New screening approach to detecting congenital syphilis in China: a retrospective cohort study

Fang Hu,1 Shuai-Jun Guo,2,3 Jian-Jun Lu,4,5 Ning-Xuan Hua,1 Yan-Yan Song,1 Sui-Fang Lin,1 Sui Zhu 6

ABSTRACT

Background Diagnosis of congenital syphilis (CS) is not straightforward and can be challenging. This study aimed to evaluate the validity of an algorithm using timing of maternal antisyphilis treatment and titres of non-treponemal antibody as predictors of CS.

Methods Confirmed CS cases and those where CS was excluded were obtained from the Guangzhou Prevention of Mother-to-Child Transmission of syphilis programme between 2011 and 2019. We calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) using receiver operating characteristics (ROC) in two situations: (1) receiving antisyphilis treatment or no-treatment during pregnancy and (2) initiating treatment before 28 gestational weeks (GWs), initiating after 28 GWs or receiving no treatment for syphilis seropositive women.

Results Among 1558 syphilis-exposed children, 39 had confirmed CS. Area under the curve, sensitivity and specificity of maternal non-treponemal titres before treatment and treatment during pregnancy were 0.80, 76.9%, 78.7% and 0.79, 69.2%, 88.7%, respectively, for children with CS. For the algorithm, ROC results showed that PPV and NPV for predicting CS were 37.3% and 99.5% (non-treatment during pregnancy) and 9.4% and 100% (non-treatment titres cut-off value 1:8 and no antisyphilis treatment), 9.4% and 100% (non-treponemal titres cut-off value 1:16 and treatment before 28 GWs), 4.2% and 99.5% (non-treponemal titres cut-off value 1:32 and treatment before 28 GWs), respectively.

Conclusions An algorithm using maternal non-treponemal titres and timing of treatment during pregnancy could be an effective strategy to diagnose or rule out CS, especially when the rate of loss to follow-up is high or there are no straightforward diagnostic tools.

INTRODUCTION

Congenital syphilis (CS) resulting from intrauterine infection with *Treponema pallidum* continues to be a substantial global public health problem.2 Korenromp et al estimated that the global CS rate in 2016 was 473 per 100 000 live births.3 CS is considered as a re-emerging disease in developed countries.4 The incidence in the USA increased from 9.2 to 23.3 cases per 100 000 newborns during 2013–2017.7 Similarly, in China, the reported incidence of CS sharply increased from 7.2 to 82.7 per 100 000 newborns during 2003–2011. Although this incidence rate rapidly dropped to 27.6 to 100 000 newborns in 2016,6 this is still exceeding the target of 15 per 100 000 newborns by 2020.

CS results in an estimated additional $9969 per case in hospitalisation costs,7 placing a substantial economic burden on individuals and families. Additionally, managing the high-risk population creates substantial challenges for the health service system.8 Therefore, timely and accurate diagnosis of CS is vital to avoid severe health consequences for children born to syphilis-seropositive mothers and an economic burden to their families and community.9

The diagnostic criteria for CS are complicated, requiring a careful review of maternal tests and treatment history, comparison of maternal and neonatal non-treponemal titres, and multiple blood tests and clinical follow-up of children.10 A reactive serological test before age 18 months does not necessarily indicate that the infant is infected.11 A broad spectrum of severity exists, from inapparent infection to severe cases that are present at birth.12 Therefore, diagnostic misclassification of CS in clinical practice is not uncommon. The reported rate of accurate diagnosis of CS in China ranges from 33.8% to 49.1%.13 14 In the USA, both underdiagnosis and overdiagnosis of CS exist, with 98% of CS being diagnosed by neonatologists based on the severity of the symptoms such as central nervous system calcification or hydrocephalus.15 However, 56% of neonatologists choose a treponemal instead of a non-treponemal test for CS, which results in overdiagnosis.16

The high probability of no clinical manifestations of CS at birth hinders its diagnosis and the mothers’ awareness of the importance of follow-up.4 In England, at least one-third of infants born to treated syphilis-seropositive women did not have a follow-up.16 In Brazil, the lost to follow-up rate of syphilis-exposed children was reported to be about 62.3%.8 Furthermore, we have previously shown that the lost to follow-up rate of syphilis-exposed children is 44.2%, and the rate gradually increases with age.17 This high rate of lost to follow-up is an obstacle for timely diagnosis of some CS cases.

Taken altogether, the complex diagnostic criteria and the high lost to follow-up rate hinder the timely and accurate detection of CS. Identifying predictors for CS detection at birth is of great clinical importance and could contribute to the global elimination of CS launched by the WHO in 2007.9

In this study, we aimed to evaluate the usefulness and validity of two commonly used and easy-to-collect objective CS predictors: maternal non-treponemal titres before treatment and timing of antisyphilis treatment during pregnancy. Higher maternal non-treponemal titre at the time of diagnosis was found to be a risk factor for CS.11 19 20 Similarly, timing of antisyphilis treatment during pregnancy was chosen due to the close association between inappropriate or
no treatment and CS. Previous studies have shown that antisyphilis treatment before 28 gestational weeks (GWs) is critical for CS prevention. Initiating adequate antisyphilis treatment during early pregnancy, ideally, before the second trimester, was emphasised by the WHO. Therefore, we hypothesised that maternal non-treponemal titres before treatment and timing of antisyphilis treatment during pregnancy might identify children at high risk for CS and help clinicians develop better follow-up management strategies. This study aimed to test this hypothesis.

METHODS
Participants and study design
This study was a retrospective cohort study. We included all syphilis-infected pregnant women registered in China’s Information Management System for Prevention of Mother-to-Child Transmission (PMTCT) of syphilis in Guangzhou between January 2011 and December 2019. Pregnant women received free toluidine red unheated serum test (TRUST; a non-treponemal test for syphilis) and Treponema pallidum particle agglutination test (TPPA) at their first antenatal visit at Guangzhou. Maternal syphilis was diagnosed if TRUST and TPPA were both positive. All syphilis-seropositive pregnant women were referred to designated hospitals where treatment and regular serological tests were free. Children born to mothers with syphilis were entitled to free treatment and regular serological tests were free. Children born to mothers with syphilis were treated before 28 weeks of pregnancy in designated hospitals. Only a few patients underwent this test due to its lack of availability and relatively high cost. All laboratory tests were performed according to the manufacturer’s instructions, and routine quality control procedures were carried out to reduce false positive or negative results.

Covariate assessment
Trained medical staff regularly followed pregnant women with syphilis and their children. During face-to-face interviews, medical staff recorded maternal and children’s information on structured forms. This information included maternal demographic characteristics (eg, age, ethnicity, education, occupation and marital status), clinical information (previous infection history, TRUST before treatment and before delivery, stage of infection, time of starting treatment, time of stopping treatment, name and dosage of medications used) and children’s birth information (eg, sex, gestation at birth, delivery mode and TRUST at birth). The information was collected and reported to the PMTCT surveillance system after district-municipal-provincial reviews.

All participants’ information was confidential, and only the first and corresponding authors had access to the data.

Diagnosis of CS
Cases of CS reported in the PMTCT surveillance system were verified by checking the mothers and their children’s information according to the national PMTCT programme and syphilis diagnosis guidelines issued by the Ministry of Health. The definitions of confirmed cases and cases where CS was excluded are summarised in table 1.

ALGORITHMS
Laboratory tests
Treponemal and non-treponemal tests were used in the diagnosis of syphilis. The former is highly specific but can identify syphilis infection, while the latter is less specific but reflects the response to treatment and infection activity. There are several non-treponemal tests such as TRUST and rapid plasma reagin (RPR), but Parham et al found that TRUST is comparable to RPR in all parameters. For non-treponemal test, we used TRUST (Rongsheng Biotech, Shanghai, China). For treponemal test, TPPA (Fujirebio Diagnostics, Tokyo, Japan) is used in Guangzhou, which is based on the agglutination of coloured gelatin particle carriers sensitised with T. pallidum (Nichols Strain) antigen.

Table 1 Diagnosis criteria of CS

| Classification | Description |
|----------------|-------------|
| Confirmed CS   | CS was diagnosed in infants who met any one of the following criteria: 1. Neonatal non-treponemal serological titre fourfold higher than maternal titre at delivery. 2. Reactive treponemal IgM. 3. Increasing non-treponemal serological titre and positive treponemal-specific antibody test. 4. Positive treponemal-specific antibody test after 18 months of age. |
| Excluded CS    | Any infants who had a normal physical examination, and one of the following: 1. Non-treponemal serological titres were negative at birth, 3 months and 6 months of age. 2. Both the non-treponemal serological titre and treponemal-specific antibody tests were negative at two check-ups performed every 3 months from the age of 6 months. |

CS, congenital syphilis.

Treponema pallidum IgM tests seem to be the most sensitive and specific tests for CS since they cannot cross the placental barrier. There are only two dermatology institutes in Guangzhou which perform fluorescent treponemal antibody absorption assay-195-immunoglobulin M antibody test, which is expensive and paid for by patients. Only a few patients underwent this test due to its lack of availability and relatively high cost.

Treated for maternal syphilis
Syphilis-infected pregnant women were initially divided into two groups, those who received antisyphilis treatment during pregnancy (group 1) and those who received no treatment (group 2). Pregnant women receiving treatment were further divided into two subgroups: those starting treatment before 28 weeks of gestation and those starting treatment after 28 weeks. Thus, we ended up with three groups of syphilis-infected pregnant women: women who received treatment before 28 weeks (group 1a), after 28 weeks (group 1b) and untreated (group 2).

Statistical analysis
The study participants’ sociodemographic data and clinical characteristics were summarised and compared between confirmed and non-confirmed CS using χ² test for categorical variables.
We proposed a new screening algorithm using the two predictors (maternal non-treponemal titres and timing of antisyphilis treatment) to identify children at high risk for CS (figure 1). The usefulness of these two indicators was evaluated using receiver

| Table 2  | Characteristics of mothers with syphilis associated with CS|
|----------|---------------------------------------------------------------|
| Characteristic                              | CS (n=39) | Non-CS (n=1519) | χ²/Z value | P value |
| Mother’s age (years, %)                       |           |                |            |         |
| ≤24                                            | 17 (7.1)  | 224 (92.9)     | 25.136     | <0.001  |
| 25–29                                         | 9 (2.3)   | 380 (97.7)     |            |         |
| 30–34                                         | 7 (1.4)   | 477 (98.6)     |            |         |
| ≥35                                            | 6 (1.4)   | 438 (98.6)     |            |         |
| Ethnicity (%)                                 |           |                | 0.183*     | 0.422   |
| Han                                            | 36 (2.4)  | 1445 (97.6)    |            |         |
| others                                         | 3 (3.9)   | 74 (96.1)      |            |         |
| Marital status (%)                            |           |                | 9.272*     | 0.002   |
| Married                                        | 29 (2.1)  | 1374 (97.9)    |            |         |
| Unmarried                                      | 10 (6.5)  | 145 (93.5)     |            |         |
| Educational attainment (%)†                   |           |                | 0.643      | 0.887   |
| Primary school or below                       | 4 (3.1)   | 126 (96.9)     |            |         |
| Middle school                                  | 17 (2.6)  | 637 (97.4)     |            |         |
| High school                                    | 11 (2.7)  | 394 (97.3)     |            |         |
| Bachelor or above                             | 4 (1.8)   | 214 (98.2)     |            |         |
| Employed (%)†                                 |           |                | 0.025      | 0.875   |
| No                                             | 20 (2.4)  | 816 (97.6)     |            |         |
| Yes                                            | 10 (2.3)  | 434 (97.7)     |            |         |
| Migrant resident (%)                          |           |                | 1.734*     | 0.188   |
| Yes                                            | 6 (4.6)   | 124 (95.4)     |            |         |
| No                                             | 33 (2.3)  | 1395 (97.7)    |            |         |
| History of syphilis infections (%)            |           |                | 14.005     | <0.001  |
| Yes                                            | 7 (0.9)   | 733 (99.1)     |            |         |
| No                                             | 32 (3.9)  | 786 (96.1)     |            |         |
| Maternal syphilis stage (%)                   |           |                | 3.553      | 0.059   |
| Latent                                         | 27 (2.1)  | 1234 (97.9)    |            |         |
| Stage I–III                                    | 12(4)     | 285(96)        |            |         |
| Titres of TRUST before treatment (%)          |           |                | 67.220     | <0.001  |
| <1:8                                           | 9 (0.7)   | 1196 (99.3)    |            |         |
| ≥1:8                                           | 30 (8.5)  | 323 (91.5)     |            |         |
| Period of initiating treatment (%)            |           |                | 115.138*   | <0.001  |
| Before 28 weeks                               | 9 (0.8)   | 1187 (99.2)    |            |         |
| After 28 weeks                                | 3 (1.8)   | 160 (98.2)     |            |         |
| No treatment                                   | 27 (13.6) | 172 (86.4)     |            |         |
| Drugs (%)                                      |           |                | 10.382     | 0.006   |
| Penicillin G                                   | 21 (1.5)  | 1393 (98.5)    |            |         |
| Ceftriaxone                                    | 1 (11.1)  | 8 (88.9)       |            |         |
| Erythromycin                                   | 2 (7.1)   | 26 (92.9)      |            |         |
| Mode of delivery (%)                          |           |                | 1.017      | 0.313   |
| Vaginal delivery                               | 25 (2.9)  | 846 (97.1)     |            |         |
| Caesarean section                              | 14 (2.1)  | 665 (97.9)     |            |         |
| Newborn’s sex (%)                              |           |                | 0.676      | 0.411   |
| Boy                                            | 24 (2.8)  | 834 (97.2)     |            |         |
| Girl                                           | 15 (2.1)  | 685 (97.9)     |            |         |
| Newborn receiving treatment (%)                |           |                | 0.019      | 0.892   |
| Yes                                            | 27 (2.5)  | 1036 (97.5)    |            |         |
| No                                             | 12 (2.4)  | 483 (97.6)     |            |         |
| Preterm birth (%)                              |           |                | 83.112*    | <0.001  |
| Yes                                            | 22 (13.3) | 144 (86.7)     |            |         |
| No                                             | 17 (1.2)  | 1375 (98.8)    |            |         |

Significant P-values are in bold-type.  
*The χ² correction for continuity tests were used for categorical variables.  
†There were missing values in each group.  
CS, congenital syphilis; TRUST, toluidine red unheated serum test.
to deliver a baby with CS. Premature children were more likely to have CS (table 2).

**Diagnostic value of non-treponemal titres before treatment and maternal antisyphilis treatment**

The AUC (95% CI) for maternal non-treponemal titres before treatment was 0.80 (0.72 to 0.87), and for receiving treatment during pregnancy it was 0.79 (0.72 to 0.86) (figure 2). There was no difference between the two indicators for predicting CS (p=0.87). We observed high NPV but low PPV for both indicators (table 3).

**Diagnostic value of non-treponemal titres before treatment stratified by two treatment groups**

By maximising Youden’s index, the optimal cut-off value for the prediction of CS was 1:6 for maternal non-treponemal titres before treatment (table 3). We used 1:8 for convenience. We found that non-treponemal titres (≥1:8) before treatment during pregnancy were more predictive of CS (AUC, PPV and NPV of 0.80, 37.3% and 96.4%, respectively) (table 4). Nevertheless, there was no difference between the two AUCs (p=0.38).

**Diagnostic value of non-treponemal titres before treatment stratified by three treatment groups**

We found the optimal cut-off values of non-treponemal titres before treatment for CS prediction were 1:24, 1:12 and 1:6, respectively. For convenience of use in clinical practice, the optimal cut-off values were changed to 1:32, 1:16 and 1:8 for groups 1a, 1b and 2, respectively.

Figure 3 and table 5 show the diagnostic values of non-treponemal titres for CS in the three groups. We found that non-treponemal titres (≥1:16) in group 1b had the highest predictions for CS with an AUC of 0.87 (95% CI 0.82 to 0.93) and a maximum Youden’s index of 0.73. Notably, there were significant differences between the AUCs of group 1b and group 2 (p=0.01) and between those of group 1a and group 1b (p=0.01). However, there was no difference between the AUCs of group 1a and group 2 (p=0.23).

**DISCUSSION**

This study is the first to find that maternal non-treponemal titres before treatment combined with timing of antisyphilis treatment during pregnancy could be used as surrogate indicators for the diagnosis of CS. We also found that untreated syphilis-seropositive women with non-treponemal titres higher than 1:8 had the highest PPV for their babies having CS.

Despite the effort to improve patients’ compliance, increase rates of follow-up testing and reduce misdiagnosis of CS by healthcare professionals, many practical challenges exist. These challenges include a lack of manpower and financial resources or parents’ busy schedules that lead to lost to follow-up. In practice, the detection of CS can be challenging because of complex diagnostic criteria. Our new screening algorithm has the

---

**Table 3** Statistical measures of non-treponemal titres before treatment and maternal antisyphilis treatment during pregnancy as predictions for CS

| Measure                                      | AUC (95% CI) | Cut-off | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Youden’s index |
|---------------------------------------------|--------------|---------|----------------------|----------------------|--------------|--------------|---------------|
| Maternal non-treponemal titres before treatment | 0.80 (0.72 to 0.87) | 1:6     | 76.9 (63.7 to 90.1)  | 78.7 (76.7 to 80.8)  | 8.5 (5.6 to 11.4) | 99.3 (98.8 to 99.7) | 0.56          |
| Treatment during pregnancy                  | 0.79 (0.72 to 0.86) | 0.5     | 69.2 (54.7 to 83.7)  | 88.7 (87.1 to 90.3)  | 13.6 (8.8 to 18.3) | 99.1 (98.6 to 99.6) | 0.58          |

AUC, area under the curve; CS, congenital syphilis; NPV, negative predicted value; PPV, positive predicted value.
potential to simplify the diagnosis of CS and subsequently allow cost-effective follow-up strategies.

CS occurs when mothers with syphilis are inadequately or not treated. Our study found that 13.6% of the children born to untreated mothers developed CS, which is similar to previous studies. Using our new algorithm based on timing of initiating treatment before or after 28 weeks gestation, the cut-off values of non-treponemal titres before treatment were different, as well as PPV and NPV of CS.

Most pregnant women with syphilis are asymptomatic, and the duration of syphilis infection is uncertain. Therefore, it is clinically difficult to determine whether they have early or late latent syphilis. That is why we selected the non-treponemal titre as another surrogate indicator. Our findings show that maternal non-treponemal titres alone could be an alternative predictor of CS diagnosis, with an optimal cut-off value of 1:8. High titres of non-treponemal antibodies (≥1:8) represent significant fetal exposure to *Treponema pallidum*. The persistence of low titres (<1:8), indicating the presence of serological scarring, reduces the risk of vertical transmission.

The risk of vertical transmission is higher when lack of maternal antisyphilis treatment is combined with high non-treponemal titres. After combining the maternal non-treponemal titres and timing of antisyphilis treatment, we found that the cut-off value of non-treponemal titres became lower and the PPV became larger, with more delays of mother’s treatment initiation. Like other studies, children born to mothers with untreated syphilis were more likely to develop CS when maternal non-treponemal titres were high (≥1:8). Initiating antisyphilis treatment after 28 GWs with non-treponemal titres ≥1:16 had a sensitivity of 100% and a specificity of 81.9% to predict CS in children born to these women. This is consistent with previous findings in which 1:16 was used as the cut-off value for high non-treponemal titres for pregnant women initiating treatment less than 4 weeks before delivery. In addition, our findings show that if pregnant women with syphilis started antisyphilis treatment before 28 weeks of gestation, the lowest serological titre for CS was 1:32 and PPV was the lowest (4.2%). Results of a randomised trial showed that benzathine penicillin G (BPG) administered to high-risk newborns born to mothers with untreated syphilis whose non-treponemal titre was higher than 32 was effective. The likelihood of fetal infection is influenced by maternal non-treponemal titres and the duration of fetal exposure.

For syphilis, validation of WHO criteria was difficult due to a lack of reliable data about CS. Our study suggests that the combination of timing of antisyphilis treatment and non-treponemal titres has high predictive ability (reflected as a high NPV) and could be used as a useful clinical tool to exclude CS. About 99.5% (99.1%–99.9%) of children born to syphilis-seropositive mothers would not be infected with syphilis, if their mothers received treatment before 28 weeks of gestation and the non-treponemal titres before treatment were less than 1:32. When pregnant women received antisyphilis therapy after 28 GWs and non-treponemal titres before treatment were lower than 1:16, their children were unlikely to have CS. Therefore, reviewing maternal non-treponemal titres and timing of treatment can help clinicians focus on strengthening the management for high-risk individuals for CS.

Given the gaps in the follow-up and management of syphilis-exposed children and lack of efficient diagnostic measures, our study provided a new approach for risk stratification of CS in syphilis-exposed children. For newborn infants at high risk of CS, standardised treatment (aqueous benzylpenicillin 100 000–150 000 U/kg/day intravenously for 10–15 days or procaine penicillin 50 000 U/kg/day as a single dose intramuscularly for 10–15 days) can be used soon after delivery to eradicate the disease. Given the shortage of BPG globally, especially in resource-limited areas, it is important to ensure that children at high risk of CS receive priority treatment.

Some limitations of this study should be noted. First, the small number of CS cases might have limited the statistical power, resulting in a relatively low PPV of CS. Second, the lost to follow-up rate of syphilis-exposed children was high, reducing the representativeness of our target population. Third, because the focus of this study was to diagnose or exclude CS after birth, the CS cases in this study excluded miscarriages and stillbirths caused by syphilis infection, limiting the prediction of CS incidence in miscarriages and stillbirths. Therefore, further studies in a larger number of patients, including miscarriages and stillbirths, are needed to increase prediction accuracy.

---

### Table 4 The diagnostic values of non-treponemal titres before treatment for CS stratified by two treatment groups

| Subgroup                  | AUC (95% CI) | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) | Youden’s index |
|---------------------------|--------------|----------------------|----------------------|--------------|--------------|---------------|
| Untreated during pregnancy| 0.80 (0.72 to 0.88) | 81.5 (66.8 to 96.1)  | 78.5 (72.3 to 84.6)  | 37.3 (24.9 to 49.6)  | 96.4 (93.4 to 99.5)  | 0.60          |
| Treated during pregnancy  | 0.73 (0.59 to 0.87)  | 66.7 (40.0 to 93.3)  | 78.8 (76.6 to 81.0)  | 2.7 (0.9 to 4.6)  | 99.6 (99.3 to 100.0)  | 0.45          |

AUC, area under the curve; CS, congenital syphilis; NPV, negative predicted value; PPV, positive predicted value.
CONCLUSION
We provide a new algorithm to facilitate clinical decision-making and CS diagnosis. This new algorithm could be used to predict the probabilities of CS and non-CS in children based on maternal non-treponemal titres before treatment and timing of therapy during pregnancy. In addition, the algorithm could also be used to identify children at high-risk or low-risk for CS. Using this new algorithm, we hope to make the follow-up of syphilis-exposed children more manageable and effective.

Correction notice This article has been corrected since it first published. The provenance and peer review statement has been included.

Acknowledgements We thank all pregnant women and their children for their participation in the study. We are grateful to the obstetric and paediatric care providers who have assisted the implementation of the PMTCT program.

Contributors FH conceived the study, provided funding and drafted manuscript. J-JL and S-JG revised the paper. Y-YS and N-NH coordinated and supervised data collection. S-FL and SZ conceived the study. All authors were involved in the data interpretation and contributed to drafting and revision of the paper. All authors read and approved the final manuscript.

Funding The project was supported by The AbbVie Foundation for Maternity and Child Care and Prevention of Mother-to-child Transmission Chinese Association of STD and AIDS Prevention and Control (2020PMTCT-56) and Guangzhou Institute of Pediatrics/Guangzhou Women and Children's Medical Center (YIP-2019-001).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study was approved by the Ethics Approval Board of Guangzhou Women and Children’s Medical Center (202046801).

Provenance and peer review Not commissioned; externally peer reviewed.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work ispermits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is

ORCID ID
Sui Zhu http://orcid.org/0000-0002-0012-9045

REFERENCES
1 Plotzker RE, Murphy RD, Stolley DP. Congenital syphilis prevention: strategies, evidence, and future directions. Sex Transm Dis 2018;45:529–37.
2 Hussen S, Tadesse BT. Prevalence of syphilis among pregnant women in sub-Saharan Africa: a systematic review and meta-analysis. Biomed Res Int 2019;2019:1–10.
3 Korenromp EL, Rowley J, Alonso M, et al. Global burden of maternal and congenital syphilis and associated adverse birth outcomes–Estimates for 2016 and progress since 2012. PLoS One 2019;14:e0211720.
4 Felix MC, de Medeiros AR, Rossoni AM, et al. Adherence to the follow-up of the newborn exposed to syphilis and factors associated with loss to follow-up. Rev Bras Epidemiol 2016;19:277–39.
5 Slutsker JS, Hennessy RR, Schillinger JA. Factors Contributing to Congenital Syphilis Cases - New York City, 2010-2016. MMWR Morb Mortal Wkly Rep 2016;67:1088–93.
6 Tao Y, Chen MY, Tucker JD, et al. A nationwide spatiotemporal analysis of syphilis over 21 years and implications for prevention and control in China. Clin Infect Dis 2020;70:136–9.
7 Kroeger KA, Sangaramoorthy T, Loosier PS, et al. Pathways to congenital syphilis prevention: a rapid qualitative assessment of barriers, and the public health response, in Cadiz parish, Louisiana. Sex Transm Dis 2018;45:442–6.
8 Walker GI, Walker D, Mlano Franco D, et al. Antibiotic treatment for newborns with congenital syphilis. Cochrane Database Syst Rev 2019;2:CD12071.
9 Trivedi S, Williams C, Torrone E, et al. National trends and reported risk factors among pregnant women with syphilis in the United States, 2012-2016. Obset Gynecol 2019;133:27–32.
10 Heston S, Arnold S. Syphilis in children. Infect Dis Clin North Am 2018;32:129–44.
11 Wang Y, Wu M, Gong X, et al. Risk Factors for Congenital Syphilis Transmitted from Mother to Infant - Suzhou, China, 2011-2014. MMWR Morb Mortal Wkly Rep 2019;68:247–50.
12 Herremans T, Kortbeek L, Notermans DW. A review of diagnostic tests for congenital syphilis in newborns. Eur J Clin Microbiol Infect Dis 2010;29:495–501.
13 Li Hui JH, Yi S. Report accuracy of congenital syphilis in Jilin, 2013. Chin J Leg Skin Dis 2016;32.
14 Ye X, Tang S-K, Dai X, et al. Over-reporting of congenital syphilis in Guangzhou, China. Sex Health 2015;12:174–5.
15 Hwang J-S, Friedlander S, Rehan VK, et al. Diagnosis of congenital/perinatal infections by neonatologists: a national survey. J Perinatol 2019;39:690–6.
16 Townsend CL, Francis K, Peckham CS, et al. Syphilis screening in pregnant women in the United Kingdom, 2010-2011: a national surveillance study. Biomed J 2017;124:79–86.
17 Hu F, Xing Y-F, Chen N-N. Analysis on follow-up status and influencing factors of children born by syphilis-infected mothers in Guangzhou. Maternal and Child Health Care of China 2018;33:5.
18 World Health Organization. The global elimination of congenital syphilis: rationale and strategy for action. Available: http://apps.who.int/iris/bitstream/10665/43792/1/ 9789241595858_eng.pdf2007.
19 Hu F, Guo S-J, Lu J-I, et al. The effect of different treatment regimens and multiple risk factors on adverse pregnancy outcomes among Syphilis-Seropositive women in Guangzhou: a retrospective cohort study. Biomed Res Int 2020;2020:1–14.
20 Qin J-B, Feng T-J, Yang T-B, et al. Risk factors for congenital syphilis and adverse pregnancy outcomes in offspring of women with syphilis in Shenzhen, China: a prospective nested case-control study. Sex Transm Dis 2014;41:13–23.
21 Liu J-B, Hong F-C, Pan R, et al. A risk model for congenital syphilis in infants born to mothers with syphilis treated in gestation: a prospective cohort study. Sex Transm Infect 2010;86:292–6.
22 Hong F-C, Wu X-B, Yang F, et al. Risk of congenital syphilis (CS) following treatment of maternal syphilis: results of a CS control program in China. Clin Infect Dis 2017;65:586–94.
23 Li H, Chen N, Yu J, et al. Syphilis-attributable adverse pregnancy outcomes in China: a retrospective cohort analysis of 1187 pregnant women with different syphilis treatment. BMC Infect Dis 2019;19:292.
24 World Health Organization. Who guideline on syphilis screening and treatment for pregnant women, 2017. Available: https://www.who.int/publications/i/item/ 9789241550901.
25 Maternal and Child Health Services Division of National Health and Family Planning Commission of China. Protocol for prevention of mother-to-child transmission of HIV, syphilis and hepatitis B, 2015. Available: http://www.nhc.gov.cn/webeditor/ uploadfile/2015/06/20150615151817.docx [Accessed 26 Oct 2020].
26 Zhanga FH, Liu H, Tang J, et al. Screening for syphilis with dual algorithms: analysis of discordant and concordant serology results in a population with a low prevalence of syphilis. J Eur Acad Dermatol Venereol 2019;33:178–84.
27 Parham CE, Pettit DE, Larsen SA, et al. Interlaboratory comparison of the toluidine red heated serum test antigen preparation. J Clin Microbiol 1984;20:434–7.
28 Marangoni A, Foschi C, Capretti MG, et al. Contribution of a comparative Western blot method to early postnatal diagnosis of congenital syphilis. Clin Vaccine Immunol 2011;18:410–4.
29 Huang X, Qin G, Fang Y. Optimal combinations of diagnostic tests based on AUC. Biomarkers 2011;67:568–76.
30 Kingston M, French P, Higgins S, et al. UK national guidelines on the management of syphilis 2015. Int J STD AIDS 2016;27:421–46.
31 Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64:1–137.
32 Gomez GB, Kamb ML, Newman LM, et al. Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. Bull World Health Organ 2013;91:217–26.
33 Rodrigues DC, Domingues RMSM. Management of syphilis in pregnancy: knowledge and practices of health care providers and barriers to the control of disease in Teresina, Brazil. Int J Health Plann Manage 2018;33:329–44.
34 de Oliveira SIM, de Oliveira Saraiva COP, de França DF, et al. Syphilis notifications and the triggering processes for vertical transmission: a cross-sectional study. Int J Environ Res Public Health 2020;17. doi:10.3390/ijerph17030984. [Epub ahead of print: 05 Feb 2020].
35 Kamb ML, Newman LM, Riley PL, et al. A road map for the global elimination of congenital syphilis. Obstet Gynecol Int 2010;2010:1155/2010/312798. [Epub ahead of print: 14 Jul 2010].
36 Biswas HH, Chew Ng RA, Murray EL, et al. Characteristics associated with delivery of an infant with congenital syphilis and missed opportunities for Prevention-California, 2012 to 2014. Sex Transm Dis 2018;45:435–41.
37 Radcliffe M, Meyer M, Roditi D, et al. Single-dose benzathine penicillin in infants at risk of congenital syphilis—results of a randomised study. S Afr Med J 1997;87:62–5.
38 Visser M, van der Ploeg CP, Smit C, et al. Evaluating progress towards triple elimination of mother-to-child transmission of HIV, syphilis and hepatitis B in the Netherlands. BMC Public Health 2019;19:353.
39 World Health Organization. Who guidelines for the treatment of Treponema pallidum (syphilis), 2016. Available: https://www.who.int/publications/i/item/who-guidelines-for-the-treatment-of-treponema-pallidum-(syphilis)
40 Chen X, Li G, Gan Y, et al. Availability of benzathine penicillin G for syphilis treatment in Shandong Province, eastern China. BMC Health Serv Res 2019;19:188.
41 National Health Commission of the People’s Republic of China. Diagnosis for syphilis (WS273–2018), 2018. Available: http://www.nhc.gov.cn/wjw/s9491/201803/5103a5425f9e47d29691de38434b774.shtml [Accessed 26 Oct 2020].
Correction: *New screening approach to detecting congenital syphilis in China: a retrospective cohort study*

Hu F, Guo S, Lu J, *et al*. New screening approach to detecting congenital syphilis in China: a retrospective cohort study. *Arch Dis Child* 2021;106:231–7. doi:10.1136/archdischild-2020-320549

This article has been corrected since it first published. The provenance and peer review statement has been included.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

*Arch Dis Child* 2021, **106** e41. doi:10.1136/archdischild-2020-320549corr1