SYSTEMATIC REVIEW

Introduction of rapid syphilis testing in antenatal care: A systematic review of the impact on HIV and syphilis testing uptake and coverage

Andrea Swartzendruber, Riley J. Steiner, Michelle R. Adler, Mary L. Kamb, Lori M. Newman

1. Background

Both syphilis and HIV affect millions of families annually. In 2008, an estimated 1.4 million pregnant women had active syphilis. Further, syphilis causes an estimated 520,000 adverse pregnancy outcomes, including approximately 215,000 stillbirths or early fetal deaths, 90,000 neonatal deaths, 65,000 preterm or low birth weight infants, and 150,000 infected newborns. In 2013, an estimated 1.4 million HIV-infected women gave birth in low- and middle-income countries (LMICs) following introduction of RST; the latter did not appear to adversely impact antenatal HIV screening levels at sites already offering rapid HIV testing and may increase HIV screening among pregnant women in some settings. Qualitative data revealed that women were highly satisfied with RST. Nevertheless, ensuring adequate training for healthcare workers and supplies of commodities were cited as key implementation barriers.

Conclusions: RST may increase antenatal syphilis and HIV screening and contribute to the improvement of antenatal care in LMICs.

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Relatively inexpensive rapid syphilis tests that allow for point-of-care testing are now widely available, with several having been well evaluated in ANC settings and found to have reasonable performance [13]. Where implemented, rapid syphilis testing (RST) has improved coverage of syphilis screening and treatment among pregnant women [14–16]. However, thus far, RST has been more limited than rapid HIV testing (RHT) in most ANC settings [WHO unpublished data, Department of Reproductive Health and Research]. Further, the introduction of RST in ANC settings where RHT is not implemented well, or at all, may impact existing services; it may either serve as an opportunity to improve upon or initiate RHT or, alternatively, it may present additional barriers to optimal RHT. The primary objective of the present study was to conduct a systematic review of the impact of RST on syphilis and HIV screening among pregnant women in ANC settings. The secondary objective was to describe the factors identified as influencing the effective implementation of RST and RHT in ANC settings, as presented in eligible studies.

2. Materials and methods

We performed a systematic review in accordance with the PRISMA guidelines [17], searching PubMed (MEDLINE) using the following keyword combinations: “rapid syphilis” AND “HIV,” “point-of-care” AND “syphilis” AND “HIV,” “immunochromatographic” AND “syphilis” AND “HIV,” and “infectious disease transmission, vertical/prevention and control” [MeSH Terms] AND “HIV” AND “syphilis.” There were no language restrictions. Searches were limited to studies published after 1999. The last search was performed in November 2014. We also reviewed references in seminal papers and review articles, manually searched reference lists of included articles, and identified potential studies upon experts’ suggestions.

3. Results

Our search identified 269 unique records, all of which were screened; 40 articles underwent full-text review and six articles [19–24] met the study eligibility criteria (Fig. 1). Table 1 presents the characteristics of all eligible articles. The six studies represent data from Asia (Cambodia, China, and India), Latin America (Peru), and Africa (Kenya, Tanzania, Uganda, and Zambia). Despite Mabey et al.’s [22] multicountry study including data from Brazil, results from Brazil were excluded since RST was not conducted in ANC settings. Five studies [19–22,24] used a pre-/post-time series design to evaluate antenatal syphilis and HIV testing uptake and coverage following introduction of RST. One also compared syphilis and HIV screening coverage to a comparison area where RST was not implemented [24]. Another study employed a prospective cross-sectional design [23]. Mabey et al. [22] and Strasser et al. [21] reported on the same HIV and syphilis testing coverage outcomes from Uganda and Zambia. Since Strasser et al. [21] provided additional detail on methods and findings, testing outcomes from Uganda and Zambia are presented as reported by these authors.
RHT was available at the time RST was introduced in three [20,21,24] of the five studies presenting unique data on HIV testing. In two studies [19,23], RST and RHT were introduced simultaneously. All studies reported on screening within the first 12 months of RST implementation (range, 2–12 months).

3.1. Syphilis testing coverage outcomes

Table 2 summarizes antenatal syphilis and HIV screening outcomes by study. Baseline levels of antenatal syphilis screening varied, although screening was generally low. Four articles [19–21,24] evaluated the introduction of RST in settings where no pregnant women or only 1% to 2% were tested for syphilis at baseline. Baseline antenatal syphilis screening was highest in Zambia, where 79.9% of first-time ANC attendees were screened. However, additional retrospective data collection was necessary in Zambia owing to rapid plasma reagin test “stockouts” immediately before the introduction of RST.

Fig. 2 shows the proportion of pregnant women screened for syphilis and HIV prior to and following the introduction of RST. All studies reported substantial increases in antenatal syphilis testing at all sites following the introduction of RST. Results did not differ greatly by country, rural/urban setting, whether RHT was already offered or was simultaneously introduced with RST, or levels of syphilis screening prior to introduction of RST following initiation of an intervention to strengthen linkages and referrals between health facilities providing different levels of care and between health facilities and community-based care (‘linked response’), through which prevention of MTCT of HIV services were expanded. In the comparison area, the intervention was not implemented but other initiatives to increase prevention of MTCT of HIV services were implemented by a non-governmental organization.
3.2 HIV testing coverage outcomes

Baseline HIV testing was generally high at sites already implementing RHT. For example, the percentage of first-time ANC attendees screened for HIV prior to the introduction of RST ranged from 80.5% to 97% at the eight health facilities evaluated in Kenya [20]. Similarly, HIV screening among first-time ANC attendees was 95.6% in Uganda and 95.5% in Zambia [21].

Two [21,24] of the three studies that evaluated the introduction of RST in ANC settings where RHT was already being implemented reported increases in HIV screening coverage following the introduction of RST. In Cambodia, RST was introduced in the first quarter of 2009 in the context of an intervention to improve reproductive health services and strengthen linkages between health facilities and community-based services [24]. As part of the intervention, RHT services were decentralized in 2008. Coverage of antenatal HIV testing steeply increased during the intervention and continued to increase following the introduction of RST. HIV screening coverage among pregnant women rose from 6% in 2007 to 55% in 2008. During 2009, coverage was 86% [24]. Strasser et al. [21] reported significant increases in the proportion of first-time ANC attendees screened for HIV following RST introduction in Zambia and Uganda. In Zambia, the percentage increased from 95.6% to 97.8% (P < 0.001) and in rural (96.4% to 97.8%, P < 0.001) and urban (96.4% to 97.8%, P < 0.001) settings. In Uganda, the percentage increased from 95.6% to 97.8% (P < 0.001) and non-statistically significant decreases in two sites which also maintained stocks (88% to 87%, P = 0.84; 95% to 88%, P = 0.57).
implementation of RST, five out of eight sites experienced shortages of HIV test kits following the introduction of RST after one of the tests used in Kenya’s HIV testing algorithm was recalled owing to inadequate performance [20]. Consequently, antenatal HIV screening significantly decreased at affected sites (P < 0.05). However, antenatal HIV testing remained stable (i.e. no significant differences were observed) at the three sites that did not experience stockouts [20].

The two studies that evaluated simultaneous introduction of RST and RHT in ANC settings reported excellent coverage outcomes [19,23]. Pai et al. [23] reported that, in India, only 9% of the pregnant women included in their study had been screened for HIV, syphilis, and hepatitis B upon study entry; nevertheless, following a strategy of “triple point-of-care testing,” 98% were screened for all three infections. In Peru, Flores et al. [19] indicated that testing was conducted in the hospital laboratory during the baseline period, leading to delays in results reporting of up to 30 days and only 60% of pregnant women screened receiving their HIV results in less than 45 minutes. Following the simultaneous introduction of on-site RST and RHT, 100% of women received their results in less than 45 minutes [19].

3.3. Factors influencing effective implementation

All six studies provided information regarding the process of implementing RST and RHT in ANC settings. Box 1 lists the facilitators and barriers that affected RST and RHT implementation. Four studies [19,20,22,23] presented information regarding pregnant women’s perceptions of rapid testing, whereas three studies [19,22,23] measured pregnant women’s satisfaction with rapid testing and reported high levels of satisfaction and a preference for rapid testing. Flores et al. [19] reported that the simultaneous RST/RHT strategy reduced time burdens for pregnant women and significantly shortened the time between testing and the provision of results. Interviews with mothers in Kenya revealed that some pregnant women did not feel adequately informed with regards to testing and felt unable to request additional information from the nurses [20].

At the facility level, Flores et al. [19] noted that the simultaneous RST/RHT strategy required fewer staffing resources. Mabey et al. [22] reported that RST was well accepted by healthcare workers, who found it easy to perform and were able to test more people per day using RST. Two articles [20,22] cited ensuring adequate training for healthcare workers implementing RST (performing tests, interpreting results, maintaining records, managing stock, etc) as a challenge in the context of frequent staff transfers and high staff turnover.

At the health systems level, three studies [20–22], representing findings from seven countries, noted that widespread stockouts decreased pregnant women’s access to testing. Delvaux et al. [24] described the low quality of reproductive health care, reflected by high estimates of maternal mortality, a low proportion of births assisted by skilled personnel, and a low proportion of births in a health facility, as a challenge to the scale-up of services for pregnant women. However, two studies [21,22] highlighted the introduction of RST as a tool for health system strengthening. Strasser et al. [21] proposed that healthcare worker training and quality management procedures implemented in support of the introduction and integration of RST within ANC may have led to the significant increases in antenatal HIV screening observed in Uganda and Zambia. It was further noted that regular consultations with national and local health authorities focused on maternal and child health, HIV/AIDS, and sexually transmitted infections may have stimulated health system strengthening [20,22].

4. Discussion

This study systematically reviewed antenatal syphilis and HIV screening uptake and coverage following introduction of RST in ANC settings in LMICs. All six of the included articles were published from 2011 onward, reflecting that RST has only recently been introduced into the ANC setting. The studies reported data from eight countries in Africa, Asia, and Latin America. Hence, study findings may be relevant to a range of LMICs.

All studies and settings reported substantial increases in antenatal syphilis screening following introduction of RST, whether in urban or rural settings, low-level health facilities, or tertiary referral hospitals. Even sites where no or very few women were screened for syphilis prior to RST introduction were able to achieve high levels of screening within months of implementing RST, perhaps aided by existing infrastructure and implementation of RHT in some settings. Moreover, it appears that the introduction of RST did not negatively impact antenatal HIV screening levels at sites already conducting RHT and may have increased HIV screening among pregnant women in some settings. Simultaneous introduction of RST and RHT may be a useful strategy for increasing both syphilis and HIV screening coverage among pregnant women where neither is currently being conducted. However, it should be noted that a high syphilis testing coverage within ANC settings may still miss pregnant women who do not attend ANC, and testing coverage...
Abbreviations: RST, rapid syphilis testing; RHT, rapid HIV testing.

Factors influencing effective implementation of rapid syphilis testing and rapid HIV testing in antenatal care settings.

### Box 1

Factors influencing effective implementation of rapid syphilis testing and rapid HIV testing in antenatal care settings.

<table>
<thead>
<tr>
<th>Patient-level factors</th>
<th>Facilitators</th>
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<tbody>
<tr>
<td>• Pregnant women were highly satisfied with RST [19,22,23]</td>
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<tr>
<td>• Pregnant women preferred finger prick over venipuncture [19,22]</td>
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<tr>
<td>• Rapid testing reduced patient burdens (reduced waiting times and provided same-day results and treatment) [19]</td>
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<tr>
<th>Barriers</th>
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<tr>
<td>• Some women reported not being fully informed about testing and not feeling able to ask nurses for more information [20]</td>
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<th>Facility-level factors</th>
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<tr>
<td>• Rapid testing required fewer staff resources (time and number of personnel) [19]</td>
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<tr>
<td>• Rapid testing was well-accepted by healthcare workers [22]</td>
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<td>• RST and immediate treatment increased healthcare workers’ job satisfaction [22]</td>
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<tr>
<td>• Stockouts of HIV-related commodities limited to an individual facility negatively affected HIV testing at that site [21]</td>
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<tr>
<td>• Frequent staff transfers and turnovers was a training challenge and adversely impacted quality of testing [20,22]</td>
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<tr>
<th>Health system factors</th>
<th>Facilitators</th>
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<tr>
<td>• Additional healthcare worker training and improved quality management procedures supported introduction of RST and may have led to improvements in HIV testing outcomes</td>
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<tr>
<td>• Regular consultation among national and local health authorities concerned with maternal and child health, HIV/AIDS, and sexually transmitted infections stimulated health system strengthening [22]</td>
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<td>• Quality assurance programs enabled assessment of facility proficiency in performing RST and interpreting results and identification of healthcare workers needing training and engaged local laboratory staff to support quality testing [22]</td>
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<tr>
<td>• Decentralization of RST and RHT and systems of referral between health facilities and between health facilities and community-based services increased testing coverage [24]</td>
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<tr>
<td>• Widespread test commodity stockouts limited access to testing [20–22]</td>
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<tr>
<td>• Low access to and quality of reproductive health services limited testing coverage [24]</td>
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Abbreviations: RST, rapid syphilis testing; RHT, rapid HIV testing.

will therefore not translate to reductions in morbidity and mortality without adequate treatment coverage.

Rapid testing appeared acceptable to pregnant women. Qualitative data revealed that pregnant women were highly satisfied with and preferred rapid testing [19,22,23]. High patient satisfaction may have been due, at least in part, to reduced time burdens since rapid tests allow same-day results and treatment [19]. Only Fleming et al. [20] documented patient concerns, specifically in relation to a lack of information regarding rapid tests, which the authors suggested could be addressed by ensuring health workers are adequately trained or through stronger community outreach concerning testing. Benefits of rapid testing for healthcare providers were also documented, including increased efficiency [19,22] and job satisfaction [22]. These findings are consistent with patient and provider perspectives from other studies examining point-of-care testing and service integration in LMICs [25–27].

Challenges to effective implementation included ensuring adequate training and supplies of high-quality commodities. Frequent staff transfers, test quality, and higher-level supply management issues adversely impacted implementation of rapid testing. These are commonly cited barriers to quality clinical care and scale-up of health programs in resource-limited settings [26]. In line with the suggestion that the introduction of RST in ANC settings can serve as a tool for health systems strengthening [21,22], settings introducing RST may consider specific coordination measures related to training and stock management to support increased coverage of both antenatal HIV and syphilis screening and an improved overall quality of ANC. In addition, combined RST/RHT quality assurance protocols and proficiency testing may help to identify and address issues related to quality testing as well as potential provider error in accurately interpreting and documenting multiple rapid test results. The WHO has recently released an information note reiterating the need for improved quality assurance measures for rapid testing, particularly related to HIV [28]. Further, regular meetings with health officials responsible for maternal and child health, HIV/AIDS, and sexually transmitted infections to discuss program performance, strengths, and weaknesses may be important for stimulating health system improvements.

### 4.1. Strengths and limitations

The present study is subject to several limitations. Due to the restricted number of eligible studies and reporting differences, we were unable to conduct a meta-analysis, although this would have more accurately addressed the issue discussed. The study is also subject to limitations inherent to review studies. For example, all six articles reported on antenatal syphilis and HIV testing for a period of up to 1 year following the introduction of RST. Therefore, conclusions regarding screening after RST has been sustained for more than a year are not possible. However, other studies have reported a high, sustained coverage of antenatal syphilis screening for several years following the introduction of RST [14,29]. Additionally, testing coverage outcomes may not be directly attributable to RST. For example, RST was evaluated in the context of larger interventions in some studies [20,24]. Finally, the present study did not examine the quality of testing, gestational age at testing, outcomes related to timely and appropriate treatment, or impact on rates of MTCT of syphilis and HIV—the ultimate measure of program success.
Nevertheless, the study possesses particular strengths. The original studies are geographically varied and represent data from high- and lower-burden countries. In addition, some studies reported on large samples of pregnant women (greater than 10,000) and included data from entire districts [21,22,24].

4.2 Implications

The findings suggest that RST can quickly yield large increases in antenatal syphilis screening. Where RHT was being implemented at the time of RST introduction, antenatal syphilis screening approached antenatal HIV screening levels within 1 year, with no negative impact on HIV screening. In some sites, RST may serve as a tool for improving implementation of RHT and antenatal HIV screening coverage. Simultaneous introduction of RST and RHT, as well as other rapid tests (e.g. hepatitis B), appears feasible and may increase screening for each infection. RST may contribute to the EMTCT of both syphilis and HIV and serve as an opportunity to strengthen ANC and health systems in LMICs. Identifying women in need of services to prevent MTCT of HIV and syphilis is critical but insufficient for eliminating adverse pregnancy outcomes and infant infections due to HIV and syphilis. Future efforts and evaluations will be necessary to ensure that pregnant women who screen positive receive timely and appropriate interventions to prevent MTCT of syphilis and HIV.

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Conflict of interest

The authors declare that they have no conflicts of interest.

References