

BMJ Open Syphilis among middle-aged female sex workers in China: a three-site cross-sectional study

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ABSTRACT

Objectives: This study addresses the lack of empirical studies about the epidemic of syphilis among middle-aged female sex workers (FSWs). The objectives of this study were to investigate prevalence of syphilis, and its potential risk factors among middle-aged FSWs in China.

Design: A cross-sectional study with respondent-driven sampling (RDS).

Setting: A multisite study conducted at three Chinese cities (Nanning, Hefei, and Qingdao) with different levels of sexually transmitted diseases in 2014.

Participants: 1245 middle-aged female sex workers who were over 35 years old (about 400 per study site).

Main outcome measures: Unprotected commercial sex, and syphilis and HIV infection were biologically tested and measured.

Results: The RDS-adjusted prevalence of active syphilis was 17.3% in Hefei, 9.9% in Qingdao, and 5.4% in Nanning. The RDS-adjusted prevalence of prevalent syphilis was between 6.8% and 33.6% in the three cities. The proportion of unprotected sex in the past 48 h verified by the prostate-specific antigen test (PSA) was between 27.8% and 42.4%. Multiple log-binomial regression analyses indicate that middle-aged FSWs who had 5 or more clients in the past week prior to interviews and engaged in unprotected sex were more likely to be active syphilitic cases. Middle-aged FSWs who had rural residency were less likely to be active syphilitic cases.

Conclusions: In contrast with previous studies that reported low prevalence of syphilis and high prevalence of protected sex among FSWs in China, both the prevalence of syphilis and unprotected sex were high among middle-aged FSWs. Evidence-based intervention programmes should be developed and evaluated among this vulnerable population in China and other countries with similar settings.

INTRODUCTION

The epidemic of syphilis has spread among the older population in both developed and developing countries,^{1 2} including China.^{3 4} According to the China National Sexually Transmitted Disease (STD) Surveillance, the

Strengths and limitations of this study

- Use of respondent-driven sampling to recruit study participants.
- Conducted at three sites for different levels of sexually-transmitted diseases.
- Use of biomarkers to measure prevalent and active syphilis, and condom use.
- Temporal ambiguity bias due to the nature of a cross-section study.
- Non-response or non-appearance may bias the results.

proportion of syphilis cases aged 60 years and older increased rapidly from 9% in 2004 to 22% in 2013 among the total reported cases, most of whom were recently infected.^{4 5} The increased number of syphilis cases may reflect a real increased incidence of syphilis in the elder population or could be the result of the more thorough screening efforts that could have captured latent syphilis cases.⁴ Commercial sex is a major mode of syphilis transmission as the majority of infected older cases reported a history of commercial sex with sex workers, especially, with those charging low rates or middle-aged female sex workers (FSWs) who are over 35 years old.^{6–8}

Middle-aged FSWs in China tend to enter sex work for survival sex in their 30s.^{6 9 10} These sex workers are often married and have children, and there is a great need for them to make enough money to support their families. In contrast, young FSWs usually start sex work in their early 20s. After making enough money to start their own private business (eg, run a barbershop, restaurant, roadside hotel, small grocery store or sell clothes), young FSWs often quit sex work, typically in their 30s.¹¹ Previous research in China and other developing countries have examined the epidemic of syphilis, and its potential determinants among predominantly young FSWs.^{12–14} However,



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findings from these studies may not apply to middle-aged FSWs as they may have different behavioural risk factors for syphilis. Despite the rapid spread of syphilis among older adults, little research has focused on middle-aged FSWs, a critical source of infection.

We conducted a multisite cross-sectional survey among middle-aged FSWs in three Chinese cities. The objectives of this study were to investigate the prevalence of syphilis, and the behavioural factors that were associated with syphilis infection among this vulnerable population. We hypothesised that middle-aged FSWs who engaged in risky sexual behaviour (inconsistent condom use, multiple sexual partners and illicit drug use) were more likely to be infected with syphilis compared with those who did not.

METHODS

Study sites and study samples

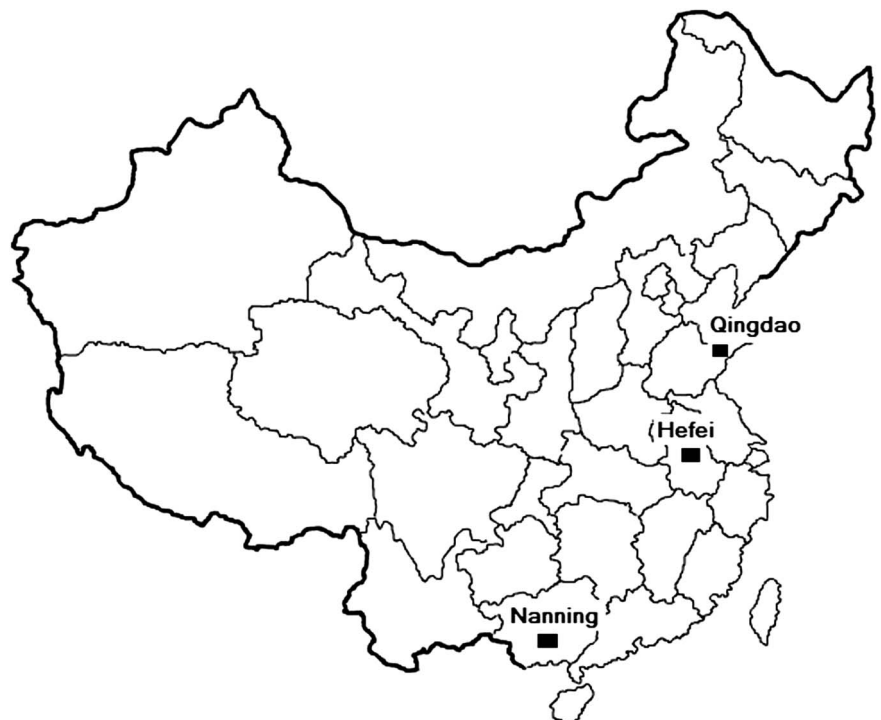
Detailed information regarding the sampling has been previously reported elsewhere.¹⁵ Briefly, this cross-sectional study was conducted in three cities in China in 2014: Qingdao, Hefei and Nanning (figure 1). In order to recruit samples that cover different levels of the STD epidemic, three different geographic regions were purposefully selected from northern China to the south that captured variation in the number of STDs. According to the local surveillance data and China National HIV/STD Surveillance,¹⁶ Nanning is located in the area with the highest HIV/STI prevalence (8618 HIV cases and 36 404 notifiable STI cases reported from 2010 to 2013), Hefei had mid-level prevalence (1105 HIV cases and 21 344 STI cases), and Qingdao had the lowest prevalence (733 HIV cases and 8748 STI cases).

The inclusion criteria defined middle-aged FSW as (1) women who over 35 years old, (2) lived in one of the three cities for at least 3 months; and (3) had commercial sex at least once a week in the past month prior to the interview. The selection of 35 years of age to define middle-aged FSWs was based on findings from our qualitative studies conducted at the three sites.⁶

Recruitment of study subjects

Respondent-driven sampling (RDS) was used to recruit participants.^{17 18} The reason for selecting RDS rather than the venue-based sampling approach was that the RDS sample covered eligible participants who did not work in venue-based brothels. Four or five seeds were selected from each site. The selection of seeds was based on the results from our qualitative study and suggestions from middle-aged FSWs. The seeds received an explanation of the study purpose and three coupons to recruit up to three eligible participants from their social networks. All new recruits in the subsequent recruitment waves participated in an anonymous interview in a private room and were offered three coupons similar to the seeds. The number of recruitment waves was 8 in Qingdao, 9 in Hefei and 11 in Nanning. Participants received compensation for their time and transportation costs, with \$10 given for their participation in the interview and \$3 for each eligible participant they recruited. Convergence plots were used to determine whether the final RDS estimates were biased by the initial convenience sample of seeds.¹⁹ Five variables were used in this convergence analysis, including age, education, marital status, migration status and location of client solicitation. In each site, after 100–300 participants were recruited,

Figure 1 Location of the three study sites (Qingdao, Hefei, and Nanning).



the proportions of the five variables reached convergence or equilibrium (eg, the proportions remained unchanged in the later recruitment waves). Therefore, our evaluation of this RDS sample at each study site indicated its success in reaching the convergence of RDS compositions that included a broad cross-section of the hidden population.

In this study, we estimated a sample size of 400 participants at each study site, which ensured that recruitment went through a sufficient number of recruitment waves (at least 5 waves required by RDS). In addition, a sample size of 400 produced a two-sided 94% CI with a width equal to 0.06 when the sample proportion was 0.10.²⁰ According to previous reports,^{21–22} the prevalence of syphilis was about 10% among FSWs in China.

Interviews

As the education level was relatively low among middle-aged FSWs,⁶ trained interviewers used computer-assisted personal interviewing (CAPI) to interview participants. Interviewers at each site received training in interviewing techniques, for developing rapport, ensuring confidentiality, and for answering questions raised by participants. Interview sites were located in the local Centers for Disease Control and Prevention, general clinics and hotels. The selection of these sites was based on two conditions: easy access (less than 1 h travel time) and protection of participants' confidentiality.

Biological tests

Trained laboratory technicians collected and tested the following specimens from each consenting participant (1) venipuncture blood specimen for syphilitic and HIV infection, and (2) a vaginal secretion specimen for prostate-specific antigen (PSA) test. Syphilis infection was first screened using a qualitative immunoassay to detect antibodies to *Treponema pallidum* (Alere Determine TP test; Alere Medical Co. Ltd, Chiba Prefecture, Japan) and was confirmed by a *T. pallidum* particle agglutination test for detection of antibodies to *T. pallidum* (TPPA; Fujirebio Inc, Tokyo, Japan). Confirmed TPPA positive samples were tested for non-treponemal antilipoidal antibodies using Tolidine Red Unheated Serum Test (TRUST; Wantai Biological Pharmacy Enterprise Co, Ltd, Beijing, China). Screening for HIV was performed with enzyme immunoassay (Alere Determine HIV-1/2; Alere Medical Co, Ltd, Chiba Prefecture, Japan), and positive screening results were confirmed with western blot (WB) confirmatory tests (MP Biomedicals Asia Pacific Pte Ltd, Singapore). Unprotected sex in the past 48 h was biologically measured by PSA. Presence of PSA was tested using ABACard p30 test (Abacus Diagnostics, West Hill, California, USA). The presence of PSA is detectable in vaginal discharge for 48 h after acts of unprotected vaginal intercourse.^{23–24} The PSA test is 100% sensitive (95% CI 98% to 100%) and 96% specific (95% CI 93% to 97%) for testing PSA within 48 h after vaginal

intercourse.²³ Our previous report had information bias for self-reported condom use when using PSA as the golden standard.¹⁵

Prevalent cases and active cases of syphilis

Middle-aged FSWs who tested seropositive for TPPA were classified as prevalent cases of syphilis (including both previous and active syphilis) as a positive test indicates evidence of the antibody to syphilis, and is interpreted as a lifetime marker of having ever been infected. Those who were tested seropositive for both TPPA and TRUST were classified as active cases (or current cases) of syphilis (including active or latent treponemal infection). While TPPA is a lifetime marker of having ever been infected, TRUST is a marker of a recent syphilis infection.

Questionnaire measurements

HIV/STI knowledge regarding STI transmission and prevention was measured by 11 true or false questions (example items: Consistent condom use can prevent STIs; If a client does not show signs of STIs, it is safe to have sex with him because there is no risk of getting the infection from him). One point was given for each correct answer (score range: 0–11). Self-perceived risk for STDs was measured by asking respondents their perceived risk of contracting STDs (impossible to be infected, somewhat possible, and possible and sure). Number of clients was measured by asking respondents to give the total number of sex clients they had relationship with in the 7 days prior to the interview. Participants who reported having ever used illicit drugs (eg, heroin, opium, methamphetamine or ketamine) were classified as illicit drug users.

Statistical analysis

The prevalence of prevalent syphilis was calculated by the number of prevalent cases divided by the total participants who received a TPPA test, while the prevalence of active syphilis was estimated by the number of active cases divided by the total participants who received both TPPA and TRUST tests.

Bivariate and multiple log-binomial regression analyses²⁵ were performed to estimate the crude prevalence ratio (cPR) and adjusted prevalence ratio (aPR), and their 95% CIs using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA). RDS data were weighted to account for potential sampling bias.¹⁷ The weight for the outcome variable was calculated using the RDS Analyst (RDS-A, V.0.42, Statistics-UCLA, Los Angeles, California, USA) (MS Handcock, IE Fellows, KJ Gile. RDS Analyst: Software for the Analysis of Respondent-Driven Sampling Data, Version 0.42. 2014. <http://hpmrg.org>). The probability-based estimator (RDS-II) was used to estimate RDS weights. Since multiple modelling techniques for analysing RDS data are still under development,²⁷ unweighted regression modelling was performed in the multivariate analysis.^{28–30}

In order to adjust for potential cluster effects incurred from the different study sites, the variable of study sites was entered into these models.³¹

RESULTS

Characteristics of the study sample

In total, 1245 middle-aged FSWs were recruited and interviewed at the three study sites: 417 from Nanning, 407 from Hefei and 420 from Qingdao. The RDS-adjusted median age was between 37 and 42 years (table 1). The majority of middle-aged FSWs had received middle school education or lower. In Qingdao, 59% of middle-aged FSWs were divorced or widowed, 29% in Nanning, and 32% in Hefei. The rural-to-urban migrants counted for more than half of the respondents (between 59% and 74%).

Middle-aged FSWs started sex work between 33 and 36 years 45–61% had worked previously in low-paid service jobs (eg, waitress, barber, home servant, babysitter, bar attender and shop assistant). Middle-aged FSWs reported financial support for their families as the

primary reason for entering into sex work (67–77%). Middle-aged FSWs duration of commercial sex work was the longest in Qingdao (6.2 years), 1.3 years in Hefei and 3 years in Nanning.

Prevalence of syphilis and sexual behaviour

The RDS-adjusted prevalence of active syphilis was 5.4% in Nanning, 9.9% in Qingdao, and 17.3% in Hefei (table 2). The RDS-adjusted prevalence of prevalent syphilis was 33.6% in Hefei, 32% in Qingdao, and 6.8% in Nanning (table 2). HIV-positive cases were only found in Nanning (9 cases, RDS-adjusted prevalence: 2.5%). The proportion of unprotected sex in the past 48 h verified by the PSA test was 58% in Qingdao, 42.1% in Hefei and 27.8% in Nanning. The median number of sex clients in the week prior to the interview was between 5 and 23. The prevalence of illicit drug use was 15.7% in Qingdao, 2.4% in Nanning and 2.2% in Hefei. The median HIV/STI knowledge score was relatively high (between 7 and 9 out of a total possible score of

Table 1 Sociodemographic characteristics among middle-aged female sex workers at three study sites

	Nanning (N=418)		Hefei (N=407)		Qingdao (N=420)	
	Per cent (n)	95% CI	Per cent (n)	95% CI	Per cent (n)	95% CI
Education						
Primary or less	34.5 (151)	28.7 to 40.2	47.9 (202)	41.8 to 54.0	43.0 (193)	36.8 to 49.3
Middle school	52.3 (213)	46.6 to 57.9	42.2 (171)	36.8 to 47.7	46.5 (193)	40.4 to 52.6
High school or above	13.3 (54)	9.5 to 16.0	9.9 (34)	6.3 to 13.5	10.4 (34)	5.9 to 15.0
Marital status						
Unmarried	13.3 (52)	9.6 to 17.0	13.1 (47)	9.5 to 16.8	2.5 (17)	0.0 to 5.6
Married	57.6 (237)	52.3 to 62.9	54.5 (226)	49.6 to 59.5	38.6 (147)	31.9 to 45.3
Divorced or widowed	29.2 (129)	24.7 to 33.6	32.4 (134)	27.4 to 37.3	58.9 (256)	52.5 to 65.3
Residency						
Urban	27.2 (103)	22.8 to 31.7	41.1 (162)	35.9 to 46.2	33.6 (115)	27.0 to 40.1
Rural	73.8 (315)	68.3 to 77.3	58.9 (245)	53.8 to 64.1	66.4 (305)	59.5 to 73.0
Place for commercial sex						
Street/park/roadside hotel	56.9 (230)	50.7 to 63.0	45.6 (179)	40.4 to 50.9	20.2 (83)	14.5 to 25.9
Barbershop/massage/sauna	35.9 (155)	30.1 to 41.7	37.8 (157)	31.5 to 43.9	19.8 (84)	12.8 to 26.8
Dancing hall and music bar	0.2 (1)	0 to 2.1	5.4 (30)	2.3 to 8.5	11.7 (40)	5.5 to 17.8
Rental home	7.1 (32)	6.6 to 7.6	11.3 (41)	6.7 to 15.8	48.3 (213)	40.8 to 55.9
Previous job						
Low-paid services*	60.5 (251)	55.5 to 65.6	56.6 (231)	50.9 to 62.3	45.4 (170)	38.9 to 51.8
Small private business†	13.2 (55)	9.2 to 17.1	13.4 (65)	9.3 to 17.5	17.1 (58)	12.3 to 22.0
Farmer	16.4 (71)	12.6 to 20.3	9.5 (44)	5.5 to 13.5	11.1 (57)	7.5 to 14.8
No job	6.7 (28)	4.0 to 9.4	13.5 (52)	10.0 to 17.2	19.8 (108)	13.3 to 26.4
Other jobs	3.2 (13)	1.2 to 5.1	6.9 (24)	3.5 to 10.3	6.5 (27)	4.4 to 8.6
Reasons for sex work						
Economic	75.2 (315)	70.2 to 80.2	77.3 (320)	72.6 to 82.0	67.0 (287)	62.0 to 72.0
Divorced/widow	13.5 (62)	9.4 to 17.5	12.4 (47)	8.8 to 16.0	16.7 (72)	12.6 to 21.2
Lost job	6.0 (19)	3.0 to 8.9	2.1 (10)	0.2 to 4.0	6.9 (23)	4.4 to 9.3
Other reasons	5.4 (22)	3.2 to 7.5	8.2 (30)	5.5 to 10.9	9.2 (38)	6.2 to 12.2
Median and 25th–75th centile						
Age (years)	37	36 to 40	38	35 to 43	42	36 to 48
Age starting sex work	33	31 to 35	36	33 to 40	35	30 to 41
Duration of sex work (years)	3	1.8 to 5.0	1.3	0.5 to 3.0	6.2	4.0 to 9.9

*Waitress, barber, hotel or building cleaner, home servant, babysitter, bar and counter attender and shop assistant.

†Beauty salon, selling cloth, food, vegetable or fruit.

Table 2 Sexual behaviours and syphilitic infection among middle-aged female sex workers at three study sites

	Nanning		Hefei		Qingdao	
	Per cent (N)	95% CI	Per cent (N)	95% CI	Per cent (N)	95% CI
Prevalence of prevalent syphilis	6.8 (30)	4.4 to 9.2	33.6 (134)	27.7 to 39.4	32.0 (125)	26.3 to 37.8
Prevalence of active syphilis	5.4 (24)	2.9 to 8.0	17.3 (68)	12.7 to 21.9	9.9 (36)	5.5 to 14.3
Prevalence of HIV infection	2.5 (9)	0.2 to 4.9	0.0 (0)	–	0.0 (0)	–
Unprotected sex in the past 48 h verified by PSA						
Yes	27.8 (123)	23.2 to 32.6	42.1 (160)	36.1 to 48.2	58.0 (240)	51.9 to 64.1
No	72.1 (294)	67.5 to 76.8	57.9 (238)	51.8 to 63.9	42.0 (180)	36.0 to 48.1
Number of clients in the past 7 days						
0–4	46.3 (160)	40.2 to 52.3	28.3 (127)	22.4 to 34.3	7.9 (33)	7.7 to 22.3
5–10	38.8 (184)	33.2 to 44.5	35.6 (135)	30.1 to 41.1	8.0 (28)	5.8 to 10.1
11–25	13.4 (64)	11.9 to 14.8	26.9 (109)	21.8 to 32.1	32.5 (118)	25.9 to 39.0
>25	1.6 (10)	0.0 to 5.5	9.1 (36)	5.5 to 12.7	44.6 (241)	35.1 to 54.0
Having ever used illicit drugs						
Yes	2.4 (7)	0.3 to 4.5	2.2 (11)	0.7 to 3.7	15.7 (77)	11.2 to 20.2
No	97.6 (411)	95.1 to 99.8	97.8 (396)	96.3 to 99.3	84.3 (343)	79.8 to 88.8
Self-perceived risk for STDs						
Impossible	39.5 (147)	34.4 to 44.6	72.9 (278)	66.7 to 79.2	30.0 (108)	23.2 to 36.8
Somewhat possible	53.6 (238)	48.4 to 58.8	22.0 (110)	15.8 to 28.2	41.1 (181)	34.5 to 47.8
Possible and sure	6.9 (33)	4.4 to 9.4	5.0 (19)	2.3 to 7.7	28.9 (131)	22.6 to 35.1
Median and 25th–75th centile						
HIV/STI knowledge	9	8.0 to 10.0	7	4.0 to 9.0	8	6.0 to 9.0

PSA, prostate-specific antigen; STD, sexually transmitted diseases; STI, sexually transmitted infections.

11). The majority of middle-aged FSWs did not perceive themselves at a risk for HIV/STDs.

Factors associated with syphilis

In the binary analysis (table 3), the following factors were positively associated with prevalent syphilis: older age, lower education, being married, divorced or widowed, urban residency, commercial sex in rental homes, more clients in the past week, unprotected sex, illicit drug use and self-perceived risk for STIs. Factors that were positively associated with active syphilis included being 45–49 years, lower education level, urban residency, being a sex worker for 2–3 years, more clients in the past week and unprotected sex.

The results of the multiple log-binomial regression analysis indicate that middle-aged FSWs who had five or more clients in the past week ($aPR_{5-10 \text{ vs } 0-4 \text{ clients}}=1.99$, 95% CI 1.21 to 3.29; $aPR_{11-25 \text{ vs } 0-4}=2.00$, 95% CI 1.19 to 3.35; and $aPR_{\geq 26 \text{ vs } 0-4}=1.59$, 95% CI 0.82 to 3.10), and had unprotected sex ($aPR=2.01$, 95% CI 1.41 to 2.86) were more likely to be active syphilitic cases. In contrast, middle-aged FSWs who had rural residency ($aPR=0.69$, 95% CI 0.49 to 0.96) were less likely to be active syphilitic cases (table 4).

Prevalent syphilis was positively associated with older age ($aPR=1.03$, 95% CI 1.02 to 1.05), and who had 11–25 clients in the past week ($aPR_{11-25 \text{ vs } \leq 4 \text{ clients}}=1.44$, 95% CI 1.08 to 1.94), unprotected sex ($aPR=1.57$, 95% CI 1.28 to 1.93), HIV/STI knowledge ($aPR=1.05$, 95% CI 1.01 to 1.09) and self-perceived risk for STDs ($aPR=1.68$, 95% CI 1.28 to 2.20). It was negatively

associated with rural residency ($aPR=0.77$, 95% CI 0.63 to 0.94), and dancing hall and music bar places for commercial sex ($aPR=0.46$, 95% CI 0.23 to 0.90).

DISCUSSION

Findings from this multisite study document the spread of syphilis epidemic among middle-aged FSWs. As a large proportion of middle-aged FSWs did not perceive themselves at high risk for syphilis and engaged in unprotected commercial sex, syphilis may continue to spread among middle-aged FSWs and their clients unless effective intervention programmes are implemented.

In contrast with recent studies using either the national surveillance data or serial cross-sectional study data that reported a low prevalence of prevalent syphilis (between 2.4% and 7.2%) among predominantly younger FSWs in China,^{32 33} this study documents much higher prevalence of prevalent syphilis (23.2%) and active infection (10.3%) among middle-aged FSWs. A serial cross-sectional study among FSWs in China reported that the prevalence of prevalent syphilis ranged from 2.4% to 3.2% between 2008 and 2012.³² Based on the China national HIV/STD Surveillance data,³³ Li and colleagues reported that the syphilis prevalence ranged from 6.9% to 7.1% between 2010 and 2012. A meta-analysis of 190 studies among predominantly young FSWs reported a decline in the HIV and syphilis prevalence between 2000 and 2011,¹³ during which the prevalence of prevalent syphilis dropped from 10% to

Table 3 Binary analysis of syphilitic infection among middle-aged female sex workers

	Prevalent syphilis			Active syphilis		
	Per cent (n/N)	cPR	95% CI	Per cent (n/N)	cPR	95% CI
Age (years)						
35–39	17.7 (133/753)	1		8.9 (67/753)	1	
40–44	26.5 (66/249)	1.50	1.16 to 1.94	10.8 (27/249)	1.22	0.80 to 1.86
45–49	36.9 (59/160)	2.09	1.62 to 2.69	16.3 (26/160)	1.83	1.20 to 2.78
≥50	37.4 (31/83)	2.11	1.54 to 2.91	9.6 (8/83)	1.08	0.54 to 2.18
Education						
Primary or less	27.8 (152/546)	1		13.4 (73/546)	1	
Middle school	19.9 (115/577)	0.72	0.58 to 0.89	8.2 (47/577)	0.61	0.43 to 0.86
High school or above	18.0 (22/122)	0.65	0.43 to 0.97	6.6 (8/122)	0.49	0.24 to 0.99
Marital status						
Married	21.5 (131/610)	1		10.2 (62/610)	1	
Unmarried	12.1 (14/116)	0.56	0.34 to 0.94	6.0 (7/116)	0.59	0.28 to 1.26
Divorced or widowed	27.8 (144/519)	1.29	1.05 to 1.59	11.4 (59/519)	1.12	0.80 to 1.57
Residency						
Urban	29.2 (111/380)	1		13.2 (50/380)	1	
Rural	20.6 (178/865)	0.70	0.57 to 0.86	9.0 (78/865)	0.69	0.49 to 0.96
Place for commercial sex						
Barbershop/massage/sauna	23.2 (92/396)	1		10.9 (43/396)	1	
Street/park/roadside hotel	19.3 (95/492)	0.83	0.64 to 1.07	9.6 (47/492)	0.88	0.59 to 1.30
Dancing hall and music bar	12.7 (9/71)	0.55	0.29 to 1.03	7.0 (5/71)	0.65	0.27 to 1.59
Rental home	32.5 (93/286)	1.40	1.10 to 1.79	11.5 (33/286)	1.06	0.69 to 1.63
Duration of sex work (years)						
0–1	21.9 (58/265)	1		9.4 (25/265)	1	
2–3	22.9 (80/349)	1.05	0.78 to 1.41	14.9 (52/349)	1.58	1.01 to 2.48
4–6	22.4 (80/357)	1.02	0.76 to 1.38	9.2 (33/357)	0.98	0.60 to 1.61
≥7	25.9 (71/274)	1.18	0.87 to 1.60	6.6 (18/274)	0.70	0.39 to 1.25
Number of clients in the past 7 days						
0–4	16.6 (53/320)	1		6.3 (20/320)	1	
5–10	19.6 (68/347)	1.18	0.85 to 1.63	12.4 (43/347)	1.98	1.12 to 3.30
11–25	28.9 (84/291)	1.74	1.28 to 2.36	12.7 (37/291)	2.03	1.21 to 3.42
>25	29.3 (84/287)	1.76	1.30 to 2.40	9.8 (28/287)	1.56	0.90 to 2.71
Unprotected sex in the past 48 h verified by PSA						
No	16.7 (119/712)	1		6.9 (49/712)	1	
Yes	32.3 (169/523)	1.93	1.57 to 2.37	14.9 (78/523)	2.17	1.54 to 3.04
Having ever used illicit drugs						
No	22.4 (258/1150)	1		10.2 (117/1150)	1	
Yes	32.6 (31/95)	1.45	1.07 to 1.98	11.6 (11/95)	1.14	0.64 to 2.04
HIV/STI knowledge						
0–5	28.3 (64/226)	1		13.7 (31/226)	1	
6–7	25.1 (46/183)	0.89	0.64 to 1.23	10.4 (19/183)	0.76	0.44 to 1.29
8–9	19.9 (108/543)	0.70	0.54 to 0.92	8.7 (47/543)	0.63	0.41 to 0.97
10–11	24.2 (71/293)	0.86	0.64 to 1.14	10.6 (31/293)	0.77	0.48 to 1.23
Self-perceived risk for STDs						
Impossible	23.3 (124/533)	1.00		10.9 (58/533)	1	
Somewhat possible	18.3 (97/529)	0.79	0.62 to 1.00	9.3 (49/529)	0.85	0.59 to 1.22
Possible and sure	37.2 (68/183)	1.60	1.25 to 2.04	11.5 (21/183)	1.05	0.66 to 1.69
Study sites						
Hefei	32.9 (134/407)	1		16.7 (68/407)	1	
Qingdao	29.8 (125/420)	0.90	0.74 to 1.11	8.6 (36/420)	0.51	0.35 to 0.75
Nanning	7.2 (30/418)	0.21	0.15 to 0.32	5.7 (24/418)	0.34	0.22 to 0.54

Boldface indicates statistical significance ($p < 0.05$).

cPR, crude prevalence ratio; PSA, prostate-specific antigen; STDs, sexually transmitted diseases; STI, sexually transmitted infections.

3%. The different level of prevalence of syphilis may be due to age or duration of sex work because TPPA is a lifetime marker of having ever been infected. However, the prevalence of recent syphilis among middle-aged FSWs reported in this study (10%) is even higher than

the life-time prevalence among young FSWs (2.4–7.2%).^{32 33} Also, as is indicated by our findings, age and duration of sex work were not significantly associated with recent syphilitic infection. The prevalence of prevalent syphilis reported in our study is much higher than

Table 4 Multiple log-binominal regression analysis of factors associated with syphilitic infection among middle-aged female sex workers

	Prevalent infection		Active or recent infection	
	aPR	95% CI	aPR	95% CI
Age (years)	1.03	1.02 to 1.05	1.03	0.99 to 1.07
Education				
Primary or less	1		1	
Middle school	0.86	0.70 to 1.06	0.71	0.49 to 1.02
High school or above	0.82	0.55 to 1.21	0.56	0.27 to 1.17
Marital status				
Married	1		1	
Unmarried	0.76	0.46 to 1.26	0.74	0.33 to 1.69
Divorced or widowed	1.05	0.85 to 1.29	1.12	0.79 to 1.59
Residency				
Rural vs urban	0.77	0.63 to 0.94	0.69	0.49 to 0.96
Duration of sex work (years)	0.99	0.96 to 1.02	0.94	0.89 to 1.01
HIV/STI knowledge	1.05	1.01 to 1.09	1.05	0.98 to 1.12
Place for commercial sex				
Barbershop/message/sauna	1		1	
Street/park/roadside hotel	0.90	0.71 to 1.15	0.94	0.64 to 1.39
Dancing hall and music bar	0.46	0.23 to 0.90	0.73	0.27 to 1.99
Rental home	1.05	0.81 to 1.36	1.10	0.69 to 1.76
Number of clients in the past 7 days				
0–4	1		1	
5–10	1.22	0.90 to 1.65	1.99	1.21 to 3.29
11–25	1.44	1.08 to 1.94	2.00	1.19 to 3.35
≥26	1.11	0.79 to 1.58	1.59	0.82 to 3.10
Unprotected sex in the past 48 h verified by PSA				
Yes vs no	1.57	1.28 to 1.93	2.01	1.41 to 2.86
Having ever used illicit drugs				
Yes vs no	1.22	0.90 to 1.65	1.38	0.76 to 2.50
Self-perceived risk for STDs				
Impossible	1		1	
Somewhat possible	1.04	0.82 to 1.31	1.17	0.80 to 1.71
Possible and sure	1.68	1.28 to 2.20	1.48	0.90 to 2.44
Study sites				
Hefei	1		1	
Qingdao	0.60	0.44 to 0.83	0.39	0.21 to 0.72
Nanning	0.23	0.16 to 0.34	0.42	0.25 to 0.69

Bold denoting p value of less than 0.05.

aPR, adjusted prevalence ratio.

PSA, prostate-specific antigen; STD, sexually transmitted diseases; STI, sexually transmitted infections.

that reported among FSWs in other developing countries, for example, 4–15% in Botswana,³⁴ and 2–9% in Sudan.³⁵ The low HIV prevalence may be due to relatively short duration of sex work as the study participants entered sex work only in their mid-30s and had been in sex work for a time period ranging from 1 to 6 years. However, further studies need to be conducted to investigate potential factors for the low HIV prevalence.

The high prevalence of prevalent syphilis and active syphilis may be due to sexual risk faced by middle-aged FSWs, including multiple sex clients and unprotected sex. The average proportion of unprotected sex verified by the PSA test during the past 48 h was 42.4% (between 28% and 59%), higher than that cited by the national surveillance data and serial cross-sectional study data in which very low unprotected sex was reported from the last commercial sex (between 11% and 28%) among

predominantly young FSWs.^{32–33} This difference may be due to the different approaches used to acquire such information (biomarker vs self-reported), and the different study populations (middle-aged FSWs vs young FSWs). According to our recent report, self-reported condom use was highly over-reported and was not a valid tool to measure actual condom use.¹⁵ In our study, condom use was verified by a biological marker (PSA), while it was self-reported in the other studies. Although middle-aged FSWs had adequate knowledge about HIV/STIs, they did not perceive themselves at risk and still engaged in unprotected sex, which may indicate that adequate HIV knowledge may not lead to perception and/or behavioural changes. Based on qualitative studies conducted in the same population at the three sites,^{6–11} we found that making more money to support their families and raise their children reduced

middle-aged FSWs' power to negotiate condom use; norms regarding condom use was low among their clients, especially older clients who reported erectile dysfunction. In contrast to middle-aged FSWs, younger FSWs usually are not burdened by commitments to support their family as a majority of them are single.⁶

In contrast to our expectation, the prevalence of both prevalent syphilis and active infection was higher among middle-aged FSWs who had urban residency than those who had rural residency. We compared sexual risk behaviour (condom use and number of clients), HIV/STI knowledge and duration of sex work between the two groups and did not find substantial differences. Further studies are needed to explore this finding. Duration of being a FSW was not associated with syphilis. The possible explanations are that they started commercial sex work late in their 30s and the length of the sex work may not change their engagement with sexual risk for STIs. We checked and found that the association between condom use and duration of sex work was very small and insignificant. While middle-aged FSWs who worked at dancing halls or music bars (high-end venues) were less likely to be infected with prevalence syphilis than those who worked in barbershops, massage or sauna places (low-end venues), places for commercial sex were not associated with active syphilis. The proportions of middle-aged FSWs in sex venues differed among the three study sites. The differences in proportions at sex venues were also documented in our qualitative studies conducted among 63 middle-aged FSWs and 55 stakeholders (pimps and owners of roadside beauty salons and roadside hotels) at the three sites.^{6 11}

Surprisingly, the prevalence of prevalent and active syphilis among middle-aged FSWs in Nanning was lower than that in Hefei and Qingdao even though the cumulative number of reported HIV and STI cases in Nanning was much larger than the numbers reported in the other two cities. The prevalence of HIV (2.5%) and syphilis (6.8%) we found in Nanning is similar to a recent study conducted among FSWs in the same region,³⁶ in which the prevalence of HIV and syphilis was 1.1% (0.4–1.8%) and 7.1% (3.4–10.7%). The proportion of illicit drug use reported in our study (2.4%) in Nanning is relatively larger than the proportion (1.7%) reported in that study. Our results document, compared to the other two cities, fewer middle-aged FSWs in Nanning engaged in unprotected sex and had a large number of clients. In addition, HIV/STI knowledge among middle-aged FSWs in Nanning was relatively higher. Since Nanning is located in the most HIV-affected area in China, many HIV/STI intervention activities have been conducted there, which may have influenced them to protect themselves from becoming infected. These findings imply that the Chinese health authorities need to pay more attention to implementing intervention programmes in geographic areas with higher HIV/STI epidemics besides the areas with small-scale epidemics.

The strengths of this study include using RDS to recruit large numbers of middle-aged FSWs from three areas, and the use of biomarkers to measure major variables. However, several limitations should be noted. First, due to the nature of a cross-sectional study, temporal ambiguity bias could not be eliminated. The use of active syphilitic incident data (ie, more recent infections) may have reduced such bias. Second, the use of the *T. pallidum* specific rapid test for syphilis may not be sensitive enough for screening syphilis. However, the manufacturer-reported 92.3% for sensitivity and 100% for specificity.³⁷ Third, non-response or non-appearance may bias the results. However, the assessment of the RDS sampling indicated high validity of the RDS sample. Fourth, the study may have limited generalisability, as it was conducted among middle-aged FSWs at three sites; however, this covered different geographic areas, and different levels of HIV and syphilitic epidemics in China. Fifth, according to a previous study among FSWs in China,³⁸ the RDS approach might have a potential to underestimate the prevalence of syphilis. If this happened in our study, the actual prevalence of syphilis should be higher than our reports.

Despite these limitations, findings of our study document the spread of syphilis epidemic among middle-aged FSWs. The prevalence is even higher than it is in the most economically-devastated countries (eg, Botswana and Sudan).^{34 35} As the epidemics of STIs spread among both middle-aged FSWs and younger FSWs, intervention priority should be placed on both groups. Combined intervention programmes that integrate both behavioural component (promotion of condom use) and biomedical component (treatment of STIs) need to be developed and evaluated among middle-aged FSWs as well as their clients. Intervention should take into consideration the unique features of middle-aged FSWs (family burden, low power to negotiate condom use, sex with older clients with erectile dysfunction) and target middle-aged FSWs from both urban areas and rural areas. Effective interventions should be implemented in geographic areas with higher HIV/STI epidemics as well as areas with small-scale epidemics.

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REFERENCES

- Nash P, Willis P, Tales A, *et al.* Sexual health and sexual activity in later life. *Rev Clin Gerontol* 2015;25:22–30.
- Minichiello V, Rahman S, Hawkes G, *et al.* STI epidemiology in the global older population: emerging challenges. *Perspect Public Health* 2012;132:178–81.
- Liu H, Lin X, Xu Y, *et al.* Emerging HIV epidemic among older adults in Nanning, China. *AIDS Patient Care STDS* 2012;26:565–7.
- Pearline RV, Tucker JD, Yuan LF, *et al.* Sexually transmitted infections among individuals over fifty years of age in China. *AIDS Patient Care STDS* 2010;24:345–7.
- Gong X, Yue X, Teng F, *et al.* Syphilis in China from 2000 to 2013: epidemiological trends and characteristics. *Chin J Dermatol* 2014;47:310–15.
- Hao C, Liu H, Sherman S, *et al.* Typology of older female sex workers and sexual risks for HIV infection in China: a qualitative study. *Cult Health Sex* 2014;16:47–60.
- Zhang C, Li X, Su S, *et al.* Prevalence of HIV, syphilis, and HCV infection and associated risk factors among male clients of low-paying female sex workers in a rural county of Guangxi, China: a cross-sectional study. *Sex Transm Infect* 2014;90:230–6.
- Han L, Zhou C, Li Z, *et al.* Differences in risk behaviours and HIV/STI prevalence between low-fee and medium-fee female sex workers in three provinces in China. *Sex Transm Infect* 2015; Published Online First 16 Oct 2015. doi:10.1136/sextrans-2015-052173
- Zhou C, Rou K, Dong WM, *et al.* High prevalence of HIV and syphilis and associated factors among low-fee female sex workers in mainland China: a cross-sectional study. *BMC Infect Dis* 2014;14:225.
- Huang ZJ, Hu D, Chang R, *et al.* Female streetwalkers' perspectives on migration and HIV/STI risks in a changing economic and social environment: a qualitative study in Shanghai, China. *Cult Health Sex* 2015;17:763–76.
- Hao C, Guida J, Morisky D, *et al.* Family network, workplace network, and their influence on condom use: a qualitative study among older female sex workers in China. *J Sex Res* 2015;52:924–35.
- Remis RS, Kang L, Calzavara L, *et al.* Prevalence and correlates of HIV infection and sexually transmitted infections in female sex workers (FSWs) in Shanghai, China. *Epidemiol Infect* 2015;143:258–66.
- Yang Z, Su J, Peng X, *et al.* A decline in HIV and syphilis epidemics in Chinese female sex workers (2000–2011): a systematic review and meta-analysis. *PLoS ONE* 2013;8:e82451.
- Weir SS, Li J, Edwards JK, *et al.* Exploring venue-associated risk: a comparison of multiple partnerships and syphilis infection among women working at entertainment and service venues. *AIDS Behav* 2014;18:S153–60.
- Liu H, Morisky DE, Lin X, *et al.* Bias in self-reported condom use: association between over-reported condom use and syphilis in a three-site study in China. *AIDS Behav* 2015 [Epub ahead of print 22 Dec 2015].
- Ministry of Health of the People's Republic of China. 2012 China AIDS response progress report. Secondary 2012 China AIDS response progress report. 10 February 2016. [http://www.unaids.org/sites/default/files/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries/ce_CN_Narrative_Report\[1\].pdf](http://www.unaids.org/sites/default/files/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries/ce_CN_Narrative_Report[1].pdf)
- Heckathorn DD. Extensions of respondent-driven sampling: analyzing continuous variables and controlling for differential recruitment. *Sociol Methodol* 2007;37:151–208.
- Liu H, Li J, Ha T, *et al.* Assessment of random recruitment assumption in respondent-driven sampling in egocentric network data. *Soc Netw* 2012;1:13–21.
- Gile KJ, Johnston LG, Salganik MJ. Diagnostics for respondent-driven sampling. *J R Stat Soc Ser A Stat Soc* 2015;178:241–69.
- Hintze JL. *PASS 13—power analysis and sample size; user's guide.* Kaysville, UT: NCSS, 2014. <http://www.ncss.com>
- Chen XS, Wang QQ, Yin YP, *et al.* Prevalence of syphilis infection in different tiers of female sex workers in China: implications for surveillance and interventions. *BMC Infect Dis* 2012;12:84.
- Lin CC, Gao X, Chen XS, *et al.* China's syphilis epidemic: a systematic review of seroprevalence studies. *Sex Transm Dis* 2006;33:726–36.
- Hobbs MM, Steiner MJ, Rich KD, *et al.* Good performance of rapid prostate-specific antigen test for detection of semen exposure in women: implications for qualitative research. *Sex Transm Dis* 2009;36:501–6.
- Abacus Diagnostics I. ABACard P30 test for the forensic identification of semen at crime scene: manufacturers' Instruction. 2006.
- Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol* 2005;162:199–200.
- Handcock MS, Fellows IE, Gile KJ. RDS Analyst: software for the Analysis of Respondent-Driven Sampling Data, Version 0.42. 2014. <http://hpmrg.org>
- Johnston LG, Malekinejad M, Kendall C, *et al.* Implementation challenges to using respondent-driven sampling methodology for HIV biological and behavioral surveillance: field experiences in international settings. *AIDS Behav* 2008;12:S131–41.
- Li J, Liu H, Luo J, *et al.* Sexual transmissibility of HIV among opiate users with concurrent sexual partnerships: an egocentric network study in Yunnan, China. *Addiction* 2011;106:1780–7.
- Strathdee SA, Lozada R, Pollini RA, *et al.* Individual, social, and environmental influences associated with HIV infection among injection drug users in Tijuana, Mexico. *J Acquir Immune Defic Syndr* 2008;47:369–76.
- Jenness SM, Begier EM, Neaigus A, *et al.* Unprotected anal intercourse and sexually transmitted diseases in high-risk heterosexual women. *Am J Public Health* 2011;101:745–50.
- Twisk JWR. *Applied multilevel analysis.* New York: Cambridge, 2006.
- Wang L, Tang W, Wang L, *et al.* The HIV, syphilis, and HCV epidemics among female sex workers in china: results from a serial cross-sectional study between 2008 and 2012. *Clin Infect Dis* 2014;59:e1–9.
- Li D, Wang L, Lin W, *et al.* HIV and syphilis infections among street-based female sex workers in China, 2010–2012. *Chin Med J* 2014;127:707–11.
- Merrigan MB, Tafuma TA, Okui LA, *et al.* HIV prevalence and risk behaviors among female sex workers in Botswana: results from the 2012 HIV/STI bio-behavioral study. *AIDS Behav* 2015;19:899–908.
- Elhadi M, Elbadawi A, Abdelrahman S, *et al.* Integrated bio-behavioural HIV surveillance surveys among female sex workers in Sudan, 2011–2012. *Sex Transm Infect* 2013;89:iii17–22.
- Chen Y, Shen Z, Morano JP, *et al.* Bridging the epidemic: a comprehensive analysis of prevalence and correlates of HIV, Hepatitis C, and syphilis, and infection among female sex workers in Guangxi Province, China. *PLoS ONE* 2015;10:e0115311.
- AlereTM. *Alere DetermineTM syphilis TP test.* Chiba Prefecture, Japan: Alere Limited, 2012.
- Weir SS, Merli MG, Li J, *et al.* A comparison of respondent-driven and venue-based sampling of female sex workers in Liuzhou, China. *Sex Transm Infect* 2012;88:i95–101.