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Prevalence of Curable Sexually Transmitted Infections in Pregnant Women in Low- and Middle-Income Countries From 2010 to 2015:

A Systematic Review

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Abstract

Background—Current literature comparing the prevalence rates of curable sexually transmitted infections (STIs) in pregnant women in various global regions is limited. As a result, antenatal screening practices for curable STIs in pregnant women, specifically *Treponema pallidum* (syphilis), *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and *Trichomonas vaginalis* (TV) vary around the world, differing by country and particular STI.

Methods—We conducted a systematic review of publications on STI prevalence among pregnant women in 30 different low- and middle-income countries. We searched PubMed for studies reporting prevalence of syphilis, CT, NG, and TV in pregnant women. English language studies published between January 1, 2010, and March 1, 2015, were included. The adjusted mean STI prevalence by region was calculated via multivariable linear regression adjusting for health care setting, women's mean age, study sample size, and sensitivity of diagnostic test.

Results—We identified 75 studies that met inclusion criteria, providing 116 point prevalence estimates for curable STIs among 3,489,621 pregnant women. Adjusted mean prevalence for NG ranged from 1.2% (95% confidence interval [CI], 1.0–1.3) in Latin America to 4.6% (95% CI, 4.0–5.2) in Southern Africa; syphilis prevalence ranged from 1.1% (95% CI, 0.5–1.6) in Asia to 6.5% (95% CI, 4.7–6.3) in Southern Africa; CT ranged from 0.8% (95% CI, 0.4–1.1) in Asia to 11.2% (95% CI, 6.0–16.4) in Latin America; and TV ranged from 3.9% (95% CI, 2.2–5.6) in Latin America to 24.6% (95% CI, 17.9–31.4) in Southern Africa.

Conclusions—Although we observed a wide variation in STI burden in pregnancy after adjusting for age, test, and health care setting, further valid comparison may depend on adjustment for access to care and screening practices.

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Curable sexually transmitted infections (STIs) in pregnant women, specifically *Treponema pallidum* (syphilis), *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and Trichomonas vaginalis (TV), may lead to various adverse outcomes including premature rupture of membranes, preterm labor, preterm delivery, chorioamnionitis, low birth weight, congenital infection, and even stillbirth or neonatal mortality.[1–9] Furthermore, recent studies have suggested the possibility of increased mother-to-child transmission of human immunodeficiency virus (HIV) among mothers with bacterial STIs.[3,10,11]

Antenatal screening practices for curable STIs vary around the world, differing by country and particular STI. The World Health Organization (WHO) has implemented guidelines for testing and treatment of syphilis in pregnancy. Early successes of the congenital syphilis elimination program have been demonstrated by the elimination of mother-to-child transmission of syphilis in Cuba.[12–14] However, no WHO recommendations exist for the screening of CT and NG in pregnancy. Although the screening of asymptomatic pregnant women at increased risk for CT and NG is currently standard of care in the United States,[15] WHO recommends a syndromic approach with presumptive treatment for symptomatic women.[10] Because most CT and NG infections are asymptomatic, syndromic management misses the majority of the CT and NG infections in pregnancy.

Current literature comparing the prevalence rates of curable STIs in various global regions is limited. A recent review article by Chico et al.[16] focused on sub-Saharan Africa, but an update of this region and other global regions has not been performed. Our systematic review summarizes the adjusted mean prevalence of curable STIs among pregnant women in low- and middle-income countries, stratified by geographic region, and adjusting for potential confounders. The Chico review covered sub-Saharan Africa, which is predominately low income.

METHODS

We used the PRISMA guidelines to conduct a systematic review to assess the prevalence of CT, NG, TV and syphilis in pregnancy from studies published between January 1, 2010, and March 1, 2015. The cited data were collected earlier in many studies, ranging from 1999 to 2014.[17] PubMed was searched to identify studies based on the following inclusion criteria: (1) English language; (2) cross-sectional/prevalence, cohort, or case-control study design; (3) conducted in a low- or middle-income country; and (4) reported on prevalence statistics for pregnant women. Exclusion criteria included (1) non-English language, (2) review article, (3) study conducted outside of a low- or middle-income country, (4) sample from women previously tested for STIs during current pregnancy, (5) data collected after postpartum women were discharged from the hospital, (6) data obtained via surveys or self-report, and (7) data obtained from high-risk pregnant women (eg, pregnant sex workers), and/or cohort of women presenting with a chief complaint of vaginal discharge (Fig. 1). H.S. reviewed the PubMed search results, and D.J.D. cross-checked results, validated the data, and resolved discrepancies. We excluded studies on sex workers, women with ectopic pregnancy and symptomatic women; however, we did include HIV-infected pregnant women in the analysis. We did not have exclusion criteria based on testing or screening protocols, other than excluding studies if the testing was syndromic or if the results were self-reported.

There were no requirements for sample size for the selected articles, though the sample size was adjusted for in the analysis.

Definitions of low- and middle-income countries were obtained from the World Bank (http://data.worldbank.org/incomelevel/LMY). When a study reported more than 1 STI prevalence, we recorded each infection and each sample size separately. Data abstraction was not blinded to authors or publication, but was performed independently. See Supplemental file for a complete list of publications included in the analysis.

We stratified our prevalence estimates by region and adjusted for health care setting (eg, hospital-, clinic-, or community-based study), age of pregnant women in the study, and diagnostic tests used. Prevalence values in the included articles were calculated as the number of pregnant women who were diagnosed with an STI over the total number of pregnant women tested.

For syphilis, tests included venereal disease research laboratory, rapid plasma reagin, *Treponema pallidum* hemagglutination, Toluidine Red Unheated Serum Test, *Treponema pallidum* particle agglutination assay, enzyme immunoassay, fluorescent treponemal antibody absorption, and rapid diagnostic test. However, 23 of 54 (43%) studies on syphilis only reported venereal disease research laboratory, rapid plasma reagin, or *Treponema pallidum* hemagglutination but no second test. For CT and NG, tests included nucleic acid amplification testing (NAAT), enzyme immunoassay, IgG antibody screen, culture, Aptima combo 2 and microscopy. For TV, tests included polymerase chain reaction, culture, and microscopy. Data for diagnostic test used was extracted from the studied articles. Due to the variance in performance of different diagnostic tests, estimated sensitivities and specificities were collected from the current literature for each reported diagnostic test used.[18–22]

All studies that satisfied the previously mentioned inclusion criteria were analyzed and those with missing data points for any factors are denoted in the final analysis. Site of data collection was stratified in a stepdown method to 3 subgroups: at a hospital, at an antenatal or community clinic, or as part of a study or community screening program. Studies reporting more than 1 type of location for data collection or crossover within a location, that is, an antenatal clinic within a hospital, were considered to have occurred at the higher-level care center. Studies directly reporting mean or median ages for the women were used for portion of the analysis whereas studies that either stratified age as a categorical variable without reporting mean age or did not report age as a factor were noted as missing in the final analysis.

Statistical Analyses

We stratified results by subregion (East Africa, West Africa, Southern Africa, Latin America, and Asia). Asia included South Asia, and the Middle East and Pacific Regions, and Latin American included both Central and South America, due to the small number of studies from these regions. We calculated the total number of positive pregnant women per STI per region, the median number with positive diagnoses, the study sample size, the mean age, and the mean sensitivity and specificity for each diagnostic test used (if not counted, then was reported as missing). We developed multivariable linear regression models to

estimate adjusted mean prevalence by STI and region, and 95% confidence intervals (CI) for all strata. We adjusted for health care setting (eg, hospital-, clinic-, or community-based study), women's mean age, study sample size, and STI test sensitivity. The specificity was not included in the final model due to collinearity with sensitivity. We used STATA 13.1 (College Station, TX) for all analyses.[23]

RESULTS

We identified a total of 376 potentially relevant reports from January 2010 to March 2015. Only 75 studies from 30 low- and middle-income countries met inclusion criteria, providing 116 point prevalence estimates for curable STIs in pregnant women, including a total of 3,489,621 women (Fig. 1). The diagnostic test used was reported in 94.7% of included articles. The greatest number of published studies were from Latin America (n = 23 studies, n = 206,848 pregnant women), followed by East Africa (n = 20 studies, n = 23,413 pregnant women), Asia (n = 18 studies, n = 3,109,314 pregnant women), Southern Africa (n = 15 studies, n = 128,467 pregnant women), and West Africa (n = 6 studies, n = 10,790 pregnant women). The total number of studies is greater than the 75 studies included because some studies had more than 1 country in the analysis. The number of women and numbers of tests per woman varied considerably from a sample size of 12 (in Brazil) to a sample size of over 2 million (in China).

Overall, the region with the highest adjusted mean prevalence of curable STIs among pregnant women was Southern Africa. Our analyses included studies in the following countries: South Africa, Malawi, Madagascar, Zambia, Mozambique, and Zimbabwe. In Southern Africa, TV was the most prevalent STI overall, with a adjusted mean prevalence of 24.6% (95% CI, 17.9–31.4) in 3 studies. Next was syphilis with a prevalence of 6.5% (95% CI, 4.70–8.3) in 8 studies. *Neisseria gonorrhoeae* and CT were similarly high at 4.6% (95% CI, 4.0–5.2) in 3 studies, and 4.4% (95% CI, 2.3–6.6) in 3 studies, respectively (Fig. 2).

In East Africa, we included studies from the following countries: Kenya, Tanzania, Somalia, Ethiopia, Uganda, and Sudan. Eight studies demonstrated a adjusted mean prevalence of syphilis of 4.6% (95% CI, 3.7–5.4), the second highest prevalence after Southern Africa. The adjusted mean prevalence was similarly high for TV in 3 studies at 6.8% (95% CI, 4.6–9.0). The adjusted mean prevalence of CT in 3 studies was 4.2% (95% CI, 2.8–5.6), followed by NG with a prevalence of 2.3% (95% CI, 2.0–2.5) in 3 studies (Fig. 2).

In West Africa, we included studies from Benin, Democratic Republic of Congo, Nigeria, and Burkina Faso. In these countries, the adjusted mean prevalence of CT was 7.2% (95% CI, 0.0–14.6) in 1 study. The adjusted mean prevalence of syphilis was 4.0% (95% CI, 1.7–6.3) in 4 studies (Fig. 2).

For Latin America, we included studies from Peru, Brazil, Ecuador, Argentina, and Guatemala. The adjusted mean prevalence of TV among pregnant women was 3.9% (95% CI, 1.1–5.6) in the 3 studies included. The adjusted mean prevalence of CT in Latin America was 11.2% (95% CI, 7.3–17.1) in 7 studies, which is higher than the mean prevalence in Southern and East Africa. Syphilis had a mean prevalence of 2.6% (95% CI, 1.2–3.9) in 15

studies. The mean prevalence of NG was very low at 0.3% (95% CI, 0.1–2.1) in 3 studies (Fig. 2).

In Asia, we included studies from China, India, Bangladesh, Papua New Guinea, Turkey, Pakistan, Iran, Myanmar, and Cambodia. The mean prevalence of STIs among pregnant women was lower here than the other regions. *Trichomonas vaginalis* was most prevalent with a mean prevalence of 13.6% (95% CI, 6.8–20.4) in 1 study, followed by NG at 2.8% (95% CI, 2.4–3.3) in 1 study, and CT at 0.8% (95% CI, 0.4–1.1) in 6 studies. The mean prevalence of syphilis was also lowest in Asia at 1.1% (95% CI, 0.5–1.6) in 13 studies controlling for potential confounders (see Table 1).

DISCUSSION

Our study found that the prevalence of curable STIs among pregnant women was substantial throughout low- and middle-income countries. Importantly, our review found a lack of recent data on STI prevalence among pregnant women in many parts of the world. We also note that the variation in diagnostic tests used and populations tested makes it difficult to compare the prevalence between the different regions. Inconsistencies between research and practice may play a role in why the WHO has not implemented clear screening guidelines and policies for STI screening, other than for syphilis and HIV, in pregnancy.[13,14] In most high-income countries, NAATs are the diagnostic standard of care for NG and CT due to their wide availability and high sensitivity and specificity.[15,16,18–23] Yet, many other nations have no tests available or rely on tests with lower sensitivities and specificities. Cultures for NG and CT have estimated sensitivities of 41% and 21%, respectively, and are dependent on strong laboratory infrastructure.[18,19]

Other systematic reviews of STI prevalence in pregnant women have found similarly high rates of STIs. A review article by Chico et al.[16] in 2012 found that the prevalence of syphilis was 3.5%, CT was 6.1% and TV was 17.8% among pregnant women in West and Central Africa. Those rates are similar to the mean prevalences we report, which include 41 additional studies from sub-Saharan Africa and expand the review to include a large proportion of low- and middle-income countries.

Despite persistent high level of STIs among pregnant women, there is still a limited focus on CT, NG, and TV. All of those are curable STIs that are risk factors for adverse birth and neonatal outcomes. Despite the well-known negative outcomes of these curable STIs, our systematic review revealed a serious lack of necessary prevalence data, which impedes an accurate assessment of the STIs among pregnant women in multiple regions worldwide, thereby preventing the timely diagnosis and treatment of pregnant women (and their partners and infants) to prevent known complications.

Our findings are particularly relevant for CT and NG, which are largely asymptomatic infections. However, TV and syphilis, which may present with the symptoms of genital discharge and ulceration, also go underdiagnosed.[8] In the past, it was difficult to determine whether women had CT or NG because the performance of the available tests was poor. Now, with the advent of point-of-care NAATs, the specificity and sensitivity of CT and NG

tests are much higher and may be cost-effective to use in resource-limited countries.[24] As a testament to the success that can be had with STI screening, point-of-care rapid syphilis tests are now being integrated into antenatal care around the world, and some countries have even started to use a dual syphilis-HIV test, which has shown excellent performance.[25] Our study found that most of the syphilis testing was done with point-of-care tests, whereas none of the other STI tests were point of care.

LIMITATIONS

Our study was subject to some limitations. We only used PubMed for the search and may have missed other publications as a result. Although PubMed (Medline) and EMBASE are similar, their coverage of the published literature differs. For example, EMBASE is used more frequently in Europe, and PubMed in the United States. As a result of limiting our search to PubMed, we may have excluded European or abstract citations. Further, the quality of the studies included in this analysis varied considerably, including different sampling strategies, diagnostic tests used, testing strategies, and HIV coinfection rates. We attempted to control for that heterogeneity by adjusting for women's mean age, sensitivity of diagnostic test used (when reported), and number of women included in the sample size. Our estimates though may be underestimations because we excluded studies on sex workers (n = 2) and symptomatic women. Additionally, in countries with limited access to STI care, the prevalence studies often used convenience sampling, which may underestimate the true burden in pregnancy. Also, diagnostic tests with poor sensitivity will tend to underdiagnose true-positive cases and underreport STI prevalence as a result. Conversely, studies not performing treponemal specific testing may overreport syphilis prevalence. The limited number of studies on NG and TV might limit generalizability or precision of the estimates. Where possible, we included more than 2 studies; however, there were instances where more than 1 recent study was not available (eg, CT in West Africa, NG and TV in Asia). We excluded studies that only reported estimates of STI prevalence, but did not present data as to where those estimates came from (eg, surveys, subjective or self-reported estimates), which could have caused underrepresentation of studies from West and Central Africa or Asia. Finally, due to the significant heterogeneity in socioeconomic status within each region, regional prevalence studies may not be representative of population-level burden of STIs among pregnant women.

CONCLUSIONS

Our study highlights the urgent need to collect reliable measures of STI prevalence in low- and middle-income countries, where the burden among pregnant women is greatest. We advocate for strengthening prevalence monitoring as a method of STI surveillance in pregnant women worldwide.[26] The sequelae of untreated STIs are well known.[1–9] However, the syndromic approach continues to direct STI management among pregnant women in low- and middle-income countries, which substantially underdetects STI prevalence in pregnant women.[12,15] Additional focus is needed to expand the clinical evidence for policy makers on the cost-effectiveness of integrating CT, NG, and TV screening and diagnostics into existing antenatal care programs already focusing on syphilis and HIV. In conclusion, the prevalence of curable STIs is substantial among pregnant women in low- and middle-

income countries in all regions, suggesting a large population-level burden of untreated curable infections. Our study revealed a lack of necessary prevalence data among pregnant women in low- and middle-income countries, where the disease burden is greatest. The lack of reliable prevalence data not only impedes an accurate assessment of STIs among pregnant women in multiple regions worldwide, but also prevents the treatment of pregnant women to prevent adverse pregnancy and neonatal health outcomes. Data from systematic and comprehensive screening programs in pregnancy are needed to support the design and implementation of effective prevention and control strategies in low- and middle-income countries.

Appendix 1 Search terms used

(“sexually transmitted infections”[text word] OR “sexually transmitted diseases”[text word] OR “genital tract infections” [text word] OR “reproductive tract infections”[text word] OR “syphilis”[text word] OR “treponema pallidum”[text word] OR “gonorrhea”[text word] OR “Neisseria gonorrhoeae”[text word] OR “chlamydia”[text word] OR “chlamydia trachomatis”[text word] OR “trichomonas”[text word] OR “trichomonas vaginalis” [text word] OR “sexually transmitted diseases, bacterial”[Mesh] OR “reproductive tract infections”[Mesh]OR“trichomonas”[Mesh] OR “treponema pallidum”[Mesh] OR “chlamydia” [Mesh] OR “Neisseria gonorrhoeae”[Mesh])

AND

(“pregnancy” [text word] OR “pregnant women” [text word] OR “antenatal” [text word] OR “pregnant women” [Mesh] OR “pregnancy” [Mesh] OR “prenatal care” [Mesh] OR “perinatal care” [Mesh])

AND

(“developing country”[text word] OR “developing countries” [text word] OR “Africa”[text word] OR “Mexico”[text word] OR “Caribbean”[text word] OR “central America”[text word] OR “Latin America”[text word] OR “south America”[text word] OR “Americas”[text word] OR “Asia”[text word] OR “China” [text word] OR “Oceania”[text word] OR “Eastern Europe”[text word] OR “developing countries”[Mesh] OR “Africa”[Mesh] OR “Mexico” [Mesh] OR “Caribbean region”[Mesh] OR “central America”[Mesh] OR “Latin America” [Mesh] OR “south America” [Mesh] OR “Asia”[Mesh] OR “Transcaucasia”[Mesh] OR “Indian ocean islands”[Mesh] OR “Pacific Islands”[Mesh] OR “Europe, eastern”[Mesh])

AND

(“prevalence” [Mesh] OR “morbidity” [Mesh] OR “epidemiology” [Subheading] OR “statistics and numerical data” [Subheading] OR prevalence [text word] OR morbidity [text word] OR epidemiology [text word] OR statistic*[text word])NOT (“animals” [Mesh] NOT “humans” [Mesh])

Appendix 2 Publications included in analysis

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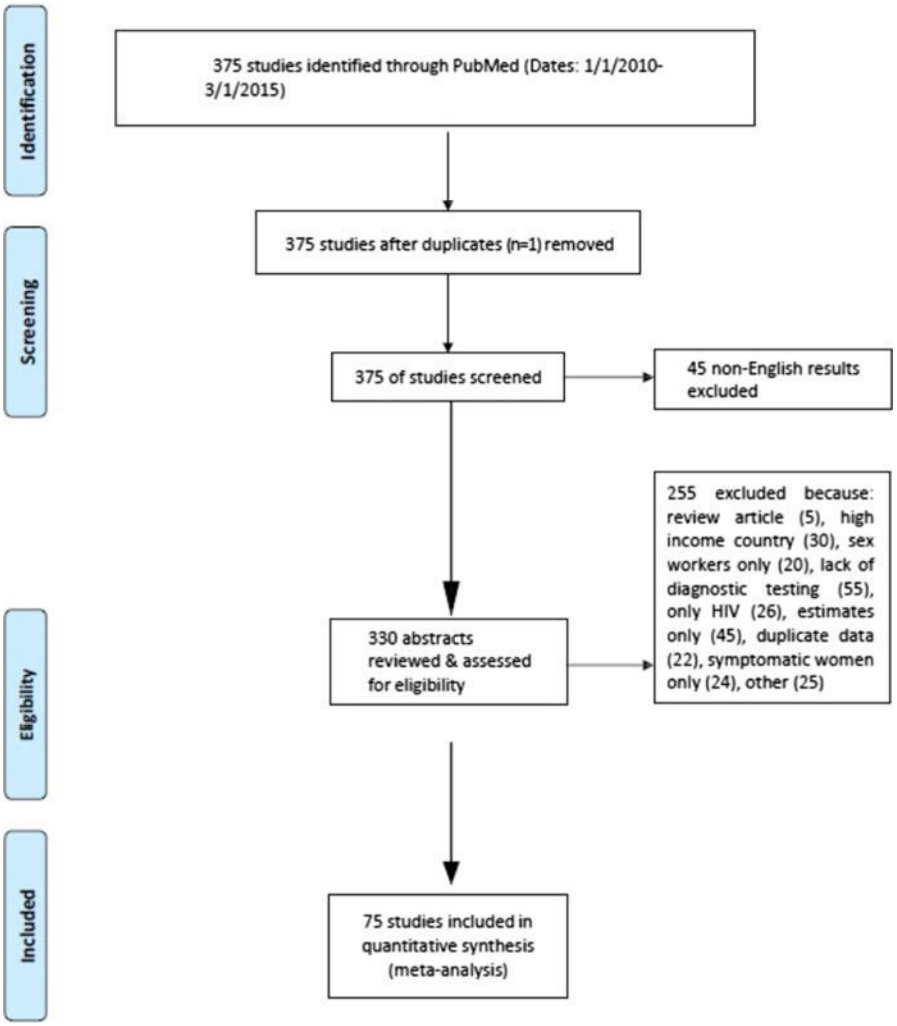

Figure 1.
PRISMA flow diagram of publications searched.

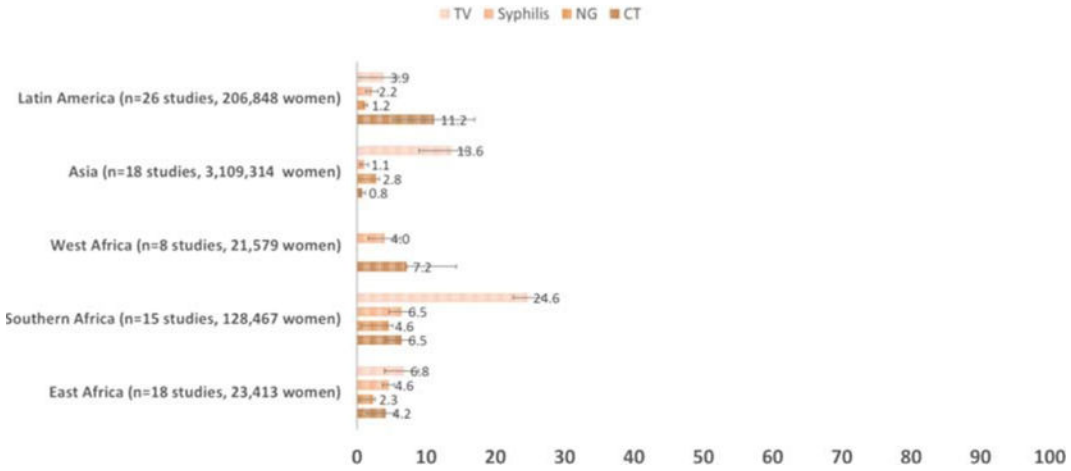

Figure 2.

Adjusted mean STI prevalence by region (N=75 studies of STI prevalence among 3,489,621 pregnant women 2010–2015).

TABLE 1

Adjusted Mean STI Prevalence Among Pregnant Women Adjusting for Potential Confounders, 2010–2015 (Stratified by Region)

STI by Sub-Region	Adjusted Mean Prevalence, % (95% CI)*	No. Positive (Total in Studies)	Tested (N)	Median No. With Positive Diagnosis	Study Sample Size, Range	No. Studies	Women's Mean age (95% CI)
Eastern Africa†							25.9 (23.0–28.7)
Syphilis	4.6 (3.7–5.4)	705	18,043	9	165–5,802	8	
N. gonorrhoeae	2.3 (2.0–2.5)	18	826	7	185–441	3	
C. trachomatis	4.2 (2.8–5.6)	161	856	19	185–441	3	
T. vaginalis	6.8 (4.6–9.0)	416	3,688	21	185–441	3	
West Africa‡							26.6 (23.9–29.3)
Syphilis	4.0 (1.7–6.3)	787	21,481	23	283–17,669	4	
C. trachomatis	7.15 (0.00–14.57)	16	98	16	98	1	
Southern Africa§							24.9 (21.7–28.0)
Syphilis	6.5 (4.7–8.3)	37134	119,962	125	149–95,663	8	
N. gonorrhoeae	4.6 (4.0–5.2)	128	1,804	27	145–1459	3	
C. trachomatis	4.4 (2.3–6.6)	306	1,840	28	151–1459	3	
T. vaginalis	24.6 (17.9–31.4)	606	4,861	38	200–1459	3	
Latin America (Central and South America)¶							25.3 (21.4–29.2)
Syphilis	2.2 (1.2–3.3)	934	196,689	17	12–162,669	15	
N. gonorrhoeae	1.2 (1.0–1.3)	21	3366	1	63–2017	3	
C. trachomatis	11.2 (6.0–16.4)	437	4592	33	63–2071	7	
T. vaginalis	3.9 (2.2–5.6)	61	2201	24	289–1315	3	
Asia ‖							26.6 (22.0–31.2)
Syphilis	1.1 (0.5–1.6)	11,057	3,107,741	35	113–2,077,362	13	
N. gonorrhoeae	2.8 (2.4–3.3)	4	113	4	113	1	
C. trachomatis	0.8 (0.4–1.1)	100	1,375	8	85–784	6	
T. vaginalis	13.6 (6.8–20.4)	6	85	6	85	1	

Note: study references are listed in the Appendix.

*Syphilis and CT models adjusted for health care setting (hospital, clinic or community-based study), women's mean age, study sample size, and sensitivity of diagnostic test; TV, model adjusted for study sample size and health care setting; NG, model adjusted for study sample size.

† Study references: 4, 6, 10, 18, 27, 29, 30, 32, 34, 39, 49, 55, 57, 59, 64, 65, 66, 68, 70, 72.

‡ Study references: 8, 9, 18, 23, 52, 53.

§ Study references: 7, 17, 18, 20, 28, 31, 38, 41, 48, 56, 57, 63, 67, 70, 71.

¶ Study references: 2, 11, 14, 21, 22, 24, 25, 28, 35, 36, 37, 40, 45, 46, 54, 55, 58, 61, 62, 64, 69, 74, 75.

‖ Study references: 1, 3, 5, 12, 13, 15, 16, 19, 26, 33, 42, 43, 44, 47, 50, 51, 60, 73.