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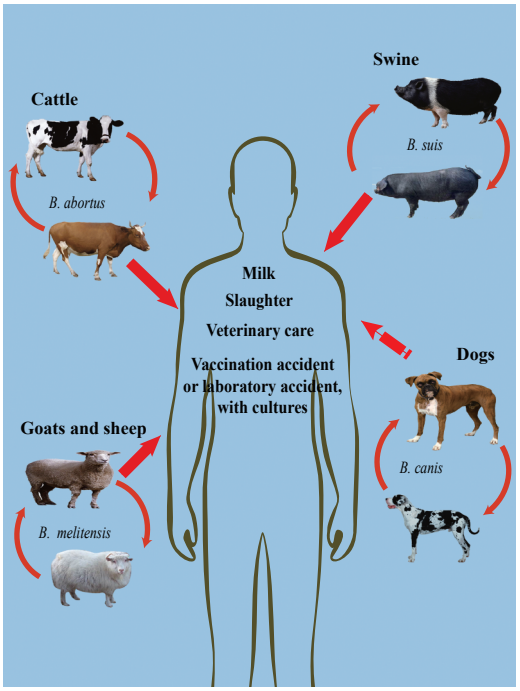

Preplanned Studies

Policy Notes

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Cover Image: A diagram of brucellosis transmission, a neglected zoonotic disease.

Preplanned Studies

High Risk Behaviors for HIV and STIs Among Men Who Have Sex with Men Aged 15–19 Years — Guangzhou City and Tianjin Municipality, China, 2018

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Summary

What is already known on this topic?

There has been a steady increase of new reported HIV infections in individuals aged 15–24 years, primarily from self-reported men who have sex with men (MSM).

What is added by this report?

MSM aged 15–19 years practiced behaviors that put them at high risk for HIV and other sexually transmitted infections (STIs). Systems to address their unique risks and vulnerabilities in both school settings and in high impact HIV interventions may be inadequate.

What are the implications for public health practice?

Special needs of MSM aged 15–19 years must be met by starting sex education in junior high school and sensitizing health workers in and out of school settings on quality counselling, testing, and referral. Piloting approaches that address age of consent issues are also suggested.

Adolescents and young people represent a growing share of people living with human immunodeficiency virus (HIV) globally (*1*). In China, new reported HIV cases among Chinese youth aged 15–24 years reached 16,307 in 2017 (*2*). The 2016 sentinel surveillance indicated that 82% of newly reported HIV cases among students were among males who reported having sex with males (MSM) (*3*). Of new HIV cases diagnosed in China, the male to male sexual transmission rate increased from 3.4% in 2007 to 28.2% in 2015, and remained at around 28.2% from 2017 to 2018. (*4*). Also, China has 146 million adolescents, the second largest adolescent population in the world (*5*), but the population of adolescent MSM (AMSM) in China has not been well-studied. In 2018, an online survey was conducted in Guangzhou City and Tianjin Municipality to measure risk factors and behaviors for HIV and STIs to better plan prevention programs and service.

Eligible participants were male, aged 15–19 years, reported having oral or anal sex with a male in the past 12 months, and were living or working in Guangzhou or Tianjin. Online sampling used standard respondent driven sampling (RDS) method (*6*), which are a chain referral method used to sample members of hidden and hard-to-reach populations starting by choosing 'seed' participants who have large social networks and are well-known within their communities (*7*). Once the seed participants complete the survey, they are asked to recruit a set number of their eligible peers (usually up to three) using a uniquely coded coupon. Ongoing successive recruitment of peers results in multiple recruitment waves with the intended goal of eliminating common chain referral biases by the time the calculated sample size is reached. A payment system is used to remunerate participants for completing the survey (primary) and for successfully recruiting eligible participants (secondary).

Due to the hidden nature and vulnerability of AMSM and the popularity of online social networks among this age group in China, this study used a web-based peer-to-peer probability-based sampling technique using WeChat, a Chinese multi-purpose messaging, social media, and mobile payment app. The surveys were conducted in Tianjin (2015 population: 14,722,100) and Guangzhou (2015 population: 12,926,800), both of which have a strong presence of community-based organizations (CBOs) and adolescent networks and are also program sites for the China Comprehensive AIDS Response (China CARES) and UNICEF's adolescent HIV prevention collaboration with the Chinese government. Formative research and training were conducted with managers from CBOs and adolescent representatives from Guangzhou and Tianjin to identify potential sampling

issues related to RDS, to resolve study logistics, to determine AMSM web-use behaviors for rolling out the surveys online, and to design the questionnaire.

A WeChat-based online program accessible via quick response (QR) code was developed and rolled out by CBOs in the two cities. Respondents who received a valid recruitment e-coupon could scan their unique QR code and respond to a set of eligibility questions. Eligible persons were then requested to read the purpose of the survey and provide informed consent, and complete the online questionnaire. Those who completed the entire questionnaire received an 8-digit password for an online payment of 30 CNY (~4.24 USD) via Alipay, administered by the survey software manager. After completing the questionnaire, the respondent received up to 5 coupons with unique QR codes which were used to recruit eligible peers into the survey. Respondents received an additional incentive of 30 CNY for each person they recruited who enrolled and completed the survey. These incentives were also provided online via Alipay and administered by the software manager.

No personal identifying information was collected, no response could be traced back to respondents, and, to avoid duplicates, each IP address could only enroll once. The questionnaire collected data on sociodemographic characteristics, social network sizes, use of MSM social networks, sexual and drug risk, knowledge on HIV and testing services, sexual experiences, perceptions, experience with buying and selling sex, condom use, social support, and access to and utilization of HIV related services.

Data were directly entered into a database as participants responded to the online questionnaire. Data were monitored by an information technology manager as well as the survey coordinator and an international consultant. Data were formatted and coded in Microsoft Excel (version 14.0; Microsoft Corporation) and SPSS (version 23.0; IBM Corporation) before being downloaded into RDS-Analyst (www.hpmrg.org), a specialized software for analysing RDS data. Data were assessed for bottlenecks and convergence and population proportions, and 95% confidence intervals (CI) were derived with RDS-analyst using the Gile successive sampling estimator (*8*–*9*) adjusted for differential recruitment and social network sizes. Given that the online survey format resulted in some unreliable social network size responses, social network sizes were imputed with the visibility imputation function in RDS Analyst (*10*). This survey received ethical approval from the ethics review committee of the National Centre for AIDS/STD Control and Prevention of China CDC.

The survey in Guangzhou recruited 288 MSM aged 15–19 years resulting in 3 recruitment chains with a maximum of 13 waves. In Tianjin, 258 were recruited resulting in 5 recruitment chains and a maximum of 9 waves (Figure 1A and Figure 1B, highlighted by age groups). The mean age of MSM aged 15–19 years was 17 years old in Guangzhou and 18 years old in Tianjin. Homosexual identity was reported by 32% of MSM aged 15–19 years in Guangzhou and 69% in Tianjin. Most respondents reported that their parents

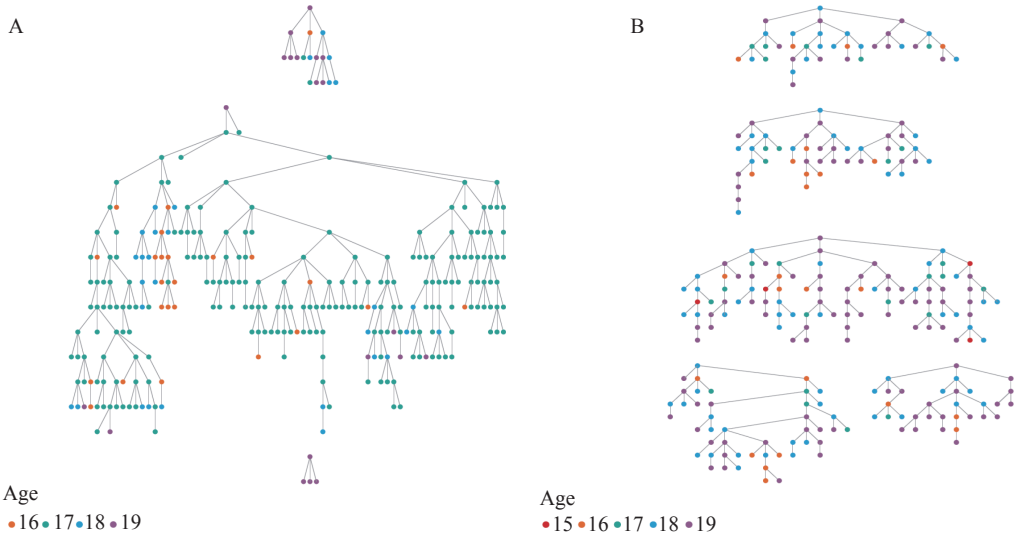

FIGURE 1. Recruitment chains of adolescent men who have sex with men (AMSM) sampling in Guangzhou, April−May, 2018 (n=288) (A) and in Tianjin, April−September, 2018 (n=258) (B).

did not know about their sexual attraction to males, and 75% of MSM aged 15–19 years in Guangzhou and more than 94% in Tianjin reported using any MSM online social network app (Table 1).

The age group with the highest percentage for first anal sexual experience was 16 years old in Guangzhou and 18 years old in Tianjin. Most MSM aged 15–19 years in the 2 cities reported having had an anal sexual experience in the past 6 months, with over half having multiple sex partners. One third of respondents in both cities who reported having anal sex were primarily receptive partners. Forty-two percent of AMSM in Guangzhou and 9% of AMSM in Tianjin reported experience of selling sex. Among them 56% and 54% reported having consistent condom use respectively. Among MSM aged 15–19 years who ever used a condom, the age at first condom use during an anal sexual experience most frequently reported was 16 years in Guangzhou and 18 years in Tianjin. An estimated 61% of AMSM in Guangzhou and 43 % in Tianjin reported using any drug before anal sex with a male. Although as much as 65% of MSM aged 15–19 years in Guangzhou and 93% in Tianjin knew that the proper use of condoms during each sexual intercourse reduces the risk of HIV transmission, only 26% of MSM aged 15–19 years in Guangzhou and 12% in

TABLE 1. Sociodemographic characteristics and communication factors of adolescent men who have sex with men (AMSM) in Guangzhou City and Tianjin Municipality, 2018.

Item	Guangzhou (n=288)		Tianjin (n=258)	
	N	Percentage (CI)	N	Percentage (CI)
Currently in school				
Yes	270	94.7 (91.9–97.5)	228	83.1 (79.9–94.3)
No	18	5.3 (2.5–8.1)	30	12.9 (5.7–20.1)
Education level				
≤Junior high school	58	19.1 (13.8–24.4)	18	8.0 (2.2–13.9)
Senior high/vocational/second	202	71.2 (65.2–77.2)	105	46.0 (35.8–56.2)
≥Vocational college	28	9.6 (5.4–14)	135	46.0 (35.5–56.5)
Sexual orientation				
Gay/homosexual	96	32.1 (25.2–38.9)	173	68.7 (59.2–78.2)
Bisexual	59	24.1 (16.8–31.3)	45	18.0 (10.1–25.8)
Straight	51	17.2 (11.5–23)	2	2.9 (0–6.6)
Unsure	43	17.2 (11.7–22.8)	18	7.2 (2.1–12.4)
Other	5	1.8 (0–3.9)	2	0.3 (0–0.7)
Do not know	16	7.5 (2.5–12.6)	3	2.9 (0–6.7)
Talked about same sex behaviour among circle of friends				
Yes	143	55.2 (48.2–62.4)	129	57.7 (46.4–68.9)
No	121	44.8 (37.6–51.8)	110	42.3 (31.1–53.6)
Parents know about sexual attraction to males				
Yes	101	39.8 (31.4–48.2)	30	11.2 (3.8–18.4)
No	163	60.2 (51.8–68.6)	210	88.8 (81.6–96.2)
How MSM network was entered				
Acquaintances outside school	83	28.7 (21.5–25.9)	14	7.3 (3.2–11.5)
Classmates	72	25.2 (18.5–32)	34	12.4 (6.9–17.8)
From internet	75	28.6 (20.3–36.9)	174	64.2 (55.9–72.5)
Other	3	1.9 (0–4.2)	5	2.6 (0–5.7)
Can't remember	45	15.6 (9.6–21.5)	29	13.5 (7.7–19.2)
Uses any MSM online social network app				
Yes	215	74.7 (67.5–81.9)	252	94.3 (88.8–99.9)
No	73	25.3 (18.2–32.5)	6	5.7 (0.1–11.2)

Tianjin knew that a healthy-looking person can have HIV, and only 27% of AMSM in Guangzhou and 25% in Tianjin knew that having sex with one faithful, uninfected partner, reduces the risk of HIV transmission. Percentages of MSM aged 15–19 years in Tianjin who were aware of anti-retroviral therapy and self-testing for HIV were 91.6% and 85.6%, respectively, whereas in Guangzhou the awareness rates of anti-retroviral therapy and HIV self testing were 59.5% and 45.8%, respectively. The percentages of MSM aged 15–19 years reporting ever having a HIV test were 46.9% in Guangzhou and 79.4% in Tianjin. Self-reported positive results of HIV was 17.6% in Guangzhou and 2.1% in Tianjin (Table 2).

TABLE 2. HIV-related knowledge/awareness and behaviours among adolescent men who have sex with men (AMSM) in Guangzhou City and Tianjin Municipality, 2018.

Item	Guangzhou (n=288)		Tianjin (n=258)	
	N	Percentage (CI)	N	Percentage (CI)
Age at first anal sexual experience				
≤12 years	18	6.1 (3.1−9.1)	4	3.0 (0−7.2)
13 years	10	2.6 (0.6−4.8)	8	1.4 (0−3.0)
14 years	25	9.9 (5.7−14.1)	7	3.9 (0.5−7.3)
15 years	44	16.5 (10.9−22.1)	30	7.3 (2.5−19.5)
16 years	63	22.1 (16−28.1)	39	12.6 (5.7−17.8)
17 years	49	21.2 (14.9−27.5)	40	11.4 (5.0−17.8)
18 years	28	10.1 (5.8−14.3)	62	30.2 (20.1−40.4)
19 years	6	2 (0.3−3.6)	29	11.0 (4.5−18.7)
Do not remember	25	9.6 (5.5−13.6)	25	18.5 (9.9−27.2)
Age at first use of condom during anal sexual experience				
≤12 years	10	3.5 (0.4−6.6)	2	2.3 (0−7.8)
13 years	8	3.0 (0−6.3)	4	1.2 (0−3.5)
14 years	16	9.1 (3.0−15.2)	7	3.1 (0.2−6.1)
15 years	39	20.4 (10.2−30.5)	17	4.6 (1.4−7.8)
16 years	68	28.5 (20.0−37.0)	32	16.0 (8.8−23.1)
17 years	53	19.4 (11.6−27.1)	38	12.8 (7.8−17.8)
18 years	33	12.6 (5.5−19.7)	57	31.6 (23.7−39.6)
19 years	12	3.5 (0−7.0)	53	28.3 (20.4−36.2)
Anal sexual experience in the past 6 months				
Yes	211	78.6 (73.1−84)	233	91.0 (84.4−97.5)
No	59	21.4 (16.0−26.8)	11	9.0 (2.5−15.6)
Number of anal sex partners (among those who had anal sex in past 6 months)				
1	102	48.2 (39.5−56.9)	87	42.8 (30.2−55.3)
2–5	58	25.7 (18.3−33.1)	98	42.4 (31.8−53.1)
6–10	23	11 (5.6−16.4)	37	9.4 (3.4−15.4)
11–20	24	12.8 (7.2−18.3)	7	1.5 (0−3.3)
21 and above	4	2.3 (1.4−3.3)	4	4.0 (0−8.8)
Age range of sex partners* in past 6 months				
Under 20 years	185	68.6 (61.5−75.8)	110	45.5 (35.4−55.6)
20–30 years	53	18.3 (12.3−24.2)	113	47.6 (37.0−58.0)
31–40 years	26	10.1 (6.2−14.1)	9	6.9 (0.9−12.9)
41 years or above	6	2.9 (0.6−5.3)	1	0.1 (0−0.2)

TABLE 2. (Continued)

Item	Guangzhou (n=288)		Tianjin (n=258)	
	N	Percentage (CI)	N	Percentage (CI)
Usual role in anal sex experience in past 6 months				
Insertive	93	40.6 (30.2−50.9)	77	37.4 (26.6−48.4)
Receptive	70	33.8 (23.1−44.5)	97	38.0 (27.3 48.7)
Insertive and receptive	46	25.6 (17.0−34.2)	54	24.6 (15.2−33.9)
Ever paid someone money for sex				
Yes	117	44.6 (37.0−52.4)	13	5.3 (0.2−10.5)
No	148	55.4 (47.7−63)	228	94.7 (89.5−99.8)
Frequency of using a condom when paying for sex				
Every time	74	57.9 (47.0−69.0)	2	29.2 (0−76.2)
Sometimes	37	36.5 (25.5−47.4)	7	38.8 (0−76.0)
Never	6	5.6 (5.6−5.6)	4	32.0 (0−73.4)
Ever received money or other benefit in return for sex				
Yes	112	41.7 (33.2−50.1)	21	9.4 (2.4−16.4)
No	153	58.4 (49.9−66.8)	220	90.6 (83.6−97.6)
Frequency of using a condom when selling sex				
Every time	65	55.5 (39.3−71.7)	10	53.6 (25.8−81.6)
Sometimes	40	39 (27.6−50.5)	10	45.1 (17.2−72.8)
Never	7	5.5 (0−14.2)	1	1.3 (0.4−2.2)
Ever been forced or coerced to have anal sexual experience with a male				
Yes	116	43.7 (35.0−52.2)	19	8.8 (3.8−13.8)
No	148	56.4 (47.7−65.0)	222	91.2 (86.2−96.2)
Frequency of condom use when forced to have anal sexual experience				
Every time	66	58.3 (44.5−72.1)	9	53.5 (26.6−80.5)
Sometimes	42	36.5 (23.7−49.4)	3	18.3 (3.8−40.4)
Never	8	5.2 (1.2−9.0)	7	28.2 (14.2−42.2)
Can always negotiate with a partner to use condoms when wanting to				
Yes	185	74.9 (67.8−82.1)	212	88.7 (83.3−94.1)
No	46	21.4 (15.3−27.5)	17	9.0 (3.8−14.2)
Never want to use	9	3.7 (0.2−7.2)	6	2.3 (0−4.7)
Used a condom during last anal sexual experience				
Yes	206	85.3 (78.4−92.2)	143	62.7 (51.1−74.3)
No	34	14.7 (7.8−21.6)	93	37.3 (25.7−48.9)
Used any drug before anal sex with a man to enhance sexual experience				
Yes	160	61.4 (53.6−69.3)	107	42.5 (32.9−52.3)
No	105	38.6 (30.7−46.4)	135	57.5 (47.4−67.2)
Awareness that a healthy-looking person can have HIV				
Yes	75	25.7 (19.0−32.4)	33	12.2 (5.3−19.2)
No	130	50.4 (42.7−58.2)	184	73.7 (64.6−82.7)
Do not know	65	23.9 (19.0−30.8)	27	14.1 (6.9−21.4)

TABLE 2. (Continued)

Item	Guangzhou (n=288)		Tianjin (n=258)	
	N	Percentage (CI)	N	Percentage (CI)
Awareness that having sex with one faithful-uninfected partner reduces the risk of HIV transmission				
Yes	94	26.6 (26.7−39.2)	45	25.3 (15.8−34.7)
No	101	37.8 (30.3−45.3)	178	65.3 (55.0−75.7)
Do not know	75	29.3 (21.7−36.9)	21	9.4 (3.3−15.4)
Awareness that proper use of condoms during each sexual experience reduces the risk of HIV transmission				
Yes	180	65.3 (57.8−72.7)	231	93.4 (88.1−98.6)
No	51	20.9 (15.5−26.2)	8	3.4 (0−7.0)
Do not know	39	13.9 (7.4−20.3)	5	3.2 (0−6.9)
Aware of anti-retroviral therapy				
Yes	167	59.5 (51.3−67.6)	216	91.6 (86.3−96.8)
No	103	40.5 (32.4−48.7)	28	8.5 (3.2−13.7)
Aware of a test to take by oneself to test for HIV				
Yes	128	45.8 (37.1−54.5)	201	85.6 (78.5−92.6)
No	142	54.2 (45.5−62.9)	43	14.4 (7.4−21.5)
Ever tested for HIV				
Yes	123	46.9 (37.4−56.2)	198	79.4 (70.5−88.3)
No	141	53.2 (43.8−62.6)	47	20.7 (11.7−29.5)
Result of last test (among those who ever had an HIV test)				
Negative	78	59.7 (45.7−73.6)	183	84.1 (76.8−91.3)
Positive	22	17.6 (9.8−25.3)	4	2.1 (0−5.5)
Do not know results	23	22.8 (11.6−33.9)	11	8.3 (0.3−16.4)
Self-perceived level of HIV infection risk				
No risk	51	18.8 (13.4−24.1)	43	18.6 (9.4−27.9)
Some risk	116	47.9 (41.3−54.6)	91	36.3 (26.3−46.2)
High risk	63	25.2 (18.5−31.9)	75	30.9 (19.9−41.9)
Do not know	0	−	17	8.3 (1.9−14.7)

* Type of sex is not defined; sex of partner not defined; question asks about multiple partners whose ages may not be in the same range.

DISCUSSION

This survey found that AMSM have many intersecting risks including high percentage of inconsistent condom use during anal sex, of early sexual initiation, of recreational drug use, and use of sexual enhancement drugs that are likely leading to unprotected sex or sex with multiple partners. They also have high rates of self-reported HIV infection.

These findings strongly indicated that education on STI/HIV prevention and on risks of drug use must begin at younger ages. Educators in school settings must be trained on and sensitized to the specific needs for knowledge of and services for AMSM and other key adolescent populations to provide early and targeted interventions in response to the high prevalence of risky sex and substance abuse. Both AMSM and service providers should be informed about the actual age of consent of 16 years for independent testing, to encourage more adolecents at high risk of HIV to get tested and receive counselling. In addition, utilization of self-testing should be explored for AMSM.

Because AMSM have large social networks and rely on peers for information, more activities should be explored on how to use the highly active social networks and peer communications to improve AMSM's knowledge and access to services. Creative technology-based interventions should be enhanced to

leverage social media to expand and improve connections with AMSM, to better understand their behaviors, to more effectively disseminate knowledge on HIV prevention, counselling, and testing, and to improve access to services.

This survey had some limitations. Although recruitment through peers using WeChat was effective, the reporting of accurate network sizes could not be verified. Some variables had small values, which resulted in wide confidence intervals that limited the ability to derive accurate estimates. However, this is the first use of online RDS among AMSM in China and provides essential information about their behaviors and needs. Additional surveys using online techniques should be conducted in other cities to gain a more expanded epidemiological picture of AMSM in China.

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Preplanned Studies

Screening and Treatment of Syphilis for Pregnant Women — China, 2011–2018

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Summary

What is already known on this topic?

The national program of prevention of mother-to-child transmission (PMTCT) of syphilis was initiated in 2011 and scaled to a national level since 2015. A better understanding of the implementation and outcomes of the program on PMTCT of syphilis is needed for future strategies to achieve the World Health Organization (WHO) goal of elimination of mother-to-child transmission (EMTCT) of syphilis.

What is added by this report

Between 2011 and 2018, as the coverage of syphilis screening of pregnant women and treatment for syphilis-seropositive pregnant women and their infants have increased consistently, the incidence of congenital syphilis was significantly reduced from 91.6 cases per 100,000 live births to 18.4 cases per 100,000. Treatment rates and adequate treatment rates of syphilis-seropositive pregnant women were below the criteria of validation of EMTCT of syphilis and regional disparities were found.

What are the implications for public health practice?

We recommend continuing to strengthen the current PMTCT intervention strategies with further commitments to achieve the targets set by the WHO's dual EMTCT of HIV and syphilis. Barriers to achieving high coverage of adequate treatment should be investigated and addressed at the provincial level to ensure prompt treatment for syphilis-seropositive pregnant women.

Syphilis caused by *Treponema pallidum* can be transmitted transplacentally from a pregnant woman to her fetus. Without treatment, maternal syphilis is estimated to result in adverse birth outcomes (ABOs) in 50%–80% of affected pregnancies (*1*). Congenital syphilis (CS) as one of the ABOs can be prevented by early detection of maternal syphilis through testing and prompt treatment to cure maternal and fetal infections (*2*). The World Health Organization (WHO) launched the global initiative to eliminate mother-to-child transmission (EMTCT) of syphilis in 2007 and integrated interventions of maternal syphilis into the existing elimination of HIV in 2015 (*3*). Syphilis screening for cases and treatment for infected pregnant women and their infants as a vital component of the national program on preventing mother-to-child transmission (PMTCT) of HIV, syphilis, and HBV has been available freely in China since 2010 and achieved universal coverage since 2015 (*4*). A better understanding of the implementation and outcomes of the program on PMTCT of syphilis is needed for future strategies to achieve the WHO goal of EMTCT of syphilis. The data from the surveillance systems revealed that there was a marked increase in the coverage of syphilis screening of pregnant women and treatment for syphilis-seropositive pregnant women and their infants in China between 2011 and 2018. Meanwhile, the incidence of CS significantly dropped from 91.6 cases per 100,000 live births to 18.4 cases per 100,000 live births. However, treatment rates and adequate treatment rates of syphilis-seropositive pregnant women were below the criteria of validation of EMTCT of syphilis and regional disparities were found. Hence, the current PMTCT intervention strategies need to be strengthened continuously with further commitments. More effort is needed to remove roadblocks to achieving high coverage of adequate treatment.

The report described the coverage of maternal syphilis screening and treatment for syphilis-seropositive pregnant women and their infants in China using the 2011–2018 national information system of PMTCT of HIV, syphilis, and HBV management data. The national information system of PMTCT of HIV was established in 2007 by the National Center for Women and Children's Health of China CDC. Since 2011, the system started to collect data on PMTCT of syphilis and HBV. Data on syphilis screening of pregnant women and treatment of syphilis-seropositive pregnant women and their infants was collected through mandatory case-reporting and

monthly work statements by health facilities, including general hospitals, maternal and children's hospitals, and other health providers across China. Data on CS cases from the national sexually transmitted disease (STD) surveillance system during 2011–2018 were analyzed (*5*). Birth data, used for determining the number of live births, were derived from the annual report of maternal and child health.

Syphilis-seropositive diagnosis required positive results from both types of serologic tests for syphilis: non-treponemal and treponemal. The diagnosis of CS cases was based on the national PMTCT action plan (*6*). Prophylaxis treatment referred to treatment of eligible newborn infants with one dose of intramuscular benzathine benzylpenicillin after birth. Eligible infants included: 1) born to seropositive mothers without standard treatment, or 2) born to seropositive mothers with standard treatment and with a reactive non-treponemal serology titer less than fourfold more than that of the mother before delivery (*5*). Treatment for seropositive pregnant women referred to treating seropositive women with penicillin, ceftriaxone, or erythromycin where appropriate during pregnancy. Adequate treatment defined by the WHO referred to treating seropositive women with at least one dose of intramuscular benzathine benzylpenicillin at least 30 days before delivery (*3*). The SPSS software (version 23.0, IBM Corp, Armonk, NY, USA) was used for all analyses. The rates of screening and treatment were presented as frequencies and proportions. Pearson's Chi-square test and trends Chi-square test were applied to compare rates in different years. A p-value of <0.05 was considered statistically significant and calculated for 95% confidence intervals (95% CI).

During 2011–2018, the number of pregnant women screened for syphilis raised from 7,303,093 to 15,060,037, which indicated a twofold increase. The rates of maternal syphilis screening during pregnancy (predelivery and at labor) and predelivery increased from 85.0% (7,303,093/8,590,863) and 47.5% (4,084,096/8,590,863) to 99.5% (15,060,037/15,132,674) and 93.9% (14,203,528/15,132,674), respectively. A total of 263,154 syphilis-seropositive pregnant women had been detected, with a maternal syphilis positive rate of 2.40 ‰ (95% CI: 2.39 ‰– 2.41 ‰) between 2011 and 2018. The rate increased from 2.03‰ (95% CI: 2.00‰–2.06‰) to 3.05 ‰ (95% CI: 3.03 ‰– 3.08 ‰) (trend χ^2 = 3 575.84, p<0.001) during the study period. (Table 1)

The treatment rates of syphilis-seropositive pregnant women and the prophylaxis treatment rates of their newborn infants consistently raised during the study period. In 2018, the treatment rate and the prophylaxis rate were 84.3% (29,982/35,578) and 69.5% (24,799/35,671), respectively. Along with increasing uptake of treatment for infected mothers and their infants, the incidence of CS reduced from 91.6 cases per 100,000 live births to 18.4 cases per 100,000 live births between 2011 and 2018. (Figure 1)

Among 31 provincial-level administrative divisions (PLADs) of the mainland of China, the treatment rates of 7 (22.6%) PLADs were higher than 90% and that of 4 (12.9%) PLADs were higher than 95%. None of the provinces achieved an adequate treatment rate of 95% in 2018. Compared with 2017, the treatment rates and the adequate treatment rates of 19 (61.3%) provinces significantly increased (p<0.05), but of 2 provinces (Hainan and Qinghai) decreased (p<0.05) in 2018. No statistically significant differences were found in 2 rates

TABLE 1. Testing rates and positive rates of maternal syphilis among pregnant women, China, 2011−2018.

Year	No. of pregnant women	Syphilis test during pregnancy		Syphilis test predelivery		Syphilis-seropositive pregnant women	
		n	%	n	%	n	‰ (95% CI)*
2011	8,590,863	7,303,093	85.0	4,084,096	47.5	14,822	2.03 (2.00−2.06)
2012	12,061,754	11,470,728	95.1	7,446,927	61.7	23,101	2.01 (1.99−2.04)
2013	13,074,271	12,597,061	96.4	8,749,303	66.9	27,435	2.18 (2.15−2.20)
2014	13,796,336	13,724,595	99.5	10,481,076	76.0	31,757	2.31 (2.29−2.34)
2015	13,983,083	13,823,676	98.9	11,495,493	82.2	33,279	2.41 (2.38−2.43)
2016	18,325,702	18,223,078	99.4	16,051,482	87.6	40,213	2.21 (2.19−2.23)
2017	17,566,853	17,517,666	99.7	15,971,783	90.9	46,562	2.66 (2.63−2.68)
2018	15,132,674	15,060,037	99.5	14,203,528	93.9	45,985	3.05 (3.03−3.08)
Total	112,531,536	109,719,934	97.5	88,483,688	78.6	263,154	2.40 (2.39−2.41)

* ‰=the proportion of syphilis-seropositive pregnant women among pregnant women who received syphilis test during pregnancy.

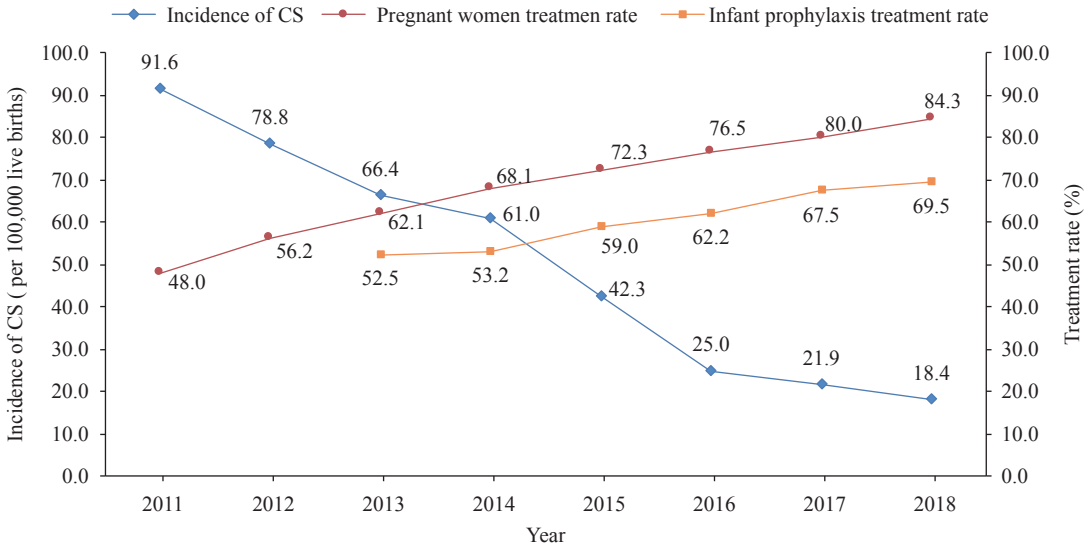

FIGURE 1. Treatment rates of syphilis-seropositive pregnant women and their newborn infants, and the incidence of congenital syphilis (CS), China, 2011–2018.

of Beijing, Liaoning, Shanghai, and Jilin between 2017 and 2018. (Table 2)

DISCUSSION

This analysis was a comprehensive overview of the national program on PMTCT of syphilis in China since 2011. The findings showed that the overall uptake of PMTCT program continued to increase and reached a high level, and perinatal transmission of syphilis decreased since the initiation of the PMTCT program. But the results showed that the positive rate and the disease burden of maternal syphilis increased yearly, and in 2018 nearly 46,000 syphilis-seropositive pregnant women were detected. The study confirmed that the interventions of PMTCT of syphilis were effective and need to be carried on consistently.

The findings showed that the coverage of syphilis screening among pregnant women increased consistently and was over 99% in 2018. Meanwhile, the rate of hospital delivery was 99.8% in China in 2018. Thus, the program has covered almost every pregnant woman in China. The PMTCT services were integrated with antenatal care (ANC), perinatal care, and child health care in China. The work of the maternal and child health (MCH) network guarantees the implementation of PMTCT services to a high level. As a result, the expansion of the screening coverage was in line with the increasing coverages of ANC and hospital delivery nationwide.

Our results showed that gaps still existed in achieving the national targets of treatment rate of syphilis-seropositive pregnant women and prophylaxis rate of their newborn infants over 90% by 2020. The study also found that the average level of adequate treatment (69.6% in 2018) was below the WHO treatment goal of 95%. Previous studies in China reported that third-trimester syphilis diagnosis, no treatment, or initiation of treatment after 37 weeks of gestation were significantly associated with increased risk of CS, and treatment before the third trimester and adequate treatment were protective factors (*7–9*). Late diagnosis and initiation of treatment might contribute to low adequate treatment rates and affect the effectiveness of the program. More effort is needed to improve uptake of screening during the first trimester, early diagnosis, and early initiation of treatment for maternal syphilis in the future.

The CS cases are mainly distributed in Xinjiang, Qinghai, Sichuan, Chongqing, and Guizhou in China (*10*). The result indicated that the rate of treatment in some PLADs with a high number of CS cases were relatively low or had no significant progress between 2017 and 2018. The differences in the program performed at the provincial level might be due to comprehensive factors embedded in the local context. Further studies are needed in PLADS to provide evidence to develop specific strategies to improve the uptake of treatment for maternal syphilis.

The study is subject to at least a few limitations. CS cases reported from the national information system of PMTCT of HIV, syphilis and HBV might be lower than the real figure due to lost follow-ups of infants

TABLE 2. Treatment rates and adequate treatment rates of syphilis-seropositive pregnant women at the provincial level in China, 2017–2018.

PLADs	2017					2018				
	No. of sero-positive pregnant women	Treatment		Adequate treatment		No. of sero-positive pregnant women	Treatment		Adequate treatment	
		No.	%	No.	%		No.	%	No.	%
Yunnan	1,963	1,901	96.8	1,692	86.2	1,959	1,916	97.8	1,787	91.2*
Hunan	2,420	2,269	93.8	1,838	76.0	2,615	2,527	96.6*	2,185	83.6*
Zhejiang	2,559	2,384	93.2	2,123	83.0	2,176	2,088	96.0*	1,898	87.2*
Beijing	274	255	93.1	232	84.7	218	209	95.9	196	89.9
Sichuan	2,821	2,593	91.9	1,886	66.9	2,931	2,745	93.7*	2,117	72.2*
Guizhou	2,312	2,082	90.1	1,308	56.6	2,556	2,371	92.8*	1,759	68.8*
Tianjin	313	205	65.5	173	55.3	339	307	90.6*	240	70.8*
Guangdong	3,130	2,742	87.6	2,008	64.2	3,213	2,864	89.1	2,286	71.1*
Liaoning	1,145	999	87.2	912	79.7	1,220	1,069	87.6	989	81.1
Guangxi	2,190	1,835	83.8	1,609	73.5	2,071	1,799	86.9*	1,594	77.0*
Ningxia	189	139	73.5	105	55.6	209	180	86.1*	123	58.9
Anhui	1,803	1,386	76.9	1,164	64.6	1,684	1,442	85.6*	1,247	74.0*
Shanxi	655	457	69.8	306	46.7	677	568	83.9*	421	62.2*
Xinjiang	1,151	886	77.0	723	62.8	1,182	973	82.3*	843	71.3*
Jiangsu	1,817	1,400	77.1	1,170	64.4	1,885	1,537	81.5*	1,336	70.9*
Hainan	321	295	91.9	186	57.9	162	129	79.6*	75	46.3*
Chongqing	841	607	72.2	479	57.0	773	602	77.9*	512	66.2*
Jiangxi	717	531	74.1	341	47.6	716	554	77.4	406	56.7*
Shanghai	436	313	71.8	243	55.7	365	282	77.3	219	60.0
Fujian	1,447	1,006	69.5	851	58.8	1,479	1,135	76.7*	1,006	68.0*
Qinghai	273	235	86.1	152	55.7	424	324	76.4*	195	46.0*
Henan	889	595	66.9	308	34.6	986	744	75.5*	475	48.2*
Hebei	639	280	43.8	236	36.9	794	562	70.8*	461	58.1*
Shaanxi	587	334	56.9	238	40.5	616	410	66.6*	322	52.3*
Heilongjiang	890	529	59.4	398	44.7	761	499	65.6*	400	52.6*
Inner Mengolia	552	257	46.6	172	31.2	614	387	63.0*	292	47.6*
Hubei	589	313	53.1	243	41.3	624	382	61.2*	313	50.2*
Shandong	1,161	618	53.2	420	36.2	1,400	854	61.0*	673	48.1*
Jilin	654	379	58.0	297	45.4	653	389	59.6	313	47.9
Gansu	129	63	48.8	35	27.1	153	80	52.3	60	39.2*
Tibet†	NA	NA	NA	NA	NA	123	54	43.9	33	26.8
Total	34,867	27,888	80.0	21,848	62.7	35,578	29,982	84.3*	24,776	69.6*

Note: Adequate treatment: at least one injection of 2.4 million units of intramuscular benzathine benzylpenicillin at least 30 days prior to delivery.
Abbreviation: PLADs=provincial-level administrative divisions; NA= not available.
* chi-square test statistically significant $p<0.05$.
† Tibet Autonomous Region starts to report the data in 2018, the data in 2017 was not available.

born to infected mothers or lack of essential laboratory capacities. Hence, we used CS case data from the national STD surveillance system instead. Another limitation is that we could not analyze the screening rates during different trimesters of pregnancy because of a lack of data on gestational weeks of screening.

In conclusion, China has achieved universal coverage of PMTCT of syphilis for all pregnant women.

However, comprehensive interventions need to be further strengthened to improve early screening, early diagnosis, and early initiation of treatment. Barriers to achieving high coverage of adequate treatment should be investigated and addressed at the provincial level to ensure prompt treatment for infected pregnant women.

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Preplanned Studies

Cervical Cancer Screening Rates Among Chinese Women — China, 2015

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Summary

What is already known about this topic?

Cervical cancer is the fourth most common cancer of women around the world. Age-adjusted incidence and mortality rates of cervical cancer were 11.78 and 3.29 per 100,000, respectively, in China in 2015.

What is added by this report?

Cervical cancer screening rates were 25.7% for women aged 20–64 years old and 31.4% for women aged 35–64 years old in China in 2015. Screening rates were lower in rural areas than in urban areas and varied across provinces.

What are the implications for public health practice?

Efforts should be made to continue to strengthen national and local policy initiatives, financial support, health education, and accessibility to women in rural areas for cervical cancer screening coverage.

Cervical cancer is the fourth most common cancer of women around the world, and the only cancer deemed preventable and treatable with effective screening. Cervical cancer screening rates in China reached 20.7% for women aged 18 years old and above in 2010 and 21.4% for women aged 21 years old and above in 2013 (*1*–*2*). It is unknown whether cervical cancer screening rates improved in China after the country's serious efforts to strengthen screening coverage over the past decade. In order to understand the latest cervical cancer screening coverage in China, data from a nationally and provincially representative cross-sectional survey were analyzed, and screening rates were estimated based on answers to questionnaire interviews. Key demographic and geographic factors were analyzed via Rao Scott chi-square tests and logistic regression models. This study reported that cervical cancer screening rates improved from the past but remained at low levels among women in China. Efforts should be made to strengthen national and local policy initiatives and financial support on cervical cancer screening, carry out health education for women, and strengthen the accessibility of screening services to women in rural areas or areas with limited health-related resources.

According to the latest estimates, in 2018 there were 570,000 new cases and 311,000 new deaths of cervical cancer around the world, and without intervention the death tolls could increase 47.6% by 2040 (*3*). Cervical cancer is deemed preventable and treatable with mature prevention and control measures. The World Health Organization (WHO) was expected to adopt the draft entitled "Global Strategy Towards the Elimination of Cervical Cancer as a Public Health Problem" in 2020, which proposed cervical cancer intervention goals by 2030 such as 70% of women being screened with a high-precision test between 35–45 years of age (*4*). In China, cervical cancer had an age-adjusted incidence rate of 11.78 per 100,000 and a mortality rate of 3.29 per 100,000 in 2015, ranking the sixth and eighth respectively among all cancers in women (*5*). While numerous measures including policy initiatives, financial support, and health education were taken to improve cervical cancer screening in China over the past decade, little is known about the latest screening coverage in China, especially in rural areas.

The latest cervical cancer screening rates were estimated in this study. In 2015, a cross-sectional survey was conducted in 298 districts/counties across 31 provincial-level administration divisions (PLADs), which were selected randomly from over 2,400 districts/counties to be representative of the whole population in the mainland of China as well as the population in every PLAD and specific regions, including urban and rural areas. The respondents aged 18 years old and above within every district/county were selected using a multi-stage, cluster-randomized sampling method (*6*). A set of questionnaires was used to collect data on chronic diseases and related behaviors by trained professionals from the local CDCs in China (*7*). In order to understand cervical cancer

screening coverage, all female participants were asked whether they have ever had cervical cancer screening and the time of the most recent screening.

In 2015, of 88,250 households sampled, 100,543 female participants completed the survey from August to December, which yielded a 95.4% response rate. After excluding 18,948 female participants who were less than 20 years or over 64 years of age, 5,205 participants who were unclear whether they have been screened, 586 participants who did not respond to the cervical cancer screening question, and 517 participants who had incomplete sociodemographic data, a final sample of 75,287 women aged 20 to 64 years old was analyzed in this study. The study was approved by the Ethical Committee of the National Centre for Chronic and Non-communicable Disease Control and Prevention, China CDC. All participants provided written informed consent.

Weighting was applied to all statistical analyses for both national and region-specific estimates (*8*). The weighted proportion for the characteristics of Chinese women aged 20 to 64 years old was reported. Chi-square tests were used for comparisons between unordered categorical variables, whereas logistic regression models were used to examine the trend for ordered categorical variables. Taylor linearization methods with a finite population correction were used to estimate standard errors (SE) accounting for the complex sampling design. Statistical significance was determined as a two-sided $p<0.05$. All statistical analyses used software SAS (version 9.4, SAS Institute Inc., Cary, USA).

According to the weighted proportions, 41.7% of women aged 20 to 64 years old were from urban areas and 42.4% from China's eastern region. (Table 1) A total of 5,205 participants who were unclear about their screening history were excluded from the final analysis and constituted about 7% of the final sample. These participants had similar age and health insurance status but were slightly more rural, less educated, and had lower likelihood of health examination in the past three years than the final sample.

Overall, cervical cancer ever screening rate was 25.7% in women aged 20–64 years old and 31.4% in women aged 35–64 years old. The urban screening rate was significantly higher than rural screening rate (30.0% *vs.* 22.6%, $p<0.001$). The 35–44 age group had significantly higher screening rate (36.9%) than other age groups ($p<0.001$). The eastern region showed significantly higher screening rate (33.7%) than other regions only for women in urban areas ($p<0.001$), whereas there was no statistically significant difference in screening rate across the geographical regions for women in rural areas. (Table 2)

Moreover, among the women who were screened, about 90% of them were screened within the past three years.

Women with college or above education and with high school education had significantly higher screening rates (30.8% and 30.5%, respectively) than women with middle school education (25.6%) and with primary or less education (21.2%, $p<0.001$). Although about one-fifth of participants did not reveal their household income, available data showed that screening increased with advancing income ($p<0.001$).

Retired women had significantly higher screening rates (34.4%) than employed women (27.2%), women doing housework (21.4%), and unemployed women (17.2%, $p<0.001$). Women without health insurance had significantly lower screening than women with health insurance (12.9% *vs.* 26.2%, $p<0.001$). Women without a health examination in the past three years had significantly lower screening rate than women with health examinations in the past three years (16.6% *vs.* 40.0%, $p<0.001$). Women with self-assessed poor or fair health status had significantly higher screening rate than women with self-assessed good health status (27.9% *vs.* 23.1%, $p<0.001$).

Provincial-level data further showed that screening rates varied widely across the 31 PLADs. The screening rates in 5 provinces, including Beijing and Shanghai, exceeded 35%, whereas three provinces, Tibet, Anhui, and Hebei, had screening rates of less than 15%. (Figure 1)

DISCUSSION

This study showed that cervical cancer screening rates remained low in China, especially for women in rural areas. In 2015, 25.7% of women aged 20–64 years old and 31.4% of women aged 35–64 years old ever had cervical cancer screening. About 90% of screened women were screened within the past 3 years. Efforts should be made to continue to strengthen national and local policy initiatives, financial support, health education, and accessibility for women in rural areas for cervical cancer screening coverage. Cervical cancer is preventable and treatable, and increasing cervical cancer screening is critical to allow for early detection of precancerous lesions and protect women against cervical cancer.

Gaps still exist in cervical cancer screening coverage

TABLE 1. Sociodemographic characteristics of female participants aged 20–64 years old of China Chronic Disease and Nutrition Surveillance, 2015.

Characteristics	No. of participants (n=75,287)	Weighted Proportion (%)*
Age (years old)		
20–24	2,707	15.3
25–34	11,251	22.2
35–44	15,107	26.9
45–54	24,392	20.3
55–64	21,830	15.4
Residence		
Urban	32,639	41.7
Rural	42,648	58.3
Location		
East	28,365	42.4
Middle	21,649	32.3
West	25,273	25.4
Education		
Primary or less	36,781	35.3
Secondary	22,500	32.5
High	9,444	15.6
College or above	6,562	16.6
Household income per capita (CNY)		
Q1 (<6,000)	14,503	15.6
Q2 (6,000–11,999)	15,543	19.7
Q3 (12,000–21,600)	17,165	23.0
Q4 (21,600 and above)	15,745	24.6
Don't know/refused to answer	12,331	17.1
Employment status		
Employed	51,746	69.8
Housework	14,694	18.4
Retired	5,325	4.2
Unemployed	3,522	7.6
Health insurance coverage		
No	2,194	4.3
Yes	73,093	95.7
Health examination in the past 3 years		
No	46,702	53.6
Yes	28,585	46.4
Self-assessed health status		
Poor or fair	43,475	61.1
Good	31,812	38.9

* Proportions are weighted to represent the national total population with poststratification for age, gender, and urban/rural residence.

in China with 36.9% screening rates in China compared to the 70% WHO goal for the 35–44 age group, which was mainly due to the absence of an organized, population-based cervical cancer screening system in China. However, screening rates in China showed significant improvement from the past.

TABLE 2. Cervical cancer screening rates among Chinese women aged 20–64 years old by sociodemographic factors — China, 2015*.

Item	Total (%)(95%CI)	Urban (%)(95%CI)	Rural (%)(95%CI)	*p*-value
Total	25.7(24.1−27.2)	30.0(27.7−32.2)	22.6(20.3−24.9)	<0.001
Age (years old)				
20–24	7.5(6.1−8.9)	7.0(4.7−9.3)	7.9(6.2−9.6)	0.569
25–34	22.1(20.1−24.0)	26.6(23.6−29.5)	18.3(15.5−21.2)	<0.001
35–44	36.9(34.5−39.4)	43.6(39.4−47.8)	32.2(29.4−35.1)	<0.001
45–54	32.4(30.4−34.5)	38.3(35.2−41.4)	28.8(25.8−31.9)	<0.001
55–64	20.2(18.6−21.9)	25.1(22.5−27.6)	17.1(14.7−19.5)	<0.001
p-value for trend	<0.001	<0.001	<0.001	
Geographic location				
East	29.1(27.0−31.3)	33.7(30.1−37.2)	24.4(21.1−27.7)	0.001
Middle	22.3(19.0−25.6)	26.9(22.9−31.0)	20.3(15.9−24.7)	0.041
West	24.1(21.9−26.4)	25.0(21.8−28.3)	23.6(20.3−26.9)	0.582
p-value for difference	<0.001	0.001	0.275	
Education				
Primary or less	21.2(19.2−23.1)	22.0(18.9−25.2)	20.9(18.4−23.4)	0.607
Middle	25.6(23.5−27.7)	30.2(26.9−33.4)	23.2(20.3−26.1)	0.005
High	30.5(28.3−32.7)	33.0(30.1−36.0)	26.9(23.1−30.7)	0.024
College or above	30.8(27.9−33.7)	32.6(29.1−36.1)	24.3(19.5−29.1)	0.013
p-value for trend	<0.001	<0.001	0.013	
Household income per capita (CNY)				
Q1 (<6,000)	19.4(17.4−21.4)	19.2(16.6−21.8)	19.4(17.0−21.9)	0.913
Q2 (6,000–11,999)	22.0(20.3−23.8)	24.6(21.5−27.7)	21.0(18.8−23.2)	0.072
Q3 (12,000–21,599)	27.8(25.9−29.7)	29.6(27.1−32.1)	26.3(23.2−29.4)	0.142
Q4 (21,600 and above)	33.7(31.4−35.9)	35.3(32.4−38.3)	30.4(26.7−34.2)	0.074
Don't know/refused to answer	21.2(18.7−23.8)	27.2(22.8−31.6)	17.9(15.0−20.8)	<0.001
p-value for trend †	<0.001	<0.001	<0.001	
Employment status				
Employed	27.2(25.7−28.7)	31.7(29.1−34.3)	24.1(22.0−26.2)	<0.001
Housework	21.4(18.5−24.3)	25.0(20.8−29.1)	19.8(15.9−23.7)	0.105
Retired	34.4(31.4−37.3)	34.8(31.5−38.0)	31.5(24.0−39.0)	0.469
Unemployed	17.2(14.8−19.6)	19.9(17.6−22.2)	14.4(10.1−18.6)	0.048
p-value for difference	<0.001	<0.001	<0.001	
Health insurance coverage				
No	12.9(10.4−15.4)	11.5(8.8−14.2)	15.5(10.3−20.7)	0.181
Yes	26.2(24.7−27.8)	31.3(28.9−33.6)	22.8(20.5−25.1)	<0.001
p-value for difference	<0.001	<0.001	0.021	
Health examination in the past 3 years				
No	16.6(15.3−17.9)	16.5(14.8,18.2)	16.6(14.8−18.4)	0.95
Yes	40.0(37.9−42.1)	42.3(39.6,44.9)	37.1(33.7−40.5)	0.029
p-value for difference	<0.001	<0.001	<0.001	
Self-assessed health status				
Poor or fair	27.9(26.2−29.5)	32.5(30.3−34.7)	24.6(22.2−27.1)	<0.001
Good	23.1(21.5−24.8)	27.1(24.4−29.8)	20.2(17.8−22.5)	<0.001
p-value for difference	<0.001	<0.001	<0.001	

* Screening rates are all weighted proportions.
† Participants answering "don't know/refused to answer" were not included in the trend test.

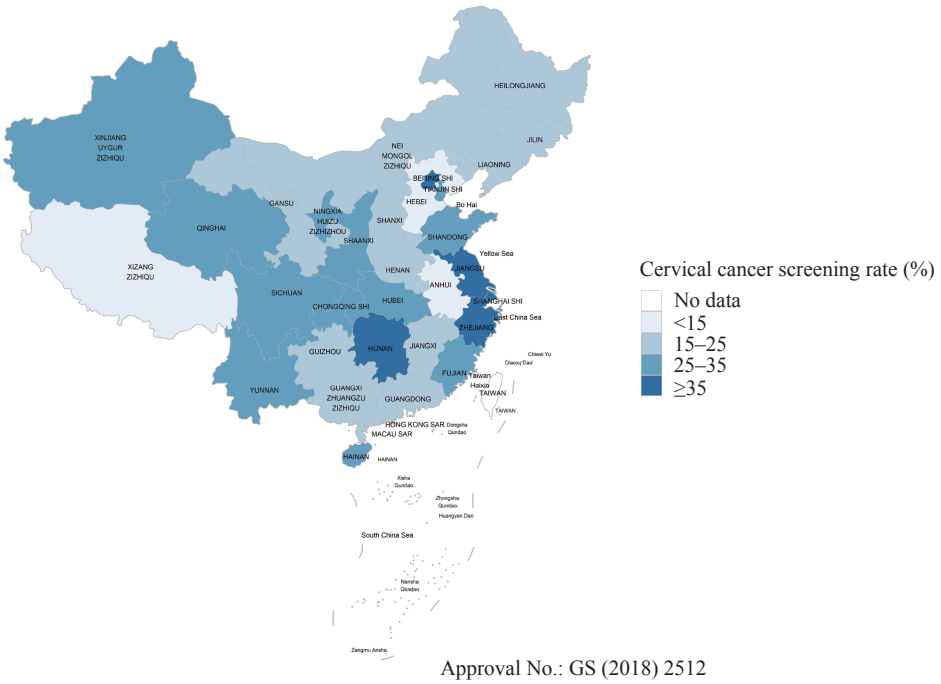

FIGURE 1. Cervical cancer screening rates among Chinese women at the provincial level in China in 2015.

Compared to the current screening rates of 25.7% for women aged 20 to 64 years old, screening rates were only 20.7% for women aged 18 years old and above in 2010 and 21.4% for women aged 21 years old and above in 2013. In particular, screening rates for the 35–64 age group increased remarkably from 26.7% in 2013 to 31.4% in 2015, which was the target age group of China's cervical cancer screening program in rural areas launched in 2009 (*9*). Rural screening also increased remarkably from 16.9% in 2010 to 22.6% in 2015, and rural screening coverage in the western region notably caught up with rural screening coverage in the middle and eastern regions. Furthermore, over 90% of screening took place within the past 3 years among women who ever had the screening, which indicated that most women followed the guidelines for screening every 3 years. The main reason may be attributable to China's national policy efforts in increasing cervical cancer screening coverage. For example, China's Women Development Program (2011–2020) strived for 80% screening coverage of women's common diseases. The National Screening Program for Cervical Cancer and Breast Cancer in Rural Areas provided free cervical cancer screening to about 10 million women aged 35–64 years old in rural areas annually since 2009, constituting about 20% of all women aged 35–64 years old in rural China in 2012–2014 (*10*). Efforts were also made to strengthen the screening system and technical personnel training, especially training of screening techniques of local staff. In addition, the study reveals significant variances in screening coverage across PLADs, indicating that different policies and strategies may be at work on the ground. Given the positive improvement in cervical cancer screening rates, the central and local governments should continue to strengthen policy and financial support as well as health education to women in order to increase cervical cancer screening coverage in China.

This study also found that women in rural areas, as well as women who were unemployed, who did not have health insurance, and who did not have a health examination in the past three years had significantly lower cervical cancer screening rates. These suggest that with limited resources, targeting women of these subgroups should be a priority.

This study is limited by response bias as 7% of the initial respondents that were unclear of their screening history were excluded from the final analysis, and those excluded were slightly more rural, were less educated, and had less health examination than the final sample. Assuming these respondents were all unscreened would lower final screening rates by about 1%–2%, though this would not change the conclusion. Misclassification may also occur as the respondents might incorrectly recall their screening history. Furthermore, the questionnaire did not ask for the reason of not having had cervical cancer screening, which thus fails to offer

an additional opportunity to examine the factors affecting screening accessibility.

In conclusion, this study provides a 2015 updated assessment of the largest nationwide and population-based self-reported history of cervical cancer screening in China. About one-quarter of Chinese women ever had cervical cancer screening. Efforts should be made to continue to strengthen national and local policy initiatives and financially support cervical cancer screening coverage, enhance health education, and improve the accessibility of screening services to women in rural areas, without employment, without health insurance coverage, and without health examination in the past three years.

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Policy Notes

Updated Guidelines for the Diagnosis of Human Brucellosis — China, 2019

Hai Jiang[1]; Lan Feng[1]; Jinxing Lu[1,#]

Brucellosis is a neglected infection that has a widespread geographic distribution. Based on an evaluation from the World Health Organization (WHO), brucellosis cases have been reported in more than 170 countries with about 500,000 new cases being reported each year. However, the actual number of brucellosis patients is much higher, and it is believed to be approximately 10–25 times the number of reported cases (*1*). This big discrepancy between the reported rate and the actual incidence rate is largely due to misdiagnosis and underdiagnosis, especially in endemic areas. With the aim of improving the diagnostic capacity, the National Health Commission of China released its updated Guidelines for the Diagnosis of Human Brucellosis (WS 269–2019) on July 1, 2019. Compared with the old guidelines (WS 269–2007), there are three major changes in the new guidelines including new detection methods, revised classification of brucellosis stages, and biosafety requirements. In particular, the new guidelines mention lateral flow assays (LFA) as one of the new detection methods that are expected to provide fast and simple point-of-care testing at county-level clinics and CDC labs.

BACKGROUND

The classification of brucellosis by the WHO, US CDC, and China CDC differ as shown in Table 1. According to WS 269–2019 (the updated guidelines of China CDC), brucellosis cases are classified as suspected, probable (clinically diagnosed), confirmed (laboratory confirmed), and covert infection. Probable cases of brucellosis are diagnosed based on a combination of epidemiologic exposure, clinical manifestations, and positive results of presumptive laboratory tests including the Rose Bengal test (RBT), enzyme-linked immunosorbent assay (ELISA), LFA, and Gram staining of *Brucella* spp. Confirmed cases are probable cases with a positive result for one of the following tests: standard agglutination test (SAT), complement fixation test (CFT), Coombs test, or isolation of *Brucella* spp. In contrast, the WHO only classifies cases as suspected, probable, and confirmed, and does not list LFA, Gram staining, or CFT as diagnostic tests. Similarly, US CDC only classifies cases as probable and confirmed, and while it does not include RBT, CFT, Gram staining, or LFA, it does include PCR and BMAT.

The definitive diagnosis of brucellosis requires isolation of the pathogen from blood or other tissue and body fluids; however, the inability to isolate the pathogen does not rule out the infection. In contrast to bacterial culture, serological testing is more sensitive and, therefore, preferred in routine clinical practice. The main serology methods currently used in China are serum agglutination tests. One such test is RBT, which is a practical screening test that has low diagnostic specificity but is used in combination with SAT, a commonly-used test that is used as a confirmatory test. However, there is a lack of consensus about the diagnostic endpoint titer: the WHO and US CDC have set the minimum antibody endpoint titer at 1:160, but the minimum antibody endpoint titer in China is 1:100. When the result of the SAT test is suspicious, the Coombs test is recommended for confirmation as it can improve the accuracy of diagnosis. However, because the Coombs test kit has not been licensed by the China Food and Drug Administration (CFDA), it is not used in clinical or medical institutions and is only used for research.

ELISA (IgG and/or IgM) is another serological test that is sensitive, fast, and convenient for the detection of brucellosis. It shows high sensitivity and specificity and should be used as a routine lab test when brucellosis is suspected in clinical practice. LFA, another serological test, does not require extensive laboratory infrastructure or technical expertise, and compared to the standard SAT and/or culture, the sensitivity and specificity are higher at 92%–95% and 97%, respectively, in endemic settings (*2*). Thus, it seems that there are several viable options with regard to serological testing for the diagnosis of brucellosis. Therefore, based on newly published studies and

TABLE 1. Definition and classification of brucellosis by China CDC, WHO, and US CDC.

Case classification	China CDC	WHO	US CDC
Suspected case	Epidemiologic exposure+clinical manifestations	Epidemiologic exposure+clinical manifestations	None
Probable case	Suspected case+presumptive diagnosis (RBT, ELISA, LFA, Gram staining of *Brucella* spp.)	Suspected case+presumptive diagnosis (RBT+SAT ≥160)	Epidemiologic exposure+clinical manifestations+presumptive diagnosis (SAT≥ 160, BMAT, PCR)
Confirmed case	Probable case+confirmatory diagnosis (SAT≥100, Coombs IgG, CFT, Culture)	Probable case+confirmatory diagnosis (ELISA IgG, Coombs IgG, Culture)	Probable case+confirmatory diagnosis (a fourfold or higher increase in *Brucella* antibody titer between acute- and convalescent-phase serum specimens obtained ≥2 weeks apart; Culture)
Covert infection	Epidemiologic exposure+confirmatory diagnosis+asymptomatic manifestations	None	None

clinical practices, China CDC initiated a process to assess the performance of new tests with the support of the National Health Commission.

METHODS OF ASSESSMENT

China CDC considered several factors and the opinions of many experts in determining whether to update its guidelines. First, China CDC referred to a systematic review that was conducted before the creation of the WS 269–2019 guidelines: the review covered 157 studies and 716,280 samples from 25 provincial-level administrative divisions (PLADs) and covered the period 1954–2012 (*3*). China CDC also invited 8 provincial experts to act as reviewers of the collected evidence and the updated WS269-2019 recommendations. The reviewers were selected based on their expertise in *Brucella* infection, diagnosis, or the intersection of these topics. The reviewers participated in several conferences with China CDC staff members from 2015 to 2019, and during this period, China CDC staff members presented the process and outcome of the updated WS 269–2019 recommendations. The participants provided their individual input about (*1*) whether the updated evidence might influence clinical practice in China, and (*2*) how the updated WS 269–2019 recommendations might translate to clinical practice in China. After the final conference, China CDC assessed the evidence, the updated WS 269–2019 recommendations, and the individual perspectives provided by the expert reviewers.

RATIONALE AND EVIDENCE

The findings of the systematic review showed that RBT and SAT were the most widely used in county-levels of CDC labs. LFA and ELISA are not only in keeping with international criteria but also have high concordance with SAT. With regard to the development of future tests, CDC has conducted a comprehensive evaluation of three approved LFA kits. The internal report generated based on the evaluation indicated that there was no significant difference between the results of the kits and SAT according to the results of the kappa and χ^2 tests (p>0.05). Another study showed that among 235 patients with brucellosis, 232 (98.7%) tested positive with ELISA (*4*). Based on this finding, it was concluded that ELISA has higher sensitivity and specificity for the detection of brucellosis than the agglutination test, as reported in other previous studies (*5*–*7*). This means that its performance is "substantially equivalent to or better than" that of the currently commercially available predictive tests.

RECOMMENDATIONS

LFA and ELISA were cleared by the CFDA and were considered acceptable alternatives for the laboratory diagnosis of brucellosis. Based on the criteria established by the 2019 Diagnostic Guidelines for Human Brucellosis, clinicians and laboratories should consider serological tests to be cleared by the CFDA as China CDC-recommended procedures for the serodiagnosis of brucellosis. Considering the importance of the disease, the international brucellosis research community should focus on viable diagnostic options. Therefore, I will highlight below a small selection of the recently reported advanced tests. Fluorescence polarization assay seems to be a valuable method for the diagnosis of brucellosis in humans (*8*). Another option is MALDI-TOF mass spectrometry, which is revolutionizing the clinical diagnosis

procedure (*9*). Additionally, China CDC has developed a spectral database for the identification of *Brucella* called the Pathogen Identification System. The system is now used in developed provincial-level CDCs and is becoming the diagnostic choice in modern clinical laboratories in China. It is expected that the advances in diagnostic technology will lead to the standardization of brucellosis guidelines in the future.

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