

## 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  $\chi^2 = 3\,575.84$ ,  $p < 0.001$ ) 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.

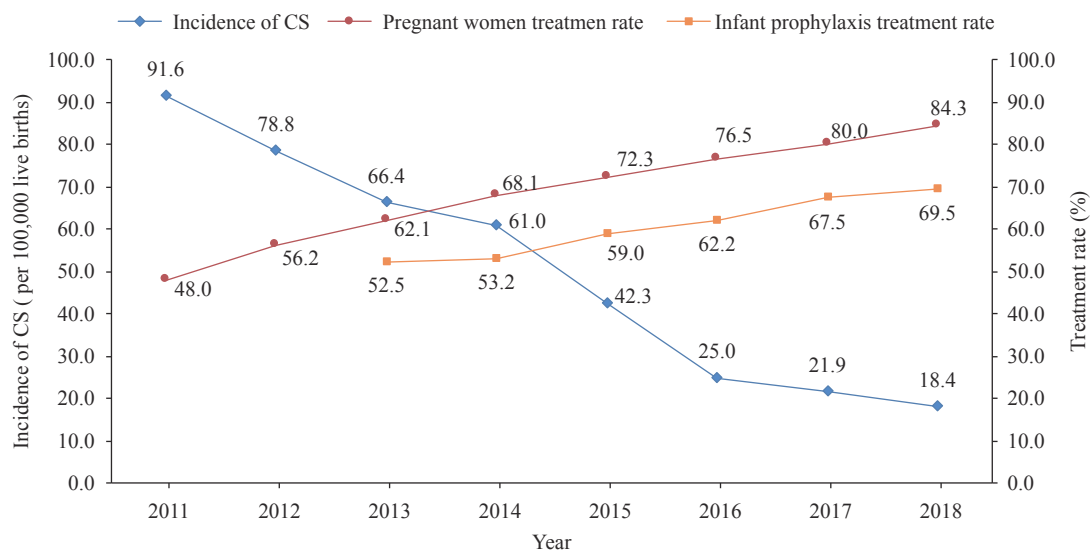


FIGURE 1. Treatment rates of syphilis-seropositive pregnant women and their newborn infants, and the incidence of congenital syphilis (CS), China, 2011–2018.

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 Mongolia	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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## REFERENCES

- Gomez GB, Kamb ML, Newman LM, Mark J, Broutet N, Hawkes SJ. Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. *Bull World Health Organ* 2013;91(3):217 – 26. <http://dx.doi.org/10.2471/BLT.12.107623>.
- World Health Organization. WHO guideline on syphilis screening and treatment for pregnant women. Geneva: WHO, 2017. <https://apps.who.int/iris/handle/10665/259003>.
- World Health Organization. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV and syphilis. 2nd ed. Geneva: WHO, 2017. <https://apps.who.int/iris/bitstream/handle/10665/259517/9789241513272-eng.pdf;jsessionid=A984732EB390529D4E8F04CCDF30BBDD?sequence=1>.
- Wang AL, Qiao YP, Wang LH, Fang LW, Wang F, Jin X, et al. Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China. *Bull World Health Organ* 2015;93(1):52 – 6. <http://dx.doi.org/10.2471/BLT.14.139626>.
- Gong XD, Yue XL, Teng F, Jiang N, Men PX. Syphilis in China from 2000 to 2013: epidemiological trends and characteristics. *Chin J Dermatol* 2014;47(5):310 – 5. <http://dx.doi.org/10.3760/cma.j.issn.0412-4030.2014.05.002>. (In Chinese).
- National Health and Family Planning Commission of the People's Republic of China. Action plan to prevent mother-to-child transmission of HIV, syphilis and Hepatitis B virus. 2015. <http://www.nhc.gov.cn/ewebeditor/uploadfile/2015/06/20150615151817186.docx>. [2019-1-10]. (In Chinese).
- Dou LX, Wang XY, Wang F, Wang Q, Qiao YP, Su M, et al. Epidemic profile of maternal syphilis in China in 2013. *Biomed Res Int* 2016;2016:9194805. <http://dx.doi.org/10.1155/2016/9194805>.
- Zhang X, Yu Y, Yang HJ, Xu HY, Vermund SH, Liu KB. Surveillance of maternal syphilis in China: Pregnancy outcomes and determinants of congenital syphilis. *Med Sci Monit* 2018;24:7727 – 35. <http://dx.doi.org/10.12659/MSM.910216>.
- Hong FC, Wu XB, Yang F, Lan LN, Guan Y, Zhang CL, et al. Risk of congenital syphilis (CS) following treatment of maternal syphilis: results of a CS control program in China. *Clin Infect Dis* 2017;65(4):588 – 94. <http://dx.doi.org/10.1093/cid/cix371>.
- Wang YJ, Gong XD, Yue XL, Li J. Spatial distribution characteristics and patterns of congenital syphilis in 2010 and 2015 in China. *Chin J Dermatol* 2018;51(5):337 – 40. <http://dx.doi.org/10.3760/cma.j.issn.0412-4030.2018.05.004>. (In Chinese).