STATE-OF-THE-ART DIAGNOSTICS FOR SYPHILIS

Epidemiology & Burden: In 2012, ~17.7 million individuals (15–49 years) globally had syphilis, with an estimated 5.6 million new cases every year (WHO); Highest prevalence in Africa and >60% of new cases occurring in LMICs; Most infections asymptomatic but syphilis in pregnancy can lead to congenital syphilis and is the leading cause of preventable stillbirths; greatest burden of maternal syphilis in Africa

Prevention & Management: Prenatal Screening, early case detection, prompt treatment with an effective antibiotic regimen and treating sex partners of a person with infectious syphilis.

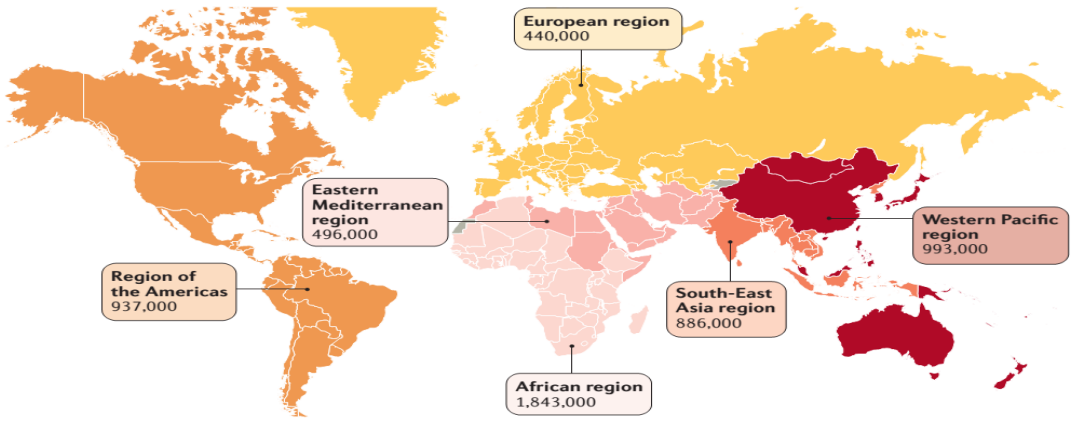


Fig 1: Estimated annual Incidence of Syphilis worldwide

Diagnostic Methods

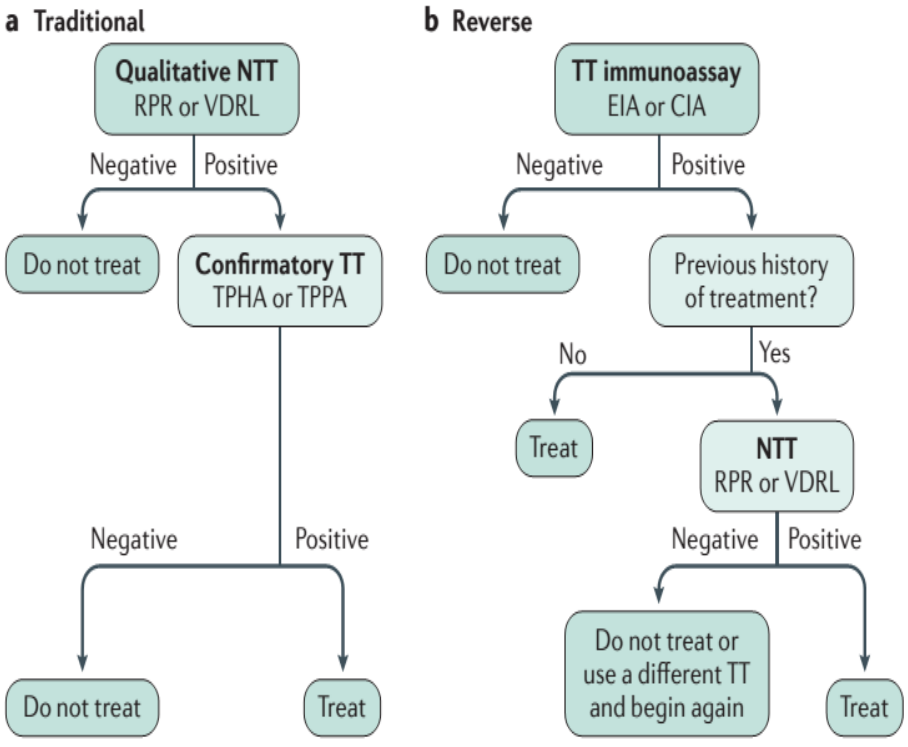


Fig 2: WHO recommended Screening algorithm for Syphilis

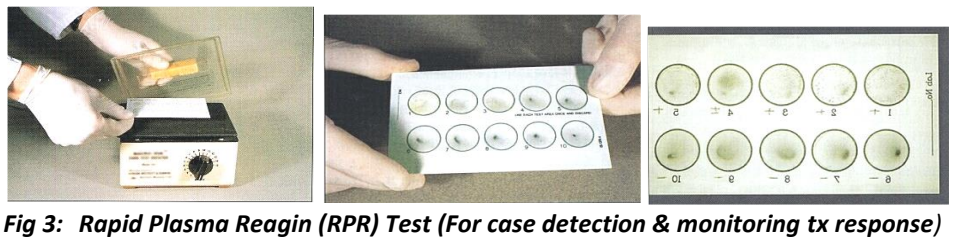


Fig 3: Rapid Plasma Reagin (RPR) Test (For case detection & monitoring tx response)

A.TRADITIONAL ALGORITHM	B.REVERSE SCREENING ALGORITHM
Advantages • begins with a qualitative non-treponemal test (NTT) that is confirmed with a treponemal test (TT) • has a high positive predictive value when both tests are reactive, although early primary and previously treated infections can be missed owing to the lower sensitivity of NTTs • less costly than reverse screening algorithms and does not require highly specialized laboratory equipment **Disadvantages** • Subjective interpretation • false negative NTT results can arise from the prozone effect (when there is an excess of antibody) • previously treated, early untreated and late latent cases can be missed and biologically false-positive cases can be overtreated as not always followed by a confirmatory TT	**Advantages** • uses a TT with recombinant *T. pallidum* antigens in enzyme immunoassay (EIA) or chemiluminescence immunoassay (CIA) formats that, when reactive, is followed by an NTT • permits treatment of 99% of syphilis cases, compared to the traditional algorithm in a low-prevalence setting • false negative tests due to the Prozone effect do not occur as TTs are not flocculation assays **Disadvantages** • higher initial setup costs and ongoing operational costs • in high-risk populations, screening with a TT can result in a high rate of positive results due to previously treated infections, leading to increased clinician workload needed to review cases and determine appropriate management

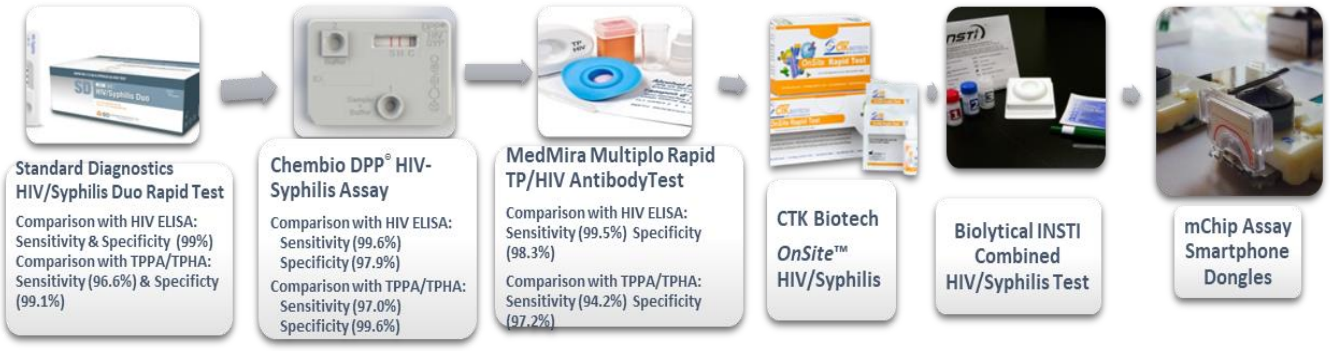
The European Centre for Disease Prevention and Control uses a variation of this approach: a reactive TT immunoassay is followed by a second (different) TT of any kind (that is, not followed by an NTT).

Ideally, a positive TT should be supplemented by another TT or an NTT. However, given the serious consequences of syphilis in pregnancy, treatment is recommended in a patient with a positive TT result.

The Dual Elimination of Mother to Child Transmission of HIV and Syphilis: WHO has set criteria for the validation of dual elimination including the following targets: (i) Antenatal care coverage (at least one visit) of ≥95%, (ii) Coverage of HIV and/or syphilis testing of pregnant women of ≥95%, (iii) Antiretroviral coverage of HIV positive pregnant women of ≥90% (iv) Treatment of syphilis-seropositive pregnant women of ≥95%.
A dashboard to track country-specific progress towards dual elimination is on the IDC website:
http://www.idc-dx.org/dashboards/dual-elimination-of-mother-to-child-transmission-of-hiv-syphilis

HIV/Syphilis Duo-test performance and laboratory evaluation

http://www.who.int/reproductivehealth/topics/rtis/Diagnostic_Landscape_2017.pdf



A.Summary ROC Curve for HIV diagnosis **B. Summary ROC curve for Syphilis diagnosis**

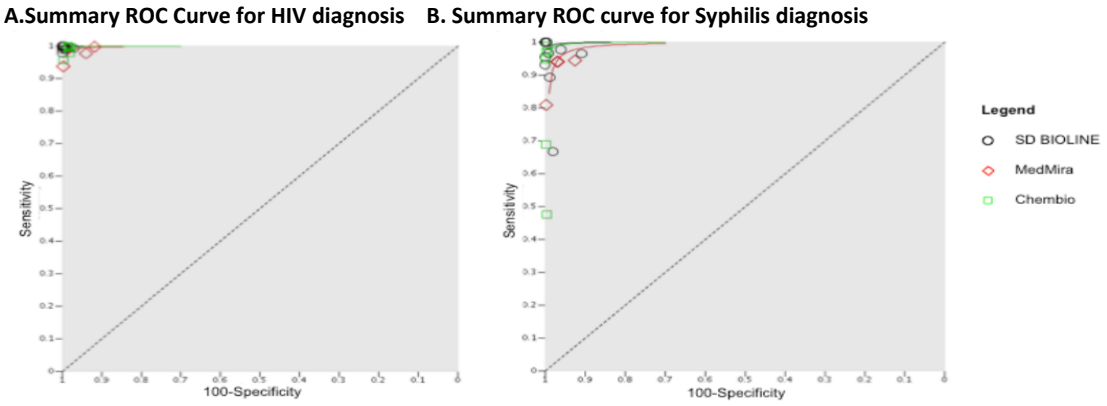


Fig 4: Summary Receiver Operating Characteristic curves showing the diagnostic performance for:
HIV: The MedMira Multiplo Rapid TP/HIV Antibody test shows lower performance compared to the other 2 tests
Syphilis: SD BIOLINE HIV/syphilis Duo Test gives the highest syphilis diagnostic accuracy, followed by the Chembio DPP HIV/Syphilis Assay and then the MedMira Multiplo Rapid TP/HIV Antibody Test; however, these differences are not statistically significant.
Source: Gliddon H. D. et al. STI 2017

Unmet Diagnostic Needs

- Develop tests for active infection, neurosyphilis and congenital syphilis
- Develop point‑of‑care tests with data connectivity or data transmission capability to facilitate automated surveillance and to improve the efficiency of health systems
- Identify & validate biomarkers to accurately distinguish between active and past, treated syphilis & can identify patients who are re-infected and can provide a test of cure

References

- Gliddon, H.D., Peeling, R.W., Kamb, M.L., Toskin, I., Wi, T.E. and Taylor, M.M., 2017. A systematic review and meta-analysis of studies evaluating the performance and operational characteristics of dual point-of-care tests for HIV and syphilis. Sex Transm Infect, pp.sextrans-2016.
- Peeling, R. W. et al. Syphilis. Nat. Rev. Dis. Primers 3, 17073(2017).
- Yin, Yue-Ping, et al. "Laboratory evaluation of three dual rapid diagnostic tests for HIV and syphilis in China and Nigeria." International Journal of *Gynecology & Obstetrics 130.S1 (2015).*
- World Health Organization, 2017. WHO information note on the use of dual HIV/Syphilis rapid diagnostic tests (RDT). In WHO information note on the use of dual HIV/Syphilis Rapid Diagnostic Tests (RDT). Accessed from: http://apps.who.int/iris/bitstream/10665/252849/1/WHO-RHR-17.01-eng.pdf?ua=1