

Rapid Syphilis Testing Study in Zambia and Uganda

This document outlines the quality management processes established as part of a study looking at the impact and feasibility of offering rapid syphilis testing together with rapid HIV testing. The study was conducted in antenatal care (ANC) facilities offering prevention of mother-to-child transmission of HIV (PMTCT) services. The information provided is intended to support policy development, program planning, and implementation of rapid syphilis testing in resource-limited settings.



photo: Olivier Asselin

Background

Syphilis is a major cause of morbidity and mortality among women and children in developing countries. There are an estimated 12 million new cases of syphilis globally each year, with the majority of cases occurring in developing countries.¹ In sub-Saharan Africa, the prevalence of syphilis among pregnant women attending ANC clinics ranges from 2.5% to 17%.^{2,3,4} Untreated syphilis during pregnancy is associated with spontaneous abortion, stillbirth, premature delivery, low birth weight, congenital syphilis, and perinatal death.⁵ Penicillin is an affordable and accessible cure for syphilis and a means of prevention against congenital syphilis.

While policies on routine syphilis screening are present in many countries, comprehensive implementation of screening has not been achieved due to logistical challenges associated with conventional test procedures, which require electricity, refrigeration, and laboratory equipment. The Elizabeth Glaser Pediatric AIDS Foundation (the Foundation), with support from the World Health Organization Special Programme for Research and Training in Tropical Diseases (WHO/TDR) Sexually Transmitted Disease Diagnostic Initiative (SDI) and the London School of Hygiene and Tropical Medicine conducted a study to assess the impact and cost effectiveness of introducing rapid syphilis testing for pregnant women at ANC sites offering PMTCT services in Zambia and Uganda. The study in Zambia was conducted in partnership with the Center for Infectious Disease Research in Zambia.

Implementation

Between February and March 2010, rapid syphilis testing was initiated in 9 ANC clinics in Uganda and 15 ANC clinics in Zambia. The test used was a one-step, point-of-care rapid test (SD Bioline Syphilis 3.0, Kyonggi-Do, Korea). Unlike conventional syphilis tests, the rapid syphilis test requires minimal training, can be used on whole blood, plasma, or serum, and does not require laboratory equipment, cold storage, or electricity. For these reasons, the test was considered by the study team as a promising tool for facilitating syphilis screening and treatment in lower-level health-care facilities in resource-limited settings.

A quality management system is important for any laboratory or testing site to ensure the accuracy and reliability of test results. Quality management guidelines (outlined in the following section) were developed by study investigators to support use of rapid syphilis tests at all study sites, and were largely adapted from the London School of Hygiene and Tropical Medicine and WHO-produced *Guidelines for Assuring Accuracy and Reliability of Treponemal Syphilis Rapid Testing: Applying a Quality Systems Approach*.⁶ Quality measures were successfully implemented at all participating sites, and were integrated into the quality management systems already in use for rapid HIV testing.

Components of the Quality Management Guidelines

DOCUMENTS AND RECORDS: To ensure that rapid syphilis testing quality control procedures were carried out correctly and consistently, standard operating procedures (SOPs) were developed and distributed to sites. SOPs were developed for all laboratory activities, including administration of the rapid syphilis test, internal quality control, and external quality control (see Process Control). Stock cards to manage the test-kit supply, daily quality control logs to record quality processes and corrective action, and dated and version-controlled SOPs were introduced and made accessible to appropriate staff (i.e., midwives and laboratory technicians).

ORGANIZATION AND PERSONNEL: Personnel files were created to document employee qualifications at each participating site, including education, work history, trainings, and competency assessments. Files were stored at each ANC clinic and employees were responsible for updating their files after participating in trainings and competency assessments.

At least one health-care worker from each ANC clinic attended a didactic and practical training, led by the study coordinator and internal monitor. Training covered operation of the rapid syphilis test, quality control testing, stock management, and biosafety. All attendees received WHO/Foundation training certificates. The trained health-care workers were then able to provide on-the-job training to other clinic staff.

INTERNAL AUDIT: Internal auditing proved to be a valuable tool in maintaining quality systems. At least one Foundation-associated study monitor in each country was appointed and tasked with visiting sites once per month to assess issues related to supply management and internal and external quality control. Study monitors also provided on-the-job support and additional training when necessary. The monitors used a checklist to guide their assessments, which enabled them to easily track progress and problems and ensure that consistent support was provided.

PROCESS CONTROL: All rapid syphilis test kits were inspected for damage and expiration date before distribution to ANC clinics. Damaged or expired kits were destroyed and this action was documented.

Parallel testing was conducted when there was a new shipment or new lots of test kits. A confirmed positive sample and a confirmed negative sample were tested using the old and new kits. If the two test results yielded discrepant results, action was taken according to the quality control SOP and corrective action algorithm, and documented in a corrective action log.

INTERNAL QUALITY CONTROL: Internal quality control for client testing was performed by conducting weekly testing of an aliquot of a known rapid plasma reagin (RPR) positive and negative control. Internal quality control was also performed when new staff used the rapid syphilis tests for the first time or when temperatures were outside the recommended range (2°C to 30°C) in the space where the test kits were stored. The central public health laboratory in each country prepared controls from samples that were confirmed positive or negative by conventional RPR testing. The control samples were then distributed to participating ANC sites for result comparison with the rapid syphilis test.

As defined in this study, **internal quality control** assesses the ability of the test to distinguish between samples that are known to be either positive or negative and ensures day-to-day (or week-to-week) consistency of testing.

Corrective action procedures for discrepancies and repeat testing were outlined in the SOPs and documented in a corrective action log.

EXTERNAL QUALITY CONTROL: External quality control was done by repeat confirmatory testing and proficiency testing. Central public health laboratories retested 2% of the samples collected by ANC sites using the same rapid syphilis test and the internal monitor or study coordinator followed up on any discrepant results.

Additionally, the central public health laboratories prepared proficiency panels (i.e., serum samples of known positive, weak positive, and negative status) and distributed the panels to participating sites twice annually. The positive samples were prepared by serially diluting a confirmed, strongly positive sample (confirmed by RPR) to create strong, medium, and weak samples. The panel contained between four to six samples and was sent to participating sites as dried tube specimens (DTS), which are serum samples that are completely dried out to form pellets. DTS are easily transportable and stable for up to four weeks. Health-care workers responsible for performing routine rapid syphilis testing tested these known panels, allowing for test sites and test operators to be assessed on correctly interpreting negative, strong, and weak positive syphilis samples. The central laboratory staff and project supervisor analyzed the proficiency panel test results. A scoring system was established and personnel who received a score below 67% were required to undergo training and repeat the panel. This proficiency testing was instrumental in determining health-care workers' accuracy in reading the test and properly diagnosing clients.

As defined in this study, **external quality control (proficiency testing)** is the ability of health-care providers to correctly perform rapid tests according to the manufacturer's guidelines.

Lessons Learned

- Quality management measures are essential for high-quality laboratory services, ensuring that results delivered to clients are both accurate and reliable.
- Quality systems for rapid syphilis testing can be implemented easily into laboratory activities or quality schemes, and can be extended or adapted for other laboratory tests, such as HIV testing.
- Confirmatory testing and in-house preparation of proficiency panels are efficient ways of performing external quality control.

¹ World Health Organization (WHO). Global prevalence and incidence of selected curable sexually transmitted infections. Overview and estimates. Geneva: WHO; 2001.

² Ratnam AV, Din SN, Hira SK, et al. Syphilis in pregnant women in Zambia. *Br J Vener Dis*. 1982;58:355-358.

³ Wilkinson D, Sach M, Conolly C. Epidemiology of syphilis in pregnancy in rural South Africa: opportunities for control. *Trop Med Int Health*. 1997;2:57-62.

⁴ Mayaud P, Uledi E, Cornelissen J, et al. Risk scores to detect cervical infections in urban antenatal clinic attenders in Mwanza, Tanzania. *Sex Transm Infect*. 1998;74 (suppl 1):S139-146.

⁵ Di Mario S, Say L, Lincetto O. Risk factors for stillbirth in developing countries: a systematic review of the literature. *Sex Transm Infect*. 2007;34(7 Suppl):S11-21.

⁶ London School of Hygiene and Tropical Medicine (LSHTM) and WHO. *Guidelines for Assuring Accuracy and Reliability of Treponemal Syphilis Rapid Testing: Applying a Quality Systems Approach*. In press.

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About the Foundation

The Elizabeth Glaser Pediatric AIDS Foundation is a global leader in the fight against pediatric HIV and AIDS, and has reached more than 11.6 million women with services to prevent transmission of HIV to their babies. The Foundation works at 5,400 sites in 17 countries to implement prevention, care, and treatment services; to further advance innovative research; and to execute strategic and targeted global advocacy activities in order to bring dramatic change to the lives of millions of women, children, and families worldwide.

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