The costs of accessible quality assured syphilis diagnostics: informing quality systems for rapid syphilis tests in a Tanzanian setting

Objectives: To determine the costs of RSTs as compared to RPR when implemented in a Tanzanian setting, and to determine the relative impact of a quality assurance (QA) system on the cost of RST implementation.

Methods: The incremental costs for RPR and RST screening programs in existing antenatal care settings in Geita District, Tanzania were collected for nine months in subsequent years from nine health facilities that varied in size, remoteness, and scope of antenatal services. The costs per woman tested and treated were estimated for each facility. A sensitivity analysis was constructed to determine the impact of parameter and model uncertainty.

Findings: In surveyed facilities a total of 6,362 women were tested with RSTs compared with 224 tested with RPR. The range of unit costs was $1.76 - $3.13 per woman screened and $12.88 - $32.67 per woman treated. Unit costs for the QA system came to $0.51 per woman tested, of which 50% were attributed to salaries and transport for project personnel.

Conclusions: Our results suggest that rapid syphilis diagnostics are very inexpensive in this setting and can overcome some critical barriers to ensuring universal access to syphilis testing and treatment. The additional costs for implementation of a quality system were found to be relatively small, and could be reduced through alterations to the program design. Given the potential for a quality system to improve quality of diagnosis and care, we recommend that QA activities be incorporated into RST roll-out.

Introduction

The burden of curable sexually transmitted diseases remains high in many low-income countries. According to a WHO estimate, 12 million people are infected with syphilis each year, and 90% of infections take place in low-income countries[1]. Syphilis in pregnancy is a leading cause of adverse birth outcomes, and is believed to contribute to 650,000 fetal and neonatal deaths each year in developing countries[2]. These adverse birth outcomes can be easily prevented with treatment, however symptoms of primary syphilis are often unnoticed in women and later stages are often asymptomatic. Routine screening for syphilis during pregnancy has been found to reduce adverse birth outcomes [3] and is therefore policy in most sub-Saharan African countries [4-7].

Adverse outcomes attributable to maternal syphilis infection can be prevented with a single dose of benzathine penicillin[8]. As symptoms of primary syphilis are often unnoticed in women and later stages are often asymptomatic, universal screening for syphilis infection during pregnancy is the preferred intervention for control of congenital syphilis and is policy in most sub-Saharan African countries[9-12].

The traditional lab-based diagnostic for detection of syphilis, the Rapid Plasma Reagin (RPR) test, is often not implemented in low-resource settings due to a number of implementation barriers such as electricity, equipment and training; according to Gloyd, et al. (2001) only 38% of all pregnant women are screened for syphilis in sub-Saharan Africa[13 14]. The RPR test cannot be performed on whole blood, and requires a refrigerator for the reagents and a rotator for test processing[9-12]. Furthermore, even where screening is available, diagnostics such as RPR are commonly operated by users without lab training and in the absence of a quality system or supportive supervision. While RPR has good sensitivity and specificity when performed in a lab setting, ranging from 86-100% and 93-98% respectively, environmental and infrastructural factors can compromise the validity of the tests or lead to variability in test results.

Rapid diagnostics could drastically improve access to and quality of syphilis screening programs in low-resource settings [13 14]. Unlike RPR, RSTs can be stored at room temperature, performed using whole blood, give results within 30 minutes, and do not require additional laboratory infrastructure[15]. Diagnostic accuracy of RSTs vary by type; sensitivity and specificity of the SD Bioline using whole blood in clinic was found to range from 85.2-100% and 98.1-99.4% respectively[2].

As with many other diagnostics, however, RST validity and accuracy can be compromised due to exposure to high temperatures or humidity, manufacturing issues, or operator errors. In order to ensure accuracy of diagnosis and quality of care, implementation of a quality assurance (QA) system alongside rapid diagnostics is widely advocated [16-19]. A QA system will often be made up of several components, including: an in-built control in the test device to verify the specimen was adequate (Internal Quality Control); an incoming inspection of test kits to ensure their accuracy has not been compromised during transport; regular testing with known positive and negative samples to evaluate accuracy of the test kits (External Quality Control); and regular proficiency testing of the operator with blinded positive and negative samples (External Quality Assessment). In addition, adequate training and re-training, monitoring and supervision are essential to ensure the quality of diagnostic testing. Each component of a QA system can be implemented at differing frequencies and intensities, in order to match the specific need of the health system in question; the ideal mix of QA components will vary by setting.

The costs of monitoring and supervision, training, and QA as part of rapid diagnostic test implementation are often overlooked[19]. There is very little information on the costs of a QA system as implemented alongside rapid tests. The objective of this study is to estimate and compare the costs of RSTs to RPR in this Tanzanian setting, and to determine the relative impact of a QA system on the cost of RST implementation.

Methods

The Intervention

Prior to the introduction of RSTs, RPR tests were routinely conducted within MCH units by staff nurses, with no regular training or quality assurance in place. The typical RPR testing process in Tanzania is described in further detail by Terris Pretholt, et al[20].

In September 2009, a pilot program for RST implementation was established by the National Institute for Medical Research (NIMR) in Geita District. All health workers conducting screening were given intensive training at the start of the project, and routine monitoring and supervision were conducted by NIMR staff to assess compliance and ensure quality of diagnosis and patient care. In addition, a robust QA system was introduced in February 2010 to ensure diagnostic accuracy. The QA system included each of the components described above. External Quality Control was conducted with known positive and negative serum samples, which were prepared from whole blood at the NIMR lab in Mwanza and delivered to health facilities on a monthly basis. External Quality Assurance was conducted with Dried Tube Specimens – a relatively new approach to quality control specimens which does not require cold-chain support and can be easily produced from whole blood[21]. These were also produced at the NIMR lab, and delivered alongside serum samples.

Cost Analysis

We collected cost and output data from 9 health facilities which varied in size, remoteness, and scope of The incremental costs for RPR and RST screening programs in existing antenatal services provided, including three dispensaries (D), five health centers (HC), and one district hospital (DH). Incremental financial and economic costs were collected retrospectively from a provider's perspective, for a nine-month period in 2009-10 for RSTs. RPR costs were retrospectively collected for a nine-month period in 2007-08 from six of the nine facilities; three facilities were excluded from the RPR analysis due to unavailability of output data (D2, HC5 and DH). Cost data was collected using a combination of standard step-down accounting and micro-costing methods[20 22-24]. Costs were collected in Tanzanian shillings (TZS) and converted to United States Dollars (USD) using the average exchange rate for 2010 (TZS

1,569.04 = 1 USD)[25], then adjusted to 2012 USD using inflation rates from the Consumer Price Index[26]. All costs are presented in 2012 USD.

Cost components include capital and recurrent costs for testing and treatment at the health facility level, as well as startup, capital and recurrent costs for RST implementation and quality assurance. In line with the existing literature on syphilis screening in antenatal care, our approach in cost analysis was incremental to existing antenatal care services. We only considered new inputs required to add syphilis screening to existing ANC services; general administrative or overhead costs required to run the health facilities were not included [20]. Where syphilis screening was conducted alongside HIV screening, costs such as personnel time and building space were considered to be 'shared costs' and divided equally between HIV and syphilis screening [20]

Project outputs and unit costs

Project outputs were collected retrospectively from patient registers for RST and RPR over the same periods as the costs. Intermediate outputs include number of: pregnant women tested, reactive tests, and women treated. Unit economic costs per woman tested, and per woman treated were calculated for each facility, and for all facilities combined.

Sensitivity Analysis

A univariate sensitivity analysis was constructed to determine the impact of uncertainty in cost and output collection. We analyzed factors in the sensitivity analysis which could not be directly observed, or which varied significantly amongst facilities, including: clinic opening hours, supply wastage, staff time taken for testing, staff salaries, and building costs, discount rate, and life of the project. In addition, we conducted a multivariate analysis of cost and output factors, simultaneously varying all factors above with uniform distribution between the minimum and maximum values observed, over 1,000 iterations.

Results

Project Outputs

Over a period of nine months in 2009-10, a total of 9,372 pregnant women were tested with RSTs in the nine surveyed facilities, covering 87% of women attending antenatal care. Nine hundred twelve (10%) tested positive, of which 92% (841 women) were treated. At some facilities, more women were screened than were enrolled in ANC – these women were either residents outside the ANC catchment area and not captured by the recording system or had been previously enrolled in ANC but not tested until the introduction of RSTs.

[table 1 here]

Over a similar time period in 2007-08, a total of 838 women were screened with RPR in six facilities. Disaggregated ANC attendance rates during this period were not available, however we found that testing rates overall for Geita District during this time were 17.8% [27]. Assuming that ANC attendance rates remained relatively constant from 2007/8 to 2009/10 for the facilities included in this analysis, this would represent about 12% of women attending ANC at these facilities. Outcome data were unavailable from two facilities, and one facility conducted no testing during this period; these three facilities were therefore dropped from RPR cost analysis. Two hundred and thirty women (27%) were recorded as reactive, although reactivity rates varied from 9%-59% of all women presenting for screening (Table 1). As there was no re-testing of samples with a gold standard, the true prevalence of syphilis in these facilities is unknown, however a study conducted in 2001 found an average of 8% RPR reactivity in the area[28]. This suggests that some facilities had high false-positive rates. Treatment rates for RPR also varied widely (11%-90%) but overall only 66% of those testing positive were treated.

Costs

Total economic costs incurred at the health facility level for screening and treatment using RSTs over a nine-month period ranged from $751.43 to $5,862.71. RST costs at the health facility level were driven by the high unit costs of rapid syphilis tests ($1.10 per test kit); test kits accounted for 41-73% of total health facility costs. Personnel time accounted for 11-32% of costs.

Total costs for the QA system ranged from $513.37 to $554.74 by health facility over the 9-month costing period. Costs varied due to differences in transportation costs associated with reaching more remote clinics and differences in staff salaries. An incoming inspection of test kits cost $36.46 at the district level for each shipment of kits, or an average of $0.70 per health facility. One External Quality Control panel cost an average of $22.72 per health facility, while one External Quality Assessment panel cost an average of $33.11 per health facility. Salaries and transport for NIMR personnel accounted for 61% of costs for External Quality Control, and 50% of costs for External Quality Assessment. One monitoring and supervision visit from NIMR personnel cost an average of $23.49 per health facility. Finally, start-up and training costs ranged from $184 - $401 by facility, dependent on the number of nurses trained. Inclusion of start-up and training, monitoring and supervision, and QA costs increased total costs for RST screening to $1,540-$6,777.

Total economic costs for screening and treatment using RPR ranged from $203.21 to $506.86. Personnel accounted for 23%-34% of costs, while supplies accounted for 35%-47%. A significant proportion of costs were incurred due to refrigeration of the reagent for RPR; combined equipment and operation /maintenance costs represented 13%-34% of costs.

[table 2]

Costs were not collected for start-up/training or QA as these activities did not occur under observation period of the RPR costing. Costs incurred in district supervision were excluded from both RST and RPR cost analysis due to unreliability of reported supervision rates. The total economic cost of one supervisory

visit from District Coordinators was found to be $111.09. As District Coordinators are responsible for oversight of ANC, PMTCT, and syphilis screening activities, this cost is shared amongst all activities.

Unit costs

Unit costs for RST screening at the health facility level were $1.92 per woman screened and $21.35 per woman treated. Costs per woman screened varied from $1.74 at HC_4 to $3.13 at D_1.

QA costs varied from $0.15 - $2.25 per woman tested. Inclusion of start-up, training and QA costs increased unit costs to $2.67 per woman screened (ranging from $2.03 - $6.42) and $29.70 per woman treated ($19.19 - $66.96). Economies of scale were apparent in RST testing; costs per woman screened were lower at larger health facilities, reflecting a spreading of fixed costs over more women. As QA is a large fixed cost, economies of scale are more evident when QA costs are included.

For RPR screening, unit costs were $2.17 per woman screened (ranging from $1.70-$2.97), and $12.69 ($5.96 - $74.34) per woman treated. Variations in RPR unit cost did not reflect facility size.

[Table 3]

Sensitivity Analysis

We conducted a univariate sensitivity analysis in order to understand the impact of assumptions made in collection of cost data and output measures on unit costs at the health facility level. RST costs were sensitive to estimates surrounding staff time and supply wastage, while RPR costs were highly sensitive to staff time estimates. Decreasing staff time by 50% reduced the average unit cost per woman tested with RPR to 1.93. Increasing the estimated supply wastage by 50% increased the estimated unit cost per woman tested with RST to 2.42, higher than the base case scenario for RPR.

[Table 4]

A multivariate sensitivity analysis was conducted varying staff time and working hours, supply wastage, salaries and discount rate, as well as output factors including testing rates,syphilis prevalence, and

treatment rates for positive women and their partners. All factors were varied over a uniform distribution between the minimum and maximum values observed. Over 1,000 iterations, unit costs for RST testing were lower than those for RPR 83% of the time (Figure 1). Lower cost is largely related to economies of scale achieved through higher utilization under RST; further research is needed to determine whether this increased access is sustainable over a longer term.

[Figure 1]

Discussion

Cost of Screening

This analysis found the average unit cost at the health facility level for routine screening with RSTs to be $1.92 per woman screened. This was lower than the estimated unit cost for RPR ($2.17 per woman screened), although direct comparisons varied by health facility. Our results suggest that rapid syphilis diagnostics are very inexpensive in a Tanzanian setting, and less expensive than RPR, even where RPR is feasible.

Previously published costs per woman screened with RSTs vary between $1.25 and $4.87 depending on prevalence rates, outcome probabilities used, and costs included in the analysis [29-32]. Our finding that RST costs for testing and treatment are lower than those for RPR is unique; previous studies have reported RST costs per woman screened to be $0.17 – $1.07 higher than those for RPR. The lower costs for RST are largely a reflection of economies of scale in implementation – greater access allows fixed costs to be spread over a larger number of women. This may also reflect higher personnel costs for RPR testing in Tanzania than those previously recorded, incurred through manual completion of tasks which could be performed by equipment in settings with better laboratory infrastructure.

The Tanzanian Ministry of Health and Social Welfare has expressed plans to scale up RST implementation throughout the country following this demonstration project, and has accordingly

changed the national syphilis screening guidelines. We found the startup and training costs to vary

between $184 - $401 per facility

Access to Screening

During the study period, syphilis screening rates for women in antenatal care increased under RST

implementation. In surveyed facilities, the total number of women screened under RSTs was 88% of total

ANC attendees, as compared to only 12% of ANC attendees screened with the RPR method.

The increase in number of women tested may be attributable to increased acceptability of the tests by

health care workers, additional monitoring by project staff, or a reduction in stock outs of essential

supplies during the RST period. Because they can be ordered in bulk and stored for long periods of time

without refrigeration, RSTs may be less susceptible to stock-outs than RPR test supplies. RSTs were

preferred by both health care workers and ANC clients, and found to motivate staff who were happy to

provide a diagnostic service and immediate treatment to patients [27].

This study did not evaluate whether increased access to screening was sustained after the project period

completed; further research is therefore needed to determine the long-term utilization patterns of RST as

compared to RPR.

Access to Treatment

Treatment of reactive patients also increased under RST implementation. The introduction of RST

witnessed a 30% increase in the number of reactive cases treated compared to RPR. Due to the rapid

nature of the tests, RST results are available the same day, reducing loss-to-follow up and increasing

access to treatment.

Increased access to prompt treatment has the potential to greatly reduce adverse pregnancy outcomes. A

single dose of penicillin in pregnancy has been proven to reduce the likelihood of adverse birth outcomes

due to syphilis. A study conducted in 2002 in a neighbouring district in Tanzania found that following treatment, there was no increased likelihood of adverse outcomes among women with high-titre active syphilis, which was determined thought to be correlated with adverse pregnancy outcomes[28], as compared to RPR-negative women. A more recent panel of experts with the WHO / child health epidemiology reference group (CHERG) has evaluated the literature on maternal syphilis, and estimated that treatment can avert adverse outcomes in 48.7% of all women with untreated syphilis in pregnancy, regardless of titre [33]. In this study setting, this would mean that treatment has prevented 111 stillbirths, 68 miscarriages, 163 cases of congenital syphilis, and 106 neonatal and infant deaths.

Cost of QA

The QA costs reported reflect current QA implementation for the quality system alongside RST in Tanzania. This includes joint monitoring and supervision / QA visits to all health facilities once per month, with External Quality Control and External QA conducted simultaneously. QA costs were not observable for RPR testing, and therefore not reported in this study. However QA would theoretically be a necessary component of any syphilis screening program, and a robust QA system supporting screening with RPR would likely carry similar costs.

The costs and effects of QA are variable according to implementation, and a QA program can be designed for different settings with different disease prevalence levels and to suit different budgets. In areas of high disease prevalence, WHO guidelines recommend that quality controls and monitoring are performed weekly or even daily to ensure high accuracy of testing and proficiency of personnel[34]. Increasing the frequency of on-site External Quality Control samples to a weekly basis would increase External Quality Control costs from $21.79 to $35.52 per month. In areas of low disease prevalence, periodic External Quality Assessment at a lower frequency is advisable as part of a continuous proficiency assessment of personnel, thereby reducing re-training events and increasing confidence of operators. Decreasing the frequency of External Quality Assessment schemes from monthly to quarterly would reduce costs by a third, assuming samples are also manufactured quarterly.

Altering the frequency of QA activities will influence the cost of the program, although care should be taken to ensure the scheme is sufficient to meet the needs of the system. Reduced intensity of Quality Assurance could lead to inaccuracy in testing, especially in areas where there is high turnover of staff. This might result in high numbers of false positive or false negative test results. The importance of QA in ensuring the quality and accuracy of testing is further discussed by Mabey, et al[27].

The number of events necessary to validate the test kits after shipment can be reduced by centralizing the supply and inventory system, reducing the number of actors in the distribution channel, and ensuring adequate temperature monitoring, although minimum performance requirements should be established to avoid unnecessary time-consuming and unproductive testing.

Decentralization of QA responsibilities to the District level and integration with other projects can also influence QA cost. The majority of costs for both External Quality Control and External Quality Assessment presented reflect transport and personnel costs associated with bringing NIMR personnel from Mwanza for delivery of QA materials, monitoring and supervision. Where District Coordinators are already conducting monitoring and supervision for other programs the incremental cost of integrating a QA component would be minimal.

Finally, QA is a fixed cost at clinic level and therefore exhibits economies of scale in implementation. Unit costs for QA activities varied from $0.15 per woman tested at the largest health facility (DH) to $2.25 per woman tested at the smallest health facility (D_1). Given the economic gains from implementing QA at larger health facilities, a valid interim solution may be to implement QA at larger health facilities first, expanding to smaller health facilities when economically possible. However it is often the small clinics that need it most.

Limitations

There are a number of limitations to this study which may affect generalisability of the results. Primarily, it is difficult to determine the potential changes in access to and cost of services upon scale-up of rapid

testing and transfer of QA responsibility to the MoH. Although the pilot project was designed to maintain

minimal impact on the health system, NIMR did provide support that may not be sustainable under the

MoH. For example, NIMR provided additional support to the supply chain throughout the project,

decreasing the frequency of supply stock-outs and thereby increasing access to screening and treatment

for syphilis. It is also possible that frequency and intensity of monitoring/supervision will change

substantially if decentralized to the district level, possibly impacting the success of the QA system.

This study also did not confirm diagnoses with a gold standard, making it difficult to estimate health

outcomes (such as DALYs). The lack of a gold standard also prevented confirmation that the introduction

of RSTs along with a robust quality system improved the accuracy of diagnosis. We also found some

gaps in cost data for RPR testing. We used original RPR cost data from a previously published study in

Geita District [35] where data was lacking, inflated to 2012 USD[26]. Finally, the impact of QA on total

costs of RST screening per woman is likely underestimated. QA activities were not started in Tanzania

until February 2010 after the screening program had been running for three months, thus potentially

underestimating costs by up to a third. Table 3 provides the building blocks to estimate the replication

costs of QA under different configurations.

As noted by McIntiyre et al.[36], access to health care or health services is a multidimensional concept

and not directly measureable from utilization data. Further dimensions of access include hours and

location of services, expectations and attitudes between providers and patients, and range of services

provided relative to need. Mabey et al.[27] further discuss acceptability of RSTs amongst clients and

health care workers in this setting, however this project was not designed to estimate other components of

health care access.

Conclusions

The cost-effectiveness of RSTs has been previously proven. This study reports the relative costs of a

quality control system, when implemented alongside RST testing in a Tanzanian setting. We find that QA

has a small additional cost to rapid syphilis screening, but potentially improves quality of diagnosis considerably. QA costs could be further reduced through alterations in the program design, including changes in frequency of QA activities, integration with other programs, and decentralization to the district level. Rapid syphilis screening services are currently being expanded throughout the country as part of the Ministry of Health's efforts to increase access to syphilis screening in antenatal care. Given the small incremental costs and potentially significant improvements in quality of diagnosis, we argue that roll-out of RSTs should include a QA and monitoring/supervision system in order to improve the validity and quality of diagnosis and treatment.

References

1. World Health Organization. The Global Elimination of Congenital Syphilis: Rationale and Strategy for Action, 2007.

2. Kamb ML, Newman L, Riley P, et al. A Road Map for the Global Elimination of Congenital Syphilis. Obstet Gynecol Int. 2010

3. Hawkes S, Matin N, Broutet N, et al. Effectiveness of interventions to improve screening for syphilis in pregnancy: a systematic review and meta-analysis. The Lancet Infectious Diseases 2011;**11**(9):684-91

4. Gloyd S, Chai S, Mercer MA. Antenatal syphilis in sub-Saharan Africa: missed opportunities for mortality reduction. Health Policy and Planning 2001;**16**:29-34

5. Molyneux E, Weber MW. Avoiding HIV and dying of syphilis. The Lancet 2001;**358**:596-96

6. Walker GJ, Walker DG. Congenital syphilis: a continuing but neglected problem. Seminars in fetal & neonatal medicine 2007;**12**:198-206

7. Walker DG, Walker GJ. Forgotten but not gone: the continuing scourge of congenital syphilis. Lancet Infect Dis 2002;**2**(7):432-6 doi: S1473309902003195 [pii][published Online First: Epub Date]|.

8. Watson-Jones D, Gumodoka B, Weiss H, et al. Syphilis in Pregnancy in Tanzania II - The Effectiveness of Antenatal Syphilis Screening and Single-Dose Benzathine Penicillin Treatment for the Prevention of Adverse Pregnancy Outcomes. Journal of Infectious Diseases 2002;**186**:948-57

9. Hook EW, Peeling RW. Syphilis control--a continuing challenge. The New England Journal of Medicine 2004;**351**:122-4

10. Peeling RW, Mabey D, Herring A, et al. Why do we need quality-assured diagnostic tests for sexually transmitted infections? Nature reviews. Microbiology 2006;**4**:909-21

11. Peeling RW, Ye H. Diagnostic tools for preventing and managing maternal and congenital syphilis: an overview. Bulletin of the World Health Organization 2004;**82**:439-46

12. Mabey D, Peeling RW, Perkins MD. Rapid and simple point of care diagnostics for STIs. Sex Transm Infect 2001;**77**(6):397-8

13. Loubiere S, Moatti J-P. Economic evaluation of point-of-care diagnostic technologies for infectious diseases. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 2010;**16**:1070-6

14. Bates I, Maitland K. Are laboratory services coming of age in sub-Saharan Africa? Clin Infect Dis 2006;**42**(3):383-4 doi: CID38323 [pii]

10.1086/499368[published Online First: Epub Date]|.

15. Initiative WTSTD. Evaluation of rapid diagnostic tests: syphilis. Nature Reviews Microbiology 2006;**Supplement**:S33-S40

16. Peeling R, Holmes K, Mabey D, et al. Rapid tests for sexually transmitted infections (STIs): the way forward. Sexually Transmitted Infections 2006;**82 Suppl 5**:v1-6

17. Peeling R, Mabey D, Herring A, et al. Why do we need quality-assured diagnostic tests for sexually transmitted infections? Nature reviews. Microbiology 2006;**4**:909-21

18. Schmid GP. Economic and programmatic aspects of congenital syphilis prevention. Bulletin of the World Health Organization 2004;**82**:402-09

19. TDR. Evaluating Diagnostics: Introducing evidence-based measures in an unregulated world. TDRnews 2009;**83**(June 2009)

20. Terris-Prestholt F, Santos A, Peeling RW. The Costing Guidelines for Syphilis Screening Strategies, 2010.

21. Parekh BS, Kalou MB, Alemnji G, et al. Scaling up HIV rapid testing in developing countries: comprehensive approach for implementing quality assurance. American Journal of Clinical Pathology 2010

22. Kumaranayake L, Pepperall J, Goodman H, et al. Costing Guidelines for HIV Prevention Strategies. October. Geneva, Switzerland, 2000.

23. Creese A, Parker D, Kahn F, et al. *Cost analysis in primary health care*, 1990.

24. Drummond MF, Sculpher MJ, Torrance GW, et al. *Methods for the economic evaluation of health care programmes*: Oxford University Press, 2005.

25. OANDA. Historical Exchange Rates, 2010.

26. Statistics BoL. Consumer Price Index: United States Department of Labor, 2012.

27. Mabey D, Sollis K, Kelly H, et al. Point-of-Care Tests to Strengthen Health Systems and Save Newborn Lives: The Case of Syphilis. PLoS Med 2012;**9**(6)

28. Watson-Jones D, Changalucha J, Gumodoka B, et al. Syphilis in pregnancy in Tanzania. I. Impact of maternal syphilis on outcome of pregnancy. The Journal of infectious diseases 2002;**186**:940-7

29. Blandford JM, Gift TL, Vasaikar S, et al. Cost-Effectiveness of On-Site Antenatal Screening to Prevent Congenital Syphilis in Rural Eastern Cape Province, Republic of South Africa. Sexually Transmitted Diseases 2007;**34**

30. Levin CE, Steele M, Atherly D, et al. Analysis of the operational costs of using rapid syphilis tests for the detection of maternal syphilis in Bolivia and Mozambique. Sexually Transmitted Diseases 2007;**34**(7 Suppl):S47-54 doi: 10.1097/01.olq.0000245986.62775.b6[published Online First: Epub Date]|.

31. Schackman BR, Neukermans CP, Fontain SNN, et al. Cost-Effectiveness of Rapid Syphilis Screening in Prenatal HIV Testing Programs in Haiti. PLoS Medicine 2007;**4**

32. Rydzak CE, Goldie SJ. Cost-Effectiveness of Rapid Point-of-Care Prenatal Syphilis Screening in Sub-Saharan Africa. Sexually Transmitted Diseases 2008;**35**:775-84

33. Newman L, Hawkes S, Kamb M, et al. Challenges in Global Estimates of Syphilis in Pregnancy. ISSTDR. Quebec City, Canada, 2011. .

34. WHO. Guidelines for Assuring the Accuracy and Reliability of HIV Rapid Testing: Applying a Quality System Approach. Geneva: World Health Organization, 2005.

35. Terris-Prestholt F, Watson-Jones D, Mugeye K, et al. Is antenatal syphilis screening still cost effective in sub-Saharan Africa. Sexually Transmitted Infections 2003;**79**:375-81

36. McIntyre D, Thiede M, Birch S. Access as a policy-relevant concept in low- and middle-income countries. Health economics, policy, and law 2009;**4**:179-93 doi: 10.1017/S1744133109004836[published Online First: Epub Date]|.

Table 1: Screening and Treatment Output

	D1	D2	D3	HC1	HC2	HC3	HC4	HC5	DH		TOTAL
Total ANC Clients	196	594	735	707	792	723	1667	1412	3885		10,711
RPR											
Total Tested	85	38	81	197	217	110	110	0	N/A		838
Total Positive	50	14	27	95	21	13	10	0	N/A		230
Total Treated	23	N/A	3	85	19	8	5	0	N/A		143
% of ANC Tested	43%	6%	10%	28%	27%	15%	7%	0%	-		12%
% Reactive	59%	37%	33%	48%	10%	12%	9%	-	-		27%
% of Positive Treated	46%	-	11%	89%	90%	62%	50%	-	-		62%
RST											
Total Tested	240	481	666	809	819	517	1135	1371	3334		9,372
Total Positive	23	53	105	74	122	58	107	102	268		912
Total Treated	23	52	88	70	116	51	105	102	234		841
% of ANC Tested	122%	81%	91%	114%	103%	72%	68%	97%	86%		87%
% Reactive	10%	11%	16%	9%	15%	11%	9%	7%	8%		10%
% of Positive Treated	100%	98%	84%	95%	95%	88%	98%	100%	87%		92%

N/A – Data not available
RST outputs: 1st October 2009 through 30th June 2010
RPR outputs: 1st May 2007 – 31st January 2008

Table 2: Total Screening Costs

	RPR Costs						RST Costs								
	D1	D3	HC1	HC2	HC3	HC4	D1	D2	D3	HC1	HC2	HC3	HC4	HC5	DH
Start-up and Training Costs				N/C			249	221	212	187	197	184	298	262	402
Quality Assurance Costs							539	896	555	844	535	534	533	545	513
Monitoring and Supervision Visit (x5)							24	23	24	26	23	22	23	25	21
Incoming Inspection (x4)							1	1	1	1	1	1	1	1	1
External Quality Control Panel (x5)							23	23	23	24	23	22	23	23	22
External Quality Assurance Panel (x5)							33	33	33	33	33	33	33	33	32
Testing and Treatment Costs															
Capital	31	37	48	40	30	30	43	142	22	89	60	48	48	24	194
Personnel	88	67	182	134	51	101	435	741	570	656	435	361	412	543	1,217
Supplies	97	77	240	166	85	103	457	868	1,027	1,235	1,188	928	1,705	2,119	4,595
Other	40	41	43	42	41	40	41	61	56	52	48	44	25	36	66
Total Testing Costs	**256**	**223**	**512**	**382**	**207**	**274**	**1,540**	**2,399**	**2,206**	**2,573**	**2,242**	**1,877**	**2,802**	**3,301**	**6,778**

N/C: Data not collected
All values rounded to the nearest dollar

Table 3: Unit Costs per Woman Tested

	RPR				RST			
	Average	Min	Max	Percent	Average	Min	Max	Percent
Startup and Training Costs								
Training					0.18	0.10	0.78	
Other start-up					0.06	0.02	0.26	
Total Startup Costs					**0.24**	**0.12**	**1.04**	
Quality Costs		N/C						
Monitoring and Supervision					0.32	0.07	1.27	
Incoming Inspection					0.00	0.00	0.01	
External Quality Control					0.11	0.03	0.48	
External Quality Assurance					0.16	0.05	0.69	
Total Quality Costs					**0.59**	**0.15**	**2.25**	
Testing and Treatment Costs								
Buildings and Storage	0.06	0.03	0.11	3%	0.07	0.02	0.30	4%
Equipment	0.20	0.12	0.43	9%	-	-	-	0%
Personnel	0.74	0.46	1.04	34%	0.33	0.19	1.00	17%
Supplies	0.92	0.76	1.22	41%	1.51	1.38	1.80	78%
Test Kits	*0.73*	*0.64*	*0.85*	*33%*	*1.29*	*1.29*	*1.29*	*67%*
Treatment Supplies	*0.14*	*0.03*	*0.33*	*6%*	*0.08*	*0.05*	*0.14*	*4%*
Other Supplies	*0.05*	*0.04*	*0.09*	*2%*	*0.14*	*0.04*	*0.50*	*7%*
Building Operation and Maintenance	0.29	0.19	0.49	13%	0.00	-	0.03	0%
Waste Management	0.01	0.00	0.01	0%	0.01	0.00	0.05	1%
Total Testing and Treatment Costs	**2.21**	**1.76**	**3.02**	**100%**	**1.92**	**1.74**	**3.13**	**100%**
Total Costs	**2.21**				**2.74**			

N/C: Not collected

Table 4: Univariate Sensitivity Analysis

Univariate Sensitivity Analysis Results
(% divergence from base case)

| Parameters Varied | Observed Values | | RST | | RPR | |
	Minimum	Maximum	Minimum	Maximum	Minimum	Maximum
Discount rate	1%	6%	1.92 (0%)	1.92 (0%)	2.30 (1%)	2.35 (1%)
Working hours per day	7	4	1.85 (3%)	2.06 (7%)	2.20 (5%)	2.70 (17%)
Supply wastage	0%	50%	1.80 (6%)	2.42 (26%)	2.23 (4%)	2.67 (15%)
Staff time (+/- 50%)	- 50%	+ 50%	1.77 (8%)	2.07 (8%)	1.93 (17%)	2.71 (17%)
Staff Salaries	$139	$624	1.76 (8%)	2.37 (24%)	3.32 (44%)	1.94 (16%)
RST Outcomes						
Syphilis Prevalence	7%	16%				
% Positives Treated	84%	100%				
% Partners Treated	14%	100%		Varied only in		
RPR Outcomes				Multivariate Sensitivity Analysis		
% ANC Tested	7%	43%				
Syphilis Prevalence	9%	59%				
% Positives Treated	11%	90%				

Figure 1: Multivariate Sensitvity Analysis