

UK National Screening Committee

A pilot of the triage approach to assess whether existing population screening programmes should be continued

Screening Topic

Antenatal screening for Syphilis

V. Final consultation

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1. Executive Summary

Triage reviews are high level reviews which scan the literature to identify 'red flags' suggesting that further exploration of programme cessation may be necessary. These reviews have a surveillance function and are not intended as a comprehensive review of the programme.

This triage review identified two studies that discussed a limitation of the screening programme although none advocated its cessation. A Cochrane review reported limited benefits of on-site screening compared with a conventional screening programme and a cost-effectiveness model considered the benefits and harms of the addition of routine re-screening in the third trimester.

There were no findings in either of the studies that could be interpreted as a harm. Instead, both studies touched upon areas of improvement that are acknowledged internationally and domestically. Specifically, the pursuit of more accurate tests that reduce false positives and detect disease at a stage that presents a significant risk of mother to child transition and the appropriate pathways for effective antibiotic treatment after detection.

The 2013 UK National Screening Committee recommendation to offer antenatal syphilis screening considered the benefits of screening to outweigh the harms. It is the conclusion of this triage review that there is no evidence suggesting that programme cessation should be explored further.

2. Background

Introduction to the condition

Syphilis is a sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum*.

In adults syphilis infections are usually described by the stage of the infection:

- The first (or primary) stage of infection is commonly asymptomatic. In those that do present with symptoms they may be limited to a sore on the genital region or mouth. The primary stage of the infection typically lasts between 4 and 12 weeks.
- The **second stage** of the disease (lasting up-to 2 years after infection) may also be asymptomatic, although symptoms are more common than in primary infections. When present, symptoms will typically include a red skin rash, pain in the joints and swollen lymph nodes.
- The **latent stage** is usually asymptomatic. During this period infectivity is low, but up to one-quarter of patients will experience recurrence of symptoms. This stage is often further divided into "early latent" and "late latent". Approximately one third of people with untreated secondary syphilis will develop latent infections.
- The final stage of the infection, also known as the **tertiary stage**, occurs when the infection remains untreated and follows up to 20 years of latency. Symptoms can be very severe at this stage, including complications with the heart and brain.

Untreated maternal infections can result in serious adverse pregnancy outcomes, including early fetal loss, stillbirth, prematurity, low birth weight, neonatal and infant death, and congenital disease of the newborn. Clinical manifestations of congenital syphilis are influenced by gestational age, stage of maternal syphilis, maternal treatment, and the immunological response of the fetus.

Mother to child transmission usually occurs through fetal exposure via the bacteria crossing the placenta. The likelihood of vertical transmission increases with gestational age. Conversely, the severity of fetal infection decreases with gestational age. When left untreated, the rate of vertical transmission is between 60% and 100% in women with a primary or secondary syphilis infection. The rate decreases in women in the later stages of infection to approximately 40% in early latent infections and <10% in late latent infection.

Penicillin is the most effective treatment for all stages of syphilis. Treatment during the early stages of the infection is preferable to help prevent further complications and to avoid onward transmission of the infection. Early treatment in pregnancy can significantly reduce the risk of congenital syphilis;

approximately 70% to 100% of infants born to untreated mothers will be infected compared to 1% to 2% of those born to women adequately treated during pregnancy.

Congenital syphilis, in those neonates that survive beyond delivery, is usually described as either early or late presenting depending on whether symptoms present before or after 2 years. It is common for neonates to be asymptomatic at birth. In those that do present “early”, symptoms will usually emerge within 3 months.

The manifestations of early infections can be varied, although persistent rhinitis (snuffles) is often the earliest presenting symptom; occurring in up to 40% of affected neonates. Later congenital infections manifest with facial deformities, keratitis, sensorineural hearing loss, dental deformities, intellectual impairment, hydrocephalus and skeletal deformities. Neonates are not routinely screened for syphilis and diagnosis is often missed because of the non-descript symptoms of early congenital infection.

3. NHS screening and treatment pathways

The UK National Screening Committee (UKNSC) recommends that women are screened for syphilis at their first antenatal appointment. Syphilis is one of three infectious diseases screened via a blood test at that first appointment, that fall under the remit of the Infectious Diseases in Pregnancy Screening programme in England.

The UK Standards for Microbiology Investigations recommend that an enzyme immunoassay (EIA) or chemiluminescent immunoassay (CLIA) is used as the primary screening test (PHE 2016). Confirmation of positive screening test results should involve a repeat enzyme immunoassay to confirm reproducibility and a further highly sensitive and specific treponemal test.

The management of syphilis in pregnant women and neonates in the UK is outlined in a British Association for Sexual Health and HIV (BASHH) guideline (Kingston et al., 2015).

4. Review methodology

Triage review

The UKNSC has committed to assess the viability of all national screening programmes every three years. Triage reviews will be the starting point for each of these assessments.

The purpose of a triage review is to search for evidence that indicates that a screening programme may cause harm in the screened population. The definition of harm in these reviews can be a clinical risk, a social complication or a reason to consider disinvestment. Evidence associated with the modification of the existing screening programme, for example diagnostic studies regarding improvements to screening test accuracy, is outside the scope of these triage reports.

Depending on the direction and volume of the evidence identified, the triage review may recommend that further investigation through a more rigorous evidence review is warranted or that no further investigation is required until the next three-year cycle. If no studies are identified then this report will recommend continuation of the programme without any further review until the next cycle. As such, triage reviews have a surveillance function.

Each triage review will undergo a three month public consultation on the UKNSC website. The screening committee will then make the final recommendation on the next stage of the review based on the findings of the triage review and the stakeholder consultation comments.

Search strategy and Inclusion criteria

The triage review will be based on a literature search over the last 10 years or since the publication date of the last formal UK NSC review, whichever is most recent. As noted above, studies will only be included that report on outcomes that highlight a reason for the cessation of the existing national screening programme. The search and inclusion criteria will therefore only consider studies that are relevant to one or more of the criteria below:

- The study reports outcomes that address screening programme cessation (including publications about the ending of screening programmes in countries similar to the UK)
- The study reports on the harms of screening for syphilis
- The study reports on the balance of harms and benefits of screening for syphilis in pregnancy

Triage reviews prioritise higher quality studies; systematic reviews, randomised controlled trial and large prospective cohort studies. Lower quality of evidence (i.e. case-series, narrative reviews etc.) are considered if they report a significant finding and there is no higher quality evidence to refute or support the outcome(s).

The process for study inclusion was undertaken in two stages. The first stage was undertaken by a UKNSC information scientist and aimed to remove studies that are clearly not relevant to the review (for example, animal studies, studies in a foreign language and duplicates). The second stage was undertaken by a single reviewer and considered the remaining studies and applied the above criteria; all studies excluded at this stage were noted in the excluded studies table in the appendix.

5. Evidence summary

Antenatal screening for syphilis was last assessed against the UKNSC criteria in 2013. That report found no publications that suggested that there should be a change in the screening policy. It concluded that syphilis screening during pregnancy is a cost-effective intervention for which the benefits currently outweigh the harms (UKNSC 2013).

The 2013 UKNSC review also addressed the harms of screening, identifying one study. It stated the following:

Potential harms may include false-positive results that require clinical evaluation (unnecessary utilisation of resources), unnecessary anxiety to the patient in case of false-positive result, and unnecessary use of antibiotics. There is also evidence of the women experiencing fear of gender-based violence from a partner following the disclosure of sexually transmitted infection status

Strategies to overcome such potential harms include: use of highly sensitive and specific diagnostic testing; and identifying women at potential increased risk of violence from an intimate partner when giving them a positive diagnosis. Such women have been shown to prefer provider-initiated referral mechanisms (rather than patient-initiated), and may need additional counselling and support strategies to be implemented

Description of the evidence

The literature search identified seven studies and three conference abstracts that matched the specifications outlined in the methodology. Two studies met the inclusion criteria, also outlined above. The full search strategy is outlined in appendix 1 and the rationale for the exclusion of each of the studies included after the first stage of the review can be found in appendix 2. Full details of the two included studies can be found in appendix 3.

A Cochrane review, published in 2014, assessed the effectiveness of point of care (same day) testing compared to the more conventional antenatal screening programme with laboratory testing (Shahrook et al., 2014). The advantage of same-day screening in comparison to the conventional screening programme would primarily be found in the time saved analysing the blood sample and avoidance of the delay in treatment that is associated with conventional screening. The review included two cluster randomised controlled trials, the outcomes of which could not be used in a meta-analysis and so were reported separately. The first study compared point of care testing with conventional screening in 7700 Mongolian women. The findings of the study are summarised in the table below. Although there were observed advantages of the point of care tests, there was no evidence that screening should be stopped. No outcomes were reported that considered adverse screening outcomes (for example false positive rates), the rate of neonatal transmission or perinatal mortality.

One American cost-effectiveness model considered whether re-screening in the third trimester would reduce the incidence congenital cases and frequency of adverse perinatal outcomes (Albright et al., 2015). The model compared re-screening women who screened negative in the first trimester with no rescreening. The model assumed that the base-case incidence of seroconversion was 0.012%. The model estimated that rescreening 4,000,000 women would prevent 60 cases of congenital syphilis, at a cost of \$419,842 per case of congenital syphilis prevented. The model also estimated that 7 fetal and 4 neonatal deaths would be prevented at a cost of \$3,621,144 and \$6,052,534, respectively. The study did not report on how many cases of congenital syphilis would be prevented through only one screening test. The authors concluded that re-screening would only be cost effective at a seroconversion incidence of 0.017%, with a willingness to pay \$285,000 to prevent one case of congenital syphilis. It is unclear how applicable this economic analysis or the model assumptions would be for a screening programme in the UK.

UK screening programme performance

Between 2010 and 2011, the UCL institute for Child Health was funded by Public Health England to evaluate the performance of the screening programme and the epidemiology of syphilis in pregnant women through a national surveillance study. The "Antenatal Syphilis Screening Study (SASS)" was published in 2016 (Townsend et al., 2016), although data from the study had already prompted the IDSP to revise screening pathways, programme standards and data collection for 2016/17 (PHE 2015).

The study found that, between 2010 and 2011, 1939 pregnant women screened positive for syphilis. Of these, 1840 were classified and 1425 cases were confirmed, meaning that 415 screening results were false positives. Of the 1425 confirmed cases; 374 were newly diagnosed and all were treated, 1010 were previously diagnosed with syphilis (of which 155 required treatment) and leaving 41 with an unclear aetiology who were also all treated. Over 96% of women indicated for treatment were treated, the median gestation at treatment initiation was 17.4 weeks. There were 6 cases of congenital syphilis, 2 were born to women who were untreated and the other 4 cases were born to women who received inadequate treatment (late commencement or incomplete treatment).

In addition to the Antenatal Syphilis Screening Study, Public Health England has also funded the British Paediatric Surveillance Unit (BPSU) to complete a 5 year surveillance study of children under the age of 24 months with a confirmed or presumptive diagnosis of congenital syphilis or acquired syphilis. The data collection stage of the study has now finished and the findings are awaiting analysis and publication. Provisional data from the BPSU study found that the incidence of congenital syphilis was: 0.0136 per 1000 live and still births in 2011 and 0.0025 per 1000 in 2011 (PHE 2013).

6. Conclusion

No studies were identified that discussed the cessation of antenatal screening for syphilis. Two studies were identified that considered potential limitations associated with the test and treatment, although none of these studies advocated that screening should be stopped or altered.

Both studies considered the limitations of the timelines of testing. The first, an American cost-effectiveness study, noted that some cases of congenital syphilis may not be prevented through a single screening test early in pregnancy. The study concluded that, despite this, it was not cost effective to introduce re-screening in the third trimester. It is unclear how generalisable these findings are in a UK setting. This uncertainty is perhaps most pertinent in light of the yearlong UK surveillance study data which found only one case of congenital syphilis that was likely caused by an maternal infection after the first screening test.

The other study, a 2014 Cochrane review, inferred that point-of-care on-site testing may be advantageous when compared to conventional screening test because of the time required for laboratory testing. Although the authors considered that point of care testing could have promising screening and treatment uptake outcomes, there was no conclusive evidence that it was more beneficial compared with conventional screening or that conventional screening programmes caused any harm that would be removed through the introduction of point of care testing.

In addition to the findings of the papers described above, the screening test accuracy, specifically the number of false positives and the detection of disease at a stage that poses little or no risk of mother to child transmission has been raised in a UK surveillance study (Townsend et al., 2016), the previous UKNSC review (UKNSC 2013) and in international WHO supported literature (Ham et al., 2015). However none of these reports advocated cessation of screening or the significant alteration of current screening practice.

Antenatal syphilis screening is part of routine care in most developed countries. It is the conclusion of this report that there is no evidence suggesting that programme cessation should be explored further.

7. References

Albright et al., 2015

Albright CM, Emerson JB, Werner EF, Hughes BL. Third-Trimester Prenatal Syphilis Screening: A Cost-Effectiveness Analysis. *Obstetrics & Gynecology*. 2015;126(3):479-85

Ensari et al., 2015

Ensari T, Kirbas A, Ozgu-Erdinc AS, Gokay Saygan S, Erkaya S, Uygur D, et al. An eight-year retrospective analysis of antenatal screening results for syphilis: is it still cost effective? *Journal of Infection in Developing Countries*. 2015;9(9):1011-5

Ham et al., 2015

Ham DC, Lin C, Newman L, Wijesooriya NS, Kamb M. Improving global estimates of syphilis in pregnancy by diagnostic test type: A systematic review and meta-analysis. *Int J Gynaecol Obstet*. 2015 Jun;130 Suppl 1:S10-4. doi: 10.1016/j.ijgo.2015.04.012. Epub 2015 Apr 25.

Hawkes et al., 2013

Hawkes SJ, Gomez GB, Broutet N. Early antenatal care: does it make a difference to outcomes of pregnancy associated with syphilis? A systematic review and meta-analysis. *PLoS One*. 2013;8(2):e56713. doi: 10.1371/journal.pone.0056713. Epub 2013 Feb 28.

Kiarie et al., 2015

Kiarie J, Mishra CK, Temmerman M, Newman L. Accelerating the dual elimination of mother-to-child transmission of syphilis and HIV: Why now? *Int J Gynaecol Obstet*. 2015 Jun;130 Suppl 1:S1-3. doi: 10.1016/j.ijgo.2015.05.002.

Kingston et al., 2015

M Kingston, P French, S Higgins, O McQuillan, A Sukthankar, C Stott, B McBrien, C Tipple, A Turner, AK Sullivan. UK national guidelines on the management of syphilis 2015. *Int J STD AIDS OnlineFirst*, published on December 31, 2015 as doi:10.1177/0956462415624059

Klein et al., 1990

Klein VR, Cox SM, Mitchell MD, et al. The Jarisch-Herxheimer reaction complicating syphilotherapy in pregnancy. *Obstet Gynecol* 1990;75(3 Pt 1):375-80.

Shahrook et al., 2014

Shahrook S, Mori R, Ochirbat T, Gomi H. Strategies of testing for syphilis during pregnancy. *Cochrane Database of Systematic Reviews*. 2014;10:CD010385

PHE 2013

Recent epidemiology of infectious syphilis and congenital syphilis. *Infection reports* Volume 7 Number 44 Published on: 1 November 2013

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/336760/hpr4413_sphls.pdf

PHE 2015

Public Health England 2015. Antenatal screening for infectious diseases in England: summary report for 2014. Infection reports Volume 9 Number 43 Published on: 4 December 2015

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/482642/hpr4315_ntntls_crng.pdf

PHE 2016

Public Health England 2016. UK Standards for Microbiology Investigations Syphilis serology Virology | V 44 | Issue no: 2.1 | Issue date: 20.07.16

PHE 2016a

Public Health England 2016. NHS Infectious Diseases in Pregnancy Screening Programme Laboratory Handbook 2016 to 2017. Accessed at

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/539597/V_44i2.1.pdf

PHE 2016b

Public Health England 2016. *NHS Infectious Diseases in Pregnancy Screening Programme Standards 2016 to 2017*. Available at:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/512083/IDPS_Programme_Standards_2016_2017_final.pdf

Townsend et al, 2016

Townsend C, Francis K, Peckham CS, Tookey P. Syphilis screening in pregnancy in the United Kingdom, 2010–2011: a national surveillance study, BJOG Volume 124, Issue 1, January 2016

UKNSC 2013

United Kingdom National Screening Committee 2013. Screening for syphilis in pregnancy External review against programme appraisal criteria for the UK National Screening Committee (UK NSC).

Wallace et al., 2013

Wallace H, Isitt C, Broomhall H, Wilson J. Treatment of syphilis in pregnancy prevents congenital syphilis but other severe adverse outcomes remain high in the UK. International Journal of STD and AIDS. 2013;24:2-3

WHO 2014

World Health Organisation. 2014. GLOBAL GUIDANCE ON CRITERIA AND PROCESSES FOR VALIDATION: Elimination of Mother-to-Child Transmission of HIV and Syphilis. Accessed at:

http://apps.who.int/iris/bitstream/10665/112858/1/9789241505888_eng.pdf?ua=1&ua=1

Appendix 1 – Search strategy

SCOPE:

- Addressing screening programme cessation
- Reporting harms from screening
- Reporting balance of harms and benefits from screening

SOURCES SEARCHED:

- Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
- Embase 1996 to 2016 Week 36
- Cochrane Library : Issue 9 of 12, September 2016

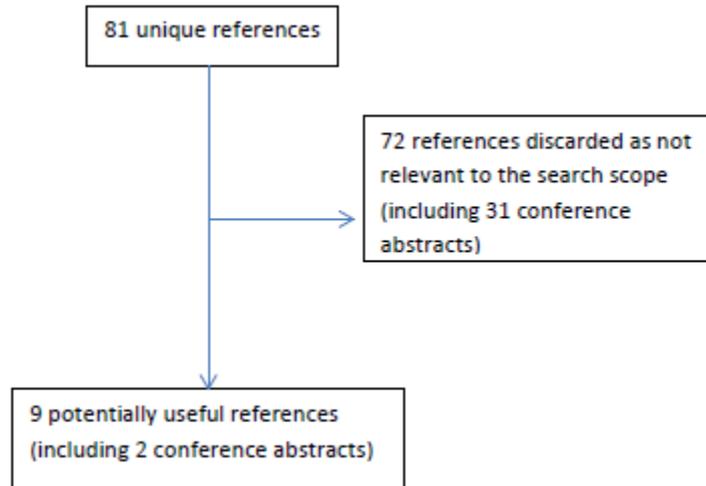
DATES OF SEARCH: January 2011 – September 2016

SEARCH STRATEGY:

1. exp Syphilis/ (26108)
2. syphil*.tw. (24717)
3. Treponema pallidum/ (3607)
4. treponema pallidum.tw. (3659)
5. 1 or 2 or 3 or 4 (35389)
6. Prenatal Diagnosis/ (33391)
7. ((antenatal or prenatal or pregnan\$) adj2 screen\$3).tw. (6360)
8. Mass Screening/ae [Adverse Effects] (623)
9. 6 or 7 or 8 (38033)
10. (ceas\$ or cessation or stop or stopped or continu\$ or discontinu\$).tw. (1054204)
11. (appropriate\$ or inappropriate\$ or unnecessary or question\$).tw. (1235870)
12. (harm\$ or adverse).tw. (488808)
13. (benefit\$ and (risk\$ or harm\$)).tw. (133318)
14. ((side or adverse) adj effect\$).tw. (316352)
15. (overdiagnos?s or over diagnos?s).tw. (2950)
16. Program Evaluation/ (52508)
17. Patient Safety/ (10403)
18. Patient harm/ (79)
19. exp Health Services Misuse/ (8775)
20. Risk Assessment/ (208201)
21. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (2982956)
22. 5 and 9 and 21 (147)
23. limit 22 to yr="2011 -Current" (43)

Similar searches were also carried out in Embase and the Cochrane Library.
All searches carried out on 8 September 2016

Medline	43
Embase	75
Cochrane Library	2
Total	120



After automatic and manual de-duplication, 81 unique references were sifted for relevance to the search scope above.

Appendix 2 – Excluded studies table

Reference	Reason for exclusion
Ensari T, Kirbas A, Ozgu-Erdinc AS, Gokay Saygan S, Erkaya S, Uygur D, et al. An eight-year retrospective analysis of antenatal screening results for syphilis: is it still cost effective? <i>Journal of Infection in Developing Countries</i> . 2015;9(9):1011-5	Screening test used in the study is not used in the UK
Manabe YC, Namale G, Nalintya E, Sempa J, Ratanshi RP, Pakker N, et al. Integration of antenatal syphilis screening in an urban HIV clinic: a feasibility study. <i>BMC Infectious Diseases</i> . 2015;15:15	Study undertaken in sub-Saharan Africa. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal syphilis screening programme or the cessation of a screening programme..
Lawi JD, Mirambo MM, Magoma M, Mushi MF, Jaka HM, Gumodoka B, et al. Sero-conversion rate of Syphilis and HIV among pregnant women attending antenatal clinic in Tanzania: a need for re-screening at delivery. <i>BMC Pregnancy & Childbirth</i> . 2015;15:3	Study undertaken in Tanzania. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal syphilis screening programme or the cessation of a screening programme..
Larson BA, Lembela-Bwalya D, Bonawitz R, Hammond EE, Thea DM, Herlihy J. Finding a needle in the haystack: the costs and cost-effectiveness of syphilis diagnosis and treatment during pregnancy to prevent congenital syphilis in Kalomo District of Zambia. <i>PLoS ONE</i> . 2014;9(12):e113868	The economic analysis included too many assumption that would be significantly different to UK model – notably incidence and treatment uptake rates. The findings in the model are therefore not generalizable to a UK screening population
Molloy EJ, Owoeye C, Knowles S. Is antenatal screening for syphilis still necessary? <i>Irish Medical Journal</i> . 2012;105(2):37-8	Secondary narrative review. Study did not present any new evidence.
Mahomed M, Gimbel S, Hoek R, Rustagi A, Come C, Newman L, et al. Testing for syphilis in pregnancy and associated adverse outcomes in mozambique. <i>Sexually Transmitted Infections Conference: STI and AIDS World Congress</i> . 2013;89(no pagination)	Study undertaken in Mozambique. Not generalizable to a UK screening population. Study did not report harm outcomes associated with an antenatal syphilis screening programme or the cessation of a screening programme..
Wallace H, Isitt C, Broomhall H, Wilson J. Treatment of syphilis in pregnancy prevents congenital syphilis but other severe adverse outcomes remain high in the UK. <i>International Journal of STD and AIDS</i> . 2013;24:2-3	Conference abstract.

Appendix 3 – Included studies summary table

Publication details	Study details	Population	Intervention/test and comparator	Main findings	Comments										
Screening cessation															
No studies identified															
Harms of screening															
Shahrook S, Mori R, Ochirbat T, Gomi H. Strategies of testing for syphilis during pregnancy. Cochrane Database of Systematic Reviews. 2014;10:CD010385	Two randomised cluster trails	<ol style="list-style-type: none"> 7700 Mongolian women 793 South African women with syphilis 	Point of care "same-day" screening vs. conventional screening programs (including laboratory assessment)	<p>Study one</p> <table border="1"> <tbody> <tr> <td>Proportion of women tested for syphilis at the first antenatal visit</td> <td>OR 989.80 (95% CI 16.27 to 60233.05)</td> </tr> <tr> <td>Proportion of women tested for syphilis at the third trimester visit</td> <td>OR 617.88, (95% CI 13.44 to 28399.01)</td> </tr> <tr> <td>Adequate treatment</td> <td>AOR 10.44, (95% CI 1.00 to 108.99)</td> </tr> <tr> <td>Syphilis cases detected at first trimester visit</td> <td>AOR 2.45, (95% CI 1.44 to 4.18)</td> </tr> <tr> <td>Syphilis cases detected at third trimester visit</td> <td>AOR 6.27, (95% CI 1.47 to 26.69)</td> </tr> </tbody> </table> <p>Study two</p> <p>Perinatal mortality reduction (odds ratio (OR) 0.63; 95% CI 0.27 to 1.48; 18/549(3.3%) versus 8/157 (5.1%)).</p> <p>After loss to follow up, 396/618 (64.1%) women with positive test results received adequate treatment(two or more doses of 2.4 mega units of benzathine penicillin) in the intervention cluster versus 120/175 (68.6%) in</p>	Proportion of women tested for syphilis at the first antenatal visit	OR 989.80 (95% CI 16.27 to 60233.05)	Proportion of women tested for syphilis at the third trimester visit	OR 617.88, (95% CI 13.44 to 28399.01)	Adequate treatment	AOR 10.44, (95% CI 1.00 to 108.99)	Syphilis cases detected at first trimester visit	AOR 2.45, (95% CI 1.44 to 4.18)	Syphilis cases detected at third trimester visit	AOR 6.27, (95% CI 1.47 to 26.69)	The review included evidence from two cluster-randomised trials at high or unclear risk of bias for most of the 'Risk of bias' domains. Data were not combined in meta-analysis because the trials used non-comparable measures of effectiveness. More trials are therefore warranted to determine the effectiveness of available testing strategies for improving syphilis-associated adverse outcomes in pregnant women and neonates, especially in high-risk regions.
Proportion of women tested for syphilis at the first antenatal visit	OR 989.80 (95% CI 16.27 to 60233.05)														
Proportion of women tested for syphilis at the third trimester visit	OR 617.88, (95% CI 13.44 to 28399.01)														
Adequate treatment	AOR 10.44, (95% CI 1.00 to 108.99)														
Syphilis cases detected at first trimester visit	AOR 2.45, (95% CI 1.44 to 4.18)														
Syphilis cases detected at third trimester visit	AOR 6.27, (95% CI 1.47 to 26.69)														

the control (OR0.82; 95% CI 0.57 to 1.17).					
Albright CM, Emerson JB, Werner EF, Hughes BL. Third-Trimester Prenatal Syphilis Screening: A Cost-Effectiveness Analysis. Obstetrics & Gynecology. 2015;126(3):479-85	Cost-effectiveness model	N/A	Re-screening women in the third trimester who screened negative in the first trimester vs. no rescreening	Rescreening 4,000,000 women would prevent 60 cases of congenital syphilis, at a cost of \$419,842 per case of congenital syphilis prevented 7 fetal and 4 neonatal deaths would be prevented at a cost of \$3,621,144 and \$6,052,534, respectively	Re-screening would only be cost effective at a seroconversion incidence of 0.017%, with a willingness to pay \$285,000 to prevent one case of congenital syphilis. It is unclear how applicable this economic analysis would be for a screening programme in the UK.
Balance of benefits and harms					
No studies identified					