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COST-EFFECTIVENESS

The cost-effectiveness of 10 antenatal syphilis screening and treatment approaches in Peru, Tanzania, and Zambia

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ABSTRACT

Objective: Rapid plasma reagin (RPR) is frequently used to test women for maternal syphilis. Rapid syphilis immunochromatographic strip tests detecting only *Treponema pallidum* antibodies (single RSTs) or both treponemal and non-treponemal antibodies (dual RSTs) are now available. This study assessed the cost-effectiveness of algorithms using these tests to screen pregnant women. *Methods:* Observed costs of maternal syphilis screening and treatment using clinic-based RPR and single RSTs in 20 clinics across Peru, Tanzania, and Zambia were used to model the cost-effectiveness of algorithms using combinations of RPR, single, and dual RSTs, and no and mass treatment. Sensitivity analyses determined drivers of key results. *Results:* Although this analysis found screening using RPR to be relatively cheap, most (>70%) true cases went untreated. Algorithms using single RSTs were the most cost-effective in all observed settings, followed by dual RSTs, which became the most cost-effective if dual RST costs were halved. Single test algorithms dominated most sequential testing algorithms, although sequential algorithms reduced overtreatment. Mass treatment was relatively cheap and effective in the absence of screening supplies, though treated many uninfected women. *Conclusion:* This analysis highlights the advantages of introducing RSTs in three diverse settings. The results should be applicable to other similar settings.

1. Background

Antenatal syphilis causes a high burden of disease worldwide, with over half of pregnancies in women with untreated syphilis leading to adverse effects, including stillbirth, neonatal deaths, prematurity, and low birth weight [1]. Despite syphilis treatment being effective and inexpensive [2–4], many pregnant women remain undiagnosed owing to lack of symptoms and the unavailability of laboratories equipped to offer syphilis screening using traditional tests, such as rapid plasma reagin (RPR), in most antenatal care (ANC) clinics [5–7]. Recent improvements in syphilis screening have been made possible by the introduction of rapid syphilis tests (RSTs), which hold several advantages over the traditional RPR [8], including not requiring laboratory infrastructure (e.g. electricity and equipment) and their ability to be used correctly by different health professionals [9]. As such, they can be performed at the point of care, allowing for immediate treatment, and have been shown to be acceptable to patients [10,11]. However, most current RSTs are treponemal tests and are therefore reactive to both current and past syphilis infections [9]. In contrast, RPR is a non-treponemal test used to diagnose active infection despite its low sensitivity [12,13]. New dual RSTs with both treponemal and non-treponemal components have been recently developed [14,15], but currently cost US $2.50 per test, which is two to five times more than single treponemal tests.

Numerous studies have reported on the cost or cost-effectiveness of antenatal syphilis screening interventions [2,16–20,35], while others have modeled the cost-effectiveness of different screening approaches

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[21–25] or the burden and cost-effectiveness of national or regional screening programs [3,26]. All of these studies show that antenatal syphilis screening and treatment is highly cost-effective, but none has compared a broad range of possible screening and treatment approaches, nor have they accessed a detailed dataset for multiple countries to parameterize their models.

Using cost and outcome data from evaluations of the RPR and single RST in three countries, this study models the cost-effectiveness of maternal syphilis screening and treatment approaches in Peru, Tanzania, and Zambia.

2. Materials and methods

The present analysis considers 10 screening and treatment approaches (Fig. 1). Four approaches involve single tests (Fig. 1A–D), four entail a sequence of tests (Fig. 1E–H), and additional scenarios consider no screening or treatment (Fig. 1NS) and mass treatment without screening (Fig. 1I). Standardized facility-based data were used to model the cost-effectiveness of each approach.

2.1. Setting and primary data

Between 2009 and 2010, study clinics in Peru, Tanzania, and Zambia undertook operational research to estimate the cost-effectiveness of introducing treponemal-based RSTs for the screening of maternal syphilis in ANC and prevention of mother-to-child transmission of HIV programs [8,27]. Prior to introducing RSTs, a baseline assessment of current syphilis screening using the RPR test was undertaken, including collection of the numbers of women screened and treated, and the associated costs (Supplementary Material S1). Data from these studies [18,28; unpublished data] were used to parameterize the models.

Table 1 presents characteristics of the clinics in Peru, Tanzania, and Zambia. These three settings represent a range of maternal syphilis prevalence: 1.2% in Peru, 10.0% in Tanzania, and 12.4% in Zambia. Although all three countries had a national policy of universal antenatal syphilis screening, in the period prior to RST introduction, only about 60% of the studied facilities in these countries performed any syphilis screening using RPR. Average country screening rates during the baseline RPR period ranged from between 17.8% and 91.1%, improving to between 86.1% and 97.3% during the RST pilot. Average treatment rates also improved from between 56.7% and 76.8% at baseline to between 77.4% and 93.9% during the RST pilot. These improvements can be attributed to both the point-of-care nature of the RST test and the increased supervision given to clinics [8]. More details on each setting can be found elsewhere [18].

2.2. Modeling

Outcomes and costs were modeled initially at the average observed scale of screening per country, converted to a common denominator of 1000 ANC attendees.

Data from each setting were collected on the number of women attending the clinic, number screened, proportion reactive for the RPR and single RST, number of women treated, and loss to follow-up (Table 1). An active syphilis case is traditionally defined as RPR positive, confirmed by a laboratory-based treponemal assay such as the *Treponema pallidum* particle agglutination (TPPA) or *Treponema pallidum* hemagglutination assay (TPHA). Field performance data (sensitivity and specificity) of the single RST and clinic-based RPR test against a laboratory-based RPR and TPPA test (Table 2) were used to estimate the proportion of reactive tests that were likely true syphilis cases. For Peru, detailed data were available to assess field performance. For Zambia and Tanzania, data from a field performance evaluation in South Africa were used [29]. The sensitivity of the dual RST was obtained from the literature [14,30]. The percentage of women with a single positive or negative RST result with different laboratory RPR and/or TPHA results is presented in Supplementary Table S1.

The impact model estimated both the intermediate outcomes as well as final outcome measures: true cases treated, cases missed, and overtreatment. Further details of how specific outputs for each algorithm were calculated are given in Supplementary Material S2.

Standard approaches were used to estimate disability-adjusted life years (DALYs) averted from treating pregnant women with syphilis [17,19,26]. Adverse outcomes averted were obtained from Gomez et al. [1]. Disability weights for congenital syphilis and low birth weight were 0.315 and 0.291, respectively. Stillbirth was treated as a full life lost and attributable adverse outcomes were captured through to end of life; country-specific life expectancies and a 3% discount rate were applied. Ranges applied in the sensitivity analysis were taken from the literature [3,31,32]. All DALY inputs are shown in Supplementary Table S2.

Total and unit costs were estimated. Total costs allowed for basic comparisons of budget impact, while unit costs allowed for comparison

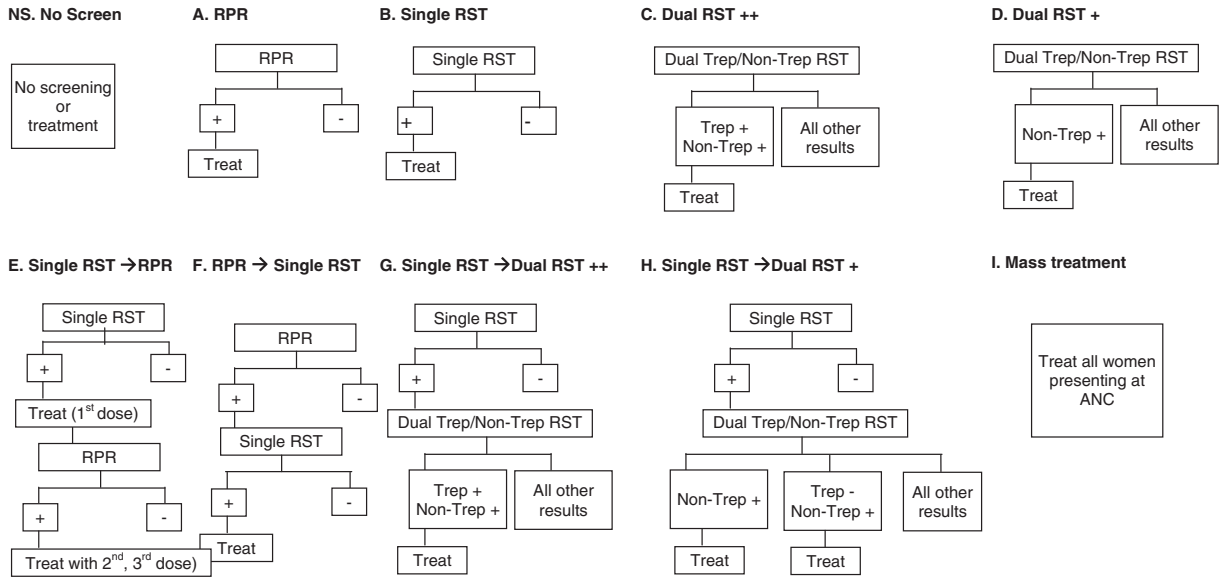

Fig. 1. Screening and treatment approaches. +, Only non-treponemal antibody test results used; ++, Dual RST – both treponemal and non-treponemal antibody test results used to determine a positive case; Trep, Treponemal antibody test result; non-Trep, Non-treponemal antibody test result; RPR, Rapid plasma reagin; RST, Rapid syphilis test.