



Published in final edited form as:

*Lancet Glob Health*. 2018 January ; 6(1): e26–e28. doi:10.1016/S2214-109X(17)30422-9.

## Revisiting strategies to eliminate mother-to-child transmission of syphilis

**Melanie Taylor, Harriet Gliddon, Stephen Nurse-Findlay, Maura Laverty, Nathalie Broutet, Lee Pyne-Mercier, Jerker Liljestrand**

WHO Department of Reproductive Health and Research, STI Program, Geneva 1211, Switzerland (MT, SN-F, ML, NB); US Centers for Disease Control and Prevention, Division of STD Prevention, Atlanta, GA, USA (MT); London Centre for Nanotechnology, University College London, London, UK (HG); and Bill & Melinda Gates Foundation, Seattle, WA, USA (LP-M, JL)

Mother-to-child transmission of syphilis, so-called congenital syphilis, can result in adverse pregnancy outcomes such as fetal loss, stillbirth, neonatal death, preterm birth, low birthweight, and congenital anomalies.<sup>1</sup> Roughly 1 million pregnant women are estimated to be infected with syphilis worldwide, with the highest prevalence in east and southern Africa.<sup>2</sup> Antenatal screening and treatment with a single dose of benzathine benzylpenicillin successfully cures both maternal and congenital syphilis and prevents adverse pregnancy outcomes due to syphilis.<sup>3</sup>

10 years have elapsed since the release of the WHO Strategy for the Global Elimination of Congenital Syphilis in 2007.<sup>4</sup> This document called for political commitment and advocacy to address the issue of congenital syphilis through increasing access to and quality of maternal and newborn health services, increasing screening and treatment of pregnant women and their partners, and establishing surveillance, monitoring, and evaluation systems. In June, 2017, a meeting was organised by the WHO Department of Reproductive Health and Research and the Bill and Melinda Gates Foundation to review the progress that has been made in the elimination of congenital syphilis, to discuss existing tools (panel),<sup>5–16</sup> and to identify challenges ahead.

The general consensus at the meeting was that little progress has been made in the elimination of congenital syphilis over the past decade because of several challenges. Communicating the burden of congenital syphilis has been challenging because adverse health outcomes, such as stillbirth, are not always attributed to congenital syphilis. Additionally, many awareness efforts have been unsuccessful because of the stigma surrounding syphilis and the poor visibility of important advocates and stakeholders, which

This is an Open Access article published under the CC BY-NC-ND 3.0 IGO license which permits users to download and share the article for non-commercial purposes, so long as the article is reproduced in the whole without changes, and provided the original source is properly cited. This article shall not be used or reproduced in association with the promotion of commercial products, services or any entity. There should be no suggestion that WHO endorses any specific organisation, products or services. The use of the WHO logo is not permitted. This notice should be preserved along with the article's original URL.

mtaylor@who.int.

LP-M reports personal fees from the Bill & Melinda Gates Foundation during the conduct of the study. All other authors declare no competing interests.

For more on the **Spectrum STI modelling tool** see <http://avenirhealth.org/software-spectrum.php>

gives the perception that congenital syphilis is not a major public health problem. The participants acknowledged that reframing screening of syphilis in pregnancy as a matter of healthy pregnancy and healthy infants would deliver a more positive message, which could ultimately help raise awareness and garner support for the elimination of mother-to-child transmission of syphilis.

Poor access to benzathine benzylpenicillin, the only recommended treatment for pregnant women with syphilis, is a major issue, with shortages reported in many parts of the world.<sup>17</sup> This issue is further complicated by the absence of an easily administered paediatric formulation of benzathine benzylpenicillin, the fear of allergic reactions to the drug, and resistance to using the drug because of its intramuscular administration. The misperception that benzathine benzylpenicillin is an outdated drug that could be replaced by newer, more effective drugs (that might be orally administered) has led health-care professionals to select alternative, ineffective treatments. A penicillin allergy desensitisation protocol (in consideration for guideline development by WHO) could reduce the use of alternative treatments because of concerns related to allergic reactions. Alternative treatments to benzathine benzylpenicillin are needed, in particular an alternative oral regimen that could increase access to treatment in settings and among populations where administration of injections is not feasible.

An important advancement in the screening of syphilis is the fairly recent availability of rapid diagnostic tests, either for detection of antibodies to *Treponema pallidum* alone or jointly with detection of antibodies to HIV. A systematic review<sup>18</sup> of these dual rapid diagnostic tests for HIV and syphilis found that, in most cases, the minimal criteria specified in the target product profile for a dual HIV and syphilis test were met and that dual testing was cost-effective, feasible to implement at the programme level, and acceptable to testing clients. The WHO Department of Reproductive Health and Research is developing formal guidelines for the use of these dual tests, including diagnostic algorithms for their use in various settings and prevalence levels, which builds on interim WHO guidance published in 2017.<sup>6</sup>

Four tools for the surveillance and monitoring of national and global burdens of maternal and congenital syphilis were reviewed and endorsed at the meeting. First, the WHO surveillance case definition, which includes the requirement for treatment of pregnant women diagnosed with syphilis with benzathine benzylpenicillin to prevent congenital syphilis, can align national-level surveillance case definitions for consistent case reporting and global congenital syphilis estimations.<sup>13</sup> Second, countries can report maternal syphilis screening and treatment data and incidence of congenital syphilis to the Global AIDS Monitoring system operated by UNAIDS.<sup>15</sup> These data are used by WHO for national, regional, and global estimations of syphilis burden. Third, the Avenir Health Spectrum STI modelling tool allows programme staff to estimate the prevalence and incidence of sexually transmitted infections in their national adult population. The model, which is freely available online, contains country-level syphilis prevalence data for more than 150 countries. Fourth, WHO has expanded the Microsoft-Excel-based congenital syphilis estimation tool<sup>7</sup> to allow national-level-programme staff to generate estimates of congenital syphilis incidence and averted adverse birth outcomes with treatment projected through to 2030.

Although an investment case for accelerated congenital syphilis elimination activities has been available since 2012,<sup>14</sup> stakeholder support and investment in elimination remain to be secured for global congenital syphilis prevention. Screening and treatment of syphilis during pregnancy is highly cost-effective, even in low-prevalence settings.<sup>19</sup> A consensus was reached to prioritise activities to expand and ensure availability of benzathine benzylpenicillin for treatment of syphilis and to expand use of rapid diagnostic tests in antenatal-clinic settings. Support at the national level, increased cooperation between and within UN agencies, and broader stakeholder involvement in syphilis prevention are needed to make provider-level screening and treatment common practice in antenatal-clinic settings. These activities will determine the advances made in the next decade of congenital syphilis prevention and elimination.

## References

1. 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: 217–26. [PubMed: 23476094]
2. Wijesooriya NS, Rochat RW, Kamb ML, et al. Global burden of maternal and congenital syphilis in 2008 and 2012: a health systems modelling study. *Lancet Glob Health* 2016; 4: e525–33. [PubMed: 27443780]
3. Blencowe H, Cousens S, Kamb M, Berman S, Lawn JE. Lives Saved Tool supplement detection and treatment of syphilis in pregnancy to reduce syphilis related stillbirths and neonatal mortality. *BMC Public Health* 2011; 11 (suppl 3): S9.
4. WHO. The global elimination of congenital syphilis: rationale and strategy for action. Geneva: World Health Organization, 2007.
5. WHO. WHO guideline on syphilis screening and treatment for pregnant women. Geneva: World Health Organization, 2017.
6. WHO. WHO information note on the use of dual HIV/syphilis rapid diagnostic tests (RDT). Geneva: World Health Organization, 2017.
7. WHO. Syphilis in pregnancy. Tool to estimate burden of maternal syphilis and adverse outcomes. 2017 [http://www.who.int/reproductivehealth/topics/rtis/syphilis/measurement\\_tool/en](http://www.who.int/reproductivehealth/topics/rtis/syphilis/measurement_tool/en) (accessed May 14, 2017).
8. WHO. WHO guidelines for the treatment of *Treponema pallidum* (syphilis). Geneva: World Health Organization, 2016.
9. WHO. Methods for surveillance and monitoring of congenital syphilis elimination within existing systems. Geneva: World Health Organization, 2011.
10. DualElimination.org. Dual elimination of HIV and syphilis. <http://www.dualelimination.org> (accessed Aug 22, 2017).
11. CDC. Management of persons who have a history of penicillin allergy. 2015 <https://www.cdc.gov/std/tg2015/pen-allergy.htm> (accessed Aug 7, 2017).
12. WHO. Global health sector strategy on sexually transmitted infections, 2016–2021. Geneva: World Health Organization, 2016.
13. WHO. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV and syphilis. 2nd edn Geneva: World Health Organization, 2017.
14. WHO. Investment case for eliminating mother-to-child transmission of syphilis. Geneva: World Health Organization, 2012.
15. UNAIDS. Global AIDS Monitoring 2017—indicators for monitoring the 2016 United Nations Political Declaration on HIV and AIDS. <http://www.unaids.org/en/resources/documents/2016/Global-AIDS-Monitoring-2017> (accessed June 27, 2017).
16. WHO. WHO Global Health Observatory data repository. Data on syphilis. 2016 <http://apps.who.int/gho/data/node.main.A1357STI?lang=en> (accessed Nov 24, 2017).

17. Taylor MM, Zhang X, Nurse-Findlay S, Hedman L, Kiarie J. The amount of penicillin needed to prevent mother-to-child transmission of syphilis. *Bull World Health Organ* 2016; 94: 559–9A. [PubMed: 27516630]
18. Gliddon HD, Peeling RW, Kamb ML, Toskin I, Wi TE, Taylor MM. A systematic review and meta-analysis of studies evaluating the performance and operational characteristics of dual point-of-care tests for HIV and syphilis. *Sex Transm Infect* 2017; 10.1136/sextrans-2016-053069.
19. Kahn JG, Jiwani A, Gomez GB, et al. The cost and cost-effectiveness of scaling up screening and treatment of syphilis in pregnancy: a model. *PLoS One* 2014; 9: e87510. [PubMed: 24489931]

**Panel: Tools to aid the screening, treatment, and elimination of congenital syphilis**

**Provider tools**

- Antenatal-care syphilis testing recommendations<sup>5</sup>
- Rapid HIV and syphilis test interim guidance<sup>6</sup>
- Current and projected use of benzathine penicillin G (BPG) in maternal syphilis<sup>7</sup>
- Syphilis treatment guidelines<sup>8</sup>
- Congenital syphilis case definition<sup>9</sup>
- Staff training on BPG administration<sup>10</sup>
- Penicillin desensitisation protocol<sup>11</sup>

**Advocacy tools**

- Congenital syphilis elimination strategy<sup>4</sup>
- Partnerships with stakeholders
- WHO global strategy on sexually transmitted infections (STIs)<sup>12</sup>
- WHO global guidance on elimination of mother-to-child transmission<sup>13</sup>
- Investment case for eliminating mother-to-child transmission of syphilis<sup>14</sup>

**Surveillance tools**

- WHO congenital syphilis surveillance case definition<sup>9</sup>
- UNAIDS Global AIDS Monitoring system<sup>15</sup>
- WHO Global Health Observatory<sup>16</sup>
- WHO congenital syphilis estimation tool<sup>7</sup>
- Avenir Health Spectrum STI modelling tool
- WHO STI surveillance report<sup>9</sup>