High-Throughput Profiling of the IgG and IgA Response to the *Treponema pallidum* subsp. *pallidum* Proteome in Syphilis Patients

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Background
Syphilis is a chronic sexually transmitted infection that can result in severe clinical outcomes without adequate treatment. Furthermore, vertical transmission of its etiological agent, the spirochete Treponema pallidum subsp. pallidum (T. pallidum), is significantly associated with stillbirth and neonatal death. Syphilis serodiagnosis requires the combined use of lipoidal tests for screening and treponemal tests to confirm the screening result. Unlike lipoidal assays, treponemal tests cannot monitor response to treatment. Neither type of test can stage syphilis.

Description
To identify antigens and reactivity patterns that could facilitate early syphilis diagnosis, and possibly serve as markers for disease staging and monitoring response to treatment, we developed an array carrying 98.8% of the annotated proteomes of two T. pallidum strains (Nichols and SS14). We probed the array with 217 sera collected pre- and post-treatment from 120 syphilis patients for detection of IgG and IgA antibodies.

Findings
Although a very limited IgA response was detected in these sera, significantly higher IgG reactivity allowed us to define the most recognized antigens during natural infection and identify a subset of targets differentially recognized by baseline (pre-treatment) sera when factoring in covariates such as syphilis stage, syphilis history, and HIV status. Differential reactivity to a subset of antigens was also detected in sera collected pre-and post-treatment.

Conclusion
These antigens could be further evaluated to improve the performance of treponemal serological tests. Additionally, antigens inducing a detectable IgA response during infection in adults, albeit few, could be evaluated as diagnostic markers for congenital syphilis in future studies using serum samples from newborns.

Topic category: Program & Implementation Sciences

Title: Barriers and Facilitators to HIV Pre-Exposure Prophylaxis Implementation for Key Populations in India

Authors: Katherine Lewis, Suchith Kumar, Jayee Chowdhury, Sukanta Paul, Asim Sen, Akram Pasha, Bhagyma Lakshmi, Pranathi Prakash, Syed Hafeez Ur Rahman, KT Venukumar, Sara Piao, Katarina Scala, Natasha Glendening, Dr. Dallas Swendeman, Dr. Protim Ray, Dr. Sushena Reza-Paul, Dr. Anne Fehrenbacher

Abstract:

Background: India has the second largest HIV epidemic in the world, but HIV Pre-Exposure Prophylaxis (PrEP) has not been implemented into national HIV Targeted Intervention programs. This study aims to identify barriers and facilitators to PrEP implementation and PrEP use in India to inform advocacy and risk reduction programs.

Description: This research was guided by the EPIS Framework for Implementation Science (Exploration, Preparation, Implementation, Sustainment). Individual in-depth interviews were conducted through Durbar Mahila Samanwaya Committee in Kolkata and Ashodaya Samithi in Mysore to explore factors influencing PrEP implementation, including how strategies should be tailored for key populations. Interviews were conducted with 23 external stakeholders and 20 stakeholders internal to Targeted Intervention programs. External stakeholders represented individuals from Indian national, state, and regional agencies; medical practitioners; and individuals from Indian and global non-governmental organizations, universities, and pharmaceutical companies. Interview transcripts were analyzed using deductive thematic coding in Dedoose.

Findings: Institutional Barriers: Participants described a need for operational guidelines on PrEP for Targeted Intervention programs, funding for PrEP efforts, and the need to overcome supply chain challenges. Institutional Facilitators: Stakeholders described community groups for peer educators, raising community awareness, PrEP-related advocacy efforts, and the existing Targeted Intervention programs through which PrEP could be distributed.

Community Barriers: Barriers to PrEP use included stigma towards sex workers and other key populations, some key populations being highly mobile, and concerns about PrEP adherence and potential condom use impacts. Community Facilitators: Participants described the role of existing community-based organizations, peer educators, and community education efforts as facilitators for PrEP use among key populations.

Conclusion: We identified community and institutional level barriers to PrEP implementation in India. We also identified facilitators of PrEP implementation and use which can be leveraged to address existing barriers. Our findings highlight future targets to improve PrEP implementation and advocacy efforts.

Title: "Virtual Avatars for Enhancing HIV Prevention Access and Education among MSM of Color: Service Provider Perceptions"

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Background

HIV pre-exposure prophylaxis (PrEP) uptake is lower among men who have sex with men (MSM) of color compared to their white counterparts in the United States. Common barriers to PrEP access include stigma, limited awareness, and lack of trust or familiarity with healthcare contexts. User-controlled avatars may help overcome these barriers by increasing feelings of privacy and safety, potentially facilitating engagement with HIV prevention services.

Methods

We developed a web-based interactive PrEP experience (e.g., museum-style exhibit featuring PrEP infotainment, sex-positive messaging, and HIV stigma art), to educate MSM of color about PrEP, explored via avatars. This was demonstrated over three iterations to staff from three HIV service providers in Los Angeles County (Feb–Mar 2024). After the demonstrations, we conducted three focus groups (N = 32 participants) and a Stakeholder Advisory Board meeting (N = 13 participants). After obtaining verbal consent, all communications were audio-recorded, transcribed via Sonix transcription services, and analyzed using inductive coding to assess feasibility and identify software preferences.

Results

The 45 participants (58% male, 49% Hispanic/Latinx, 62% gay, 56% aged 25-34) reported they felt the Avatar platform was feasible for helping users learn about HIV prevention and offering personalized services, such as role-playing to practice skills (e.g., sharing and discussing personal information). Providers suggested improvements, including enhanced security features (e.g., clearing history and enabling "trigger" words for emergency situations) and emphasized the need for human interaction in certain contexts, such as receiving diagnoses or finding peer support. Logistical barriers to PrEP adoption (e.g., finances, travel) remained a persistent challenge.

Conclusions

Service providers working with MSM of color find avatars a promising tool to engage patients remotely seeking information about HIV prevention services. This approach could improve engagement and access to PrEP, though further improvements are needed in areas such as security and human interaction.

Table 1: Demographics & Perceptions of Avatar Models of Care among Avatar Pilot Study Participants *(N = 45)*

	N (%) or Median
Age *(years)*	
18-24	6 (13%)
25-34	25 (56%)
35-44	12 (27%)
45 or Older	2 (4%)
Gender Identity	
Man	21 (47%)
Non-Binary	11 (24%)
Trans Woman	7 (16%)
Woman	6 (13%)
Racial Identity	
Black	15 (33%)
White	13 (29%)
Prefer Not to Say	8 (18%)
Multiracial/Other	6 (13%)
American Indian/Alaskan Native	3 (7%)
Ethnic Identity	
Hispanic/Latinx-Identified	22 (49%)
Sexual Orientation	
Gay	28 (62%)
Heterosexual	9 (20%)
Bisexual	6 (13%)
Queer	2 (4%)
Avatar Models of Care	
Appropriate	**4** out of 5
YMC would be Comfortable	**4** out of 5
Engage New YMC	**4** out of 5
Intuitive	**4** out of 5
Improve HIV Knowledge	**4** out of 5
Recommend to YMC Clients	**5** out of 5
Exciting Potential for HIV Services	**5** out of 5

Multiplex PCR for Genital Ulcer Disease Etiology in East London, South Africa

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Word Count: 300/300

Background

Genital ulcer disease (GUD) remains a significant public health challenge in sub-Saharan Africa, contributing to an increased risk of HIV acquisition. Understanding the microbial etiology of GUD may help facilitate treatment, control, and prevention of sexually transmitted infections.

Methods

As part of an ongoing genomic study of syphilis in sub-Saharan Africa, we enrolled patients with syphilitic skin lesions at primary healthcare facilities in East London, South Africa. Lesion swabs were collected and analyzed using an in-house multiplex PCR assay to detect *Haemophilus ducreyi* (HD), *Treponema pallidum* (TP), and herpes simplex virus types 1 (HSV-1) and 2 (HSV-2). Positive detection was defined as a cycle threshold value below 40. Chi-squared analysis was performed to assess differences in pathogen distribution by sex and HIV status.

Results

Between October 2023 and November 2024, 73 participants presenting with genital ulcers were recruited. Of these, 39 (53.4%) were female, and 25 (34.2%) were living with HIV. Pathogens were detected in 35/39 (89.7%) ulcers in females. Of these, 13 (37.1%) tested positive for TP alone, 13 (37.1%) tested positive for HSV-2 alone, and 9 (25.7%) were co-infected with TP and HSV-2. Pathogens were detected in 31/34 (91.2%) ulcers in males. Of these, 11 (35.5%) tested positive for TP alone, 9 (29.0%) tested positive for HSV-2 alone, 10 (32.3%) were co-infected with TP and HSV-2, and 1 (3.2%) was co-infected with TP and HSV-1. All ulcers were negative for HD. Chi-squared analysis revealed no significant differences in the pathogen distribution (TP alone, HSV-2 alone, and TP/HSV-2 coinfection) by sex ($p=0.75$) or HIV status ($p=0.21$).

Conclusion

Our findings highlight the substantial burden of TP and HSV-2 in GUD cases in this population, with frequent co-infections, regardless of sex or HIV status. These results underscore the importance of molecular diagnostics to guide effective STI management and prevention strategies.

Missed syphilis diagnosis by rapid treponemal antibody testing of individuals with Treponema pallidum PCR-positive genital ulcers and condylomata lata, East London, South Africa

Word Count: 294/300

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Background
Rapid point-of-care treponemal antibody tests are increasingly used to screen patients for syphilis. Laboratory-based treponemal antibody tests may also be used for screening or confirmation of syphilis. Performance of these tests in diagnosing patients with syphilitic lesions is unknown.

Methods
We recruited adults with syphilitic skin lesions in an ongoing study at five primary healthcare facilities in East London, South Africa. The Abbott Detemine™ Syphilis *Treponema pallidum* (TP) rapid test was performed on finger prick capillary blood specimens. We compared the performance of the rapid versus in-house laboratory-based test among patients with TP PCR positive lesions. We report the sensitivity and specificity of the rapid TP test with 95% confidence intervals (CI).

Results
From October 2023 to November 2024, we recruited 100 participants. Of these, 73 presented with genital ulcers and 27 with *condylomata lata*. The median age was 26 years; 38% were living with HIV. For those with TP PCR+ genital ulcers, the rapid test versus the laboratory test was 61% (23/38; 95% CI 43.4-76.0%) vs 97% (37/38; 95% CI 86.19%-99.93%) sensitive and 94% (33/35; 95% CI 80.8-99.3%) vs 77% (27/35; 95% CI 59.86%-89.58%) specific. While in those with TP PCR+ condylomata *lata*, the rapid test was 79% (15/19; 95% CI 54.4-94.0%) vs 95% (18/19; 95% CI 73.97%-99.87%) sensitive and 100% (8/8; 95% CI 63.1-100%) vs. 63% (5/8; 95% CI 24.49%-91.48%) specific.

Conclusion
The rapid treponemal test showed lower sensitivity, particularly for genital ulcers, compared to lab-based testing. The Abbott Determine rapid test may be falsely negative in those with syphilitic lesions while laboratory-based testing may be positive in patients with negative TP PCR. Clinical interpretation of syphilis test results is needed.

Differences in Levels of Cytokines by Syphilis History, HIV Status, Stage and Treatment

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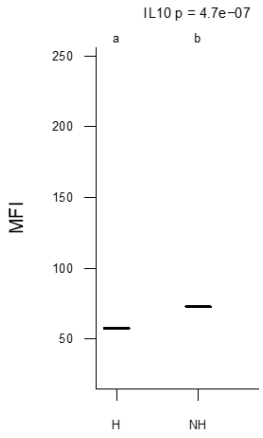
Background: Recently, cytokine expression analysis has become of interest as an approach to facilitate syphilis diagnosis. Infection with *Treponema pallidum* is treatable but can be difficult to diagnose due to the limitations of lipoidal tests, especially in cases of repeated infections. We sought to compare cytokine levels in patients at baseline and post-treatment taking covariates such as syphilis history, HIV status, and stage into account.

Methods: We characterized the longitudinal patterns of 45 cytokines in samples from a cohort of individuals from Peru diagnosed with syphilis based on serologic and clinical criteria. The analysis included 192 individuals tested quarterly up to 12 months post-treatment. Cytokines were measured in duplicate using a Luminex Flex3D-H2 instrument (Thermo Fisher, Waltham, MA) at the Immunology Laboratory at Stanford University, and the average median fluorescence intensity (MFI) values from each sample were used for analysis. We estimated the changes in cytokine levels 1) at baseline by syphilis history (anova), 2) at baseline by HIV stage (t-test), 3) at baseline by syphilis stage (anova), and 4) between baseline and 1-month post-treatment (linear mixed models with Bonferroni corrected p-values).

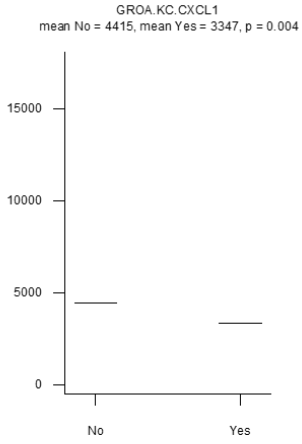
Results: We were able to identify statistically significant differences in cytokines by history (5 cytokines including IL10, IL18, Leptin, RANTES.CCL5, and TNFA), HIV (6 cytokines including RANTES.CCL5, TGFA, TRAIL.TNFSF10, Leptin, IL22, IL10, and GROA.KC.CXCL1), and stage (3 cytokines including IL18, RANTES.CCL5, and EOTAXIN.CCL11). We were also able to identify differences from pre to 1-month post treatment in cytokines: EGF, GROA.KC.CXCL1, IL3, IL7, IL10, IL18, IP.10.CXCL10, MIP1B.CCL4, TNF-α, and VEGF.

Conclusion: Cytokines have significantly different values comparing pre-post treatment, syphilis stage, syphilis history, and HIV status. These characteristics may be able to lead to improvements in syphilis diagnosis, including exploration of machine learning models.

Figure 1: Selected cytokine MFI values comparing a) Syphilis history for IL-10, b) HIV status for GROA.KC.CXCL1, c) Syphilis stage for EOTAXIN.CCL11, and d) Stage by study visit for EGF

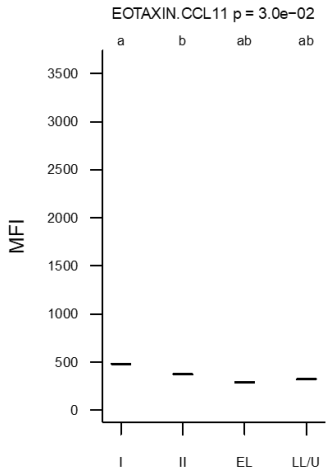
a) 

Average MFI values for cytokine IL10 with syphilis history (H) and no history (NH).

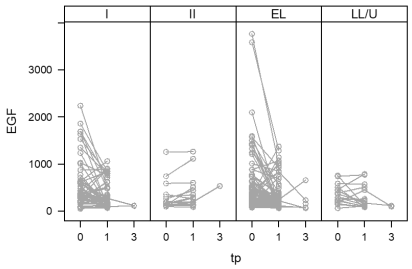
b) 

Cytokine GROA.KC.CXCL1 mean MFI values in samples without HIV (“no” x-axis) and with HIV (“yes” x-axis).

c)



Cytokine EOTAXIN.CCL11 mean MFI values in samples with primary (I), secondary (II), early latent (EL), and late latent (LL) syphilis.



	Est.	p-value	
(Intercept)	493	NA	
Visit1	−183	3.2e−06	***
Visit3	−302	1.2e−02	*

d) Cytokine EGF mean MFI values at baseline, visit 1 (1-month), and visit 3 (3-month) post treatment as time passed (tp), differentiating between primary, secondary, early latent, and late latent syphilis samples. Estimated mean MFI value recorded as decreasing by 183 over one month.

Title (max 125 characters): Neonatal Herpes Simplex Virus in the US: Regional Trends and Comparison 2017-2021

Submission Category: Epidemiology

Authors: Che' Harris, Katherine Lewis, Jeffrey Klausner

Abstract (Scientific Research Format) (currently 293 words)

Background: Neonatal Herpes Simplex Virus (HSV) infection is one of the most serious complications of genital HSV infection. However, recent disease burden estimates using nationally representative data are lacking. We address this gap by comparing US trends in neonatal HSV infection by region from 2017-2021.

Methods: We identified neonatal HSV infection cases from the nationally representative National Inpatient Sample (NIS) database using ICD-10 codes. Disease incidence was calculated by comparing the number of cases in each year to the total number of live births using NIS sample weights. We used linear regression with an interaction term to compare 5-year incidence trends by region.

Results: We identified 1,895 neonatal HSV infection cases, for an average of 379 cases per year and an average annual incidence of 10.28 cases per 100,000 live births. Of these, 47% were in the South, 19% in the Midwest, 19% in the West, and 15% in the Northeast. The total number of cases in the South was persistently higher than in other regions, and half of all cases in the South were in zip codes of the lowest household income quartile. There was no significant change in national neonatal HSV incidence over the 5-year period (coefficient = 0.06, p=0.801), but there was significant moderation in incidence by region. In the Northeast, incidence decreased by an average of 1.52 cases per 100,000 live births (p=0.018). Relative to the Northeast, the incidence was significantly higher in the Midwest and West (interaction coefficients: 2.84 [p=0.003], 2.17 [p=0.017]).

Conclusion: Neonatal HSV infection incidence was stable and varied by region. Neonatal HSV has been widely neglected in pediatric infectious disease and sexual health research and policy but remains an important cause of infant morbidity. Improved national data and attention to this condition are needed to inform targeted risk-reduction programs

TITLE: What do people who care about herpes want?

Authors: Kimberly Neff[1]; Karly Kern[2]; Nicole Hanley, FNP-BC, PMHNP-BC[1]; Simon Delgrave, PhD[1]; Luis Schang, PhD[1]; Che Harris, MD[1], Gary Richwald, MD MPH[1]; Jeffrey D. Klausner, MD MPH[1]

Affiliations: 1. Herpes Cure Advocacy, Pennsylvania, US

Background: Herpes Cure Advocacy (HCA) is a community-based volunteer organization committed to helping to find a cure, new treatment, and vaccines for herpes simplex viruses (HSV) 1 and 2. The organization launched in 2021 and today has over 5,000 members from various backgrounds, including patients, researchers, healthcare providers, and policymakers.

Methods: Given the growth of HCA's membership and the organization's impact on governmental funding and research for HSV, we surveyed HCA members. The survey sought to understand members' current demographics and preferences for intra-membership interactions and their hopes for the direction of future HSV policies and research. A 14-item survey was distributed via email and online to HCA members over three weeks in October 2024. Following the initial distribution, one weekly reminder was sent over the remaining two weeks.

Results: Four hundred members responded to the survey (~8% response rate). Over 70% (>280) were 35 years and older. Sixty-four percent (257) identified as female, and 62.5% (252) lived in the U.S. Most members, 43% (171), preferred Zoom events to connect with other members on National Herpes Day.

On a ranking scale, members ranked 'Increasing HSV research' at 93.3% (373), 'Increasing HSV awareness and education' at 85.6% (342), and 'Enhancing HSV prevention strategies' at 68.5% (274) as their highest policy priorities. Goals for 'Finding a cure' 99.1% (396), 'developing HSV vaccines' 95.3% (381), and increasing research funding' 60.5% (242) were chosen as their highest research priorities.

Conclusion: HCA members selected funding research, finding a cure, increasing education and awareness, and prevention as their top HSV policy and research priorities. Ongoing and future HSV advocacy efforts that target membership needs and preferences are essential for engagement and promoting the future direction of the HSV field.

Title

Urine-Based Human Papillomavirus Screening: Performance, Challenges, and Opportunities to Expand Access in the United States

Authors:

Lily Yang[1], BA, Chibuzor Babalola[1], MD, MPH, Jeffrey D. Klausner[1], MD, MPH

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Background
In the United States, about 12,000 new cases of cervical cancer are diagnosed each year, largely due to 30% of eligible women remaining unscreened. Underscreening is most common in rural populations and in populations where healthcare access is difficult. Urine-based testing for Human Papillomavirus (HPV) offers a non-invasive, self-sampling method that could improve access to screening. FDA-approved tests detect HPV in cervical and vaginal samples, but none are currently approved for urine detection. We conducted a narrative review of urine-based HPV testing, focusing on diagnostic performance and feasibility.

Methods
Studies were identified through PubMed using combinations of search terms including 'urine,' 'screening,' 'diagnostic tests,' and 'HPV' from January 1, 2006, to December 31, 2024. Studies reporting test performance for detecting HPV and acceptability of urine-based HPV testing compared to current cervical/vaginal detection were included. Studies comparing detection to precancerous lesions were excluded. Weighted averages for sensitivity and specificity were calculated based on study performance values and sample sizes.

Results
We identified 14 studies (N=67 to N=561) evaluating test performance for detecting any HPV in urine specimens. Weighted sensitivity was 57% (range 56.6 to 98.6%), and specificity was 82% (range 61 to 100%), compared to vaginal/cervical sampling. In studies that reported higher sensitivities, the samples were processed more promptly after collection and preservatives were added. Regarding acceptability (n=5 studies), one quantitative study reported that 95% of participants felt comfortable with urine sampling compared to 82% for cervical sampling, and qualitative assessments ranked urine as the easiest collection method.

Conclusion
Urine-based HPV testing has variable performance and high acceptability among patients eligible for cervical HPV detection. The lack of FDA-approved urine-based HPV tests represents a gap in improving accessibility to under-screened populations.

STI & HIV 2025 World Congress Abstract Submission

Title: **Adverse Birth Outcomes among Syphilis-Treated versus Syphilis-Seronegative Pregnant Women in East London, South Africa**

Chibuzor M. Babalola[1], Mandisa M. Mdingi[2], Freedom Mukomana[2], Msindisi Gqirana[2], Christina A. Muzny[4], Christopher M. Taylor[3], Andrew Medina-Marino[5,6], Remco P.H. Peters[2], Jeffrey D. Klausner[1]

Institutions: 1) Keck School of Medicine University of Southern California, USA; 2) Research Unit, Foundation for Professional Development, East London, South Africa; 3) Division of Infectious Diseases, University of Alabama at Birmingham, USA; 4) Department of Microbiology, Immunology & Parasitology, Louisiana State University Health Sciences Centre, New Orleans, USA; 5) Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, USA; 6) Desmond Tutu Health Foundation, South Africa

Presenting Author: Chibuzor M Babalola

Background

Syphilis in pregnancy remains a leading cause of adverse birth outcomes globally. Screening and treatment with benzathine penicillin G is highly effective. However, residual risks may exist in treated mothers due to factors such as delayed treatment initiation, reinfection, or inadequate maternal immune response.

Methods

We compared adverse birth outcomes in syphilis-treated versus syphilis-seronegative mothers, using data from singleton pregnancies (2021–2024) across four primary healthcare facilities in East London, South Africa. Women were identified by syphilis serostatus at their first antenatal visit (< 27 weeks) and/or a third trimester visit (30–34 weeks). We calculated frequencies and risk differences (RDs) in both groups with 95% confidence intervals (CIs) for preterm birth (<37 weeks) or low birth weight (<2,500g) among live births, and for stillbirths.

Results

Among 1,888 singleton pregnancies, 92 (4.9%) were treated for syphilis based on a positive rapid treponemal antibody test, with 78% (n=72) diagnosed and treated at the first antenatal visit. Overall, adverse birth outcomes were observed in 22.5% (n=425). Comparing syphilis-treated to syphilis-seronegative pregnancies (**Table**), adverse birth outcomes occurred in 26.1% vs. 22.3% (RD: +3.8%; 95% CI: -5.4%, 12.9%). Preterm birth was observed in 15.4% vs. 16.5% (RD: -1.1%; 95% CI: -8.8%, 6.5%), low birth weight in 14.7% vs. 11.6% (RD: +3.1%; 95% CI: -4.4%, 10.7%), composite preterm birth or low birth weight in 25.3% vs. 20.3% (RD: +5.0%; 95% CI: -4.1%, 14.1%), and stillbirth in 1.1% vs. 2.6% (RD: -1.5%; 95% CI: -3.7%, 0.8%).

Conclusion

In this South African cohort with a relatively high syphilis prevalence, adverse birth outcomes were frequent. However, no excess risks were observed among syphilis-treated pregnancies; the majority treated before the third trimester. Our findings reinforce the effectiveness of antenatal syphilis screening and treatment in mitigating risks to the fetus. Prioritizing syphilis screening and treatment programs remains essential in high-prevalence settings.

Table. Risks and Risk Differences, Comparing Adverse Birth Outcomes by Maternal Syphilis Status

Birth Outcome[a]	**Total**	**Treated for Syphilis[b]**	**Seronegative**	**Risk Difference (95% CI)**
Preterm Birth (N=1841)	303 (16.5%)	14 (15.4%)	289 (16.5%)	-1.1% (-8.8, +6.5)
Low Birth Weight (N=1756)	207 (11.8%)	13 (14.7%)	194 (11.6%)	+3.1% (-4.4, +10.7)
Preterm Birth or Low Birth Weight (N=1841)	378 (20.5%)	23 (25.3%)	355 (20.3%)	+5.0% (-4.1, 14.1)
Stillbirth (N=1888)	47 (2.5%)	1 (1.1%)	46 (2.6%)	-1.5% (-3.7, +0.8)
Any Adverse Birth Outcome (N = 1888)	425 (22.5%)	24 (26.1%)	401 (22.3%)	+3.8% (-5.4, +12.9)

Footnotes

a) *Denominators*:
- Stillbirth and any adverse birth outcome: N = 1888 (All pregnancies)
- Preterm Birth and composite preterm birth or low birth weight: N = 1841 (Live births only)
- Low birth weight: 85 Live births *missing* birthweight data are excluded

b) *Syphilis Cases*
- 92 treated for syphilis among all 1888 pregnancies (4.9%)
- 91 treated for syphilis among all 1841 live births (4.9%)
- 88 treated for syphilis among the 1756 live births contributing birthweight data (5.0%)

STI & HIV 2025 World Congress Abstract Submission

Title: **Adverse Birth Outcomes in Pregnant Women Getting Fewer vs. Standard 3-Dose Benzathine Penicillin G for Late Latent or Syphilis of unknown Duration**

Chibuzor M. Babalola[1], Mandisa M. Mdingi[2], Freedom Mukomana[2], Msindisi Gqirana[2], Christina A. Muzny[4], Christopher M. Taylor[3], Andrew Medina-Marino[5,6], Remco P.H. Peters[2], Jeffrey D. Klausner[1]

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Presenting Author: Chibuzor M Babalola

Background

In South Africa, syphilis screening in pregnancy is routine, with a 3-dose regimen of intramuscular benzathine penicillin G (BPG) administered weekly after a positive rapid treponemal diagnostic test. Pregnant women with syphilis are treated as having late latent or unknown-duration disease due to limited clinical history and delayed confirmatory results. However, patient- and healthcare-related factors, including missed visits and supply shortages, can result in incomplete regimens by delivery. We explored whether fewer BPG doses increase the risk of adverse birth outcomes.

Methods

Nested within the Philani study (NCT04446611) in East London, South Africa, which investigates screening strategies for sexually transmitted infections and impact on adverse birth outcomes, we conducted a chart review of women with singleton pregnancies treated for syphilis per routine care. We identified preterm birth, low birth weight, or stillbirth outcomes, comparing women who received fewer doses (2 or 1) of BPG before delivery to those who received the full 3-dose regimen.

Results

Among 1,888 pregnancies, 92 (4.9%) were treated for syphilis. Of these, 24 (26.1%) experienced an adverse birth outcome. Dosing data have been retrieved for 38 women to date. Among the 38, 10 received fewer doses (2 doses: n=2; 1 dose: n=8), while 28 received 3 doses. Adverse outcomes (all being preterm birth or low birth weight) occurred in 26.3% of this subset (10/38); 20% in the fewer-dose group (2/10) vs. 28.6% in the 3-dose group (8/28) (*Risk Difference*: -8.6%; 95% CI: -38.5%, 21.3%; *Relative Risk*: 0.70; 95% CI: 0.18, 2.73).

Conclusion

In this small cohort, receiving fewer BPG doses was not associated with worse adverse-birth-outcomes. Although limited by a small sample and statistical uncertainty, our findings preliminarily support the potential non-inferiority of reduced-dose regimens in late maternal syphilis or syphilis of unknown duration. Larger studies are needed to clarify these findings and optimize syphilis care in this population.

Title: Comparing Cefixime and Penicillin G for Early Syphilis: Rapid Plasma Reagin Titer Decline and Preliminary Treatment Outcomes

Authors: Gjermayne Wilson[3], Kori Keith[1], Chrysovalantis Stafylis[1], Kelika A. Konda[1], Michael Reyes-Diaz[2], Jeffrey D. Klausner[1]

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Background: Syphilis is a global health problem. Benzathine penicillin G (penicillin) is the standard treatment for early syphilis; however, a prior pilot study found oral cefixime likely efficacious, leading us to conduct a larger clinical trial to evaluate cefixime as a potential treatment alternative.

Methods: We are conducting a randomized, open-label, non-inferiority multisite clinical trial comparing the efficacy of cefixime (400 mg orally, twice daily for 10 days) to penicillin (2.4 million units intramuscularly) in participants with and without human immunodeficiency virus (HIV). During penicillin shortages, doxycycline hyclate (100 mg orally, twice daily for 14 days) was used instead of penicillin. Participants were evaluated at 3-, 6-, and 9-months. Primary outcome is defined as ≥4-fold decline in rapid plasma reagin (RPR) titers by 6 months. Treatment failure is defined as insufficient RPR decline, a ≥4-fold increase, or symptom recurrence.

Results: As of December 17, 2024, 156 participants were enrolled (78 received cefixime, 70 received penicillin, and 8 received doxycycline), with 67.3% living with HIV and 93.5% identifying as men who have sex with men or transgender women. Reported 10-day cefixime adherence was 92.3% (62/67).

Treatment success across treatment arms by 6-months is: 89.5% for cefixime, 96.0% for penicillin, and 100% for doxycycline (Figure).

Eight participants (7.0%) experienced treatment failure: 6 cefixime participants— 2 without HIV (≥4-fold increase) and 4 with HIV (insufficient RPR decline by 6 months), and 2 penicillin participants, both with HIV (insufficient RPR decline by 6 months). There were no observed doxycycline failures (N=7).

Conclusion: Cefixime and penicillin demonstrated similar efficacy at 6 months. These preliminary findings support study continuation.

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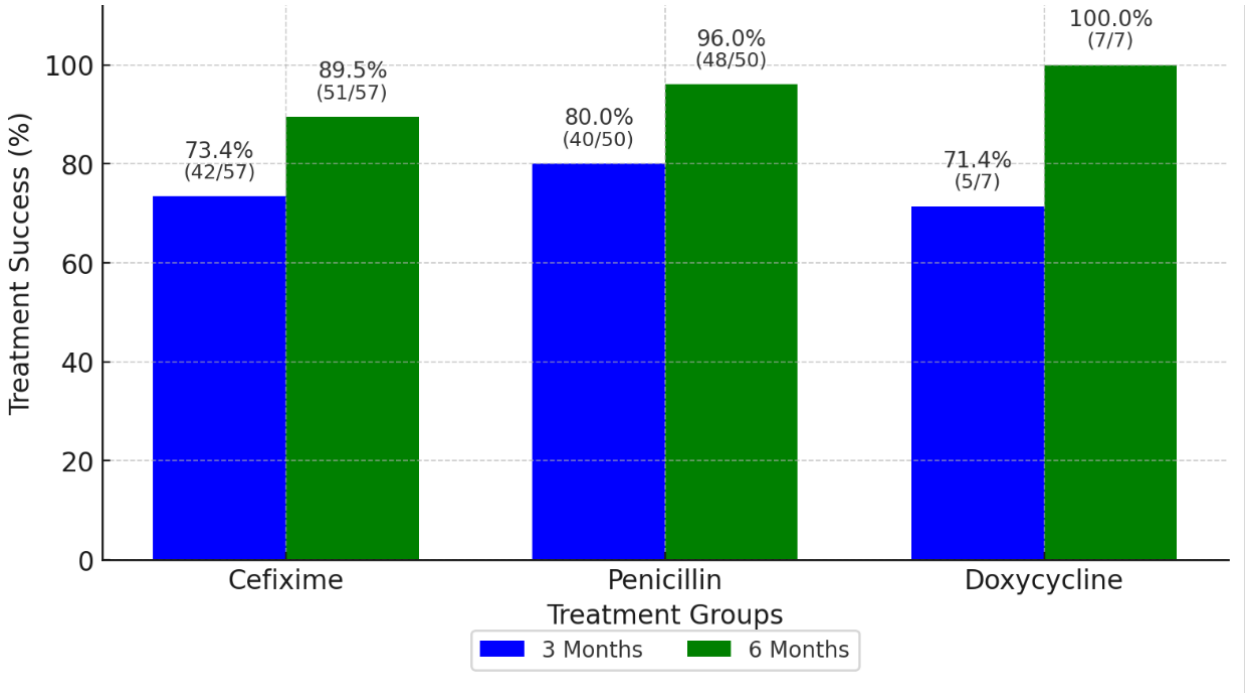

Figure 1. Treatment response by 3- and 6- months after treatment initiation among cefixime, penicillin, and doxycycline participants.

Title: Impact of Additional Antibiotic Use on Rapid Plasma Reagin Titer Declines in Early Syphilis Treatment

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Background: Syphilis has reemerged as a global health problem. Benzathine penicillin G (penicillin) is the standard treatment for early syphilis. We evaluated oral cefixime as a potential alternative and assessed the impact of additional antibiotic use on rapid plasma reagin (RPR) decline.

Methods: Participants with early syphilis were randomized to cefixime (400 mg twice daily for 10 days) or benzathine penicillin G (2.4 million units intramuscularly). Doxycycline hyclate (100 mg twice daily for 14 days) was used during penicillin shortages. Those on recent antibiotics or at baseline were excluded. Treatment success was defined as a ≥4-fold RPR decline by 6 months. We evaluated whether additional antibiotic use after treatment influenced treatment success, with antibiotic use self-reported at 3-, 6-, and 9-month follow-ups by treatment arm and time to response.

Results: Of 114 participants, 14 (12.3%) reported additional antibiotic use.

Of cefixime participants with additional antibiotics (n=8), 4 succeeded by 3 months (3 doxycycline, 1 penicillin), and 4 by 6 months (3 doxycycline, 1 unknown) versus among those allocated to cefixime (n=49) 39 succeeded by 3 months and 43 by 6 months.

For penicillin (n=5 who received azithromycin, levofloxacin, amoxicillin, doxycycline, or unknown) all succeeded by 3 months versus 35 of 45 succeeded by 3 months, and 43 by 6 months of in those not receiving additional antibiotics (n=45.

For doxycycline (n=1) all succeeded by 6 months. Among those without additional antibiotics (n=6), 5 succeeded by 3 months, and all by 6 months.

Conclusions: All participants reporting additional antibiotic use achieved treatment success, while some without additional antibiotics did not achieve treatment success by 6 months. These findings suggest that additional antibiotics may accelerate RPR decline.

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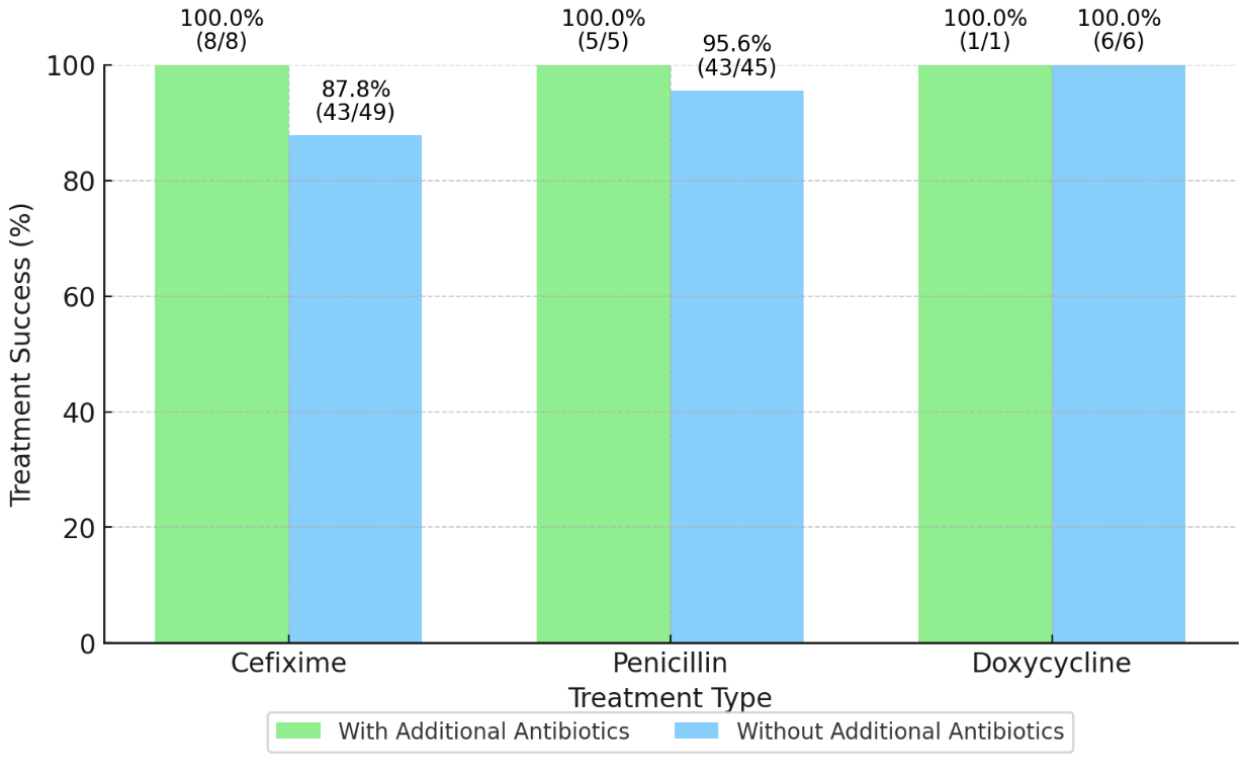

Figure 1. Treatment Success (With and Without Additional Antibiotics) by Treatment Group at 3 or 6 Months

Title: Efficacy of Oral Cefixime versus Benzathine Penicillin G for Early Syphilis by HIV Status

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Background: Rising syphilis rates pose significant public health challenges. Decline in rapid plasma reagin (RPR) titer is a key indicator of syphilis treatment effectiveness. Evidence suggests that people living with human immunodeficiency virus (HIV) experience slower RPR decline compared to those without HIV. We investigated RPR decline timelines by comparing treatment outcomes for cefixime and penicillin in early syphilis by HIV status.

Methods: In our clinical trial, patients with early syphilis were randomized to receive cefixime (400 mg orally, twice daily for 10 days) or penicillin (2.4 million units intramuscularly). Participants living with HIV must have undetectable HIV viral load < 200 copies/mL or CD4 T cell count >350 cells/mm^3 and be on antiretroviral treatment. Participants are followed at 3, 6, and 9 months for clinical evaluation and RPR testing. The primary outcome is a ≥4-fold decline in RPR titer by 6 months.

Results: As of December 17, 2024, 114 participants (32 without HIV; 75 living with HIV) completed 6 months of observation. Of those without HIV, 20 received cefixime, and 12 received penicillin. Among participants with HIV, 37 received cefixime, and 38 received penicillin.

The Figure shows treatment outcomes by HIV status and treatment arm.

Conclusion: Participants without HIV appear to achieve faster RPR declines across treatment arms. By 3 months, most participants without HIV achieved treatment success with both cefixime and penicillin, while success rates over time for those with HIV appear lower for cefixime than those with penicillin. Our preliminary analysis highlights the importance or considering HIV status in syphilis treatment evaluations. Future analysis will look at history of prior syphilis and its relationship to titer decline and HIV status.

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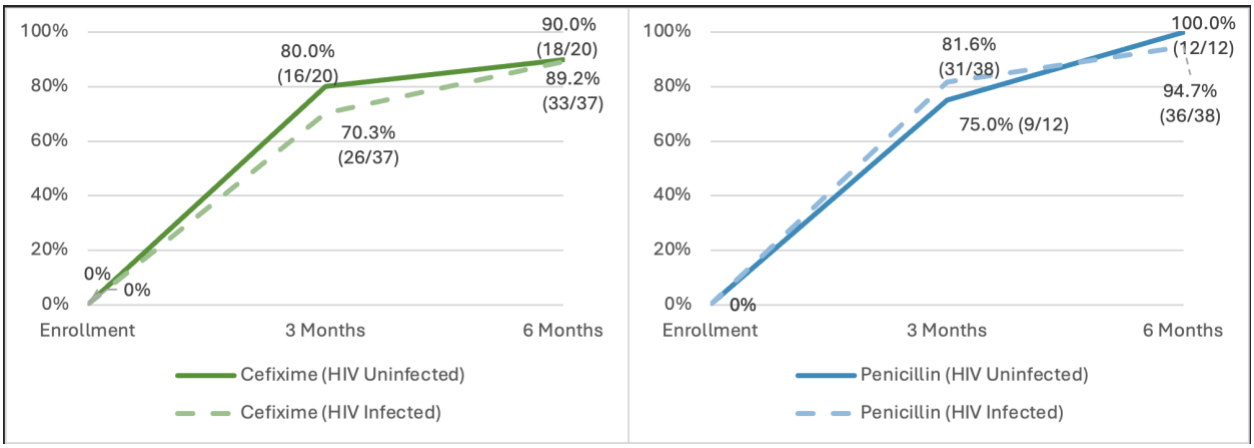

Figure. Rapid Plasma Reagin (RPR) titer treatment rates by HIV status and treatment arm at 3 and 6 months

High Test-of-Cure Positivity After Cefixime Treatment for Gonorrhea in Hanoi, Vietnam

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Introduction

Antimicrobial resistance in *Neisseria gonorrhoeae* (NG) is a global health challenge. Ceftriaxone is the first-line treatment, while cefixime, given as a single oral dose, is recommended as an alternative. Data on cefixime treatment outcomes are limited, especially in areas with emerging cefixime resistance.

Methods

We conducted a secondary analysis from a study on *Chlamydia trachomatis* and NG testing within an HIV PrEP program in Hanoi, Vietnam. Eligible participants were males, aged ≥16 years, with ≥1 male sex partner in the past 12 months. Between May 2022 and February 2023, participants with NG infections, detected via culture or nucleic acid amplification test (NAAT), at pharyngeal, rectal, or urogenital sites were treated with a single 800 mg oral dose of cefixime. A test-of-cure (TOC) visit was done 10-21 days post-treatment, with specimens obtained for culture and NAAT. Multivariate logistic regression was used to evaluate factors associated with TOC positivity.

Results

There were 24 participants treated with cefixime, including 12 rectal, 17 pharyngeal, and 7 urethral infections. Twenty participants (83.3%) returned for TOC, with a median of 12 days [IQR:11.5–14]. Overall TOC positivity by NAAT was 45.0% (9/20); TOC positivity was 60% (9/15) in pharyngeal, 10% (1/10) at rectal, and 0% at urogenital sites. All TOC cultures were negative. Initial NAAT cycle thresholds were associated with TOC positivity (aOR=0.82; 95%CI 0.70–0.92). Time from treatment to TOC and symptoms at treatment were not associated with TOC positivity.

Conclusions

Our findings indicate a high TOC positivity by NAAT, particularly at pharyngeal sites, among NG infections treated with oral cefixime in Vietnam. Higher NAAT cycle thresholds at treatment were less likely to have a positive TOC. No infections were culture-positive at TOC, suggesting that NAAT results might reflect non-viable bacterial DNA. These results raise concerns about the utility of NAATs for TOC.

Impact of Mycoplasma hominis on Trichomonas vaginalis in Pregnancy and Gestational Age at Birth: Cohort Study, South Africa

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Background

Trichomonas vaginalis (TV) during pregnancy is associated with preterm birth. *Mycoplasma hominis* (MH) is associated with preterm birth and increases the pathogenicity of TV *in vitro*. We aimed to investigate TV and MH co-infection among pregnant women and associations with preterm birth.

Methods

We conducted a cohort study in East London, South Africa. Pregnant women were enrolled at <27 weeks gestation, confirmed by ultrasound. *Chlamydia trachomatis, Neisseria gonorrhoeae* (GeneXpert, Cepheid) and HIV testing occurred on-site, with treatment as appropriate. Baseline vaginal swabs were PCR-tested for TV, MH*, M. genitalium* and *Ureaplasma urealyticum* (>40 cycles) at the end of the study, so specific treatment during pregnancy was not given. The prespecified outcome was gestational age at birth, in days (preterm birth, <37weeks=<259 days). Among women with known delivery date, we conducted regression analyses, adjusting for baseline sociodemographic, clinical and microbiological covariates, incorporating an interaction term between TV and MH (Table).

Results

From March 2021-October 2023, 603 pregnant women were enrolled (median gestation 13 weeks, interquartile range, IQR 10-19), 581/603 (96.4%) were followed post-delivery. Median age was 28 years (IQR 24-33) and 156/581 (26.9%) were living with HIV. MH

(427/581, 73.5%) was more common among women with TV (62/581, 10.7%, MH+TV+ 53/62, 85.5%) than without (MH+TV- 374/519, 72.1%). Median gestational ages at birth and percentages preterm were: women with TV+/MH+ (n=53, 39 weeks+0 days, 17.6%); TV+/MH- (n=9, 37+4, 22.2%); TV-MH+ (n=374, 39+0.5, 19.5%); TV-MH- (n=145, 38+6, 22.3%). In multivariable analysis for women both with and without TV, gestational age at birth did not differ by MH status (Table, p-value for interaction=0.41).

Conclusion

MH was highly prevalent in pregnancy and was associated with TV. TV was, however, not associated with shorter gestation and MH did not modify the effect. These findings, among prospectively followed South African pregnant women, challenge existing published research.

Table: Characteristics and birth outcomes among pregnant women according to *T. vaginalis* and *M. hominis* exposure at baseline.

	TV positive		TV negative	
	MH positive	MH negative	MH positive	MH negative
Number of women	53	9	374	145
Baseline characteristics				
Age in years				
Median	29	26	28	29
(IQR)	(23, 32)	(22, 32)	(23, 33)	(25, 33)
Living with HIV, n (%)				
No	32 (60.4%)	5 (55.6%)	268 (71.7%)	120 (82.8%)
Yes	21 (39.6%)	4 (44.4%)	106 (28.3%)	25 (17.2%)
Birth outcome, univariable analysis				
Gestational age, in weeks+days				
Median	39+0	37+4	39+0.5	38+6
(IQR)	(37+3, 40+0)	(37+2, 39+4)	(37+5, 40+2)	(37+1, 40+1)
Missing	*2*	*0*	*20*	*6*
Preterm birth, n (%)				
Yes	9 (17.6%)	2 (22.2%)	69 (19.5%)	31 (22.3%)
No	42 (82.4%)	7 (77.8%)	285 (80.5%)	108 (77.7%)
Missing	*2*	*0*	*20*	*6*
Birth outcome, multivariable analysis[a]				P-value[b]
Mean difference[c] in gestational age, in weeks+days				
All births (95% CI)	-0+3 (-2+6, 2+0)		0+5 (-0+4, 2+0)	0.41
Live births (95% CI)	0+6 (-0+5, 2+3)		-0+0 (-0+4, 0+3)	0.27
Risk difference[c] in preterm birth, %				
All births (95% CI)	-8.1% (-38.8%, 22.6%)		-2.1% (-10.2%, 6.0%)	0.43
Live births (95% CI)	-12.1% (-43.1%, 18.9%)		1.7% (-5.2%, 8.7%)	0.33

a. Linear regression model, adjusted for baseline covariates, including an interaction between TV and MH exposure. Baseline covariates: age, level of education, alcohol consumption, at least one prior pre-term birth, living with HIV, *C. trachomatis*, *N. gonorrhoeae*, *M. genitalium*, *U. urealyticum*;

b. P-value from Wald test for interaction;

c. Differences are calculated as MH-positive minus MH-negative;

CI, confidence interval; IQR, interquartile range; MH, *M. hominis*; TV, *T. vaginalis*.