On-site test to detect syphilis in pregnancy: a systematic review of test accuracy studies

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Running title: Accuracy of antenatal tests to detect syphilis

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Abstract

**Background** Syphilis in pregnancy can lead to fetal and neonatal death or congenital anomalies. Accurate on-site tests are an essential part of effective prevention of mother-to-child transmission of the disease.

**Objective** This systematic review assessed the accuracy of the on-site tests to detect infection with *Treponema pallidum* in pregnant women.

**Search strategy** Major databases were searched from inception to January 2016 using terms: “pregnancy”, “antenatal”, “syphilis”, “Treponema pallidum” with their variations, and the search limit for the relevant study design.

**Selection criteria** We included studies that used dual reference standard (non-treponemal and treponemal tests) to detect syphilis in pregnancy.

**Data collection and analysis** Extracted accuracy data were tabulated and pooled using hierarchical, bivariate random effects model.

**Main results** Seven studies (combined sample 17,546) reporting the accuracy of four on-site tests met the eligibility criteria. On average, Determine™ and SD BioLine Syphilis 3.0 had the highest sensitivity out of all evaluated tests 0.83 (95% CI 0.58, 0.98) and 0.86 (95% CI 0.82, 0.89), respectively with a high specificity 0.96 (95% CI 0.89, 1.00) and 0.99 (95% CI 0.94, 1.00), respectively. Qualitative Rapid Plasma Reagin card commonly used in clinical practice had a pooled sensitivity of 0.70 (95% CI 0.54, 0.88) and specificity of 0.97 (95% CI 0.96, 0.99).

**Conclusion** Immunochromatographic tests such as Determine and SD BioLine Syphilis 3.0 seem to be acceptable options in antenatal testing for syphilis, especially in resource-limited settings. Future research should seek more evidence to strengthen this claim.

**Keywords** Syphilis, Antenatal care, Test accuracy, On-site test

**Tweetable abstract** On-site test to detect syphilis - options during antenatal care
Introduction

Syphilis, a sexually transmitted infection caused by the bacterium *Treponema pallidum* (*T. pallidum*), is endemic throughout the developing world. Infection until one year is classified as early syphilis, and after one year as late syphilis. The initial manifestation of the disease can be easily overlooked and progress to the secondary stage which if undiagnosed and consequently non-treated leads to a period of latency with no visible signs of the disease. The infection is most commonly transmitted through sexual intercourse, and it can also be passed from mother to a child; in utero or during birth.

Transmission of the infection had been linked with the birth of children with reactive serology, long-term congenital abnormalities, miscarriages, and fetal and neonatal deaths. (1,2) The World Health Organization (WHO) estimated that in 2008 around 1.36 million pregnant women were expected to have an active form of syphilis. Without any screening or treatment in place these women would have experienced, overall, more than 700,000 adverse outcomes where more than half would be fetal or neonatal deaths. (3)

In order to prevent mother-to-child transmission of syphilis WHO advocates screening of all pregnant women antenatally and treating those identified with the disease and their partners. (4) The ideal Point-Of-Care (POC) test should be affordable, sensitive, specific, user-friendly, rapid and robust, equipment free, and deliverable to those who need them. Development of POC test has made syphilis testing more accessible especially in low-resource settings, as lengthy and skilled laboratory testing can be avoided. (5) Immunochromatographic tests or the on-site Rapid Plasma Reagin cards performed on-site give healthcare professionals an opportunity to administer treatment immediately and prevent the transmission of the disease. (6)
According to reviews assessing the accuracy of the immunochromatographic POC treponemal tests (7,8) they offer an alternative to laboratory-based diagnosis in resource-limited settings. However, none of the reviews focuses solely on pregnant women or compare the immunochromatographic with commonly used in clinics qualitative Rapid Plasma Reagin card which is not an ideal gold standard.(9) Our focus was to synthesise the accuracy of on-site tests used in antenatal care settings to detect syphilis using an established algorithm as a reference standard.(10)

**Methods**

We conducted the review and reported our findings in compliance with the current guidelines.(11) We searched Medline, Embase, Web of Science, Scopus, and Lilacs with no language restrictions. The original search run from inception to February 2015 was updated in January 2016 (Figure 1). The literature search strategy combined clinical terms such as ‘Pregnancy’, ‘Antenatal’, ‘Gestation’, 'Treponema pallidum' and ‘Syphilis’ with a filter for test accuracy studies.(12) The detailed search strategy is available in Appendix S1.

**Study selection**

Two independent reviewers (ER and LKN) screened references and then full text of potentially relevant articles. The study had to meet following eligibility criteria: recruit pregnant women without symptoms of syphilis (chancre, rash); use as a double reference standard comprising of non-treponemal (the Rapid Plasma Reagin test or venereal disease research laboratory (VDRL)) followed by treponemal test (treponema pallidum haemagglutination assay (TPHA), fluorescent treponemal antibody-absorbed (FTA-Abs) or the treponema pallidum particle agglutination (TPPA) test). Diagnosis of recently contracted infection with *T. pallidum* was defined as a positive result on both treponemal and non-treponemal test.(13)
We excluded studies in which the population showed symptoms of syphilis, women in labour and studies where reference standard was only a treponemal or non-treponemal test. We excluded studies with a case-control design and those where it was not possible to calculate True Positives, False Positives, False Negatives and True negatives. At each stage of the review process, the consensus was reached through a discussion. In the case of a stalemate, the opinion of a third reviewer’s was sought (KSK). We did not attempt to contact the study authors for any further information.

Data extraction and study quality assessment

All relevant data from included studies were extracted to a standardized, and pre-piloted form. Information about the country, settings, women’s characteristics, type of index test and reference standard, and type of collected blood sample were extracted and tabulated. We classified the countries where the studies were conducted by their income following the World Bank ranking.(14)

The quality of each included study was assessed by two review authors (ER, LKN) using the QUADAS-2 tool.(15) The risk of bias was evaluated for participants’ selection, use and interpretation of index test and reference standard, and participants flow and timing. First three aspects were also evaluated in the context of applicability to the review question. The review authors classified each item as “low” (sufficiently addressed), “high” (insufficiently addressed), or “unclear” (insufficient detail presented to allow judgment to be made) risk of bias. We considered a study to be of low risk of bias if; the patients were selected consecutively or randomly, the index and reference standard tests were correctly implemented, and all patients received the reference standard tests.
To construct two-by-two tables we extracted true positive, false positive, true negative, and false negative results or recalculated the numbers from available parameters (sensitivity, specificity, positive predictive value and negative predictive value). All analyses were performed using STATA version 12.1 (College Station, TX: StataCorp LP). Sensitivity, specificity, likelihood ratios for positive and negative test result and 95% confidence intervals (CIs) were computed for all individual studies. Where we had a sufficient number of studies (more than four), we pooled the accuracy parameters using hierarchical, bivariate, random effects model using the multilevel mixed logistic regression model as implemented by \textit{metandi} command.\cite{16} For meta-analysis with less than four studies, we pooled accuracy of sensitivity and specificity, and likelihood ratios separately using \textit{metaprop} and \textit{metan} commands, respectively. Between-study heterogeneity of studies was assessed graphically evaluating forest plots for sensitivity and specificity. Publication bias was not assessed due to lack of consensus over the reliability of currently available methods.\cite{17,18}

\textbf{Results}

The database searches retrieved 2,045 relevant citations; additional eight records were identified through the reference check. Out of 59 potentially relevant articles evaluated by their full text, seven publications met the eligibility criteria (Figure 1). A detailed list of excluded studies with reasons for their exclusion can be found in Table S1.

\textit{Characteristics of included studies}

Eligible studies recruited combined number of 17,546 pregnant women. The prospective studies were published between 1993 and 2015, with seroprevalence of syphilis ranging from 1 - 11\%. In three publications authors didn’t mention in the text whether women were previously treated for syphilis,\cite{19-21} one excluded this group\cite{22}, and in the remaining
studies around 7% of participants were previously diagnosed with syphilis. Included publications reported accuracy data of three immunochromatographic tests: Determine™ (Abbott Laboratories, Chicago, USA), SD BioLine Syphilis 3.0 (Standard Diagnostics Inc., Republic of Korea), VisiTect Syphilis (Omega Diagnostics, Alloa, Scotland) and the qualitative Rapid Plasma Reagin card (multiple manufacturers). The majority of studies recruited women in hospital settings, one in primary care and one in the general health centre. Three studies were conducted in upper-middle income countries, two in lower-middle income countries and two studies were in low-income countries. All studies used fresh blood samples.

Quality assessment
Six out of seven studies had an unclear risk of bias for the sample selection due to a lack of information about the selection process. The majority of studies were assessed as low risk of bias for the implementation of the reference standard and all for the index test. The bias for flow and timing was unclear in two studies due insufficient level of information. One study was classified as of high concern over applicability in sample selection as it reports physical examination findings of participants. There was no overall concern applicability of included studies in terms of index test and applied reference standard.

Accuracy of immunochromatographic tests
Two studies with a combined sample size of 9,587 women reported accuracy data of the Determine™ test. Pooled sensitivity and specificity of the Determine™ were 0.83 (95% CI 0.58, 0.98) and 0.96 (95% CI 0.89, 1.00), respectively with likelihood ratio for the positive test of 24.88 (95% CI 4.19, 147.57), and for a negative test result of 0.16 (95% CI 0.04, 0.66). Two studies reported the data on the accuracy of the SD BioLine Syphilis 3.0. Pooled sensitivity from those studies was of 0.86 (95% CI 0.82, 0.89), and sensitivity of 0.99 (95%
The likelihood ratio for the positive and negative test result was 54.87 (95% CI 6.52, 461.65) and 0.15 (95% CI 0.12, 0.20), respectively. The accuracy of the third test, VisiTect Syphilis, was reported in one study of 712 women. The sensitivity of VisiTect was 0.63 (95% CI 0.31, 0.86) and specificity 0.98 (95% CI 0.97, 0.99).

**Qualitative Rapid Plasma Reagin card**

The qualitative Rapid Plasma Reagin test was used as an index test in five studies. Pooled sensitivity was 0.70 (95% CI 0.50, 0.84) and pooled specificity 0.97 (95% CI 0.96, 0.98). The derived likelihood ratio of the positive test result was 27.07 (95% CI 15.39, 47.61) and the negative result of 0.31 (95% CI 0.17, 0.56). There was visible greater heterogeneity between sensitivity estimates than specificity with the 95% predictive region covering less than one-third of the operating space (Figure S1). The accuracy parameters of all evaluated tests have been collated and summarised in Table 3. The numbers used to calculate the parameters are available in Table S2.

**Discussion**

**Main findings**

SD BioLine Syphilis 3.0 test had, on average, the highest sensitivity out of all evaluated immunochromatographic tests, and visibly higher sensitivity than qualitative Rapid Plasma Reagin card. Specificity did not differ significantly between the identified tests.

**Strengths and limitations**

This systematic review was conducted using following current methodological standards. The use of search limit for test accuracy studies, was a pragmatic choice. The search without the limit had too-broad approach to be practicable. Even though, we identified the majority of studies with antenatal population included in the previous reviews and two
additional ones (19,22) the overall number of studies available for the analyses was small.

The bivariate analysis was possible only for the RPR card, yet its findings are weakened by a visible heterogeneity of sensitivity parameters between the individual studies.

Test accuracy studies are prone to numerous sources of bias due to patients’ selection and retention in the study, implementation of the index test and reference standard. In our review, we managed to limit spectrum bias by excluding studies with case-control design. However, the majority of included studies failed to describe recruitment method and inclusion criteria.

The risk of bias and concern over the applicability of the index tests and reference standards were generally low. Ideally, the reference standard and the index test should be entirely independent of each other.(26) This was true for the immunochromatographic test, yet the lab-based confirmatory algorithm for the qualitative Rapid Plasma Reagin card had as its non-treponemal component quantitative Rapid Plasma Reagin test. This raises concern over an incorporation bias (26), however, the extent to which use of the Rapid Plasma Reagin test as a part of gold standard could distort the results is unclear, and couldn’t be avoided due to studies’ design.

The average prevalence of double reactive sera in studies evaluating the accuracy of Determine™, SD BioLine Syphilis 3.0, VisiTect Syphilis and the qualitative Rapid Plasma Reagin card were 4.0%, 8.2%, 1.1% and 5.7%, respectively. This level of prevalence is higher than the global prevalence of the disease among antenatal care attendee and in some cases (South Africa or Senegal) even significantly higher than in the countries where the studies were conducted.(27) By definition, sensitivity and specificity do not depend on the disease prevalence. However, their parallel variability can occur due to clinical or artefactual mechanisms.(28) Clinicians before drawing any conclusion basing on the accuracy findings
should be very clear about the clinical question they want to address. The diversity of the prevalence, statistical methods used to pool the data and the quality of reporting impacts the generalisability of presented findings.

The timely delivery of treatment during prenatal period alters the risk of adverse outcomes due to syphilis infection. (29) In order to optimise the applicability of our findings to the context of antenatal care, we defined a clear research question. We focused solely on pregnant women during the perinatal period. We looked for the immunochromatographic, in detecting double positive sera to non-treponemal and treponemal components of the reference standard.

Interpretation

Two previous reviews address the issue of accuracy of the rapid, on-site testing using different methods of data synthesis.(7,8) The first review found that the immunochromatographic tests have a high sensitivity and higher specificity comparable with parameters of non-treponemal.(8) In systematic review with Bayesian approach to data synthesis the Determine test had the highest sensitivity when comparing with *T.palladium* specific reference standard. However, the authors admitted in their work that due to applied methodology the values of sensitivity were overestimated.(7) Both reviews included women tested in antenatal care settings, including women in labour, and focusing on the accuracy and value of the immunochromatographic test in rapid testing for syphilis.

Similar to the previous reviews (7, 8), the immunochromatographic tests were characterised by high sensitivity and specificity. Additionally, their average sensitivity was higher than for the qualitative Rapid Plasma Reagin on-site card (except VisiTech Syphilis) with the average specificity comparable between all the tests. The immunochromatographic tests are comparable in cost (8) and easier to operate than Rapid Plasma Reagin card (21,24) what
makes them less prone to an operator error. The average cost in low resource settings is U.S. $0.91 and U.S. $1.05 for the RPR and ICS tests. Nonetheless, their reliability depends on the background proportion of women with past-treated infection who may still test as positive, and consequently be treated unnecessarily. Furthermore, the tests can also give a positive result in various no venereal treponematoses such as yaws and pinta, these would be considered false positive results and are preferred to false negative results and there is greater benefit in over-treating all patients with positive results as opposed to the alternative.

In the high-prevalence settings (assumed 11%) around 9% of all positive tests with SD BioLine Syphilis 3.0 would be falsely positive in contrast to 21 – 28% with the other immunochromatographic tests or the Rapid Plasma Reagin card. The proportion of potentially missed cases would be 2% for SD BioLine Syphilis 3.0 and Determine™, and 4% for VisiTech and Rapid Plasma Reagin card. Syphilis in pregnancy is effectively treated with penicillin with benzathine penicillin remaining the first-line therapy for early syphilis. The treatment is administered by intramuscular injection and requires three large doses once weekly for three weeks. This requires patients to return to health care services for each dose which may prove difficult in rural settings. With no cases of antibiotic resistance reported so far (31) prevention of mother-to-child transmission of the disease is more important than overtreatment.

Conclusion

Our systematic review adds to the current body of evidence on the accuracy of the rapid and Point-of-Care test to detect infection with T.palladium in the context of the antenatal care. Future test accuracy studies should aim to improve reporting of their findings and directly compare the accuracy of available test controlling for the confounders.
When testing antenatally for syphilis immunochromatographic tests such as Determine™ and SD BioLine Syphilis 3.0 seem to be acceptable options. However, future research is needed to provide more evidence to strengthen this claim.

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Contribution to Authorship

ER selected eligible texts, data extraction form, extracted data, wrote the protocol, cleaned and analysed the data, drafted and revised the manuscript. LKN selected eligible texts, extracted data, and drafted and revised the manuscript. JZ supervised statistical analysis and revised the manuscript. KSK resolved discrepancies between reviewers and revised the manuscript.

Declaration of interest

The authors report no conflict of interest. The ICMJE disclosure forms are available as online supporting information.

Details of ethics approval

Ethical approval was not required for this project.

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Reference List


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Legends

Figure 1 Study selection diagram

Table 1 Characteristics of studies of on-site tests to detect syphilis among pregnant women

Table 2 Quality assessment of included studies using QUADAS-2 tool

Table 3 Accuracy of tests to detect syphilis among pregnant women

Supporting Information

Figure S1 Summary Point in Receiver Operating space for qualitative Rapid Plasma Reagin card

Appendix S1 Search Strategy for Medline 15th January 2015 (updated 11th January 2016)

Table S1 List of excluded full text articles with reasons for exclusion

Table S2 Test accuracy data extracted from included studies
Records identified through database searching from inception up to January 2016 (n = 2,045)

Additional records identified through other sources (n = 8)

Records after duplicates removed (n = 1,540)

Records screened (n = 1,540)

Records excluded* (n = 1,481)

Full-text articles assessed for eligibility (n = 59)

Full-text articles excluded due to:
- Reference standard (n = 18)
- Data reporting (n = 11)
- Population (n = 10)
- Publication type (n = 3)
- Study aim (test technical performance) (n = 7)
- Study design (n = 3)

Studies included in the review (n = 7)

*full text of nine papers was not available for the assessment
Table 1 Characteristics of studies of on-site tests to detect syphilis among pregnant women

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Country</th>
<th>Settings</th>
<th>Sample size</th>
<th>Reference standard</th>
<th>Type of the index test</th>
<th>Index test</th>
<th>Type of blood sample</th>
<th>Sero-prevalence* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzaken 2011</td>
<td>Brazil</td>
<td>Antenatal clinic</td>
<td>712</td>
<td>VDRL</td>
<td>Treponemal test - ICS</td>
<td>VisiTect Syphilis test</td>
<td>Whole blood</td>
<td>0.01 (0.01, 0.02)</td>
</tr>
<tr>
<td>Bronzan 2007</td>
<td>South Africa</td>
<td>Primary Care clinic</td>
<td>1,250</td>
<td>Quantitative RPR</td>
<td>Treponemal test - ICS</td>
<td>Determine™</td>
<td>Whole blood</td>
<td>0.06 (0.05, 0.08)</td>
</tr>
<tr>
<td>Delport 1993</td>
<td>South Africa</td>
<td>Antenatal clinic</td>
<td>1,237</td>
<td>Quantitative RPR</td>
<td>Non-treponemal test - RPR</td>
<td>Qualitative RPR card</td>
<td>Plasma</td>
<td>0.07 (0.05, 0.08)</td>
</tr>
<tr>
<td>Kashyap 2015</td>
<td>India</td>
<td>University Hospital</td>
<td>200</td>
<td>VDLR</td>
<td>Treponemal test - ICS</td>
<td>SD BioLine Syphilis</td>
<td>Serum</td>
<td>0.02 (0.01, 0.05)</td>
</tr>
<tr>
<td>Montoya 2006</td>
<td>Mozambique</td>
<td>Antenatal clinic</td>
<td>4,789</td>
<td>Quantitative RPR</td>
<td>Treponemal test - ICS</td>
<td>SD BioLine Syphilis</td>
<td>Whole blood</td>
<td>0.08 (0.08, 0.09)</td>
</tr>
<tr>
<td>Tinajeros 2006</td>
<td>Bolivia</td>
<td>Maternity Hospital</td>
<td>8,892</td>
<td>Qualitative RPR</td>
<td>Non-treponemal test - RPR</td>
<td>Qualitative RPR card</td>
<td>Whole blood</td>
<td>0.04 (0.03, 0.04)</td>
</tr>
<tr>
<td>Van Dyck 1993</td>
<td>Senegal</td>
<td>Health Centre</td>
<td>466</td>
<td>Quantitative RPR</td>
<td>Treponemal test - ICS</td>
<td>Determine™</td>
<td>Whole blood</td>
<td>0.11 (0.08, 0.14)</td>
</tr>
</tbody>
</table>

*reactive both non-treponemal and treponemal tests; ** on discordant samples
RPR - Rapid Plasma Reagin
ICS - Immunochromatographic strip
FTA-Abs - Fluorescent treponemal antibody absorption
TPHA - Treponema pallidum hemagglutination assay
TPPA - Treponema pallidum particle agglutination assay
VDRL - Venereal disease research laboratory
Table 2 Quality assessment of included studies using QUADAS-2 tool

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Sample selection</th>
<th>Index test</th>
<th>Reference standard</th>
<th>Flow and timing</th>
<th>Concern over applicability</th>
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<tr>
<td>Benzaken 2011</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Unclear</td>
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<tr>
<td>Bronzan 2007</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Unclear</td>
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<tr>
<td>Delport 1993</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
<td>Unclear</td>
<td>Unclear</td>
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<td>Kashyap 2015</td>
<td>Unclear</td>
<td>Low</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Montoya 2006</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
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<tr>
<td>Tinajeros 2006</td>
<td>Unclear</td>
<td>Low</td>
<td>Low</td>
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<tr>
<td>Van Dyck 1993</td>
<td>Unclear</td>
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<td>Low</td>
<td>Low</td>
<td>Unclear</td>
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<tr>
<td>Index test</td>
<td>Study ID</td>
<td>Reactive/Non-reactive</td>
<td>Sensitivity (95%CI)</td>
<td>Specificity (95%CI)</td>
<td>Likelihood ratio for a positive test result (95%CI)</td>
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<td>------------</td>
<td>----------</td>
<td>-----------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Determine</td>
<td>Tinajeros 2006</td>
<td>342/8,850</td>
<td>0.92 (0.88, 0.95)</td>
<td>0.99 (0.98, 0.99)</td>
<td>61.33 (51.49, 73.04)</td>
</tr>
<tr>
<td></td>
<td>Bronzan 2007(^)</td>
<td>44/651</td>
<td>0.70 (0.56, 0.82)</td>
<td>0.93 (0.91, 0.95)</td>
<td>9.97 (7.11, 13.98)</td>
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<tr>
<td></td>
<td>Pooled estimates</td>
<td>386/9,201</td>
<td>0.83 (0.58, 0.98)</td>
<td>0.96 (0.89, 1.00)</td>
<td>24.88 (4.19, 147.57)</td>
</tr>
<tr>
<td>SD BioLine Syphilis 3.0</td>
<td>Montoya 2006</td>
<td>381/4,105</td>
<td>0.86 (0.82, 0.89)</td>
<td>0.97 (0.96, 0.97)</td>
<td>26.41 (22.23, 31.37)</td>
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<tr>
<td></td>
<td>Kashyap 2015</td>
<td>4/196</td>
<td>0.75 (0.30, 0.95)</td>
<td>1.00 (0.98, 1.00)</td>
<td>275.80 (16.32, 4660.18)</td>
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<td></td>
<td>Pooled estimates</td>
<td>385/4,301</td>
<td>0.86 (0.82, 0.89)</td>
<td>0.99 (0.94, 1.00)</td>
<td>54.87 (6.52, 461.65)</td>
</tr>
<tr>
<td>VisiTech Syphilis</td>
<td>Benzaken 2011(^^^)</td>
<td>8/704</td>
<td>0.63 (0.31, 0.86)</td>
<td>0.98 (0.97, 0.99)</td>
<td>40.00 (18.07, 88.57)</td>
</tr>
<tr>
<td>Qualitative Rapid Plasma Reagin card</td>
<td>Bronzan 2007(^)</td>
<td>35/520</td>
<td>0.46 (0.29, 0.63)</td>
<td>0.97 (0.95, 0.98)</td>
<td>14.86 (8.13, 27.14)</td>
</tr>
<tr>
<td></td>
<td>Van Dyck 1993</td>
<td>50/402</td>
<td>0.46 (0.32, 0.61)</td>
<td>0.97 (0.94, 0.98)</td>
<td>13.21 (7.28, 23.97)</td>
</tr>
<tr>
<td></td>
<td>Montoya 2006</td>
<td>381/4,105</td>
<td>0.71 (0.67, 0.76)</td>
<td>0.96 (0.96, 0.97)</td>
<td>19.80 (16.70, 23.48)</td>
</tr>
<tr>
<td></td>
<td>Tinajeros 2006</td>
<td>342/8,847</td>
<td>0.76 (0.71, 0.80)</td>
<td>0.99 (0.99, 0.99)</td>
<td>82.98 (66.01, 104.33)</td>
</tr>
<tr>
<td></td>
<td>Delport 1993</td>
<td>83/1,154</td>
<td>0.93 (0.85, 0.97)</td>
<td>0.96 (0.95, 0.97)</td>
<td>24.90 (18.46, 33.59)</td>
</tr>
<tr>
<td></td>
<td>Pooled estimates</td>
<td>891/14,728</td>
<td>0.70 (0.50, 0.84)</td>
<td>0.97 (0.96, 0.98)</td>
<td>27.07 (15.39, 47.61)</td>
</tr>
</tbody>
</table>

\(^\) combined high & low titre (both define active syphilis)
\(^^^\) Missing VDRL samples assumed as positive