, Institute of Dermatology, Nanjing, Jiangsu, China
[4]Lake Forest Park, Washington, USA
[5]The Carolina Population Center and the Department of Biostatistics in the Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
[6]Department of Social Medicine, The School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

**Correspondence to**
Dr Sharon S Weir, The Carolina Population Center and the Department of Epidemiology in the Gillings School of Global Public Health, Campus Box 8120, University of North Carolina at Chapel Hill, Chapel Hill, NC 27546, USA; sharon_weir@unc.edu

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## ABSTRACT

**Objectives** To compare two methods for sampling female sex workers (FSWs) for bio-behavioural surveillance. We compared the populations of sex workers recruited by the venue-based Priorities for Local AIDS Control Efforts (PLACE) method and a concurrently implemented network-based sampling method, respondent-driven sampling (RDS), in Liuzhou, China.

**Methods** For the PLACE protocol, all female workers at a stratified random sample of venues identified as places where people meet new sexual partners were interviewed and tested for syphilis. Female workers who reported sex work in the past 4 weeks were categorised as FSWs. RDS used peer recruitment and chain referral to obtain a sample of FSWs. Data were collected between October 2009 and January 2010. We compared the socio-demographic characteristics and the percentage with a positive syphilis test of FSWs recruited by PLACE and RDS.

**Results** The prevalence of a positive syphilis test was 24% among FSWs recruited by PLACE and 8.5% among those recruited by RDS and tested (prevalence ratio 3.3; 95% CI 1.5 to 7.2). Socio-demographic characteristics (age, residence and monthly income) also varied by sampling method. PLACE recruited fewer FSWs than RDS (161 vs 583), was more labour-intensive and had difficulty gaining access to some venues. RDS was more likely to recruit from areas near the RDS office and from large low prevalence entertainment venues.

**Conclusions** Surveillance protocols using different sampling methods can obtain different estimates of prevalence and population characteristics. Venue-based and network-based methods each have strengths and limitations reflecting differences in design and assumptions. We recommend that more research be conducted on measuring bias in bio-behavioural surveillance.

In recognition of the importance of HIV/sexually transmitted infectionepidemics among sex workers, WHO recommends HIV and syphilis surveillance of sex workers.[1] A common surveillance strategy is trend analysis of periodic cross-sectional bio-behavioural surveys.[2] Methodological challenges arising from the hidden culture and illegal status of sex work make results difficult to interpret. These challenges include how to identify sex workers, how to sample the population and how to adjust crude estimates to account for differences in the probability of recruitment.

In this study, we compare two different methods to sample sex workers for the purpose of obtaining unbiased estimates of the characteristics of the population in a defined geographic area: a venue-based method named the Priorities for Local AIDS Control Efforts (PLACE) and a network-based method known as respondent-driven sampling (RDS). The methods were independently and concurrently implemented in Liuzhou prefecture (population 3.6 million) in Guangxi Province, China. The two strategies vary in assumptions, recruitment and analytic methods.

## METHODS

PLACE identifies and maps venues where people meet new sexual partners, selects a probability sample of venues and recruits participants from sampled venues. Data are analysed using statistical methods designed for complex surveys.[3–6] The disadvantages of venue-based methods include the additional fieldwork required for mapping and visiting venues and the potential bias arising from missing non-venue-based sex workers. PLACE differs from other time–space sampling protocols[7] used in surveillance of key populations in that venues are visited at peak times rather than randomly selected times; venue eligibility extends to any venue where people meet sexual partners, rather than only those with sex workers (or other target populations); and stratified sampling is often used to obtain estimates for more than one subgroup of interest. Target groups for surveillance, such as female sex workers (FSWs), are identified as a subgroup during analysis of PLACE data based on responses to survey questions (eg, did you exchange sex for money in the past 4 weeks?). The comparison with RDS presented here is based on the PLACE subsample of female venue workers who met the study definition of a sex worker.

RDS is a chain referral sampling method in which purposively selected 'seeds' initiate recruitment and invite others from their peer network for an interview conducted in a location selected for privacy, acceptability and convenience to participants.[8–10] Chains of recruitment are documented, and recruitment continues until stopped by investigators. For sex worker studies, RDS assumes that sex workers are able to tell how many women they know who meet the eligibility criteria of the survey and to whom they would potentially be able to pass a coupon; that participants will recruit sex workers randomly from their network alters; and that the network consists of one connected component. Estimates account for different probabilities of selection arising from differences in the reported number of sex workers known by respondents. RDS has been used widely[11 12] in studies of injecting drug users, sex workers and men who have sex with men.[13–15]

The disadvantages of RDS include the potential bias arising from non-random recruitment of network alters, from impersonation of eligible respondents in order to participate, from inability to inaccurately report of the number of eligible respondents known and from failure to include eligible respondents who are not socially networked. Recent computer simulations of RDS suggest that the variance in RDS estimates may be greater than previously expected.[16]

### Study population, outcome measures and power calculation

Our primary comparison measure is the prevalence of a positive rapid test for syphilis among FSWs, defined as self-identified female subjects aged 15 or older living in Liuzhou prefecture who report exchanging sex for money in the previous 4 weeks. Assuming a design effect of two, we estimated that a sample size of 380 in each arm would have 80% power to detect an absolute difference of 5% in the estimated prevalence. We identified the geographic boundary of the study to include all of Liuzhou prefecture including the four urban districts of Liuzhou City and the six Liuzhou counties. The decision was based on formative research in Liuzhou that found that recruitment chains initiated in Liuzhou City would extend to Liuzhou counties and that precluding recruitment from Liuzhou counties would cut-off recruitment chains prematurely in the RDS arm.

The rapid test (Wantai anti-TP Antibody Rapid Test, Wantai Biological Pharmacy Enterprise, Beijing, China) measures the antibody response to a treponemal antigen using whole blood obtained from a finger prick and provides a result within 30 min. Participants testing positive were offered free supplemental testing with a non-treponemal test (TRUST, Rongsheng Biotechnical Company, Shanghai, China) and free treatment if indicated. RDS participants could initiate supplemental testing immediately in the RDS interview office; PLACE participants were referred to a clinic. The rapid test is convenient in outreach settings, holds value for participants and provides a biomarker comparison measure not subject to respondent reporting bias. The disadvantage of this test for surveillance purposes is that the treponemal antibody is a lifetime marker of infection and consequently does not distinguish between current and past infection.

### PLACE methods

A sampling frame of venues was compiled based on brief anonymous interviews with 400 community informants aged 18 and older. Community informants were asked to identify venues where people meet new sex partners, including but not limited to venues with sex work. Using strata defined by geographic area, type of venue and the number of informants reporting it, a stratified random sample of venues was identified, visited and characterised based on a face-to-face interview with a knowledgeable person onsite. We used these venue-level data to construct three strata of venues from which to sample workers for the PLACE RDS comparison: Stratum 1: Venues in urban districts where at least five female workers were sex workers and/or 50% of female venue workers were sex workers; Stratum 2: Other venues in urban districts; and Stratum 3: County venues. In order to reach our target of 380 sex workers, we oversampled venues from Stratum 1. All female workers at selected venues in Stratum 1 and Stratum 2 were eligible. In county venues, a maximum of five female workers were randomly selected and interviewed. (Female venue patrons were not eligible for the study because venue-level data and a pilot patron study found very few sex workers among female patrons. See also the online supplementary material.)

### RDS methods

Established RDS methods[8 9] were used to identify and recruit sex workers. The RDS protocol in Liuzhou was mainly based on an RDS protocol used in Shanghai among FSWs. Meetings were held in Liuzhou with people working with sex workers to adapt the Shanghai protocol to Liuzhou. Waves of recruitment were initiated by seven seeds selected by the study team from diverse sex work settings. RDS participants were first screened with questions to confirm their eligibility and prevent impersonation. They were then interviewed, tested for syphilis and instructed how to recruit up to two other eligible FSWs using uniquely coded coupons. Participants could drop in to the RDS office, which was centrally located in an urban district, or call for an appointment. Interviewers collected limited biometric data to prevent repeat participation. After the 15th wave, participants were restricted to one coupon[17] to restrict sample growth. Network size was assessed using the question: 'How many sex workers do you know in Liuzhou (including Liuzhou counties)? By knowing, I mean: you know their names and they know yours, and you have met or contacted them in the past month.' Interviewers were trained to explain the eligibility criteria to participants, check the eligibility of each participant and to identify impersonators. When participants returned for their payments, they were asked information about the characteristics of those who refused a coupon.

### Ethical review

Respondents provided verbal informed consent prior to participation. Surveys were administered face-to-face by trained interviewers in Mandarin Chinese or Zhuang. In the PLACE arm, study staff located private settings within venues for the interview and no unique identifiers were obtained. PLACE participants received ¥100 (about $14). An RDS participant received ¥100 initially and ¥50 for each recruit. The amounts of the incentives were determined locally. The Research Ethics Committee of the National Center for STD Control, China and the Institutional Review Boards at the University of North Carolina and Duke University approved the protocol.

### Data analysis

In the PLACE arm, the sampling weight for each worker was the inverse of the probability of selection into the sample, taking into account the probability that the venue was selected and willing to participate and the probability that the respondent was selected. In the RDS arm, estimates were obtained using both the RDS Analysis Tool (RDSAT) V.6.0.1[18] and an RDS-II estimator.[12] Only RDS-II estimates are presented here. (See online supplementary material for a description of the RDS-II methods including the bootstrap estimator for CIs and for comparison of RDS-II and RDSAT estimates.[12 19]) To compare the characteristics of sex workers recruited by each method, the Cochran–Mantel–Haenszel statistic was used in Proc Freq in SAS, using weighted frequencies and ignoring the design effect. To compare the proportion with a positive test, PLACE estimates and CIs were estimated using Proc Survey Freq in SAS[20] to account for clustering, the design effect and probability of selection. RDS estimates and CIs used RDS-II bootstrapping methods, further described in the online supplementary material given for this report. For the multivariate analysis, we combined PLACE and RDS datasets and used binomial regression with generalised estimating equations to account for clustering by venue strata (PLACE) and seeds (RDS).

## RESULTS

### PLACE arm: worker and sex worker samples

Community informants identified 971 venues, in urban districts (67%) and in the counties (33%). Over half (53%) of the venues were named by two or more informants. The most common types of venues were massage parlours (24%), hair salons (12%) and karaoke clubs (11%), but parks, hotels, outdoor markets and streets were also named. Of the 971 venues named, 385 were selected for a venue visit and 64 venues were ultimately selected for worker interviews, including all 16 venues reporting significant sex work (stratum 1), 14 randomly selected venues in urban districts (from Stratum 2) and 23 randomly selected county venues (Stratum 3). Of the 64 venues selected, eight were not in operation when worker interviews were conducted (2–28 January 2010) and 11 venues refused to participate. Interviewers counted 806 female workers at the 45 participating venues and interviewed 680 female workers. Of the 126 female workers not interviewed, 36 worked at county venues where the five-worker limit had been reached and 58 worked at a large venue in an urban district and left before their interviews could be initiated. There were no direct refusals by female workers and no information was collected about the workers who were counted but not interviewed.

One-fourth of the female workers reported ever receiving cash or gifts in exchange for sex and 18.2% of the female workers (n=161) had done so in the last 4 weeks, thereby meeting the study definition for FSW. FSWs had a lower age at first sex, lower education, more arrests and more sexual partners than other female workers.

### RDS arm: sex worker sample

RDS recruited 583 FSWs in Liuzhou between 26 October 2009 and 29 January 2010. Six of the seven seeds recruited additional participants, generating 9–20 recruitment waves. A total of 310 recruiting respondents recruited a mean of 1.9 participants, while most of the remaining 273 respondents were terminal nodes of the recruitment tree. Of those network alters approached, 29% did not accept the invitation to participate, mainly because of fear of being identified as a sex worker (75%). Of the 583 RDS participants, 47 (8.1%) refused syphilis testing, mostly (45/47, 95.7%) because they were recently tested.

### Comparison of socio-demographic and behavioural characteristics

Socio-demographic characteristics of sex workers varied according to sampling method (table 1).

RDS estimated that 46% of FSWs lived in the district where they were interviewed, whereas PLACE estimated that half lived in the counties and only 9% lived in the urban district where the RDS office was located (figure 1A).

Compared with PLACE, RDS estimated that more FSWs were separated, divorced or widowed (24.0% vs 6.7%); that they had a higher mean monthly income (4888 renminbi vs 1994); were less likely to have solicited in counties (3.9% vs 61.4%) or outside Liuzhou (12.2% vs 31.1%); were more likely to have solicited by telephone or internet (31.6% vs 5.7%); and less likely to have been previously tested for syphilis (7.6% vs 35.2%) or HIV (28.9% vs 46.5%) in the past year. Characteristics that did not vary by sampling method included education and having 10 or more partners in the past 4 weeks (table 1).

### Comparison of syphilis test results

PLACE estimated that almost three times as many FSWs had a positive syphilis test as RDS: 24% (95% CI 13.2 to 34.8) versus 8.0% (95% CI 5.9 to 13.0) (figure 1B). If those with missing test result data are excluded, the RDS estimate is 8.5%. Among FSWs younger than 25, the PLACE estimate was an order of magnitude higher (23.9% vs 2.8%). The prevalence among RDS FSWs age 15–24 (2.8%) was similar to the percentage of all female workers aged 15–24 at PLACE (6.3%), most of whom did not report sex work (data not shown). The 20 FSWs sampled by both RDS and PLACE methods were less likely to have a positive test than those reached by PLACE alone (1.8% vs 27.5%). Soliciting in Liuzhou counties and outdoors was associated with a positive syphilis test in both samples (table 2).

The estimated unadjusted prevalence difference of a positive rapid test comparing PLACE with RDS was 16.8%; the

**Table 1** Socio-demographic and behavioural characteristics of female sex workers (FSWs) in Liuzhou recruited by respondent-driven sampling (RDS) and Priorities for Local AIDS Control Efforts (PLACE)

| | RDS-II % | PLACE % | p Value |
|---|---|---|---|
| Total | 576 | 161 | |
| Age | | | 0.002 |
| 15–19 | 11.4 | 16.9 | |
| 20–24 | 31.4 | 34.7 | |
| 25–29 | 20.2 | 29.1 | |
| 30–34 | 19.5 | 7.8 | |
| 35–39 | 10.7 | 5.4 | |
| 40+ | 6.8 | 6.1 | |
| Residence | | | <0.0001 |
| In the urban district with RDS office | 46.2 | 9.0 | |
| In one of the three other urban districts | 51.3 | 41.2 | |
| In one of the six Liuzhou counties | 2.5 | 49.7 | |
| Other socio-demographic characteristics | | | |
| Never married | 62.2 | 60.9 | 0.76 |
| Separated, divorced or widowed | 24.0 | 6.7 | <0.0001 |
| Less than a junior high education | 25.3 | 32.6 | 0.06 |
| Mean monthly income in renminbi | 4888 | 1994 | <0.0001 |
| Aged less than 15 at first sex | 2.1 | 7.3 | <0.001 |
| Ever arrested | 10.6 | 27.6 | <0.0001 |
| Drinks alcohol weekly or more | 36.6 | 27.9 | 0.04 |
| Ever injected drugs | 2.0 | 0.1 | 0.04 |
| Sexual behaviour and previous testing | | | |
| More than 10 partners in past 4 weeks | 55.7 | 58.9 | 0.11 |
| Used condom at last sex | 71.5 | 81.5 | 0.01 |
| Solicited past year in: | | | |
| Urban districts | 99.4 | 56.7 | <0.0001 |
| Liuzhou counties | 3.9 | 61.4 | <0.0001 |
| Outside Liuzhou | 12.2 | 31.1 | <0.0001 |
| Type of venue where solicited in past 6 months | | | |
| Outdoors | 4.1 | 6.5 | 0.21 |
| Phone/internet | 31.6 | 5.7 | <0.0001 |
| Karaoke TV or karaoke | 22.4 | 23.4 | 0.7882 |
| Hair salon | 12.6 | 57.2 | <0.0001 |
| Massage | 33.9 | 40.8 | <0.0001 |
| Has been tested for HIV and knows results | 28.9 | 46.5 | <0.0001 |
| Was tested for syphilis in past year | 7.6 | 35.2 | <0.0001 |

The seven RDS seeds were excluded from RDS-II estimates. The 47 RDS FSWs who participated in the survey but refused the rapid syphilis test were included in this table. The 161 sex workers are a subset of the 680 workers recruited through PLACE.

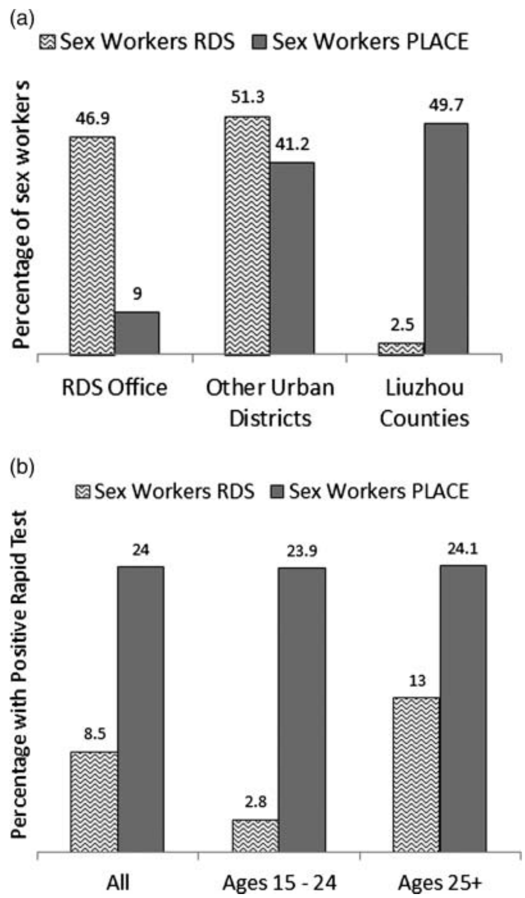


**Figure 1** Comparison of residence and rapid test results for sex workers recruited by PLACE vs RDS.

prevalence ratio was 3.3 (95% CI 1.5 to 7.2). After controlling for age and urban district/county residence, the prevalence ratio was 2.2 (1.2 to 3.9) (table 3).

## DISCUSSION

Concurrent surveys of sex workers in Liuzhou, China, using different sampling methods found significantly different estimates of the prevalence of a biomarker of syphilis (24.0% vs 8.5%) and other characteristics. This is the first study to compare biomarker outcomes from concurrently implemented venue-based and RDS investigations of sex workers. Previous studies have compared findings from different time periods or from samples not designed to compare estimates.[21–24]

We expected the two protocols to obtain similar estimates. Without a gold standard measure, interpretation is difficult, although some insight is available from comparison with a 2005 study[25] and exploratory analysis of possible explanations of the difference. The 2005 study of sex workers in urban districts of Liuzhou estimated the prevalence of syphilis to be 11% using a two-stage testing algorithm consisting of a rapid plasma regain (RPR) test followed by a Passive Particle Agglutination Test for those with a positive RPR test. We do not know what percentage of sex workers in the Lu study[25] would have tested positive using the antibody rapid test used in our study, but it would have been higher than 11% as the rapid test would be positive for people previously infected as well as the 11% currently infected. The percentage of sex workers in Liuzhou City with a positive rapid test was higher than 11% for those recruited by PLACE (17.8%) and lower among those recruited by RDS (8.2%), although the difference is not statistically significant. Comparison with the 2005 study results is complicated by the time lag between studies, the different sampling strategies and the different socio-demographic profile of the 2005 study population. A more informative analysis would compare syphilis test results for young sex workers or sex workers working in similar venues.

PLACE could have overestimated prevalence if uninfected sex workers were missed because they were not venue-based, they denied sex work, they worked at refusing venues or if PLACE oversampled older women more likely to have a biomarker for lifetime exposure. We explored these possibilities. Given that only 7% of RDS FSWs reported exclusively recruiting non-venue-based clients in the past 6 months (data not shown), it seems unlikely that PLACE missed a large proportion of non-venue-based FSWs. We assumed that infection among workers at refusing venues was similar to prevalence at participating venues, but if not, PLACE could overestimate prevalence.

**Table 2** Prevalence of a positive rapid test for syphilis by socio-demographic and other characteristics among female sex workers (FSWs) recruited by respondent-driven sampling (RDS) and PLACE in Liuzhou

| | RDS-II | | PLACE | |
|---|---|---|---|---|
| | % | 95% CI | % | 95% CI |
| Total including test refusers | 576 | | 161 | |
| Rapid test positive | 8.00 | 5.9 to 13.0 | 24.0 | 13.2 to 34.8 |
| Rapid test negative | 85.5 | 79.9 to 89.6 | 76.0 | 65.2 to 86.8 |
| Refused test | 6.5 | 3.6 to 9.7 | 0.0 | |
| FSWs tested | 530 | | 161 | |
| All tested | 8.5 | NA | 24.0 | 13.2 to 34.8 |
| Age 15–24 | 2.8 | 0.4 to 5.9 | 23.9 | 8.7 to 39.1 |
| Age ≥25 | 13.0 | 6.8 to 21.2 | 24.1 | 8.2 to 40.0 |
| Never married | 4.9 | 1.7 to 8.0 | 25.9 | 12.1 to 39.8 |
| 0–9 partners in past 4 weeks | 6.1 | 1.3 to 12.9 | 23.6 | 3.7 to 43.6 |
| More than 10 partners in past 4 weeks | 9.8 | 5.1 to 15.3 | 20.3 | 7.0 to 33.5 |
| Condom used during last sex | 4.4 | 2.1 to 7.3 | 23.8 | 12.2 to 35.4 |
| Solicited in urban district | 8.2 | 4.7 to 13.0 | 17.8 | 4.0 to 31.5 |
| Solicited in Liuzhou counties | 26.7 | 3.1 to 48.4 | 32.7 | 17.4 to 47.9 |
| Solicited out of Liuzhou | 4.9 | 0.0 to 8.9 | 27.8 | 14.5 to 41.1 |
| Venues where solicited in past 6 months: | | | | |
| Outdoors | 71.2 | 45.0 to 90.2 | 51.0 | 0.0 to 100 |
| Telephone/internet | 12.4 | 6.2 to 22.3 | 6.6 | 0.0 to 16.5 |
| Karaoke TV, karaoke | 4.1 | 0.3 to 13.8 | 20.4 | 0.6 to 40.1 |
| Hair salon | 2.1 | 0.0 to 6.5 | 30.6 | 12.7 to 48.5 |
| Massage | 4.2 | 1.4 to 7.0 | 21.7 | 6.7 to 36.7 |

RDS total (n=530) reflects the seven seeds and 46 refusals excluded from the initial 583 respondents. It is not possible to estimate the CIs for some RDS-II estimates.
NA, not available; PLACE, Priorities for Local AIDS Control Efforts.

**Table 3** Multivariable model to assess association between a positive rapid test for syphilis and method used to sample female sex workers

| Model | Variables included | Prevalence difference | 95% CI | Prevalence ratio | 95% CI |
|---|---|---|---|---|---|
| 1 | Method | 16.8 | 3.5 to 30.0 | 3.3 | 1.5 to 7.2 |
| 2 | Method, age | 16.7 | 3.6 to 29.7 | 3.3 | 1.5 to 7.2 |
| 3 | Method, age, urban district/county | 10.2 | 4.0 to 16.3 | 2.2 | 1.2 to 3.9 |

Prevalence difference refers to the absolute difference in positive rapid syphilis test between Priorities for Local AIDS Control Efforts and respondent-driven sampling (RDS). Weights for RDS respondents are from RDS-II estimation procedure.

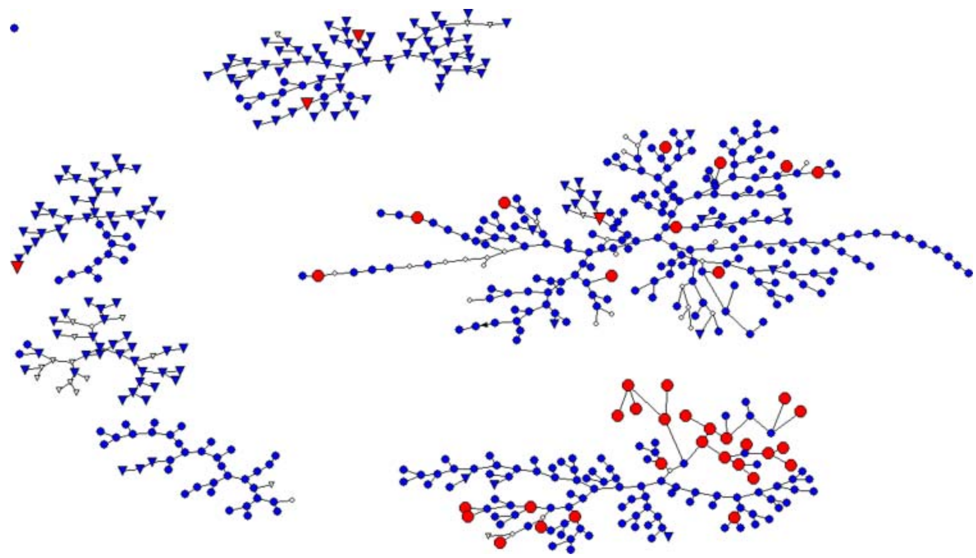

**Figure 2** RDS recruitment chains. Red indicates a positive rapid test. Blue indicates a negative rapid test. No color represents missing data. Triangles represent women working at karaoke venues.

Age composition is a less likely explanation as FSWs recruited by PLACE were younger than FSWs recruited by RDS.

Venue closings and refusal may have had a substantial effect on PLACE estimates. Significantly fewer FSWs were recruited by the PLACE protocol than the 380 FSWs expected. Obtaining a sufficient size sample is generally not a problem for venue-based sex worker surveys because protocols typically identify replacement venues to ensure targets are met. We did not anticipate that 19 of 64 venues would refuse participation or close prior to Spring Festival. Recruiting from additional venues during Spring Festival was not feasible.

The stigma and illegal status of sex work may have led to the denial of sex work and a reduction in the number of FSWs identified by PLACE. Because we interviewed and tested female workers at PLACE venues regardless of whether they reported sex work or not, we can estimate the percentage with a positive test among subgroups of workers most likely to include women actually engaged in sex work who deny it. The percentage of all female workers with a positive test (including women who reported one or no sexual partners in the past year) was 6.8%, a percentage not significantly different from the percentage among FSWs recruited by RDS (8.0%). If all PLACE workers who reported more than one sexual partner in the past year are assumed to be sex workers (an extreme and untenable assumption), the point estimate of PLACE FSW with a positive rapid test would still be twice as high as the RDS estimate (17.8% vs 8.0%). If all female workers at hair salons and massage parlours (two types of venues that are often fronts for commercial sex in China) are assumed to be sex workers, the point estimate would decrease from 24% to 14.9%.

Several scenarios could result in the RDS estimate being too low. Underestimates could arise if: (1) infected subgroups were not linked through the peer network; (2) if the interview location was less accessible to those infected; (3) if participants who refused testing were more likely to be infected than those who agreed to testing; or (4) if a large number of respondents did not meet the eligibility criteria (eg, because somehow screening methods were not effective or definitions were not clear, or the incentives attracted people who were not eligible). Underestimates could also arise if sampling weights were biased due to: inaccurate reports of network size, preferential recruitment of uninfected persons and/ or larger networks among infected individuals (leading to down-weighting of infected individuals). We explored these possibilities in a limited way.

RDS recruited few sex workers from Liuzhou counties. The finding that RDS missed geographic pockets of sex workers has been previously reported,[24] and in hindsight, establishing RDS offices in the counties may have increased participation from the counties, albeit at the risk of significantly increasing costs and introducing the complication that different recruitment sites may not recruit from the same network. Travel time to the RDS office could exceed 3 h and there were few cross-cutting ties evident in the recruitment chains between urban district and county respondents. If the comparison were limited to sex workers in urban districts, the prevalence ratio would drop from 3.3 to 2.2 (17.8% vs 8.2%).

It is possible that some other subgroups of FSWs with higher prevalence of infection were missed by RDS. Only two of six recruitment chains had more than two infections (See figure 2). Three chains with two or fewer infections primarily recruited from karaoke bars or karaoke TV. Because the RDS assumption of non-preferential recruitment constrains study managers from guiding the referral process toward members of the population who are likely to be missed, it is possible for recruitment chains to become trapped in low or high prevalence networks. There is also some indication that the RDS prevalence estimate would have been higher if all RDS recruits had agreed to be tested. For example, nine of the 47 (19%) who refused testing volunteered that they had previously tested positive.

Another possible explanation for the difference is that the PLACE sample captured women who were more frequently engaged in sex work whereas the RDS sample recruited people who were at lower risk because they less frequently engaged in sex work. It is difficult to fully assess the risk profiles of each group without information on the level of infection among clients, but there was no difference in the number of partners reported by PLACE versus RDS participants.

This study illustrates the challenges of surveillance among hidden populations. Two different sampling methods resulted in significantly different characterisations of the same target population. We focused on syphilis, but the findings are relevant to other sexually transmitted infections and relevant sexual risk behaviours as well. Our study confirms that countries should exert caution in selecting or changing surveillance methods[2] and illustrates the shift in estimated prevalence that can arise with a change in sampling methods.

Concurrent implementation afforded insights into each method. We recommend that surveillance activities routinely include investigation of bias. For venue-based methods, the proportion of non-venue-based sex workers should be estimated. The characteristics of venues that refuse and substituted venues and reasons for refusal should be analysed to assess sample representativeness. Venue-based studies may also want to assess bias arising from denial of sex work, possibly through a longer survey or an indepth interview of a subset of workers who initially deny sex work. Although obtaining information on the 519 female workers who were not sex workers allowed useful exploration of survey bias and important information on another group at risk of infection, the PLACE method was not as efficient in obtaining a large sample of sex workers as other venue-based methods that screen out non-sex workers from the survey. RDS studies would also benefit from routine investigation of key assumptions. Insight on recruitment bias and its impact on the RDS estimates can be gained by obtaining information on the characteristics of people in a participant's network, including network alters who were not invited to participate.[26] Insight on these types of bias can also be gained from mapping the work location of those recruited to identify whether any geographic pockets of the population are missed.

### Key messages

- ▶ Concurrently implemented surveillance protocols using different sampling methods can obtain different estimates of prevalence and population characteristics.
- ▶ Venue-based and network-based methods each have strengths and limitations reflecting differences in design and assumptions.
- ▶ We recommend that more research be conducted on measuring bias in bio-behavioural surveillance estimates.

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# Notes

**Supplemental Online Material**

## MATERIALS AND METHODS

### Study Setting

Liuzhou, China has a population of 3.6 million, with one million in four urban districts and 2.6 million in six surrounding rural counties. Liuzhou is known for a vibrant night life, with an estimated 5,000 women engaged in sex work. Guangxi, on the border with Vietnam, is among the provinces in China with the highest HIV and STI prevalence. In 2009, syphilis prevalence among women engaged in sex work in urban Liuzhou was estimated to be 11.0%[1].

### PLACE Methods

The venue-based strategy used in this study, the Priorities for Local AIDS Control Efforts (PLACE), constructs a sampling frame of all public venues where people meet new sexual partners. This includes venues identified as places where sex workers solicit clients. The rationale for the more generous sampling frame is that it provides information on sexual mixing among a variety of groups; the sampling frame does not depend on the definition of sex work; and it can reveal previously unknown risk groups [2]. PLACE is similar to "time-location-sampling" which randomly samples venue-time periods from an inventory of time blocks developed by listing venues where the population of interest (e.g., female sex workers) is known to congregate, and segmenting the open hours of operation at each venue into discrete time blocks. Two differences are that PLACE does not restrict the mapping and listing to venues where particular types of most-at-risk populations can be found and PLACE does not sample time-periods but interviews people when the number of people at the venue is expected to be the largest.

The PLACE method follows five steps:

1) Planning

2) Community Informant Surveys to Identify Venues

3) Venue Visits to Characterize and Map Venues

4) Interviews (and Testing) of Workers and Patrons at Selected Venues

5) Feedback to the community and use of data to improve programs

These steps were modified slightly as necessary to accommodate the comparison of the two sampling methods. See Supplementary Figure 1.

Step 1. During the planning phase we identified the geographic boundaries of the study area (i.e., urban and rural Liuzhou); selected the rapid test for syphilis as the biomarker for comparing the characteristics of the populations sampled by two methods; selected an interviewing team of people knowledgeable of Liuzhou, not affiliated with the local Centers for Disease Control, willing to visit venues late at night, and able to gain the trust of sex workers as well as administer the rapid test and provide results; developed, pre-tested and translated the data collection instruments; obtained ethical review and approval of the study; and finalized the protocol. The decision to include the rural counties reflected the desire to avoid terminating an RDS recruitment chain if a person from the rural areas was recruited into the study. Based on information available about sex work in Liuzhou suggesting that sex workers were much more likely to be workers at the venue rather than patrons, we focused efforts on interviewing workers at venues rather than workers and patrons.

Step 2. The objective of the community informant surveys is to construct a sampling frame of venues where people from Liuzhou (including but not limited to sex workers) meet new sexual partners. The rationale for identifying venues in addition to known sex worker venues was to uncover venues unknown to be places where sex workers solicit and to gain insight into high risk sexual behavior among people who do not self-identify as sex workers. The target number of community informant interviews was 15 in each of the six counties and 310 across the four urban districts. Community informants were aged 18 an older. Selection of informants was done by convenience but based on targets for various types of informants, e.g. taxi drivers, police, health workers, out of school youth, migrant workers, business men and injecting drug users. Interviewers approached people appearing to meet the target type and requested verbal informed consent for a face to face interview. No unique identifiers were obtained and no testing was performed. Each informant was asked to name places where people go to meet new sexual partners. They were asked to describe each venue named including the type of venue and its name and address. Informants identified 971 venues.

Step 3. The objective of the venue visits is to obtain information about the characteristics of the venues identified by the community informants including the number of female workers at the venue, the estimated number of female workers who exchange sex for money at the venue, and whether female patrons included sex workers. It was not feasible to visit all of the 971 unique venues identified. We selected a stratified sample of 385 venues from three strata:

- Venue Group 1: 334 Urban Venues named by only one informant
- Venue Group 2: 317 Urban Venues named by two or more informants
- Venue Group 3: 320 Rural Venues

Within each stratum, venues were sorted by geographical district and type. Venues were selected for venue visits by interval from these ordered lists using a random start. In Group 1, every third venue was selected (33% selected=111 venues); in Group 2, every third venue was not selected (66% selected=211 venues); and in Group 3, 1 in 5 were selected (20% selected=63 venues). 395 venue visits were conducted between November 19,2009 and January 9, 2010. At each selected venue, interviewers asked the manager or some other knowledgeable person aged 18 and older about the characteristics of the venue including the total number of women working at the venue and the number of women who were sex workers. Verbal informed consent was requested. Analysis of venue characteristics is weighted to account for the differences in the probability of selection.

Step 4. Female Worker Surveys. The objective of the worker surveys is to interview a stratified random sample of female workers that would yield interviews with 400 sex workers. Data from the venue visits suggested that few female patrons were sex workers. In a small sample of 95 female patrons, only three reported sex work. Therefore we focused on interviews with female workers. A sample of venues visited in Step 3 were selected for worker interviews, taking into account differences in the probabilities of selection in Step 3 and the expected number of sex workers at each venue. Venues were selected from the three strata as described below:

- Stratum 1: Urban "High Volume Venues". This stratum includes 16 venues that were confirmed during a venue visit in Step 3 as being in operation and where half or more of the female workers exchanged sex for money and where interviewing all workers would yield interviews with at least five sex workers. (Specifically, at these sites, the venue informant reported: 1) that there are sex workers at the site (c21g=1); 2) the proportion of female staff who are sex workers is at least 50% (c29c/c29a > =.5) and 3) there are at least 5 sex workers at the site (c29c>4).) All female staff at these 16 venues were eligible for an interview.

- Stratum 2: 25 Other Urban venues. The 25 selected venues are a stratified random sample of the list of urban verified venues in operation such that all venues had an equal probability of selection. All workers at these venues were eligible for an interview.
- Stratum 3: 23 Rural Venues. Every third venue of the 63 rural operational verified venues was selected for interviews with workers. All workers were eligible up to 5 workers per venue. If more than 5 workers, the 5 were randomly selected.

Interviewers requested interviews with all workers at urban venues. Verbal informed consent was requested and no unique identifiers were obtained. Partial participation was not permitted. A payment of 100 yuan was given to all who agreed to participate in the survey and syphilis testing. Interviews were conducted from January 6-28, 2010.

Women who were age 15 and older who lived in Liuzhou were identified as sex workers based on their responses to multiple questions in a face-to-face interview eliciting whether they had exchanged sex for money in the past 4 weeks. There were two questionnaires administered to participants. The first confirmed age, willingness to participate and if the respondent had participated in the RDS arm. Female workers aged 15-17 were excluded from participation if they were at the venue with their parents or at the venue on a family errand. Parental consent was not requested for the other women age 15-17. The second questionnaire included 82 items including some with multiple questions. The second questionnaire had 6 sections that covered demographic information, venue employment, health issues, sexual history, contraceptive use, and sex work. The first question about sexual behavior followed 36 prior questions. The first question about ever exchanging sex for money was asked over half-way through the questionnaire (Q43e). Other participants in the study were not aware if someone reported sex work or not based on the length of interview. Everyone received the test for syphilis regardless of whether they reported having sex or exchanging sex for money.

Step 5. Feedback to Liuzhou

The preliminary results were presented in an informal meeting with public health professionals in Liuzhou in June, 2010.

**Analysis of PLACE data**

PLACE data analysis used SAS software. Responses were weighted based on the sampling strategy and participation rates both at the venue and individual level. Estimates adjust for stratum and sample weights. Characteristics were estimated using Proc Survey Freq in SAS [3].

**RDS Methods**

**Assumptions of RDS Methods**

Unlike in venue-based sampling, RDS sampling weights are not known to researchers. Participants' number of reciprocal ties with other members of the target population is used to approximate an individual's sample inclusion probability on the assumption that the chain referral process selects respondents with probability proportional to a respondent's personal network size. RDS theory rationalizes this assumption in terms of an idealized model of how sample subjects make referrals to new subjects and potential respondents are recruited into the sample, under the following stringent conditions: (a) all eligible members of a respondent's network have an equal probability of recruitment by the respondent; (b) there is reciprocity in recruitment (that is, if individual a recruits b, then b would recruit a); (c) respondents accurately report the number of members of their social networks who meet the study definition; and (d) the network is sufficiently large to allow sampling without replacement.

Threats to the representativeness of samples and validity of population estimates obtained through RDS may be introduced in two ways. The first is if the reported personal network size does not provide the correct sampling weight[4] [5, 6]. This could arise if RDS participants inaccurately report their network size; if they recruit preferentially from their immediate social network on a characteristic associated with infection; or if infected individuals have more contacts than their uninfected counterparts, leading to proportionally down-weighting high degree individuals, underrepresentation of the infected group and a negative bias in the proportion infected[6]. The second is if other factors, in addition to network size, influence the probability that infected members of the population are included in the sample. For example, infected sub-groups of the population might be missed because they are not linked through the peer network, or the RDS assumption of non-preferential recruitment of participants constrains researchers from guiding the referral process towards members of the population who are likely to be missed. The inability to redirect the chain referral can prove particularly problematic if recruitment chains become trapped in low infection venues which would limit the ability of a potentially infected respondent to be recruited into the sample; if incentives paid to recruited peers influence the likelihood that people who do not meet the study definition will be recruited; if the location of the interview is less accessible to those infected; and if participants who refuse to be tested are more likely to be infected than those who agree to the test.

**RDS Sample recruitment**

Between October 26, 2009 to January 29, 2010, RDS methods were used to recruit FSWs in Liuzhou. Eligible participants were women 15 years and older who had sex in exchange for money during the month prior to the interview and were currently working and living in Liuzhou (including rural counties). Eligibility for participation in the RDS arm was being at least 15 years old, a first time participant in the RDS arm, and self-identified as a sex worker in response to the question: "Have you exchanged sex for money in the past month?."

Seven seeds, stratified by place where they solicited clients (massage parlour, hair salon, KTV-karaoke bar, sauna and park) were recruited with the help from experienced local outreach workers. All except one of the seven seeds recruited other participants. The six productive seeds generated between 9 and 20 waves of recruitment. 310 out of 583 respondents were recruiting participants, while the remaining 273 did not recruit any participant. Participants in the Liuzhou RDS were given from the start two coupons, a number which was further reduced to one after the 14th wave to control sample growth. The idea of systematic coupon reduction, which involves decreasing the number of coupons from two to one at a specific wave in the recruitment chains was discussed by Johnston et al.[7] Our decision to reduce the number of coupons for sample growth control was based on the theoretical consideration that this forces the sampling process to more closely resemble a non-branching random walk, a strategy that was shown to reduce the variance of RDS estimates[8].

As in the PLACE arm, interviews were administered face-to-face by trained nurses in Mandarin Chinese and Zhuang, the language spoken by the largest ethnic minority group in Liuzhou. However in the RDS arm, interviews were conducted at a single fixed interview site located in a local hospital in one of Liuzhou's urban districts, easily accessible by public transportation. Participants could drop-in or phone to make an appointment. Participants were screened upon arriving at the interview site.

Each participant received a primary incentive of 100 yuan (ca. US$ 14) for the interview and to cover transportation to the interview site and a secondary incentive of 50 yuan for each of her successful recruitments. The appropriate size of these incentives was determined after formative research was conducted prior to the fielding of the survey and in consultation with Liuzhou outreach workers who were familiar with the organization of sex work in the city.

To prevent potential respondent duplication, during screening of respondents for eligibility, biometrics (height, weight, and left/right forearm length and wrist circumference) were collected and entered in a password protected RDS coupon manager to identify potential duplicates. To minimize the threat presented by impersonators recruited into the sample by recruiters eager to fill their coupon quota or attracted by the size of the incentives, interviewers were trained to detect impersonators through a series of questions in the screening phase of the interview. Incentives were also judged not large enough as to encourage participation by imposters or coercive recruitment.

**RDS Questionnaires**

The questionnaires used to measure socio-demographic characteristics and HIV/STD-related risk behaviors were based on the RDS module provided by investigators who employed RDS to recruit female sex workers in Vietnam[9], on the FSW module of the Family Health International Behavioral Surveillance Surveys [10], on the standard PLACE protocol [2], and on a household survey of sexual behavior in Liuzhou implemented in 2008. The questionnaires included socioeconomic and demographic information, sexual behavior practices, drug use and STD symptoms. An additional set of questions on sex work history and reasons for sex work was introduced as part of this study. For RDS purposes, network size was measured using the question: "How many sex workers do you know in Liuzhou (including rural counties)? By knowing, I mean: you know their names and they know yours, and you have met or contacted them in the past month." When recruiting participants returned to the interview site to collect their secondary incentives, they were administered a brief follow-up questionnaire to collect information on basic socio-demographic characteristics, place of work, type and strength of relationship relative to all members of the participant's network, including those whom they recruited successfully, those who turned down the invitation to participate and, as a variation of the usual RDS practice, those whom they did not invite to participate. All respondents provided informed consent and anonymous interviews.

**RDS Syphilis Testing**

The RDS and PLACE arms used the same rapid syphilis test. Blood samples for rapid syphilis testing were collected by finger prick (Wantai anti-TP Antibody Rapid Test, Wantai Biological Pharmacy Enterprise, Beijing, China) on a voluntary basis. 47 out of 583 eligible RDS respondents did not agree to the test on grounds that they were tested in the past. Participants were administered the questionnaires regardless of their participation in the rapid syphilis test. (In the PLACE arm, individuals were required to participate in both the test and interview.) Test results were provided to those who agreed to take it at the end of the interview. If RDS participants tested positive, they were invited to immediately provide a blood sample using a needle for confirmatory testing (Toulidine Red Unheated Serum Test, Rongsheng Biotechnical Company, Shanghai, China). However, to increase confidentiality of results, positive-testing participants on the rapid test had the option to return on another day for the confirmatory test. Of the 40 participants who tested positive on the rapid test, 36 agreed to the confirmatory test. Of these, 20 tested positive for active syphilis. All tests were performed by trained doctors and lab technician at the same hospital of the interview site. Free treatment was offered to those with confirmed active syphilis. PLACE participants who agreed to the confirmatory test were required to visit a hospital to obtain the confirmatory testing.

**RDS data analysis**

RDS data were analyzed using the RDS Analysis Tool (RDSAT) Version 5.6.0 [11] and the RDS-2 estimator[12] implemented using R software by one of our co-authors (Neely). We used both RDSAT and RDS-2 estimators [12]to generate estimates of population proportions and their confidence intervals. The validity of estimates from RDSAT requires that the chain referral process samples individuals with probability proportional to their network sizes and that it represents a first-order Markov process that has achieved equilibrium in the sense that the overall composition of the sample has become stable with increasing numbers of recruitment waves[13, 14]. RDSAT estimates of group proportions are calculated based on cross-group recruitments, tracked through the unique codes on the recruitment coupons and used to calculate equilibrium estimates from the Markov model, and a weighted-average of participants' personal networks.

The options used in the RDSAT software were:

- Network size estimation: dual component (default)
- Mean Cell Size: 12 (default)

- Number of re-samples required for bootstrap: 2500 (default)
- Confidence interval (2-tailed alpha): 0.025 per tail
- Did not pull in outliers of network sizes. (default)
- Algorithm type: Data smoothing (default)

The RDS-2 estimator, on the other hand, requires only the assumption of sampling probability proportional to network size and computes population proportions based on a weighted average of participants' network sizes. Our decision to present RDS-2 estimates together with the more conventionally used estimates from RDSAT was motivated by the following reasons: First, simulation and empirical studies have found RDS-2 may yield estimates with less bias [12, 15]. Second, reliance on RDS-2 estimates is greater when equilibrium estimates cannot be computed and RDSAT estimates cannot be generated. This was the case for proportion estimates for a few selected socio-demographic characteristics.

RDSAT relies on a bootstrap computations presented in Salganik[16] to estimate confidence intervals. To estimate confidence intervals for proportions computed using the RDS-2 estimator, we used a variant of this bootstrap methodology. Volz and Heckathorn [12] also described an algebraic variance estimation procedure designed specifically for use with the RDS-2 estimator. However that procedure (at least in its published form) was derived under the assumption that the recruitment chain was linear (that is, there was no branching). Furthermore the Volz and Heckathorn variance estimation formula [12]has only been published in a form suitable for binary variables, while in our analyses we also deal with multi-category variables. As a result we decided to implement a simple model-based bootstrap estimator consistent with the underlying statistical model that is used throughout the RDS literature. This estimator is described in full below. All estimates were independently derived using the formulas described in Volz and Heckathorn[2008] [12] and Salganik[16] using the R statistical language **(**www.r-project.org**)**. Pre-processing of the data was performed using Stata[17].

The figure in the showing the chains of recruitment in RDS were produced by Netdraw with data output from RDSAT using the following settings: 1,000,000,000 iterations, spring embedding, distance between components:30, proximities: geodesic distances.

**RDS-2 Confidence Intervals Estimation**

In this procedure one defines a resampling scheme that can be used to create a collection of samples that, one hopes, have a distribution similar to the actual sampling process that generated the data. To make this concrete, suppose we wish to estimate the proportion of the population who are in some subgroup A (say, for example that A represents members of the population who test positive for HIV, or some other sexually transmitted disease). In this situation we wish to estimate both the proportion of the population in A, and (in order to examine the statistical significance of the result) we need to compute a confidence interval. Salganik's procedure provides a recipe for computing such a confidence interval as follows. First, construct the following algorithm for computing a single bootstrap estimate:

1. Divide the sample into two subsets: A[rec] consisting of individuals recruited by members of A, and B[rec] consisting of individuals recruited by members in the complement of A.

2. Select a "bootstrap seed" from the data by selecting an observation of the sample at random (i.e. make a random draw from the sample by selecting from amongst the observations so that each observation has equal probability of being drawn).

3. Starting with the bootstrap seed select a new observation by selecting at random (with equal probability) from either A[rec] or B[rec] depending on the group membership of the bootstrap seed. Continue this process recursively until one has selected a sequence of observations of the same size as the original sample. One then has a single bootstrap sample whose size is identical to the original data set. The data in the sample consist of an observed group membership and self-reported network size. A set of data constructed in this manner will be called a bootstrapped data set, or bootstrapped data for short.

Next we use 1-3 above to create many bootstrapped data sets:

4. Repeat 1-3 above until one has many versions of the bootstrapped data (i.e one has many artificial data sets, each constructed by the procedure above).

5. To compute a confidence interval for an estimator of p[A] (in principal any estimator, though at the time that Salganik was writing Volz's RDS-2 had not be developed yet), apply the estimator to each member of the collection of data sets above to yield a collection of bootstrapped estimates. This collection can be used to compute confidence intervals by either computing the variance of the bootstrapped variance (which is what Salganik does) or by reporting 95% central quantiles of the bootstrapped estimates. The latter strategy has the advantages that it is a standard approach in the bootstrap literature[18]and because it automatically provides intervals that are constrained to be within the interval [0,1] as is natural for a proportion estimate.

In order to examine the implications of using this procedure to compute confidence intervals, we recast this algorithm in a mathematically equivalent form that describes the model under which groups and degrees are simulated for the bootstrapped data. First, in order to simulate group memberships, we approximate the probability of transitions within and between the groups A and B by constructing a Markov transition matrix

$$\hat{P} = \begin{bmatrix} n_{AA}/(n_{AA}+n_{AB}) & n_{AB}/(n_{AA}+n_{AB}) \\ n_{BA}/(n_{BA}+n_{BB}) & n_{BB}/(n_{BA}+n_{BB}) \end{bmatrix}$$

where $n_{A,B}$ is the number of observed transitions from group A to group B seen in the original data. The terms $n_{AA}$, $n_{BA}$ and $n_{BB}$ are similarly the number of observed transitions from the group indicated by the first subscript to the group indicated in the second subscript. This matrix gives the exact probabilities of the transitions between groups under Salganik's bootstrap. In terms of statistical modeling, is the maximum likelihood estimate for the transition probabilities under a first order Markov model for the group transitions observed in the sample (see Anderson[19] for classical material on inference under this model, see either Volz[12] or Goel and Salganik[20] for detailed discussions of in the context of RDS). In Salganik's bootstrap, once groups have been simulated, we can simulate degrees by making a random draw from the observed degrees for the appropriate group. The entire process of creating a single bootstrapped data set can be described as follows.

1. Select a seed, $y_0^{boot}$ by making a random draw from the observed sample, thus $y_0^{boot}$ will be in A with probability $n_A/(n_A + n_B)$ and in B with probability $n_B/(n_A + n_B)$ where $n_A$ and $n_B$ are the number of observations in the sample from groups A and B respectively.

2. Select $y_1^{boot}$through $y_n^{boot}$iteratively by using the transition probabilities determined by.

In other terms, if $y_i^{boot}$is an A, then$y_{i+1}^{boot}$will be an A with probability $n_{AA}/(n_{AA}+n_{AB})$and in B with probability $n_{AB}/(n_{AA}+n_{AB})$.

3. After selecting $y_1^{boot}$through $y_n^{boot}$, select bootstrapped degrees $d_1^{boot}$through $d_n^{boot}$by selecting $d_i^{boot}$randomly from the observed degrees in the group corresponding too $y_i^{boot}$. Again, to be concrete, if$y_i^{boot}$is A then we select $d_i^{boot}$by making a random draw from the observed degrees for group A. If$y_i^{boot}$is B then we select$d_i^{boot}$by making a random draw from the observed degrees for group B.

The description above can be summarized quite concisely by saying that the Salganik bootstrap (i) models group membership (in A or B) as a linear first order Markov chain of length $n$with transition probabilities and (ii) models degrees as conditionally independent given group membership. Before we discuss the potential shortcomings of this approach we briefly describe the modeling assumptions behind the other variance estimation approach currently in use with RDS data.

There are two features of the above bootstrap procedure that are worth noting. First, the above procedure can be used to estimate the sampling distribution of any RDS estimator. This is because the bootstrap method is primarily a procedure for creating bootstrapped data. Thus, one uses the procedure to construct a large number of synthetic data sets whose distribution, one hopes, matches the sampling distribution of the actual RDS process. Then, in order to estimate the sampling distribution of a population estimator, one applies that estimator to each of the bootstrapped data sets in turn in order to create a large sample of bootstrapped population estimates. Consequently, one can apply this approach to any RDS estimator, including the RDS-2 estimator developed by Volz.

The second feature that is worth noting is that in Salganik's procedure there are two factors that clearly influence the ability of the bootstrap to approximate the actual sampling distribution. The first of these is that one replaces the branching observations of the RDS sampling process with a linear chain. One would expect therefore that a bootstrap method that uses the same branching procedure as the data collection process would do a better job of replicating the sampling distribution of RDS. The danger that a linear chain runs the risk of underestimating variance has been observed previously by Goel and Salganik (2009)[20]. As a result in our implementation we have used the observed branching structure of our sample, rather than a linear structure. The second feature is that Salganik samples the entire data set when selecting seeds. We believe that this approach is contrary to the very motivation for RDS: the seeds are drawn from an accessible stratum of the target population and are surely not distributed in the same manner as the actual RDS sample. As a result our bootstrap procedure treats seeds as a fixed aspect of the sampling design since they are selected by the researcher. Thus our bootstrap algorithm can be described as follows:

1. Select bootstrapped seeds, $y_0^{boot}$ by making as identical to the observed seeds.

2. For each wave in the data set, select member $y_i^{boot}$by using the transition probabilities in

and the value of the recruiter $y_j^{boot}$where $j$is the recruiter of $i$in the original data. In other terms, if $y_j^{boot}$is an A, then$y_i^{boot}$will be an A with probability $n_{AA}/(n_{AA}+n_{AB})$and in B with probability $n_{AB}/(n_{AA}+n_{AB})$.

3. After selecting $y_1^{boot}$through $y_n^{boot}$, select bootstrapped degrees $d_1^{boot}$through $d_n^{boot}$as before. Thus we select $d_i^{boot}$randomly from the observed degrees in the group corresponding too $y_i^{boot}$. Again, to be concrete, if$y_i^{boot}$is A then we select $d_i^{boot}$by making a random draw from the observed degrees for group A. If$y_i^{boot}$is B then we select$d_i^{boot}$by making a random draw from the observed degrees for group B.

In order to obtain confidence intervals we use the above method to simulate 100000 bootstrapped data sets and apply the RDS-2 estimator to each of these yielding 100000 bootstrapped population estimates. The confidence intervals reported as thus the central 0.025% to 0.975% quantiles of the bootstrapped population estimates.

**Methods to Compare Characteristics of PLACE and RDS Sampled Populations**

We expected that 15% of women engaged in sex work would have a positive rapid test. Assuming that the population of sex workers in Liuzhou is approximately 5,000, a sample size of 380 sex workers in each group would have 80% power to detect a difference of +/- 5% , assuming alpha=0.05 and the design effect is 2. We aimed for at least 400 sex workers in each group and planned on a larger sample for the RDS arm. Characteristics of the two samples and the corresponding confidence intervals were done separately. For the PLACE estimates, SAS

Proc Survey Freq was used with appropriate sampling weight and clustering by strata. We compared RDS estimates as calculated by RDSAT software and by RDS-2 estimates as described above.

For the multivariable analysis, the two data sets were combined and analyzed using Proc Genmod in SAS using the method as recommended by Cole[21]. The models were run with RDSAT weights for the RDS participants and separately with RDS-2 weights. Weights for the RDS sample were estimated using two different methods with similar results except that prevalence ratios could not be estimated using weights output from RDSAT software. Data from each PLACE worker were weighted based on the probability that the venue where the worker was interviewed was selected for a venue visit, the probability that the venue was selected for worker visits, the proportion of venues willing to participate, and the proportion of workers who participated.

We assumed an independent correlation matrix. The models were run using PROC GENMOD [21] with the weights estimated separately for persons recruited by PLACE and RDS. The natural log of the probability of the $j^{th}$ person in the $i^{th}$ cluster having a positive rapid test for syphilis was modeled as a linear function:

$$\ln[E(Y_{ij})] = \beta_0 + \beta_1 \delta_{ij} + \beta_2 Age_{ij}$$

where $[E(Y_{ij})]$ is the expected value of the probability of having a positive rapid test for the $j^{th}$ person in the $i^{th}$ cluster; $\delta_{ij}$ indicates whether the person is in the PLACE arm or not; and age is the respondent's age.

The code for the model follows. For RDS, class is the recruitment chain; For PLACE, class is the stratum from which the participant was sampled.

```
proc genmod  data=china.modeldata4 descending;
class cluster; model syphilis2 = place   / d=b link=log;
scwgt normalw1; repeated subject = cluster / type=ind;
title ratio place  all weighted;  estimate "prevalence ratio" place  1 / exp;
output out=results5 p=prevalence;
```

Supplementary Figure 2 was constructed using the predicted prevalence of a positive test from the binomial regression model similar to the model indicated above. The model-predicted probability of a positive screening test by age was lowest for RDS sex workers and highest for rural PLACE sex workers.

The model used for the graph included two indicator variables to represent the three groups on the graph (RDS, PLACE urban, and PLACE rural), and included interaction between group and age. Age was modeled using restricted cubic splines with knots at 16, 20, and 30 years. The macro "RCSPLINE" was used[22]. The figure was constructed from a model containing only individuals age 35 and younger and does not present the probability of infection at older ages. A comparison of the probability of infection by age among older women is not presented because the probability estimates were unstable at older ages among PLACE women because there were few older sex workers in the PLACE arm (n=26). In the RDS arm, women older than 35 comprised 12% of the sample and 35% had a positive rapid test compared to 3.8% of younger women. Of the 64 infections among the RDS arm, 42 were older than 35. In the PLACE arm, the proportion of women with a positive test was similar for women older and younger than 35 (26% vs 23%), although the confidence intervals were much wider around the estimate for the older women (0.0,53.5 vs. 11.9,35.0) due to the small sample size in the PLACE arm.

Overall, there was not a statistically significant difference in the RDS and PLACE estimates of the percentage of sex workers recruiting in urban Liuzhou who had a positive rapid test for syphilis (8.2 vs 17.8). The study was not powered to assess differences between the urban and rural sub-groups.

The table below compares RDSAT and RDS –II estimates.

**Comparison of Estimates from RDSAT and RDS II**

Table 1. Sociodemographic and Behavioral Characteristics of Female Sex Workers (FSW) in Liuzhou Recruited by Respondent-driven sampling (RDS): Comparison of RDSAT and RDS II estimates.

| | RDS | | | |
|---|---|---|---|---|
| | RDSAT | | RDS-II | |
| | % | 95%CI | % | 95%CI |
| total | 576 | | 576 | |
| Age group | | | | |
| 15-19 | 13.1 | 8.1, 17.8 | 11.42 | 8.0,20.2 |
| 20-24 | 32.1 | 24.6, 40.4 | 31.35 | 23.0,42.6 |
| 25-29 | 17.4 | 13.0, 22.4 | 20.23 | 12.7,23.2 |
| 30-34 | 16.5 | 10.6, 21.7 | 19.5 | 11.1,22.3 |
| 35-39 | 10.9 | 6.1, 16.9 | 10.70 | 4.8, 16.8 |
| 40+ | 10.1 | 3.8, 18.5 | 6.81 | 2.1,19.8 |
| Residence | | | | |
| District of RDS Office | 47.0 | 40.7, 53.0 | 46.21 | 40.8, 53.4 |
| Other Urban districts | 50.5 | 44.6, 57.0 | 51.28 | 44.0, 56.6 |

| | RDS | | | |
|---|---|---|---|---|
| | RDSAT | | RDS-II | |
| | % | 95%CI | % | 95%CI |
| Rural Counties | 2.5 | 1.2, 4.0 | 2.51 | 1.3, 4.1 |
| Marital status | | | | |
| Never Married | 62.9 | 55.1, 69.8 | 62.20 | 54.8, 70.7 |
| Divorced/Widowed | 23.5 | 17.9, 29.8 | 24.01 | 17.4, 29.6 |
| < Junior High Education | 25.8 | 19.7, 31.8 | 25.34 | 19.8, 31.5 |
| Monthly Income RMB | n/a | | 4,888 | |
| Aged<15 at first sex | 2.2 | 0.9, 3.9 | 2.09 | 0.9, 3.9 |
| Ever Arrested | 10.2 | 6.9, 13.9 | 10.64 | 7.2, 14.0 |
| > weekly Alcohol use | 37.7 | 30.1, 45.8 | 36.6 | 28.1, 45.6 |
| Ever injected drugs | 2.4 | 0.4, 5.1 | 1.97 | 0.4,5.4 |
| Sex work past 4 weeks | 100 | | 100 | |
| >10 Partners past 4 weeks | 56.7 | 50.0, 64.0 | 55.73 | 55.8,72.2 |
| Condom use at last sex | 71.0 | 64.9, 76.8 | 71.5 | 65.3, 76.6 |
| Solicited past year in: | | | | |
| urban Liuzhou | n/a | n/a | 99.39 | 83.4, 1.0 |
| rural Liuzhou | 3.8 | 2.0, 6.2 | 3.88 | 1.9, 6.0 |
| outside Liuzhou | 12.6 | 8.7, 16.9 | 12.17 | 8.5 16.9 |
| Solicited past 6 months | | | | |
| Outdoors | 6.4 | 1.5, 13.3 | 4.1 | 0.9,14.0 |
| Phone/Internet | 32.0 | 26.3, 37.8 | 31.6 | 26.4,37.7 |
| KTV, Karaoke | 29.0 | 17.0, 43.4 | 22.4 | 11.9, 43.8 |

| | RDS | | | |
|---|---|---|---|---|
| | RDSAT | | RDS-II | |
| | % | 95%CI | % | 95%CI |
| Hair Salon | 12.4 | 6.5, 18.7 | 12.6 | 7.4,19.7 |
| Massage | 35.2 | 26.6, 44.5 | 33.9 | 24.0, 47.1 |
| HIV tested, know results | 28.3 | 22.6, 34.1 | 28.9 | 22.9, 35.6 |
| Syphilis test past year | 7.3 | 4.5, 10.3 | 7.59 | 4.8, 10.5 |

Note: RDSAT, Respondent-driven sampling analysis tool; CI, confidence interval; n/a, not available since all RDS respondents worked in urban area. The 7 RDS seeds were excluded from RDSAT and RDS-II estimates. The 47 RDS FSW who participated in the survey but refused the rapid syphilis test were included in this table. The 161 sex workers are a subset of the 680 workers recruited through PLACE. RDSAT does not calculate means. RDS-II does not calculate medians. Income is mean monthly income.

FIGURE TITLES

Supplementary Figure 1. PLACE Study flow chart, Liuzhou, China, 2009 – 2010

Supplementary Figure 2 Predicted probability of a positive rapid test for syphilis among women age 15-35 by age and urban district-county status

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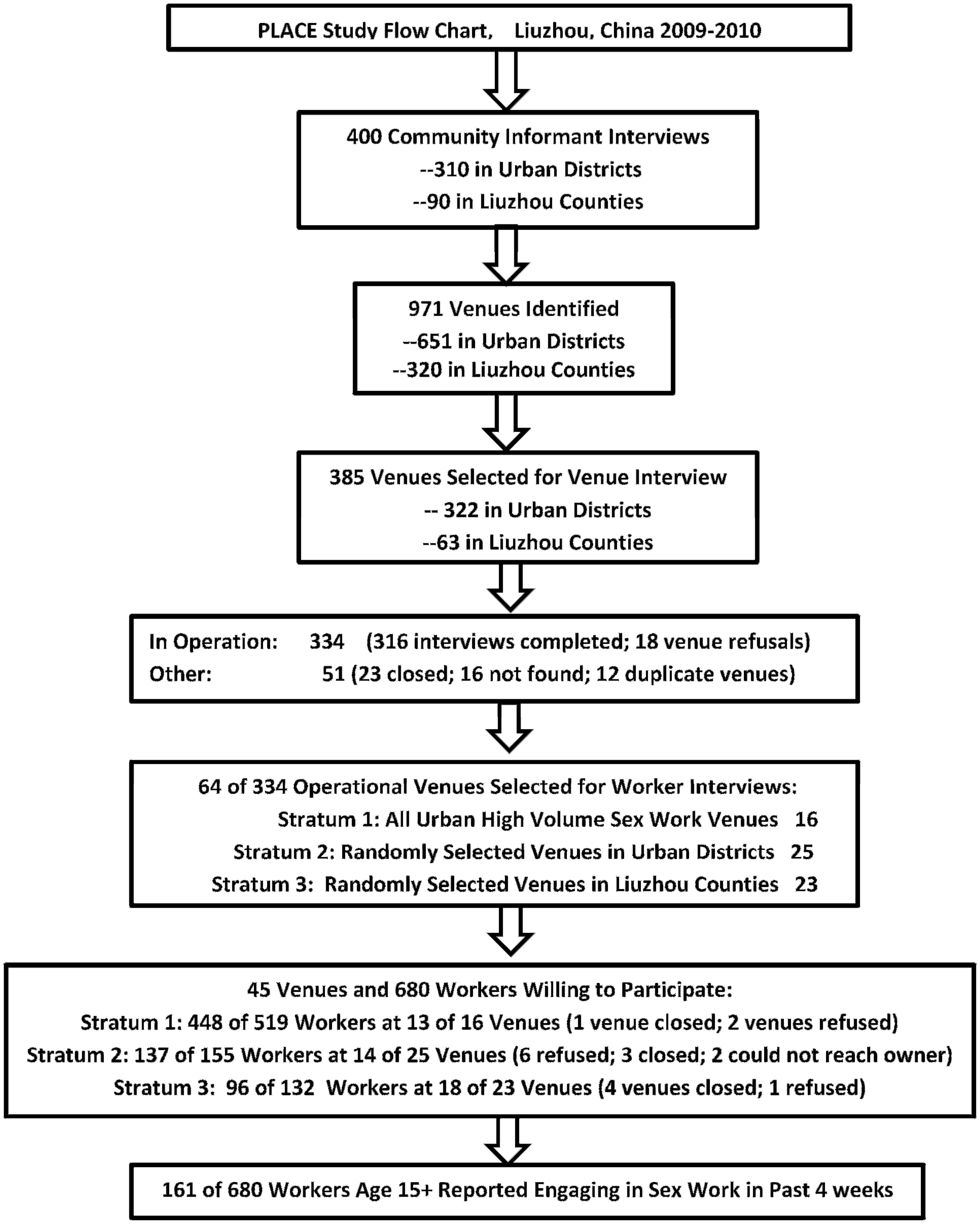
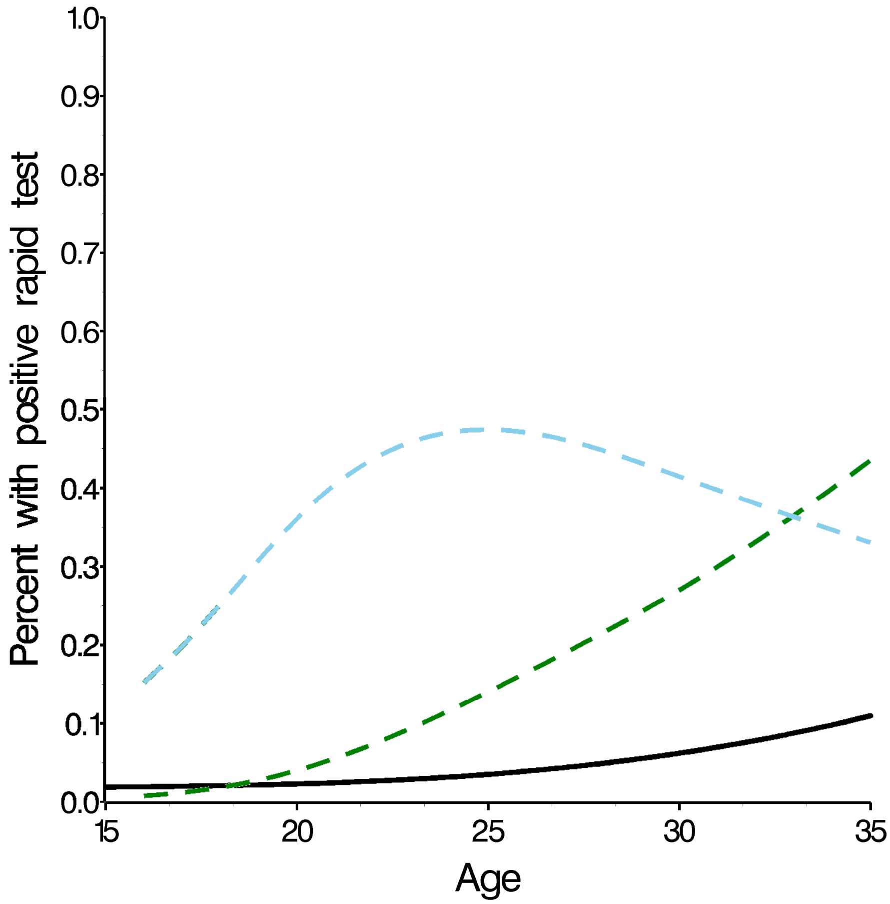

PLACE Study Flow Chart, Liuzhou, China 2009-2010
400 Community Informant Interviews
--310 in Urban Districts
--90 in Liuzhou Counties
971 Venues Identified
--651 in Urban Districts
--320 in Liuzhou Counties
385 Venues Selected for Venue Interview
-- 322 in Urban Districts
--63 in Liuzhou Counties
In Operation: 334 (316 interviews completed; 18 venue refusals)
Other: 51 (23 closed; 16 not found; 12 duplicate venues)
64 of 334 Operational Venues Selected for Worker Interviews:
Stratum 1: All Urban High Volume Sex Work Venues 16
Stratum 2: Randomly Selected Venues in Urban Districts 25
Stratum 3: Randomly Selected Venues in Liuzhou Counties 23
45 Venues and 680 Workers Willing to Participate:
Stratum 1: 448 of 519 Workers at 13 of 16 Venues (1 venue closed; 2 venues refused)
Stratum 2: 137 of 155 Workers at 14 of 25 Venues (6 refused; 3 closed; 2 could not reach owner)
Stratum 3: 96 of 132 Workers at 18 of 23 Venues (4 venues closed; 1 refused)
161 of 680 Workers Age 15+ Reported Engaging in Sex Work in Past 4 weeks



1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Percent with positive rapid test
15
20
25
30
35
Age