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Individual-level agreement between antenatal HIV/syphilis survey syphilis results abstracted from medical records and laboratory-derived results among pregnant women in South Africa, 2022

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Summary

South Africa has considered transitioning from laboratory-based sentinel surveillance to using routine data or medical records for HIV and syphilis surveillance. We describe the agreement between these two methods and determine whether relying solely on medical record abstraction is sufficient to estimate syphilis prevalence among pregnant women. We randomly selected 700 pregnant women from the 2022 South African Antenatal Care HIV/Syphilis Sentinel Survey database. Inclusion criteria included women aged 15 to 49 years, documented syphilis results extracted from both medical records and data captured in the survey database, and sufficient residual serum specimen (≥150µl) stored at the National Institute for Communicable Diseases, a division of the National Health Laboratory Service. Stored serum samples were tested for syphilis using specific and non-specific treponemal assays in the reference laboratory. Descriptive statistics were used to report on agreement between syphilis results in medical records and reference laboratory-based syphilis testing, and to determine syphilis prevalence among those whose syphilis results were missing or pending in the medical records. The overall agreement between syphilis results from medical records and that from the reference laboratory was 96.8%, with a low positive per cent agreement (PPA) of 52.6% [95% confidence interval (CI): 47.92%-57.34%] and a high negative per cent agreement (NPA) of 98.8% [95% CI: 97.76%-99.82%]. There was no difference in syphilis prevalence (based on reference laboratory testing) among those whose results were missing in medical records and those whose results were available (3.1% vs 4.4%, p=0.419). We conclude that while there was good NPA between medical records and reference laboratory-based syphilis testing, there was poor PPA, with close to half of the syphilis cases detected in the reference laboratory missing from medical records. Therefore, continued use of medical records in their current form for maternal syphilis surveillance may underestimate the true burden of disease.

Introduction

Syphilis is a curable sexually transmitted infection (STI) caused by the bacterium *Treponema pallidum* (TP).[1] Globally, about 7.1 million [range: 2.4 million–11.5 million] people were newly infected with TP and an estimated 200 000 deaths were due to syphilis in 2020.[2] Syphilis can be transmitted from mother to child during pregnancy and childbirth.[3] In pregnant women, TP can cause miscarriage, stillbirth, or early neonatal death as well as congenital infection in the baby.[4] Babies born with congenital syphilis can have bone damage, severe anaemia, enlarged liver and spleen, jaundice, neurological conditions including blindness or deafness, meningitis, or skin rashes.[4]

South Africa has a high burden of syphilis. In 2017, there were an estimated 23 000 new syphilis cases among females and 47 500 new cases among males, according to a World Health Organization (WHO)-led modelling exercise.[5] The prevalence of maternal syphilis was estimated to be 2% in 2015, increasing to 2.6% in 2019.[6] In 2023, there were an estimated 1 739 congenital syphilis cases reported to the National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service, up from 373 cases reported in 2020.[7,8] These data from South Africa suggest increased transmission within communities.

In 2007, the WHO launched an initiative to eliminate congenital syphilis globally. The initiative set targets for process indicators as follows:

i) at least 95% of pregnant women had to attend antenatal care (ANC);
ii) 95% of those attending ANC had to be tested for syphilis at least once; and
iii) 95% of those who test positive for syphilis are to be treated with at least one dose of benzathine penicillin.[2]

The initiative also set an impact target of 50 or fewer cases of congenital syphilis per 100 000 live births in 80% of countries.[2] More recent WHO global targets also include reducing new syphilis cases by 90% between 2018 and 2030.[2] Reliable surveillance methods to monitor syphilis incidence, prevalence, screening, and treatment coverage in ANC are required to monitor progress towards these targets.

South Africa does not have robust data to evaluate the country's progress towards the global targets for the elimination of congenital syphilis. The 2022 ANC human immunodeficiency virus (HIV) sentinel survey estimated the coverage of syphilis testing to be 97.5%, up from 96.4% in 2019.[9] This was defined as medical record evidence of syphilis testing at any point during pregnancy. Although close to 20% of respondents did not have the syphilis results associated with the syphilis screening on file, 3.1% had a positive result, with 94.2% having syphilis treatment with benzathine penicillin documented in the medical record.[9] Although the country seemed to be doing relatively well with respect to the process indicators, the congenital syphilis case rate was estimated to be 198 per 100 000 live births in 2023.[8] Delays in getting syphilis results to pregnant women and delays in starting treatment among syphilis-positive mothers are some identified gaps within the syphilis prevention cascade.[10]

Since the 1990s, the South African National Department of Health (NDoH) has recommended that every pregnant woman who accesses ANC at a public health care facility receive a syphilis test at the first ANC visit and, if negative, receive another at 32–34 weeks' gestation.[11,12] At that time, there was no nationally validated algorithm or quality assurance programme for rapid syphilis testing.[11, 12] The 2018 sexually transmitted infections (STI) guidelines allowed for laboratory-based testing using the Rapid Plasma Reagin Test (RPR) (non-treponemal test) first, followed by a confirmatory treponemal test such as TP Hemagglutination (TPHA) (traditional algorithm), or starting with the treponemal test and confirming with a non-treponemal test (reverse testing algorithm).[12] In late 2023, the NDoH released updated guidelines allowing for the use of rapid dual HIV/syphilis testing on site and more frequent syphilis testing, up to four times, during pregnancy. Women who were RPR positive were recommended to receive three doses (one dose per week) of benzathine penicillin, 2.4 million units, through intramuscular injection. Women who were rapid-test positive were treated with one dose of benzathine penicillin while waiting for RPR results.[13]

Since 1990, South Africa has implemented periodic (annually until 2015, then every 2–3 years thereafter) national ANC HIV sentinel surveillance to track HIV prevalence among pregnant women and to generate data for general population HIV estimates.[6] Enrolling at least 36 000 women from 1 585 facilities throughout the country, the survey measures HIV prevalence trends at national, provincial, and district levels as well as syphilis prevalence (since 1997). In 2017, the survey began reporting the coverage of syphilis testing and treatment in provinces[14] and also began estimating syphilis prevalence from medical records in 2019.[6] Both first ANC attendees and follow-up ANC attendees are eligible to enrol in the survey.

South Africa has considered transitioning from sentinel surveillance using laboratory-based testing to using routine data or medical records for HIV and syphilis surveillance to reduce costs and to strengthen the quality and use of routine data. Agreement between HIV test results obtained from routine data and those obtained in the laboratory during previous ANC surveys has been evaluated.[15,16] In the 2022 survey, the overall negative per cent agreement (NPA) between results of point-of-care and HIV immunoassays was lower than the WHO benchmark (99.5%) at 94.4% ((95% Confidence Interval (CI): 93.9–94.8%)). The positive per cent agreement (PPA) was above the WHO benchmark (98.6%) at 99.7% (95% CI: 99.6%–99.7%) nationally. However, the agreement between syphilis test results extracted from medical records and laboratory-based syphilis testing has not been evaluated.[9]

We assessed the agreement between routine (facility-based) and survey (reference laboratory-based) syphilis test results and compared the reference laboratory-based prevalence of syphilis among women with and without a documented syphilis test result in their medical records.

Methods

Study design

This was a cross-sectional reference laboratory-based study linked to the 2022 edition of the South African Antenatal HIV/Syphilis Sentinel Survey (ANCHSS22).[9]

Inclusion and exclusion criteria

From the 2022 ANC survey database, we randomly selected – from 32 828 eligible participant records – 700 survey ID numbers belonging to pregnant women who met the following inclusion criteria:

i) pregnant women enrolled in the ANCHSS22 survey;
ii) aged 15–49 years;
iii) documented syphilis screening or testing regardless of whether the result was in the file or not; and
iv) had sufficient residual serum specimen (≥150 µl) stored at the NICD.

Women were excluded from this study if they had not given consent for future testing of their stored blood specimen.

Data collection procedures

The 2022 ANC survey collected information on participant demographic characteristics, antenatal visits, and gestational age. The most recent syphilis test result was abstracted from participants' medical records, and blood specimens were collected for HIV testing. Remnant specimens from the survey were stored at the NICD. The syphilis results abstracted from medical records were from syphilis testing performed at each participant's first ANC visit and around 32–34 weeks' gestation as per national guidelines at the time.[12] The median gestational age at enrolment in the 2022 survey was 26 weeks (interquartile range 19–34 weeks), while the median gestational age at booking was 17 weeks (IQR 12–22 weeks). In the present study, we tested 700 randomly selected stored specimens for syphilis in the reference laboratory using a syphilis rapid diagnostic test (RDT) followed by confirmatory RPR testing on all positive samples. We assessed the agreement between the most recent syphilis test results extracted from medical records and the result of the syphilis testing performed in the reference laboratory. Syphilis diagnosis requires positive results from both treponemal and non-treponemal tests; however,

laboratories in public sector facilities did not use the same testing algorithm. The current STI guideline at the time of the survey allowed for both the traditional and reverse testing algorithms, i.e., testing with the non-treponemal test (RPR) first and confirming with a treponemal test such as TPHA or TP antibodies (TPAb), or starting with the treponemal test and confirming with a non-treponemal, respectively.[17] To accommodate this, for medical records, the criterion for a syphilis-positive case was a documented positive result on the RPR test, but other tests were allowed if the participant had evidence of treatment in their medical records. The reference laboratory's criterion for a syphilis-positive case was positivity on both the RDT and confirmatory RPR. A TP-specific positive test with a negative RPR confirmation test was considered negative.

Reference laboratory procedures

Serum specimens selected for inclusion in this sub-study were retrieved from storage regardless of the medical record results. Reference laboratory scientists retrieved, processed, and tested samples using either the dual HIV/syphilis or single syphilis rapid test and confirmed with an RPR if positive. Initial syphilis screening in the reference laboratory was conducted using the First Response® HIV1+2/Syphilis Combo Card Test (Premier Medical Corporation Pty Ltd, Valsad, Gujarat, Sarigam, India) or the First Response® Syphilis Anti TP Card Test (Premier Medical Corporation Pty Ltd, Valsad, Gujarat, Sarigam, India). The First Response® HIV1+2/Syphilis Combo Card Test is a rapid, qualitative screening in vitro diagnostic test for the detection of antibodies (IgG & IgM) specific to HIV (types 1 & 2) and TP in human serum, plasma or venous and capillary whole blood. The test is WHO-prequalified with in-vitro sensitivity and specificity for each analyte of ≥99%.[18] The First Response® TP Syphilis Anti TP Card Test is a rapid, qualitative screening in vitro diagnostic test for the detection of antibodies (IgG & IgM) specific to TP in human serum, plasma or venous and capillary whole blood, is also WHO prequalified and has in-vitro sensitivity and specificity ≥99%.[18] The time to result was set at 20 minutes.[18] Reactive results were confirmed using a non-treponemal test – the BD Macro-Vue™ RPR Test kit (Becton, Dickinson and Company, Sparks, Maryland, USA). Specimens positive on RPR and indicating a recent infection had antibody titre levels measured. The testing was done according to the reference laboratory standard operating procedures. Leftover specimens were discarded at the end of the study.

Data management and analysis

Data were analysed using STATA® 18.5 [Stata Corporation, College Station, United States]. Following a description of eligible women included in the random sample, positive and negative agreements between syphilis results from the medical records (defined as TP-specific test positive AND non-treponemal test positive OR evidence of syphilis treatment in the medical records) and syphilis results from the reference laboratory (defined as TP-specific rapid tests [First Response® HIV1+2/Syphilis Combo Card Test / First Response® Syphilis Anti TP Card Test] positive plus RPR-positive in the reference laboratory [Macro-Vue™ RPR Test kit]) were determined. The PPA was calculated as the number of women with a documented positive syphilis test in the medical record and a positive reference laboratory test result for syphilis divided by the total number of women with positive reference laboratory test results. The NPA was calculated as the number of women with a negative syphilis test result in the medical record and a negative reference laboratory test result divided by the total number of women with negative reference laboratory test results. Negative percent agreement and PPA were the preferred outcomes as used for similar analyses in HIV surveillance.[16] Overall agreement was determined as the total number of women who had concordant positive or negative results between medical records and reference laboratory testing. The PPA, NPA, and overall agreement were determined for all women by categories of age, ANC visit

type, gravidity, HIV status, and by the RPR/VDRL status in the medical record. The kappa statistic, representing overall agreement between syphilis results from the medical record and those from the reference laboratory beyond what would be expected by chance alone, was calculated. Syphilis prevalence based on reference laboratory-based syphilis testing among those whose results were pending or missing in the medical records was reported using frequencies and percentages with 95% CIs. Chi-squared testing was used to assess differences in prevalence among those who had available syphilis results based on medical records with those whose results were pending/missing in the medical records. A p-value of <0.05 was considered statistically significant.

Sample size considerations

The sample size was calculated assuming:

i) PPA and NPA of at least 79% between syphilis results based on medical records and those from reference laboratory-based syphilis testing;
ii) 3% precision; and
iii) 95% CI.

This gave a minimum sample size of 412 women. For measuring syphilis prevalence among pregnant women whose syphilis results were documented as pending or missing in the medical records, a sample size of at least 243 women was needed to estimate syphilis prevalence of 2.6% within 2% precision. The total minimum sample size was then determined to be 700 women, assuming that up to 6% of women selected would not have a valid blood specimen.

Results

Participants' characteristics

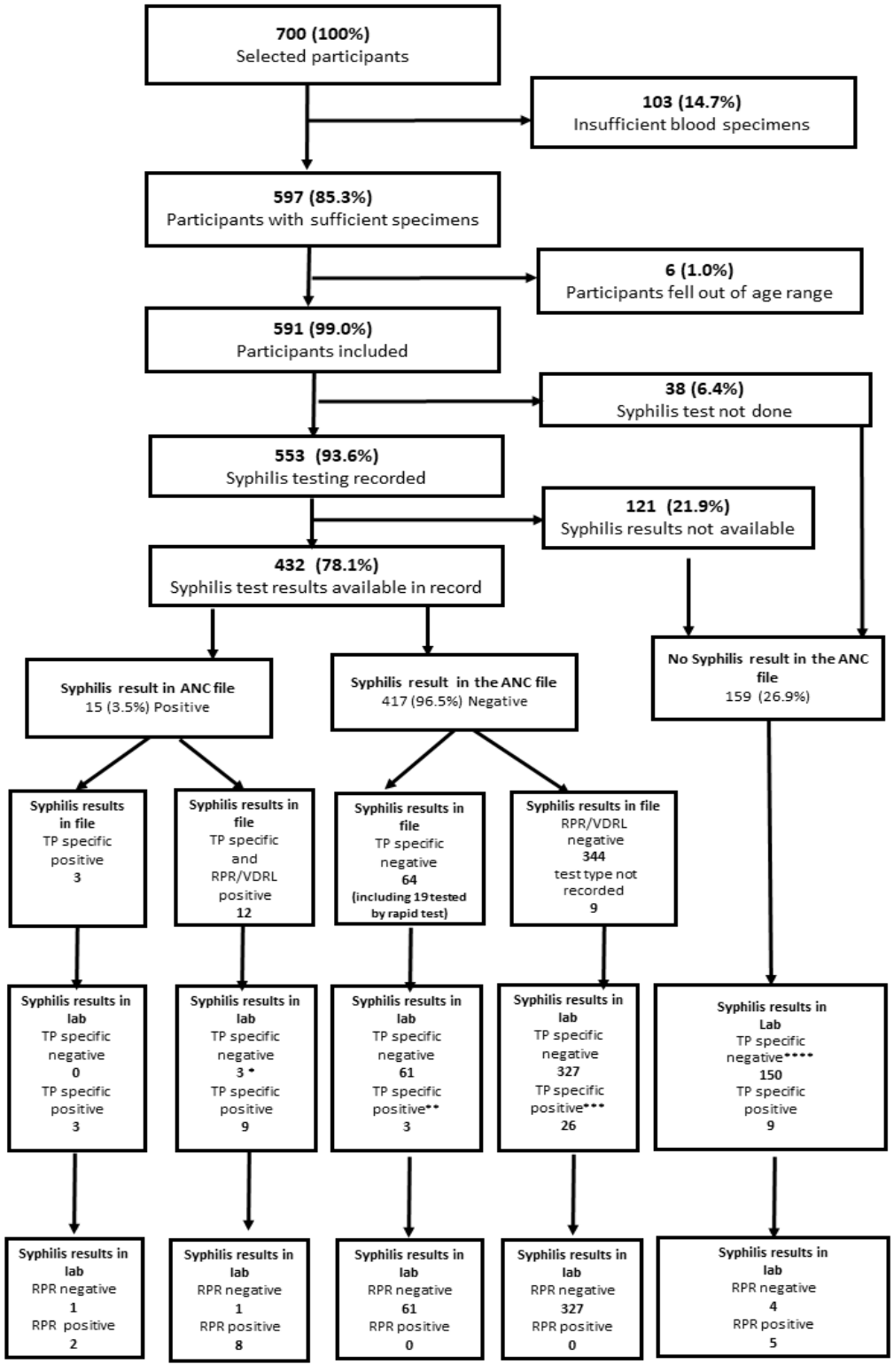
Specimens were retrieved for 700 pregnant women randomly selected from the ANCHSS22 database. Of these, 103 were inadequate for further testing and excluded, and 597 (85.3%) were tested. After testing, an additional six participants were found to be outside the age range of 15–49 years and were excluded from the analysis. The final analysis, therefore, included 591 participant records (Figure 1).

Table 1 shows the demographic, behavioural, and clinical characteristics of the included women. The median age was 25 years (interquartile range (IQR): 15–44 years). Most participants came from three provinces, namely KwaZulu-Natal (123/591; 20.8%), followed by Gauteng (95/591; 16.1%) and Eastern Cape (88/591; 14.9%). Overall, 175 (29.6%) participants were attending a first antenatal visit, 400 (67.7%) were attending a follow-up visit, and 16 (2.7%) had no indication of an ANC visit type.

Table 1. Characteristics of pregnant women enrolled in the 2022 ANC survey and who had serological testing for syphilis in the reference laboratory, South Africa, N=591.

Variable	Frequency
Age in years (median, IQR)	25 (15–44)
Race (n, %):	
Black	518 (87.6)
Other	69 (11.7)
Unknown	4 (0.7)
Province (n, %):	
Eastern Cape	88 (14.9)
Free State	26 (4.4)
Gauteng	95 (16.1)
KwaZulu-Natal	123 (20.8)
Limpopo	72 (12.2)
Mpumalanga	55 (9.3)
North West	36 (6.1)
Northern Cape	20 (3.4)
Western Cape	76 (12.9)
Level of education (n, %):	
Tertiary	84 (14.2)
Secondary	426 (72.1)
Primary	65 (11.0)
None/Unknown	16 (2.7)
Visit type (n, %)	
First antenatal visit	175 (29.6)
Follow-up visit	400 (67.7)
Unknown visit type	16 (2.7)
Gestational age in weeks (median, IQR)	
Gestational age at booking	16 (12–21)
Gestational age at enrolment	27 (19–34)
Father of the child: N= 591	
Age of father of the child (median, IQR)	30 (17–56)
Relationship with father of the child (n, %)	236 (40)
No relationship with father of the child (n, %)	347 (58.7)
Unknown	8 (1.3)

*IQR=Interquartile range



*RPR results not shown but of these 3 TP specific negative women, all 3 were RPR negative
**RPR results not shown but of these 3 TP specific positive women, 2 were RPR positive
***RPR results not shown but of these 26 TP specific test positive women, 7 were RPR positive and 1 had sample insufficient for RPR
****RPR results not shown but of these 149 TP specific negative women, all 149 were RPR negative

Figure 1. Outcomes of syphilis testing from medical records versus reference laboratory results among pregnant women enrolled in the 2022 ANC survey and who had serological testing for syphilis in the reference laboratory, South Africa, N=591.

Syphilis results from the medical record

In total, 553/591 (93.6%) women had documentation of syphilis screening or testing in their medical record during the current pregnancy, and 38/591 (6.4%) did not. Of the 553 participants who had syphilis screening or testing documented in their medical records, 432 (78.1%) had syphilis results available in their medical records. The remaining 121 (21.9%) had either missing results or results that were pending from the reference laboratory. Among the women with a documented syphilis test result in the medical record, 344/432 (79.6%) had an RPR test documented, 32 (7.4%) had a TP antibody test (TPAb) documented, 16 (3.5%) had TPHA, 12 (2.8%) had Venereal Disease Research Laboratory testing (VDRL), 19 (4.4%) were documented as rapid, and the type of syphilis testing done for nine (2.1%) participants was unknown (Figure 1). Of the 432 participants who had results in their medical records, 15 (3.5%) were documented as positive and 417 (96.5%) were documented as negative. The overall syphilis prevalence as measured by medical record review and extraction was therefore 3.5%.

Syphilis results from the reference laboratory

Among the 591 participants who had syphilis testing in the reference laboratory using the rapid TP, 50 (8.5%) were reactive. Of these 50, 49 had confirmatory testing using RPR testing in the reference laboratory, with one woman having an insufficient specimen to complete confirmatory testing. From the confirmatory testing, 24 women were reactive on RPR. Overall, 566/590 (95.9%) tested on both rapid and confirmatory tests in the reference laboratory were negative, while 24 (4.1%) were positive. The overall syphilis prevalence according to reference laboratory testing was therefore 4.1% (24/590). Figure 1 shows the distribution of the reference laboratory results according to results from the medical records and by laboratory test type. Nine out of 432 women (2.1%) with medical record results available were syphilis negative by medical record but were found to be RPR positive in the laboratory.

Percentage agreement between syphilis results on medical record and those from reference laboratory

Among 431 women who had syphilis results available from both medical records and reference laboratory testing, the overall percentage agreement in syphilis test results extracted from medical records and reference laboratory-based syphilis testing was 96.76% (95% CI: 94.60-98.07%), and the associated kappa score was 57.16% ($p<0.001$). As presented in Table 2, the PPA was 10/19 (52.63%) (95% CI: 29.74–74.47%), with 9/19 (47.37%) false negatives. The NPA was 407/412 (98.79%) (CI: 97.12–99.5%), with 5/412 (1.21%) false positives. Table 3 shows a sub-group analysis including only women who had both specific and non-specific syphilis test results in their medical records; the overall agreement was 96.90% (95% CI 94.48–98.28%) and the associated kappa score was 57.7%. The PPA was 8/15 (53.33%) (95% CI 48.14–58.52%) with 7/15 (46.67%) false negatives. The NPA was 336/340 (98.82%) (95% CI 97.70–99.95%), with 4/340 (1.18%) false positives.

Table 2. Agreement between syphilis results in the medical records and those from the reference laboratory among women who had both medical record and reference laboratory results, South Africa 2022, N=431.

		Laboratory based syphilis positive*		
Medical record syphilis positive		**No**	**Yes**	**Total**
	No	407	9	416
	Yes	5	10	15
	Total	412	19	431

*excludes one person who was *Treponema pallidum* positive in the reference laboratory but whose specimen was insufficient for RPR confirmatory testing.

Table 3. Agreement between syphilis results in the medical records and those from the reference laboratory among women who had documented specific and non-specific test results in the medical records, South Africa, 2022, N=355.

		Laboratory based syphilis positive*		
Medical record syphilis positive		**No**	**Yes**	**Total**
	No	336	7	341
	Yes	4	8	12
	Total	340	15	355

*excludes one person who was *Treponema pallidum* positive in the reference laboratory but whose specimen was insufficient for RPR confirmatory testing.

Table 4 shows the level of agreement between medical record syphilis results and reference laboratory-based syphilis results across categories of HIV status, age group, gravidity, and ANC visit type. All categories of age, ANC visit type, gravidity, and HIV status were associated with excellent NPAs, ranging from 97.53% to 100%. However, lower PPAs ranged from 28.57% to 66.67% across all categories of age, ANC visit type, gravidity, and HIV status. The PPA was particularly low among individuals who were HIV positive (28.57%), but was higher among those who were HIV negative (66.67%), those who were on their second antenatal visit (66.67%), and those who were pregnant for the first time (62.5%). Conversely, NPAs were very high among individuals who were on their second antenatal visit (100%), those aged 15–24 years (99.43%), and those who were HIV negative (99.10%). For all analyses, the kappa statistic ranged from 0.325 to 0.795, indicating minimal to moderate agreement (Table 4).[19]

Syphilis prevalence among those whose results on medical records were either pending or unknown

Of the 159 participants whose syphilis results on medical record were either pending or unknown and who had subsequent syphilis reference laboratory testing, five (3.1%) were reactive and 154 (96.8%) were non-reactive. There was no significant difference in the prevalence of syphilis as measured in the reference laboratory between those whose syphilis results were missing or pending in the medical records and those whose results were not: 3.1% vs 4.4%, p=0.491 (Table 4).

Table 4. Positive and negative percentage agreements across categories of HIV status, ANC visit, gravidity, and age among pregnant women enrolled in the 2022 ANC survey and who had serological testing for syphilis in the reference laboratory, South Africa, N=431.

Characteristics	n (Positive % agreement, 95% CI)	n (Negative % agreement, 95% CI)	kappa	p
Age (years)				
15–24	6/10 (60.0%) (52.9–67.1)	172/173 (99.4%) (98.3–100.5)	0.69	<0.001
25 and above	4/9 (44.44%) (38.3–50.6)	235/239 (98.3%) (96.7–99.9)	0.45	<0.001
Antenatal visit type				
1st antenatal visit	1/2 (50.0%) (37.6-62.5)	59/60 (98.3%) (95.2-100.0)	0.48	<0.001
2nd antenatal visit	2/3 (66.7%) (57.2-76.2)	91/91 (100.0%) (100.0-100.0)	0.79	<0.001
3rd or later antenatal visit	7/14 (50.0%) (44.0-56.0)	245/249 (98.4%) (96.9-99.9)	0.66	<0.001
Gravidity				
1st pregnancy	5/8 (62.5%) (54.9-70.2)	144/146 (98.6%) (96.8-100.0)	0.65	<0.001
2nd or more pregnancies	5/11 (45.5%) (39.5-51.39)	256/258 (98.8%) (97.6-100.0)	0.51	<0.001
HIV Status				
Positive	2/7 (28.6%) (19.1-38.0)	79/81 (97.5%) (94.39-100.0)	0.32	<0.001
Negative	8/12 (66.7%) (61.7-71.7)	329/331 (99.1%) (98.1-100.0)	0.69	<0.001

Discussion

We evaluated the PPA, NPA, and overall agreement between syphilis results from medical records and those from laboratory testing. We also assessed syphilis prevalence among those whose results were missing or pending in the medical records. We found a high NPA (99%) but a low PPA (53%), with an overall agreement of 97% between syphilis results based on review of medical records and those based on laboratory testing. A significant majority (14/24 (58.3%)) of women with reference laboratory-confirmed syphilis had a negative or missing syphilis result on their medical records. There was no significant difference in the prevalence of syphilis as measured in the reference laboratory between those whose syphilis results were missing or pending in the medical records (n=159) and those whose results were available ((n=432); 4.4% vs 3.1%; p=0.491)). This meant missing syphilis results in the medical records were unlikely to be a source of selection bias, should South Africa continue to use syphilis data from medical records for surveillance.

Our study shows that relying solely on syphilis results abstracted from medical records could underestimate syphilis prevalence among pregnant women in South Africa. South Africa has sought to transition from laboratory-based sentinel surveillance to the use of routine data or medical records for HIV and syphilis surveillance, yet the medical records abstraction identified 15 individuals with syphilis, which was lower than the 24 cases identified through reference laboratory-based testing. Some explanations for the differences between the prevalence of syphilis based on medical records and that based on reference laboratory testing include the syphilis testing algorithms used in the routine laboratories, errors during the initial recording or abstraction process, inadequate or sub-optimal performance of on-site rapid syphilis tests – although their use was not widespread at the time of data collection – or the occurrence of new infections between the time of testing recorded in the medical records and the survey. It is concerning that the medical record results missed nearly half of the pregnant women with reference laboratory-confirmed syphilis. This finding provides evidence supporting the endorsement of parallel implementation of both surveillance methods over a period, ensuring improvements in the quality of testing, reporting, and recording of syphilis testing in medical records.

According to the WHO, a syphilis prevalence of 5% or greater is considered high.[20] In this study, the prevalence was 4.1%, indicating a moderate level of disease burden in the population. However, an increase in syphilis prevalence was noted on both medical (3.5%) and reference laboratory (4.1%) records as compared to the 2019 syphilis prevalence of 2.6%, estimated from the medical records.[6] The overall syphilis prevalence estimate in the 2022 ANC survey was 3.1% based on medical records,[9] also showing an increase in comparison to the 2019 results.[6] This significant and concerning increase might suggest that existing public health policies and intervention strategies are not sufficient in combating the spread of syphilis. On the other hand, the observed increase in syphilis prevalence could also be explained by better diagnosis and reporting, although the coverage of syphilis testing at 96.4% and 97.5% was similar between the 2019 and 2022 surveys.[6,9]

In the 2019 and 2022 antenatal surveys, syphilis test results were missing or pending among 17.3% and 19.3% of women, respectively,[6,9] raising concerns that missing data could be a source of selection bias in reported estimates of syphilis prevalence. However, we found no significant difference between the syphilis prevalence (based on reference laboratory testing) among those whose results were missing in the medical records (n=159, 3.1%) and those whose results were available (n=432, 4.4%).

Ongoing scale-up of rapid syphilis testing in South Africa is expected to reduce missing data and increase the timeliness of clinically actionable results in antenatal clinics.

Our study had some limitations. We were comparing syphilis test results abstracted from participants' medical records with those from blood samples tested in the reference laboratory. The syphilis results abstracted from medical records were performed at each participant's first ANC visit and around 32–34 weeks gestation as per national guidelines at the time.[12] To the contrary, the blood samples tested at the reference laboratory were collected on the day of the survey, therefore reflecting the syphilis status of participants at the time of the survey. The median gestational age at booking was 16 weeks compared to 27 weeks at enrolment in this analysis. This indicated a median difference of 11 weeks between testing in the medical records and specimen collection for most women.[9] This difference in specimen collection times might have contributed to disagreement in syphilis results between the survey and the routine ANC syphilis test, as some women might have acquired syphilis between the first ANC visit and survey testing.

The syphilis results obtained from medical records were derived from different rapid test kits and laboratory assays, including both treponemal (such as TP) and non-treponemal (such as RPR) tests. In the reference laboratory, only two rapid test kits and an RPR test were utilised. Both rapid tests used in the reference laboratory have a sensitivity of 99% and a specificity of 99%. Based on this performance, only four false negatives were expected, as opposed to the nine false negatives observed for medical records.[18] Due to the utilisation of diverse rapid test kits and the presence of a less sensitive reference standard in the reference laboratory, it is important to acknowledge the likelihood of potential discrepancies or disagreements between these two sets of results.

Conclusion

Based on our literature search, no published studies were found to have specifically addressed the level of agreement between medical records of syphilis results and laboratory-based syphilis testing, pointing to the value of our study and the need to expand the literature base on this issue. This study found that there was good NPA between medical records and reference laboratory-based syphilis testing but poor PPA, with medical charts missing close to half of reference laboratory-confirmed maternal syphilis cases. These findings raise concerns about missed opportunities for timely treatment of pregnant women receiving ANC and underestimation of syphilis prevalence by routine data sources.

Recommendations

- Parallel implementation of surveillance-based medical records and laboratory testing is recommended, ensuring improvements in the quality of testing, reporting, and recording of syphilis testing in medical records.
- Syphilis prevention, care, and treatment for pregnant women and for communities more broadly need to be strengthened in order to minimise its transmission among pregnant women and to their unborn infants.
- Condom use, voluntary male medical circumcision, partner notification and treatment, and ensuring uninterrupted supplies of benzathine penicillin – the drug of choice for syphilis treatment – are potential priority interventions to consider strengthening and scaling up.

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Ethical considerations

This study was approved by the University of the Witwatersrand Human Research Ethics Committee (Medical), clearance number: M22/07/13. It was a sub-study linked to the already approved 2022 Antenatal HIV/Syphilis Sentinel Survey. The primary study had already obtained written consent from participants to use leftover blood specimens in future studies.

Conflict of interest

The authors declare no conflicts of interest.

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