

GUIDANCE ON SYPHILIS TESTING IN LATIN AMERICA AND THE CARIBBEAN:

Improving Uptake, Interpretation and Quality of Testing in Different Clinical Settings

Also published in:

Spanish (2015): *Orientación para el diagnóstico de la sífilis en América Latina y el Caribe: cómo mejorar la adopción, interpretación y calidad del diagnóstico en diferentes entornos clínicos*

ISBN 978-92-75-31860-7

PAHO HQ Library Cataloguing-in-Publication Data

Pan American Health Organization.

Guidance on Syphilis Testing in Latin America and the Caribbean: Improving Uptake, Interpretation, and Quality of Testing in Different Clinical Settings. Washington, DC : PAHO, 2015.

1. Syphilis, Congenital – prevention & control. 2. Syphilis, Congenital – transmission.
3. Syphilis, Congenital – therapy. 4. Public Policies. 5. Americas. I. Title.

ISBN 978-92-75-11860-3

(NLM Classification: WC 161)

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**Improving Uptake, Interpretation
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Different Clinical Settings**

Unit of HIV, Hepatitis, Tuberculosis, and Sexually Transmitted Diseases.

Washington, D.C.

2015



**Pan American
Health
Organization**



**World Health
Organization**

REGIONAL OFFICE FOR THE **Americas**

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ACRONYMS AND ABBREVIATIONS

ANC	Antenatal clinic
AO	Adverse (pregnancy or other health) outcome
BPG	Benzathine penicillin G
CIA	Chemi-immunoassay
CDC	Centers for disease control and prevention
DALY	Disability-adjusted life year
DTS	Dried tube specimen
EIA	Enzyme immunoassay
FTA-ABS	Fluorescent treponemal antibody-absorption assay
HIV	Human immunodeficiency virus
IM	Intramuscular
LAC	Latin America and the Caribbean
MCH	Maternal and child health
MHA-TP	Microhemagglutination assay for treponema pallidum
MTCT	Mother-to-child transmission
MSM	Men who have sex with men
NT	Non-treponemal test
NT/T	Non-treponemal/treponemal (dual) test
NRL	National reference laboratory
PAHO	Pan American Health Organization
POC	Point of care
PT	Proficiency testing
QA	Quality assurance
QC	Quality control
RPR	Rapid plasma reagin test
RT	Rapid test
STAT	Same-visit testing and treatment
SLMTA	Strengthening laboratory management toward accreditation program
SOP	Standard operating procedures
STD	Sexually transmitted disease
STI	Sexually transmitted infection
TPHA	Treponema pallidum haemagglutination assay
TPPA	Treponema pallidum particle agglutination assay
UFSC	Santa Catarina Federal University (Brazil)
USR	Unheated serum reagin assay
VDRL	Venereal disease research laboratory
VICITS	Vigilancia centinela y control de infecciones de transmisión sexual
WHO	World Health Organization

GUIDANCE ON SYPHILIS TESTING IN LATIN AMERICA AND THE CARIBBEAN: Improving Uptake, Interpretation and Quality of Testing in Different Clinical Settings

Background

In 2007, the World Health Organization (WHO), in collaboration with global partners, launched a global initiative for the elimination of congenital syphilis as a public health problem (1). Congenital syphilis occurs when a pregnant woman with syphilis transmits the infection to her fetus during pregnancy or delivery, also referred to as mother-to-child transmission (MTCT). Congenital syphilis can lead to stillbirth or neonatal death, low birth weight or premature infants, as well as disorders in surviving infants such as blindness, deafness, other neurologic impairment, and bone deformities. It can be prevented by early detection and treatment of the maternal infection with parenteral penicillin.

The ongoing initiative to combat this condition is based on four pillars: (i) ensuring sustained political commitment and advocacy for the elimination effort; (ii) increasing access to and quality of maternal and newborn health services; (iii) screening all pregnant women for syphilis and promptly treating those who are positive; and (iv) having adequate surveillance, monitoring and evaluation procedures in place – ideally integrated within or building upon existing health care and health information systems. While strong antenatal programs can identify and treat individual cases to prevent congenital syphilis, the syndrome cannot be eliminated without addressing syphilis prevalence among all reproductive-aged women in the community. Thus, to be most effective, a country response would work to reduce sexual transmission of syphilis within the community through prompt identification and treatment of early infections, as well as identification and treatment of all sexual partners.

The Pan American Health Organization (PAHO) and its Member States undertook congenital syphilis prevention efforts more than a decade before the launch of the WHO global initiative. With this long experience, the Region of the Americas helped to lead the global effort through its initial development and implementation of action plans and standards, which included the adoption of recommended standard case definitions (2, 3) and practical program targets

and outcome measures (4). More recently, PAHO has helped to link efforts to eliminate congenital syphilis with those to eliminate perinatal HIV, as well as to lead the development of standards on validating country-level elimination of MTCT of both infections (5).

Countries in Latin America and the Caribbean have made substantial progress in incorporating syphilis testing and treatment measures into existing Maternal and Child Health (MCH) data collection systems, and toward the program targets of at least 95% syphilis testing of all pregnant women and at least 95% treatment of women testing positive for syphilis (i.e., receipt of at least a single dose of intramuscular penicillin) (6, 7). But even as coverage and uptake of syphilis testing in pregnant women increases, many countries report continuing difficulty with ensuring prompt treatment of women testing positive, as many of these women are still lost to follow-up (8). HIV testing strategies for the region have been previously covered elsewhere (9, 10).

Syphilis serologic tests

Syphilis is a sexually transmitted infection (STI) that results from exposure to a bacterium of the *Treponema* species, *T. pallidum*. No single currently available laboratory test can provide a definitive diagnosis. Classically, the diagnosis of syphilis is based on a combination of clinical history, symptom presentation (if any), and serologic test results, including non-treponemal and treponemal tests. Non-treponemal tests (e.g., RPR, VDRL) are typically used for screening, and measure a non-specific antibody to treponemal infection. A reactive test can indicate recent infection, but could be caused by other conditions unrelated to syphilis. Treponemal tests (e.g., TPPA, TPHA, FTA-ABS, EIA) detect antibody to syphilis and thus can confirm exposure to treponemal disease. However, these tests cannot distinguish venereal infection (syphilis) from non-venereal treponemal diseases (e.g., yaws, pinta, bejel). Furthermore, treponemal antibody persists for life, and thus treponemal tests cannot distinguish between recent, active infection and previously treated or old, non-contagious infection.

The presence of a reactive syphilis test in combination with a typical clinical sign of syphilis such as a chancre, skin ulcer, or rash is highly suggestive of the disease. However, the signs and symptoms of syphilis are typically transient, and many individuals are asymptomatic or do not recognize symptoms. Furthermore, the antibody test may not yet be positive at the time an ulcer or other sign appears. Thus, when syphilis is suspected but the antibody test is negative, the test should be repeated after a week. Syphilis is easily transmissible during the primary (chancre) or secondary (rash) stages. In latent stages (asymptomatic syphilis), people with untreated disease can transmit syphilis sexually for one to two years after infection, or vertically from mother to child for four years or longer in some cases (11). Even several years after infection, when untreated syphilis may no longer be contagious, infected individuals who are not appropriately treated are at risk for developing complications of tertiary syphilis including neurologic, cardiovascular, or other chronic complications (1, 12, 13).

In the absence of symptoms, a combination of both reactive non-treponemal and treponemal tests indicates the possibility of contagious syphilis infection (sometimes referred to as "probable active" infection), and also supports the need for treatment of the individual and any sex partners.¹¹ Both non-treponemal and treponemal tests are generally inexpensive and relatively easy to perform by trained personnel. However, they require the use of appropriate reagents, equipment and supplies (e.g., specialized slides) and technicians must carefully follow standardized procedures. Laboratories with such trained personnel, equipment and supplies are increasingly limited – and non-treponemal and treponemal serologic testing are often only available in larger laboratories (e.g., national or regional laboratories or large hospitals). This situation is problematic for ensuring universal syphilis testing in antenatal care, as a majority of pregnant women receive care in decentralized health facilities without on-site laboratories capable of conducting these types of tests. Also, patients seeking STI services often do so in primary care settings where laboratory services are not immediately available.

Problems previously encountered

Ensuring appropriate testing in various clinical settings, and particularly antenatal care settings, continues to be a difficult issue for many countries. The traditional serologic testing algorithm for syphilis has used a screening non-treponemal test followed by a confirmatory treponemal test. However,

as noted, laboratory capacity for such testing is seldom available in the antenatal clinic setting. As a result, patients (e.g., pregnant women) are either referred to a laboratory with the capacity for serologic testing, or have their blood drawn at the local clinic and sent to a referral laboratory. Such approaches are subject to breakdown at a number of levels: Patients may not go to the laboratories to get the test; test samples may be lost or inadequate; patients may not return to the clinic to receive their results; positive results may not be promptly or routinely reported back to the clinics, or may not be accurately charted; and systems highlighting the need for treatment may not be in place (8). Even if all these steps are met, if treatment is not provided at the clinic, this may require another series of referrals, allowing further chance for loss to follow-up. An example of how referral systems for syphilis testing can become inordinately complicated has been reported from Peru, where women attending antenatal care may be required to make six separate visits to the health center over 27 days before receiving syphilis results (14).

Patients with positive results who are not adequately treated represent a costly public health failure, as limited funds and human resources were expended on an intervention that was only partially undertaken and did not result in a health benefit for the individuals (e.g., mother-child pair) or the community. Yet this situation is common, even in countries with relatively strong health systems. For example, national data from Brazil (2012) indicated that, among communities reporting Antenatal Clinic (ANC) program data, an estimated 2% to 22% of women with positive serologic tests were not treated at all, and a further 1% to 7% received inadequate treatment (i.e., were treated with a drug other than intramuscular penicillin) (8). The clinical and laboratory evaluation of syphilis among antenatal women and sexually transmitted infection (STI) patients represents a considerable effort for local programs. The inability to have prompt results allowing same-visit treatment at the clinic visit represents a great loss of time and resources, as well as an important missed opportunity for prevention of congenital syphilis in pregnant women and disease prevention in syphilis-infected individuals and their partners.

¹¹ CDC recommends treating all sex partners exposed through oral, vaginal or anal sex during the previous three months for primary syphilis, six months for secondary syphilis, and one year for latent (asymptomatic) syphilis infections (13).

Provision of a new strategy; rapid or point of care (POC) testing

Over the past 15 years, an increasing array of immune-chromatographic (e.g., strip and lateral flow) tests that use finger prick whole blood specimens have become available to screen for a number of diseases, including HIV and syphilis. These are generally referred to as "rapid" or "point of care" (POC) tests.

The availability of newer POC tests offers the potential for syphilis testing to be done with minimal technical training and in non-laboratory settings. Additionally, if indicated, treatment could be provided right at the clinic visit, maximizing uptake of treatment and limiting chances for adverse perinatal health outcomes. Until recently, the only available POC syphilis tests were treponemal tests measuring lifetime exposure to *T. pallidum*, and not able to distinguish recent infections from past, treated infections. However, unconfirmed treponemal tests can still have important implications in settings such as antenatal clinics in which missed infections pose a very high risk for poor health outcomes, given that treatment risks and program costs are both low (11, 15). New POC syphilis tests are continually being developed, such as treponemal and non-treponemal tests on a single cassette, supporting confirmation at the clinic level. Several large projects in the region have demonstrated that POC syphilis tests can greatly improve test uptake in antenatal women even in remote and hard-to-reach settings, and can be a cost-effective prevention strategy (11, 16-18). Laboratory evaluations of POC tests against traditional testing models indicate good test performance characteristics (19, 20).

Objectives

This document outlines guidance that countries in Latin America and the Caribbean can use to increase uptake of syphilis testing for vulnerable populations, including pregnant women and persons at risk for syphilis, and ensure prompt treatment of those persons testing positive with minimal loss to follow-up. This guidance was developed as a result of a meeting convened by PAHO and the Centers for Disease Control and Prevention (CDC) in April 2014, with representatives from the health ministries of countries of Latin America and the Caribbean; technical experts in maternal and child health (MCH), STI and HIV programs, and

laboratory diagnostics from Latin America and the Caribbean (21). The participants sought to identify and discuss the published evidence and best practices on syphilis testing algorithms for promoting disease reduction in the region. They identified the lack of regional or global guidance on syphilis testing strategies in specific clinical settings, such as antenatal clinics, as an important barrier impeding regional elimination of MTCT of HIV and syphilis (22). In addition, they recognized that limited integration of HIV and syphilis program and operations' systems, such as for procurement and quality assurance of laboratory tests, was a "missed opportunity" to leverage efficiencies, personnel and funding in many countries. The participants observed that many "best practices" existed in the region around strategies to promote appropriate syphilis testing in different clinical settings and the use of syphilis testing algorithms, but these have not been widely shared among countries. Thus, the participants recommended the development of a regional consensus document outlining syphilis testing algorithms and other strategies supporting appropriate syphilis testing in different clinical settings where laboratory services may or may not exist at the clinical site (22). Special emphasis was placed on the following five areas identified as important for national programs to effectively promote elimination of MTCT of both syphilis and HIV:

1. Guidance for health ministries to support the development of comprehensive national policies to cover syphilis testing and treatment.
2. Recommendations for use of syphilis testing algorithms in specific populations or clinical (or outreach) settings, depending on laboratory capacity. Clarification of interpretation of syphilis testing results based on the population or clinical (or outreach) setting served, including recommendations on counseling, treatment, follow-up, and partner treatment.
3. Suggested strategies to ensure the quality of syphilis testing and appropriate training of laboratory and/or health care personnel who perform the tests.
4. Mechanisms for procuring high-quality and affordable syphilis test kits, equipment, and supplies.
5. Suggested strategies to support national reporting of syphilis cases (22).

1. GUIDANCE FOR HEALTH MINISTRIES TO SUPPORT THE DEVELOPMENT OF COMPREHENSIVE NATIONAL POLICIES TO COVER SYPHILIS TESTING AND TREATMENT

In the development of national policies for syphilis testing and treatment, countries must consider the need for quick results at the clinic visit, accuracy of syphilis testing, and appropriate surveillance reporting.

To ensure accuracy of tests, countries have traditionally relied upon serologic tests conducted in laboratories, usually screening, non-treponemal tests and confirmatory, treponemal tests. These tests require trained laboratory personnel using carefully standardized operating procedures and specialized reagents, equipment and supplies. While theoretically helping ensure the quality of the testing and accuracy of the results, reliance on laboratory-based testing means that results are seldom available at the time of the clinical visit (e.g., during the antenatal or STI clinic visit). Lack of results at the clinic visit is problematic because many patients who test positive do not learn their test results or return to receive treatment and this is especially concerning in the antenatal clinic where delayed treatment can cause serious harm or death to the fetus (6, 7, 11). Furthermore, quality of testing and accuracy of results are not always assured by having tests performed at laboratories. Formal assessments have identified many barriers in laboratory settings affecting test accuracy (19, 22-24). Some countries are unable to reliably procure the commodities needed for accurate serologic testing, such as adequate quality serologic reagents, appropriate equipment for serologic testing (e.g., rotators for RPR testing) and other needed supplies (e.g., pipettes, specialized slides) (22, 24). The reasons behind this vary, and may include inadequate documentation of procedures, the complex essential commodities processes faced by some health ministries, limited supply access for districts working in decentralized health systems, diminishing funding for STI services, and increasingly limited numbers of laboratory staff well trained in syphilis serologic testing (22, 23). Standardized protocols on assuring adequate test quality and user proficiency are often either unavailable, or not routinely carried out. Standardized guidance on reporting of testing and results may be lacking, limiting the ability of health ministries to estimate burden of disease or program progress and barriers (22, 24). Furthermore, many countries have not linked systems for procurement, implementation, surveillance and quality assurance for syphilis and HIV testing, although the systems are duplicative in some settings, and especially for antenatal care (22).

POLICIES TO IMPROVE UPTAKE OF SYPHILIS TESTING

A preferred approach would be to incorporate POC syphilis testing during the clinical encounter, allowing potential for counseling and treatment right at the visit. This approach may be practical and efficient in several clinical settings, but the most obvious benefits are during the antenatal clinic visit for the prevention of MTCT of syphilis. Adoption of such POC syphilis tests at the clinic level can improve health outcomes and lead to a more efficient use of resources in settings that are currently unable to provide recommended syphilis testing and prompt (i.e., same-visit) treatment. To date, POC syphilis tests have not yet been widely adopted in the region and information on whether and how best to use these tests (i.e., appropriate algorithms to use) has not yet been available to all programs.

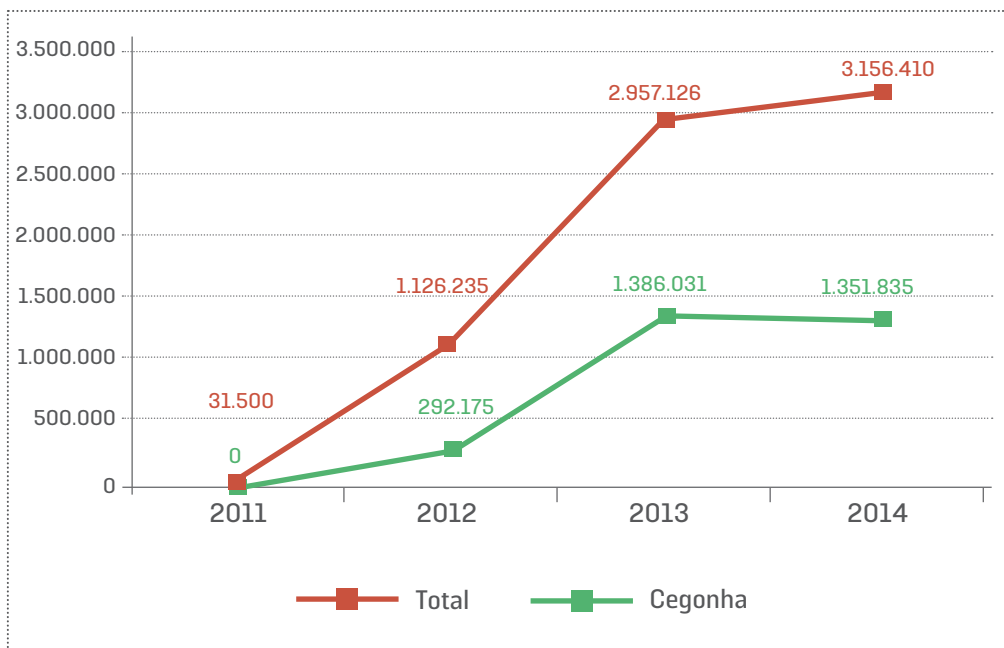
Currently marketed rapid POC tests for syphilis are primarily treponemal tests. These allow detection of treponemal (e.g., venereal syphilis) infection, but are not able to distinguish between recent and old or previously treated infections. An important benefit to these tests is that with relatively simple training they can be carried out by basic health providers at the clinic level, allowing treatment to occur at the clinic visit and thus reducing or eliminating loss to follow-up. As noted earlier, rapid POC tests for syphilis are particularly useful in clinical situations requiring prompt action, such as antenatal clinic (ANC) visits. In Brazil, coverage of syphilis testing at the municipality level has increased through technology transfer and training of health staff (Figure 1).

In addition to single treponemal POC tests, rapid "dual" non-treponemal/treponemal (NT/T) tests have been developed that allow screening and confirmation with a single finger prick whole blood specimen. The dual NT/T tests are only slightly more complicated and expensive than single treponemal POC tests, and are particularly useful in settings in which clients or patients may have been previously exposed and treated for syphilis (e.g., STI or HIV clinics, specialized clinics for sex workers or men who have sex with men [MSM], or outreach settings managing vulnerable populations).

LINKING SYPHILIS TESTING WITH HIV TESTING

Yet another category of POC tests are combination rapid syphilis and HIV tests on a single device. All currently

FIGURE 1: Distribution of rapid syphilis tests in Brazil: 2012-2014



The Brazilian Ministry of Health acquires rapid syphilis tests produced in Brazil and developed through a technology transfer mechanism. Between 2012 and 2014, 3,030,041 tests were distributed to 5,488 (98.5%) municipalities that joined the prenatal component of the Cegonha Program and trained 1,123 health professionals responsible for increasing syphilis testing in primary health care facilities. By the end of 2014, a distance learning program started through the Telelab.

Source: Department of STDs, AIDS and Viral Hepatitis – Ministry of Health of Brazil

available combination rapid syphilis/HIV tests include a syphilis treponemal test component only. Nonetheless, these combination syphilis/HIV rapid tests offer potential for on-site results and treatment and a net cost savings in settings in which detecting and treating both infections promptly is important, such as in pregnant women attending antenatal care.

An important opportunity exists in linking procurement, implementation, surveillance, and quality assurance of

syphilis testing with HIV testing strategies in antenatal care settings in Latin America and the Caribbean, to achieve the Regional initiative for Eliminating MTCT of HIV and Congenital Syphilis in the Americas by 2015 (2-4). Such integration could help maximize use of human resources, minimize costs, and build stronger and more sustainable maternal child health (MCH) systems that support healthy mothers and infants (25).

2. RECOMMENDATIONS FOR USE OF SYPHILIS TESTING ALGORITHMS IN SPECIFIC POPULATIONS OR CLINICAL (OR OUTREACH) SETTINGS

WHO and most national STI management guidelines recommend persons with signs or symptoms of primary or secondary syphilis should be treated immediately, as should their sexual partners (26). Direct diagnostic methods (e.g., dark field or direct fluorescent antibody tests) help support the diagnosis, but increasingly these tests are not available at the clinical setting. Indirect diagnosis through serologic testing can be helpful in supporting the clinical diagnosis of syphilis, and quantitative non-treponemal tests can help ensure adequate treatment is

achieved. Details on syphilis testing in symptomatic persons are well covered in existing guidelines (12, 13, 26).

SYPHILIS TESTING IN ASYMPTOMATIC PERSONS IN SPECIFIC CLINICAL SETTINGS

Testing of asymptomatic persons at risk for syphilis is more problematic given the lack of definitive diagnostics. It would be ideal to have a very precise test or combination of tests available at the clinic setting; however, the risks of delayed treatment (and possible loss to follow-up) must be weighed against the types of tests available and the timing

of results. Pregnancy is a particularly critical situation, as delayed treatment of syphilis in a pregnant woman has a high likelihood (> 50% of cases) of leading to a severely adverse outcome in the fetus or infant (11).

In asymptomatic persons, laboratory-based serologic testing algorithms for syphilis typically include traditional non-treponemal screening tests confirmed with treponemal tests (Annex 1, Figure 1), or reverse sequence algorithms using EIA or chemiluminescence immunoassay (CIA) tests confirmed with non-treponemal tests and (if negative) TPPA (Annex 1, Figure 2). While the FTA-ABS could be used as a treponemal test in these algorithms, it is more technical, time consuming and costly than the TPPA and so is increasingly less recommended (12, 26). In the clinical context, rapid syphilis tests could include POC treponemal tests or POC combined syphilis/HIV tests, alone (e.g., for the antenatal setting) (Annex 1, Figure 3) or combined with a confirmatory on-site qualitative RPR if available – or rapidly provided laboratory-based RPR or VDRL (Annex 1, Figure 4). On-site tests could also include the POC dual NT/T tests, which may be preferred in services for at-risk patients who may have been treated for syphilis in the past (e.g., MSM or sex workers) (Annex 1, Figure 5).

Some patients without clinical signs of symptoms of syphilis have high risk or vulnerability for infection, and may be infected asymptotically. In the appropriate clinical (or outreach) setting, serologic screening for syphilis can be beneficial (Table 1).

Antenatal clinics (pregnant women). As noted, for pregnant women with untreated syphilis, risk of an adverse pregnancy outcome is high (>50%) (11, 25), risks of treatment are low (15), and treatment has been proven to be highly effective in preventing perinatal morbidity and mortality (27, 28). Thus the benefits of treatment far outweigh the risks for potential unnecessary treatment. Long clinical experience suggests *in utero* syphilis transmission can occur very early in pregnancy, indicating that treatment should occur as early as possible, preferably before 24 weeks gestation (27–29).

At the population level, although published data on timing of treatment are relatively sparse, existing studies support the importance of early treatment (considered here up to and including week 27 of pregnancy) (29, 30). As noted earlier, a common problem with antenatal syphilis screening programs is loss to follow-up, as when specimens are sent out and results are not returned promptly, leading to late or missed

treatment in syphilis-infected pregnant women (14). Other scenarios that need to be considered are screening for women having miscarriages or women who come to a health facility for delivery but have not attended ANC services. In program evaluations and field studies in the region, use of rapid POC syphilis testing has been shown to greatly improve testing and treatment compliance and earlier treatment in antenatal women (14, 16–18). While some uninfected women with previously treated syphilis may be over-treated as a result of a positive POC treponemal test, the risk of treatment is small (15) and the cost of penicillin is low, while the risk of adverse outcome in untreated patients is high (11, 25, 27). Thus, a recommended algorithm for syphilis testing in pregnant women is one providing same-visit testing and treatment, at least for the first penicillin dosage (Annex 1, Figures 3, 4 or 5). In situations where confirmatory tests are available in less than 7 days (Annex 1, Figures 4 or 5), the clinician can modify the treatment plan accordingly (i.e., if confirmatory testing is positive, the pregnant woman can complete the recommended 7.2 million units long acting intramuscular [IM] penicillin [divided in three weekly doses of 2.4 million units each] to ensure latent syphilis is adequately treated, and sex partners can be treated).

Syphilis screening in pregnancy and treatment of positives is a highly cost-effective public health intervention, with cost estimates ranging from US\$ 4–19 per disability-adjusted life year (DALY) averted in resource-limited countries (17, 31, 32). A recent modeling study using generic country scenarios that varied on three factors (maternal syphilis testing and treatment coverage, syphilis prevalence in pregnant women and cost of health care) found antenatal syphilis screening and treatment programs to be highly cost-effective in every scenario, even in high-income nations (US\$ 24 – 111 per DALY averted); and cost saving in settings with high prevalence, low service coverage or high healthcare costs (< US\$ 0 per DALY averted) (32). Additionally, integrating syphilis and HIV screening has been found to increase the cost-effectiveness of HIV screening (16, 33) even in settings with very low prevalence of syphilis and HIV (33). For example in China, in a setting of 0.25% syphilis prevalence and 0.07% HIV prevalence in pregnant women, combining antenatal syphilis testing along with HIV testing would be expected to result in a 15-fold reduction in estimated cost-effectiveness ratios compared with HIV testing alone (US\$ 359 vs. US\$ 5636 per DALY averted) (33).

Other clinical settings. In addition to the antenatal clinics, there are other clinical settings in which on-site testing and

results followed by treatment (i.e., same-visit testing and treatment [STAT]) are highly desirable in order to minimize loss to follow-up and lack of treatment. These settings include dedicated STI clinics or primary care clinics providing STI services, and specialized services for high risk or vulnerable populations (e.g., adolescents, MSM, sex workers, migrant populations, HIV-infected persons). In clinical settings without on-site laboratories, rapid POC testing strategies are a means to achieve the STAT goal. In larger facilities connected with laboratories and trained technicians, traditional testing algorithms using non-treponemal tests and confirmatory treponemal tests for those testing positive (Annex 1, Figure 4) could be employed if results can be returned quickly enough to ensure immediate treatment, or if the use of "send out" RPR testing approaches still yield very high levels of treatment (e.g., < 7 day turnaround and >95% treatment rates for people testing positive). Traditional laboratory-based testing algorithms (Annex 1, Figures 1 and 2) allow a more precise diagnosis and may be more cost-effective than rapid syphilis tests when batched. However, if patients do not receive results and treatment, this testing leads to costs to the program only, with no effect on individual or community health outcomes.

Persons at high risk for syphilis. In Latin America and the Caribbean, persons with high behavioral risk for acquiring syphilis include sex workers regardless of gender, clients of sex workers, MSM, patients attending STI clinics, and patients with HIV within or outside of clinical care. Additionally, some migrant populations have higher syphilis prevalence, whether related to personal or partner risks (e.g., Garifunas in Central America) (34, 35). Routine syphilis screening may be beneficial in these subgroups, and such screening is recommended in national guidelines in some countries (e.g., monthly or quarterly screening for female sex workers) (36, 37). High risk persons may have received syphilis testing in the past, and thus testing strategies that include both non-treponemal and treponemal tests are desirable. On the other hand, untreated syphilis among persons with multiple partners increases spread of disease in the community, particularly among stigmatized or hidden populations at risk for loss to follow-up. In these cases, rapid availability of results and treatment is also highly desirable (10, 13, 38). In these situations, on-site laboratories capable of both non-treponemal and treponemal testing are ideal (Annex 1, Figures 1 and 2); however, rapid tests (including treponemal only, dual NT/T, and combination syphilis/HIV tests) have been used in clinical settings serving high risk persons with variable results (39-41) (Annex 1, Figure 4 and Table 1). Dual

NT/T tests may be especially useful in these settings (Annex 1, Figure 5).

Blood donors. Syphilis screening is routinely conducted at blood banks, often through treponemal testing. Units testing positive are not used for transfusion and the donors should be counseled to follow up with public health services to assess their need for treatment, keeping in mind that many positive tests represent previously treated infections. Because results are not immediately needed, laboratory-based testing algorithms can be cost-effective for blood bank screening (42, 43) (Annex 1, Figures 1 and 2). In addition, national laboratories may wish to collaborate with blood banks to obtain positive units, following additional confirmation to rule out false positives, as sera from these units could be useful in laboratory proficiency testing programs.

Serosurveillance studies. Serosurveillance studies can be useful in assessing syphilis rates in hidden or high-risk populations, and may also be used in assessing syphilis seropositivity in pregnant women. Any serosurveillance studies assessing HIV would ideally include syphilis, as the additional testing incurs little added cost and provides important data about patterns and burden of disease. Depending upon the surveillance processes and funding, various algorithms could be appropriate for syphilis testing; however, assessing active disease prevalence requires both treponemal and non-treponemal testing. In syphilis surveillance studies, persons with positive confirmatory tests should receive appropriate counseling, treatment, and information on partner treatment.

Recommended syphilis testing algorithms to use in surveillance include: (1) Treponemal testing with rapid tests, with additional blood drawn for lab-based non-treponemal serologic testing among those screening positive (Annex 1, Figure 4); persons with sexual risk exposure and with no reported history of benzathine penicillin G (BPG) injection could then be treated promptly, or treatment could await positive non-treponemal tests, requiring a need for follow up for counseling and treatment. (2) Treponemal/non-treponemal testing with dual rapid tests (Annex 1, Figure 5), with on-site treatment for only those with positive results on both tests. (3) Blood drawn and sent to a laboratory capable of non-treponemal screening and confirmatory treponemal testing (Annex 1, Figure 1). Persons with positive confirmatory tests would require follow-up for treatment, counseling, and partner notification.

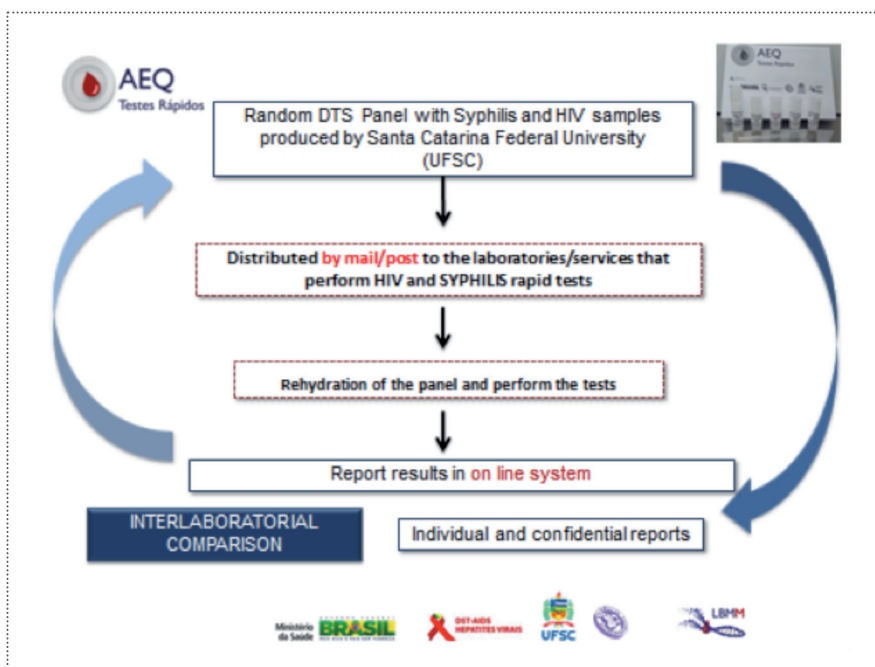
3. SUGGESTED STRATEGIES TO ENSURE THE QUALITY OF SYPHILIS TESTING

The first step in ensuring quality of laboratory testing for syphilis is maintaining adequate standards in overall laboratory operations. Developing policies at the national level will help to ensure basic, standardized public health laboratory procedures and operations. Basic policies would ideally address management structure and biosafety measures, as well as protocols for procurement and maintenance of equipment, specimen collection and processing, laboratory testing and result reporting, documentation and records management, as well as overall laboratory quality assurance. Ideally, any national or other large laboratory providing reference services to underlying laboratories would participate in a regionally or globally recognized accreditation program, such as Strengthening Laboratory Management Toward Accreditation (SLMTA) (44, 45).

To ensure quality of syphilis serologic testing, several quality control (QC) and quality assurance (QA) elements are recommended. A strict internal quality control for

all procedures, including written standard operating procedures (SOPs), should be developed and implemented. SOPs from existing programs may be used to implement standard quality practices without the need to develop new procedures. Ideally, each country's national reference laboratory (NRL) would participate in an external program, such as the CDC global proficiency program for syphilis serology testing, in order to establish the quality of its serologic tests under typical circumstances (24). In this program, CDC's Division of STD Prevention Laboratory sends a serum panel of known results to participating laboratories three times per year. Laboratory technicians who are blinded to panel results perform the treponemal (e.g., TPPA, MHA-TP, TPHA, FTA-ABS, EIA) and/or non-treponemal (e.g., VDRL, USR, RPR) qualitative and/or quantitative tests that the laboratory routinely conducts using typical reagents, equipment and procedures. Results are reported to CDC via email for analysis and feedback. Evaluation of rapid POC tests is planned to be included in the CDC proficiency testing program in the near future.

FIGURE 2: External Quality Control Evaluation



The external evaluation program of the Ministry of Health of Brazil is done in association with the Santa Catarina Federal University that produces the HIV/syphilis panels which contain four dry samples, a buffer and the package insert. These are distributed to the laboratories/services that conduct HIV and syphilis rapid tests. Each laboratory has 30 days to perform the rapid tests and report the results through the Quali-TR online system. After that period, the university analyzes the results and sends individual and confidential reports to the participant units.

There is also a need for 'local' laboratories to ensure quality of rapid POC testing, including assuring providers' ability to conduct POC tests appropriately, and routine assessment of the quality of the POC test kits being stored and used. The London School of Hygiene and Tropical Medicine has published a Toolkit for Rapid Syphilis Tests that includes guidance in these areas (46).

In order to assure quality and user proficiency in rapid POC testing at laboratories and other testing sites within the country, dried tube specimen (DTS) approaches for syphilis testing have been adapted based on procedures developed for HIV testing programs (47-50). These can be used at NRLs and other large laboratories where rapid testing is employed, but are likely most useful in ensuring quality of POC testing in lower level programs.

A desirable approach that builds country capacity, develops reporting linkages, and promotes continuous quality improvement is for the NRL to provide underlying laboratories with the tools, training, and oversight needed to maintain quality of syphilis testing (also see next section on procurement). In addition, smaller health facilities using POC tests would ideally integrate quality assurance for both

syphilis and HIV testing, given the similar performance goals. For example, Brazil has developed a national proficiency testing program for POC testing in underlying health facilities that integrates syphilis and HIV components using DTS specimens (Figure 2). This approach allows evaluation of rapid syphilis and HIV test kits, operator performance, and the need for ongoing training and supervision of clinicians conducting the POC testing (50). The Brazilian model has been employed by other countries and is relevant even in remote areas.

A model for countries to consider is one in which the NRL or a regional reference laboratory provides a series of minimal standard procedures and oversight that include: (1) syphilis testing algorithms; (2) procedures to ensure test validation and procurement (also see next section); (3) internal QA of reagents and supplies; and (4) routine, periodic evaluation of quality through proficiency testing of laboratories and competency testing of staff (e.g., through establishing an internal and/or external proficiency testing program using the DTS approach). Additionally, overseeing laboratories should provide guidance on basic laboratory training needed to conduct testing, and disseminate SOPs for testing.

4. MECHANISMS FOR PROCURING HIGH-QUALITY AND AFFORDABLE SYPHILIS TEST KITS, EQUIPMENT, AND SUPPLIES

The regional consultation on syphilis testing identified procurement of adequate equipment and supplies as an important gap affecting the quality materials such as VDRL or RPR reagents, equipment (e.g., proper rotators for conducting RPR testing), and even adequate supplies for conducting serologic tests (e.g., RPR cards, appropriate VDRL slides, u-bottom plates for TPPA). Several technical experts representing countries reported that essential commodities procurement systems tended to purchase the least expensive, often low quality, reagents rather than higher quality reagents; and some reported that procurement was possible only from certain companies with which the government had contracts rather than open tender. Several countries reported that critical supplies were often extremely limited or unavailable, requiring, for example, inappropriate reuse of RPR cards; this

situation leads to problems with reading and interpretation of results. It has been reported that decentralization of health services, while improving local access and timing of services (51), can make procurement of commodities more difficult and expensive when each sub-region or facility must procure their own supplies. Some participants from the laboratories reported that limited procurement mechanisms may be part of the reason why many countries in the region continue to use older testing approaches (e.g., FTA-ABS) rather than newer, more sensitive and user-friendly (and less expensive) approaches.

Several meeting representatives suggested that the use of regional procurement schemes, as is done for HIV testing, could improve the availability and lower the cost of higher quality reagents. Additionally, many representatives

expressed their concern about the quality of various rapid POC tests for syphilis, as performance characteristics reported in package inserts are typically based on company-supported studies. At the regional meeting, these concerns led to a call for PAHO and CDC to support external validation of available rapid POC tests using qualified regional laboratories, with publication of results to allow countries to have better evidence for justifying and purchasing specific rapid test kits. In addition, there was also a call for PAHO to develop a website providing names of companies selling critical reagents and allowing laboratories to provide feedback on their experiences.

During the consultation, CDC agreed to evaluate the most commonly used rapid POC tests in the region and provide results to PAHO for publication on their website (<http://www.paho.org/hq/>). Ongoing evaluation of syphilis POC

tests is warranted as additional tests come to market, using CDC or other laboratories in the region.

Additionally, with help from the consultation participants, PAHO has developed a list of companies that carry syphilis testing reagents and supplies, and plans to update this list as new information becomes available. Meanwhile, WHO has developed a diagnostics proficiency testing program to certify dual syphilis/HIV tests. Finally, priority was placed on sharing experiences among implementers on how the tests perform in the field. In some situations the initial laboratory evaluation of a POC test suggests reasonable performance characteristics, but in actual clinical use the test has problems that make providers and countries unsure of its usefulness. Sharing experiences can lead to a better understanding of a test's performance in real world settings and can help improve future evaluations.

5. SUGGESTED STRATEGIES TO SUPPORT NATIONAL REPORTING OF SYPHILIS CASES

Surveillance for syphilis has two main components:

- Case reporting is the process of reporting notifiable cases of syphilis to local health departments up to the national health department. Surveillance case definitions that are broad (sensitive) and simple to use may be more effective in promoting public health benefits such as communicable disease prevention than highly specific, clinical case definitions (2).¹¹²
- Prevalence monitoring is a process in which data on trends in disease prevalence are routinely collected over time in defined populations. This may be done by specific surveillance studies among certain populations or systematic collection of program data based on routine screening of populations such as pregnant women.

The adoption of new syphilis testing algorithms based on clinical settings implies that systems must be developed that allow reporting of positive results, without confirmatory testing in many cases. Figures 1 – 5 in Annex 1 are annotated to suggest reporting to national surveillance based on results of each algorithm. Case definitions of confirmed and suspect cases should be updated to reflect new testing strategies. All cases of suspected or confirmed

syphilis should be reported regardless of treatment status (see Figures 1 to 5 in Annex 1).

Reported cases should include information on the type of laboratory test conducted and the results, as well as disease stage at the time of initial examination. Stage determination should be based on available clinical and serological information (i.e., documented signs or symptoms of primary or secondary syphilis or evidence of an epidemiological link [named contact to primary or secondary case]) or history of a negative serologic test for syphilis within the past year. In contrast to case reporting, which is intended to be population-based, prevalence monitoring for syphilis is generally performed using data obtained from selected populations. When prevalence data are collected from routine program screening, the type of laboratory test used by the program is an important data element needed

¹¹² For Congenital Syphilis, PAHO recommends countries adopt a broad surveillance case definition, such as: *A live born or stillborn infant born to a mother with inadequately treated syphilis.* Syphilis is based on clinical evidence (genital ulcer or signs compatible with secondary syphilis) or on a reactive treponemal or non treponemal serologic test. Adequate treatment is defined as a parenteral injection of at least 2.4 million units penicillin, at least 30 days prior to delivery (52).

to interpret the meaning of the results. Testing algorithms for specific surveillance studies among certain populations have been previously described in this document.

NEXT STEPS IN THE REGIONAL PLAN FOR IMPROVING SYPHILIS TESTING IN THE REGION OF THE AMERICAS

In addition to creating a regional guidance on syphilis test algorithms for different clinical settings, the representatives at the Regional Consensus Meeting identified the following additional steps for PAHO to further strengthen syphilis testing in the Region (22). Both short and long-term activities were identified, and PAHO has agreed to provide support and oversight for each:

Short-term activities to be completed over the next 12 months:

1. Completion of a regional guidance on syphilis testing algorithms, recommended treatment and follow-up for Latin American and Caribbean countries (this document).
2. Development of a regional work group of laboratory and public health experts in syphilis testing able to provide technical assistance to countries on laboratory testing and quality.
3. Synthesis of existing materials on laboratory standards, training and reference materials for specific serologic and rapid syphilis tests, and QA and proficiency testing strategies. Existing materials would be vetted through the regional work group of laboratory experts and made available through the PAHO website (to be done by the regional syphilis serology work group).
4. Development of a list of tests, commodities (e.g., reagents) and equipment needed for syphilis testing that meet quality standards, and where they could be procured by national laboratories (included in this document, with plans for periodic updates).
5. Development of a regional scheme for bulk procurement of rapid POC tests, including combination HIV/syphilis tests, and other syphilis testing commodities, in order to promote more affordable pricing (under discussion).
6. Development of a regional bulk volume specimen panel by collection and characterization of discarded blood units from blood banks. This panel will be used for preparation of training panels, QC materials, proficiency testing and competency panels (under discussion).
7. Summary of experiences from countries in the region on use of POC tests, including reports on formal

training of healthcare workers where POC rapid tests are employed and formal evaluations of recommended algorithms in different clinical settings.

8. Periodic updating of the regional guidance on syphilis testing, taking into account new tests that become available and how these could be used in different clinical settings as well as new evidence (program evaluation data) based on experiences with currently recommended algorithms.
9. Financial support for operational research to better understand the appropriate use of available testing technologies. One example of such research is an ongoing comparison of the uptake of syphilis testing before and after introduction of single rapid HIV and single rapid syphilis tests against combination rapid HIV/syphilis testing in antenatal clinics in Bogotá and Cali.

Medium-term and longer, to be implemented over a three year period:

1. Development of an action plan by each country to secure commitment from those necessary for improved syphilis testing linked with HIV testing, within the next 12 months.
2. Support from PAHO on health system and program integration supporting elimination of MTCT of HIV and syphilis at national, regional and municipal levels.
3. Active engagement from PAHO in reporting advances in syphilis testing strategies and adding to an on-line free-access library of results, SOPs, training materials and QA strategies.
4. Promotion of regional laboratories that can take on external QA testing in LAC, currently done solely by the CDC STD Laboratory. South-to-south technical support is particularly desirable.
5. Evaluation of risks and benefits associated with extended use of treponemal POC test algorithms without confirmatory non-treponemal testing (extent and cost of overtreatment vs. pregnancy outcomes averted).
6. Support from PAHO on improved surveillance supporting elimination of MTCT of syphilis and HIV, including appropriate data management and reporting systems, and better documentation of fetal loss and still birth associated with syphilis.
7. Support from PAHO on improved strategies for sentinel STD surveillance, including promotion of best practices (e.g., Vigilancia Centinela y Control de Infecciones de Transmisión Sexual).

Syphilis remains a major public health problem in the region of Latin America and the Caribbean. Despite recent advances in technology and instrumentation, challenges in the diagnosis of syphilis persist. The goal of this guidance document outlining best practices on syphilis testing, including POC testing, in different clinical settings is to improve the uptake, interpretation, and quality of syphilis testing in the region. It is intended as an instrument to improve the coverage and effectiveness of syphilis screening and diagnostic test programs as well as appropriate treatment in the region, in order to reduce mortality and adverse health outcomes caused by congenital syphilis.

DOCUMENT DEVELOPMENT METHOD

There are limited data published on the development of evidence-based guidelines for syphilis testing (including POC testing) in different clinical settings. This guidance document establishing best practices was developed as a result of a PAHO meeting held in April 2014 with representatives from health ministries of the countries of Latin America and the Caribbean (21). Participants

included technical experts from PAHO, CDC and the region in MCH, STI and HIV programs, and in laboratory diagnostics. Country representatives were present from Brazil, and regions of the Caribbean, Central America, the Andean Region and the Southern Cone (21). The meeting participants identified potential syphilis testing algorithms and discussed the benefits and challenges of each. This resulting guidance document was developed by a small task force composed of meeting participants. The document development process involved mixed methodologies, including: (1) results from both in-depth discussions at the meeting and follow-up conference calls on the five special emphasis areas (page 3) (22); (2) results of a standardized, regional survey of NRL and other laboratory staff in the Americas; and (3) systematic reviews of published literature and country-level reports. All experts invited to the regional meeting, whether or not they were able to attend, were asked to review and comment on initial drafts and the final document. Comments were also elicited from technical experts in syphilis diagnostics from the World Health Organization and from other regions of the world.

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TABLE 1: SYPHILIS TESTING IN ASYMPTOMATIC PATIENTS: considerations in different clinical settings*

Setting	Management	Public health concerns	Possible testing strategies	Counseling/ partner services/reporting
Antenatal	Syphilis testing in pregnant women should be done during the 1st trimester (or 1st pregnancy visit). Testing should be repeated during 3rd trimester if there is risk for infection/re-infection. Women without testing results available at delivery should be tested.	<ul style="list-style-type: none"> - In untreated maternal syphilis, risk of adverse outcome (AO) to fetus is high (>50% AO) and increases with delayed treatment. - Ideally, same-day treatment and partner treatment. - Loss to follow-up is a public health failure, as well as costly to the program. - Treatment: One IM dose 2.4 million units BPG.† If confirmatory NT test+ or no confirmatory test available, repeat weekly x 2. 	<ul style="list-style-type: none"> - If ANC services are linked to on-site lab, use traditional screening option (RPR/VDRL with confirmatory treponemal test). Results should be available on the same day. - If no on-site lab, rapid treponemal test with treatment based on positive result. - If there is a history of prior syphilis treatment, assess possibility of re-infection for treatment decisions; and send out test for RPR with instructions/counseling on follow-up. - Reverse algorithms generally inappropriate. 	<ul style="list-style-type: none"> - Counseling should note that test suggests syphilis but we cannot be absolutely certain about presence of infection. However, treatment (first IM dose) is recommended to prevent AO in baby (later IM doses can await confirmation, if available) - Partners should be counseled that test is suggestive, we cannot be absolutely certain about presence of infection. If lab available, partner treatment can await results. If laboratory unavailable, treatment recommended to avoid AO in baby. - Reporting should ideally be done based on positive confirmatory test. If none available, reporting should still be conducted as a suspect case. Test type should always be recorded in reporting form.
High risk patient	Patients at risk for acquiring syphilis, such as sex workers, clients of sex workers, MSM, HIV+ patients whether in and out of clinical care, and certain migrant populations may benefit from annual testing.	<p>(In addition to individual risk)</p> <ul style="list-style-type: none"> - Risk for spread of syphilis in the wider community. - Risk for enhanced HIV transmission and acquisition. - In reproductive aged women, risk for MTCT of syphilis. - Patients with high syphilis risk are likely to have had previously treated or untreated syphilis. Positive treponemal tests may not represent recent disease. 	<ul style="list-style-type: none"> - If services are linked to an on-site lab, use traditional screening option (RPR/VDRL with confirmatory treponemal test). Results should be available on the same day. - If no on-site lab, consider dual rapid non-treponemal/treponemal test. - If no on-site lab, rapid syphilis tests with treatment based on positive result may be appropriate in some situations (e.g., suggestive history of exposure and no history of previous benzathine penicillin G treatment). 	<ul style="list-style-type: none"> - Counseling should indicate that patient has been exposed to syphilis and requires multiple course treatment.† - Clients should be counseled to notify partners that they are exposed to syphilis and should be treated. - Reporting should ideally be done based on positive confirmatory test. If none available, reporting should still be conducted as a suspect case. Test type should always be recorded in reporting form including information on risk behavior and factors according to national or regional guidelines.

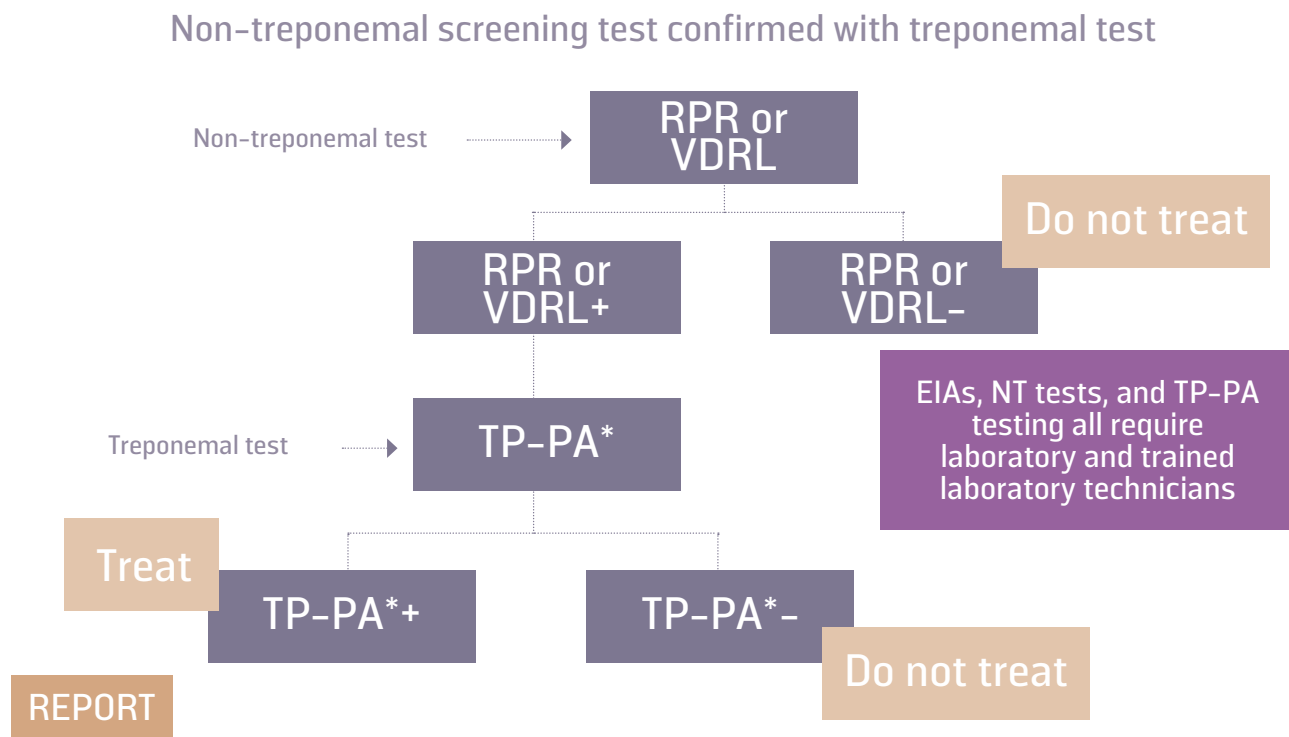
* Assumes asymptomatic clients. Clients with suggestive clinical signs or symptoms of primary or secondary syphilis (e.g., chancre; characteristic palmar rash or who are exposed to a sex partner with recent syphilis) should be treated with 2.4 million units intramuscular (IM) Benzathine Penicillin G (BPG) in a single dose.

Setting	Management	Public health concerns	Possible testing strategies	Counseling/ partner services/reporting
Surveillance	May include ANC, general or high risk populations.	– Important in assessing country situation regarding MTCT and bridging populations for HIV transmission.	<ul style="list-style-type: none"> – Multiple strategies possible depending on data/survey processes used. – If serologic tests collected, traditional algorithm (RPR/VDRL with confirmatory treponemal test). – If no serologic tests, could use dual rapid NT/T test, or rapid treponemal test with serologies drawn for NT testing among those testing positive. – Pregnant women testing positive on rapid treponemal tests should receive immediate treatment with IM BPG (see antenatal women). 	<ul style="list-style-type: none"> – It is critical that persons with positive confirmatory tests receive appropriate treatment (International Review Board concern), and are counseled on partner treatment needs. Reporting should ideally be done based on positive confirmatory test. If none available, reporting should still be conducted as a suspect case. Test type should always be recorded in reporting form including information on risk behavior and factors according to national or regional guidelines.
Blood bank	General population; may include higher risk persons with paid donations	– Important to reduce risk to recipients, thus any positive sample, regardless of test type, should be discarded.	<ul style="list-style-type: none"> – Most strategies use treponemal tests only. – Reverse algorithm could be appropriate. 	<ul style="list-style-type: none"> – Donors testing positive should be counseled to follow up with public health services for possible need for treatment. However, positive tests may represent previously treated infections. – If cases are confirmed, reporting should be conducted based on national reporting guidelines for blood banks.

† Syphilis treatment: IM BPG is the recommended treatment of choice in patients with syphilis. In patients with infectious syphilis of < 12 months duration (primary/secondary, early latent) a single dose of 2.4 million units BPG is sufficient to cure infection. Patients for whom a history of suggestive symptoms is not elicited, or in whom symptoms occurred > 12 months ago require 7.2 million units IM BPG (2.4 mu weekly doses for a total of 7.2 mu IM BPG)). Some other treatment options exist outside of pregnancy; however, oral medications are inferior as adherence is poor and potential for inadequate treatment is high. Azithromycin has been associated with resistance. There are no reliable data on the efficacy of parenteral cephalosporins in treating syphilis. Patients who are truly penicillin allergic are rare (13), but persons reporting being allergic to penicillin could be treated with certain oral medications such as doxycycline 100mg twice daily for 10 days, except in the case of pregnancy.‡

‡ Syphilis treatment in pregnancy: Because oral medications against syphilis either do not cross the placenta or are contraindicated (tetracyclines), pregnant women must be treated with parenteral penicillin to avoid adverse pregnancy outcomes, including death or disability, in the fetus or infant. Penicillin allergic women who are pregnant should be referred for desensitization (21).

FIGURE 1: Traditional laboratory-based syphilis serologic testing



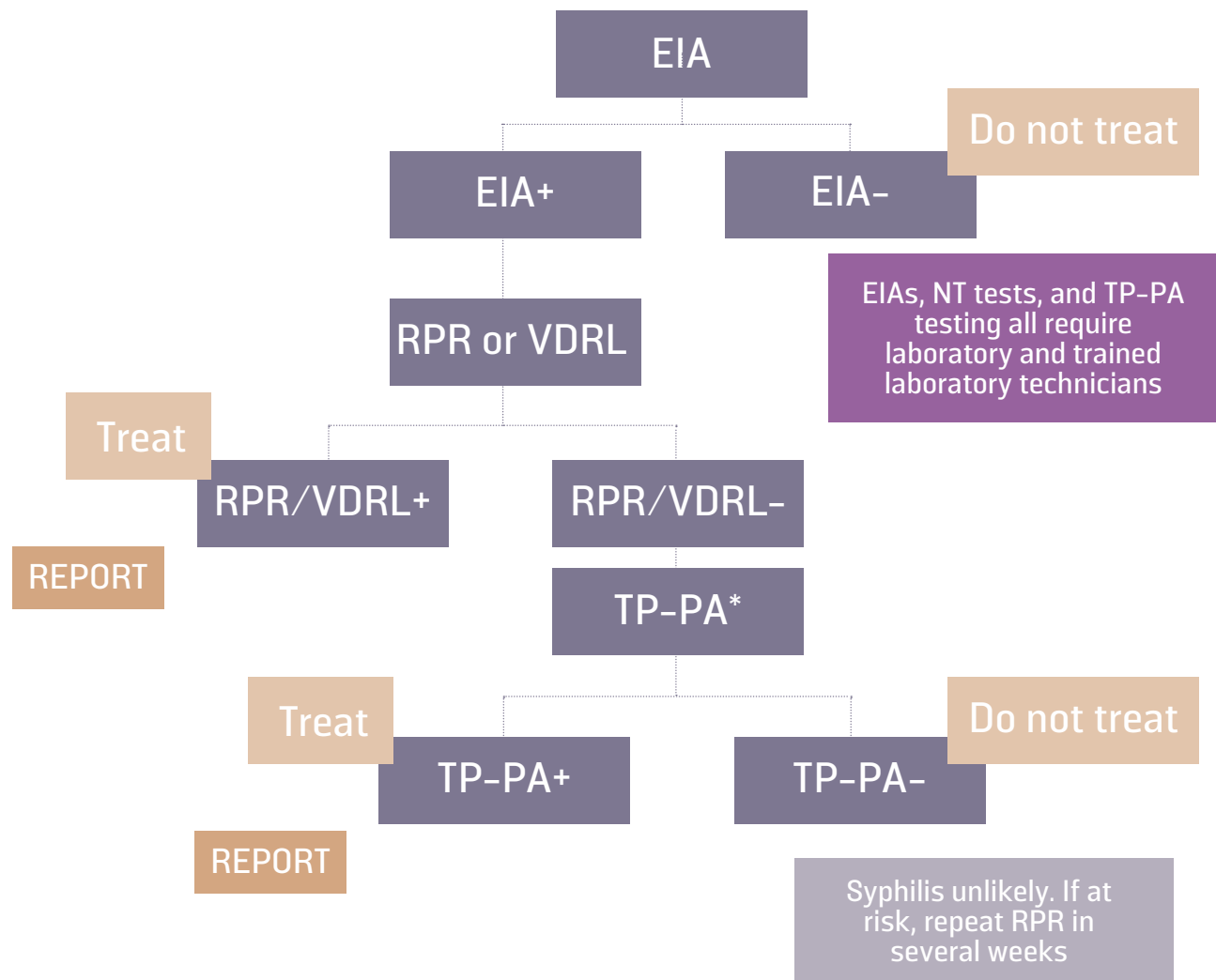
Comments:

- Approach detects active infection and can be used for routine surveillance reporting.
- RPR test has a high rate of biologic false positive, but when used with confirmatory treponemal test (TPPA) has a high positive predictive value.
- This algorithm may miss early primary or old, past infection.
- Requires a laboratory with trained technicians and appropriate equipment.
- Routine reporting of cases for surveillance.

*Other treponemal tests could be used; however, TP-PA has better performance than TPHA and FTA-ABS, and is less expensive than FTA-ABS.

FIGURE 2: Reverse sequence laboratory-based syphilis serologic testing

Treponemal screening test to allow automated screening, confirmed with non-treponemal test



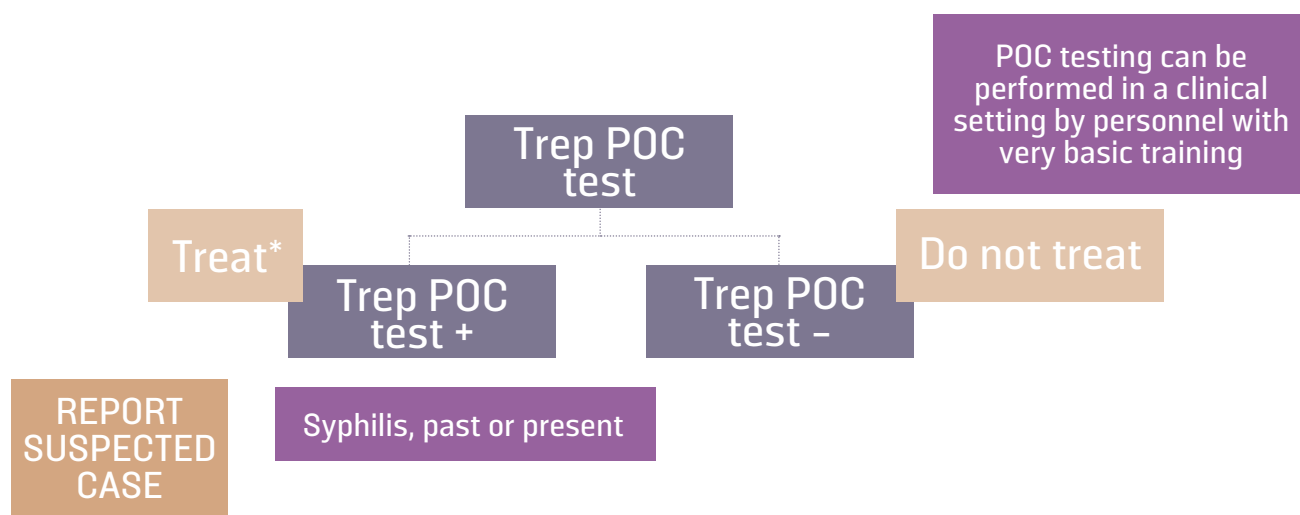
Comments:

- Approach detects early primary or past infection that might be missed with initial RPR testing. The non-treponemal test detects active infection.
- EIAs and CIAs have imperfect specificity i.e., a high rate of false positive results, and results are dependent upon risk of the population tested. Positive results should be confirmed with a TP-PA.
- Confirmatory treponemal test must have equivalent sensitivity but greater specificity than the screening EIA.
- Requires a laboratory with trained technicians and appropriate equipment.
- Approach can be automated (fewer human resources) but can be expensive and time consuming.
- This algorithm can be used for routine reporting of cases for surveillance (includes confirmatory test).

*Other treponemal tests can be used; however, TP-PA has better performance than TP-HA and FTA-ABS, and is less expensive than FTA-ABS.

FIGURE 3: Treponemal rapid point-of-care (POC) syphilis testing – without confirmatory non-treponemal test

Clinic-based testing opportunity best used in antenatal clinic setting



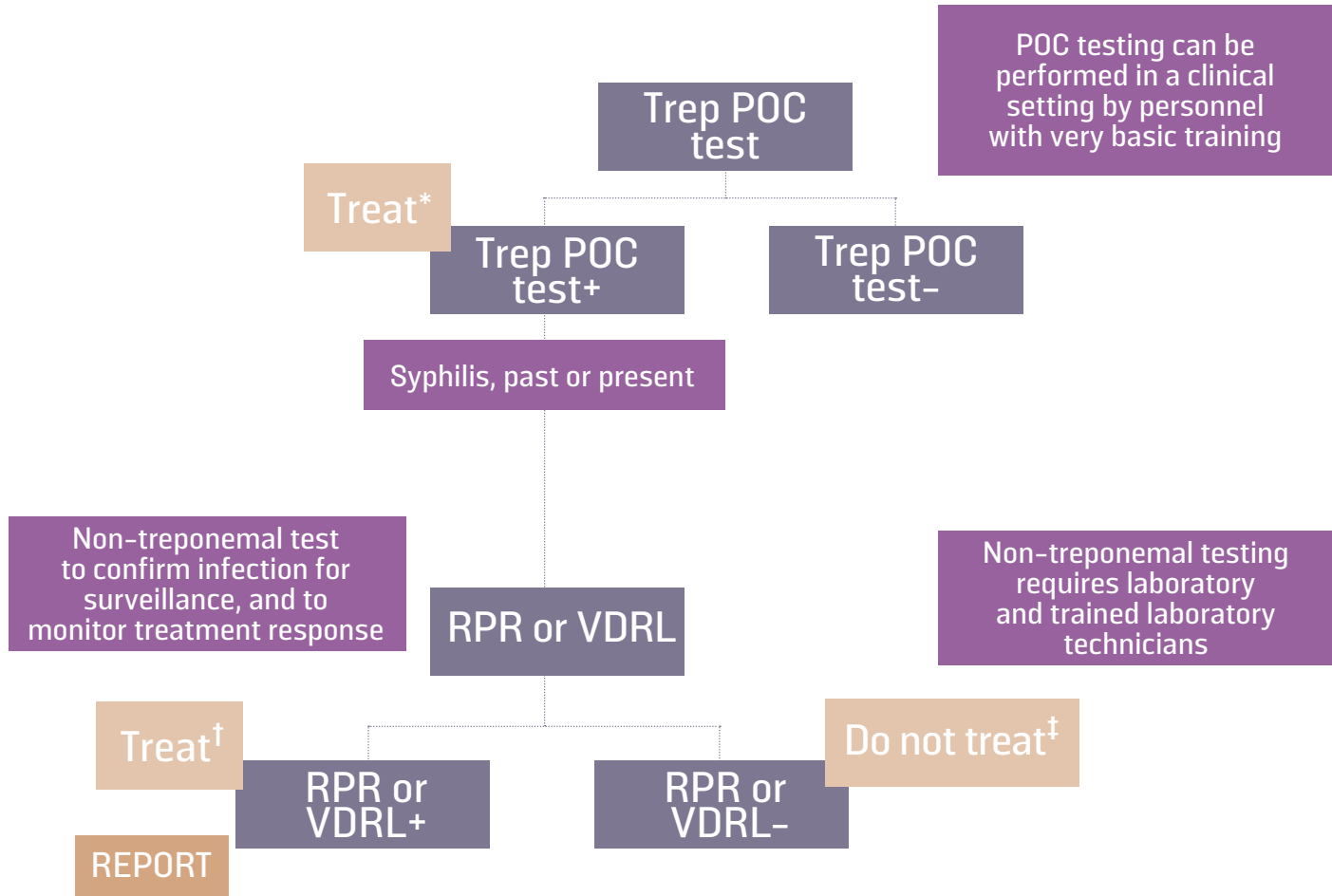
Comments:

- Point-of-care test (POC), such as a single rapid treponemal test or combined HIV/syphilis rapid test, can be performed at the site of the visit (health center), facilitating same-visit testing and treatment and minimizing loss to follow-up.
- Blood can be drawn for a laboratory-based treponemal test (RPR or VDRL) to confirm the presence of active disease for management and reporting decisions. A positive VDRL or RPR would clarify the need for further treatment of the mother and partner management, and if titers are available can monitor treatment response.
- Cost effective for the prevention of congenital syphilis.
- Reporting to surveillance should indicate test type used (i.e, POC with no confirmation). If laboratory-based non-treponemal test is later performed, the initial case report should be updated.

*Treatment benefits for infant are greater than risk from maternal treatment. Therefore, treat all pregnant women with first dose of Benzathine Penicillin G at point of care.

FIGURE 4: Treponemal rapid point-of-care (POC) syphilis testing – with confirmatory non-treponemal (NT) testing

Clinic-based testing opportunity: Consider in settings serving patients who may have been previously treated for syphilis



Comments:

- Addition of non-treponemal test identifies active infection, reduces over-treatment, facilitates same-day testing and treatment (minimizing loss to follow-up), and provides better surveillance data.
- POCT can be performed at site of visit (health center), while RPR or VDRL requires laboratory.
- This algorithm can be used for routine surveillance reporting (includes confirmatory test).

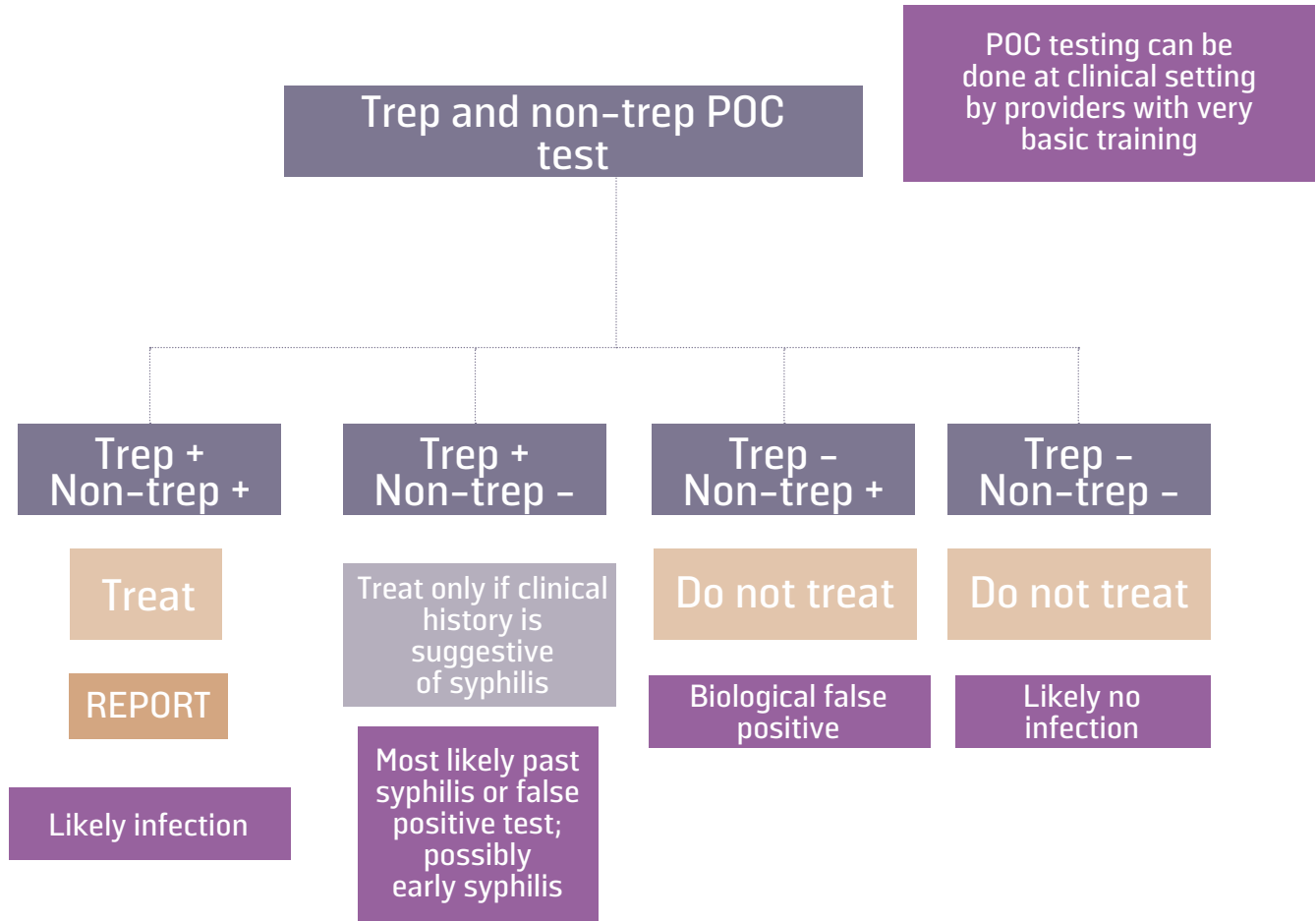
* Treat if patient cannot recall previous BPG injections. For persons who recall previous treatment, re-infection is possible: Treatment could be deferred until the non-treponemal test results are available. However, if clinical suspicion is high or loss to follow-up a possible concern, consider treating at the clinic visit.

† Treat with a total of 7.2 mu IM BCG divided into 3 weekly doses of 2.4 mu each.

‡ No treatment needed unless history suggests re-infection (i.e., early primary syphilis).

FIGURE 5: Dual non-treponemal/treponemal (NT/T) antigen rapid point-of-care (POC) syphilis testing

Clinic-based testing opportunity



Comments:

- Identification of active, confirmed infection at site of clinic visit (health center).
- Does not require laboratory.
- Facilitates same-day testing and treatment, minimizes loss to follow-up.
- This algorithm can be used for routine reporting, as confirmatory testing is part of POC.

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