World Health Organization

WHO Information Note on the Use of Dual HIV/Syphilis Rapid Diagnostic Tests (RDT)

Information Note

Advice for countries using or planning to introduce dual HIV/syphilis RDT in antenatal services and other testing sites.

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In 2015, the first multiplex rapid diagnostic test (RDT) for detection of anti- HIV and *anti-treponema pallidum* (dual HIV/syphilis RDT) was listed on the WHO list of prequalified in vitro diagnostic products (IVD) [1]. This information note provides interim advice for countries using or planning to introduce dual HIV/syphilis RDT in antenatal services and other testing sites pending forthcoming WHO programmatic guidance, including a WHO recommended testing strategy. This note also emphasizes the need to ensure the quality of HIV and syphilis testing using RDTs, as well as laboratory-based testing, to avoid false positive and false negative HIV and syphilis results.

Countries have begun using the dual HIV/syphilis RDTs in various settings. Multiple studies have demonstrated good clinical performance in diagnosing both HIV and present or past infection with syphilis [2¬–6]. The WHO prequalification performance evaluation of this RDT observed a final sensitivity for HIV antibodies of 100% (95% CI 98.2–100%) and specificity of 99.5% (95% CI 97.2–100%) compared to the reference assays. For antibodies to *treponema pallidum*, the final sensitivity was 87% (95%CI 81.5–91.3%), with specificity of 99.5% (95%CI 97.2–100%) compared to the reference assays [7].

The dual RDT detects anti-HIV and anti-*treponema pallidum* antibodies in one test device. The test results should be interpreted individually as for tests performed separately and included in WHO recommended standardized testing strategies [8–9]. Though this RDT provides the opportunity to test for HIV and syphilis together, a reactive test result for either pathogen should not be considered definitive and should be followed by additional testing according to the appropriate testing strategy as recommended by WHO.

For the anti-HIV detection component, this includes using at least two serial HIV reactive test results for two assays in high prevalence settings (HIV prevalence >5%), and three reactive HIV test results assays in lower prevalence settings (HIV prevalence <5%) [7].

Dual HIV/syphilis RDT may be selected and validated as Assay 1 of these testing strategies.

See Figures 1 and 2.

For the syphilis component, among pregnant women or in areas with a low prevalence of syphilis, treatment should be considered for anyone with a reactive anti-treponemal test result (i.e. syphilis test line reactive). In populations of high syphilis prevalence which may include key populations such as men who have sex with men (MSM) or sex workers (SW), a reactive test result may represent current infection or past-treated infection. If there is no history of previous treatment, self-reported or otherwise, treatment should be offered. Follow-up testing with a non-treponemal detecting IVD such as (RPR or VDRL) can differentiate individuals with active (untreated) infection from those who have been successfully treated for past infection [9]. This rapid dual test cannot be used to identify re-infection with syphilis in subsequent pregnancies. For this reason, pregnant women who have tested positive and received treatment during a previous pregnancy should be considered for re-treatment upon receiving a positive syphilis test result in subsequent pregnancies.

See figures 3 and 4.

Syphilis should be treated according to the updated WHO treatment guidelines [10].

Current WHO recommendations include HIV and syphilis testing for all women at least once, and preferably in the first trimester of pregnancy [11–12]. The use of the dual HIV/syphilis RDT would facilitate implementation of this recommendation.

Figure 1: WHO recommended HIV testing strategy for high prevalence settings (above 5%)

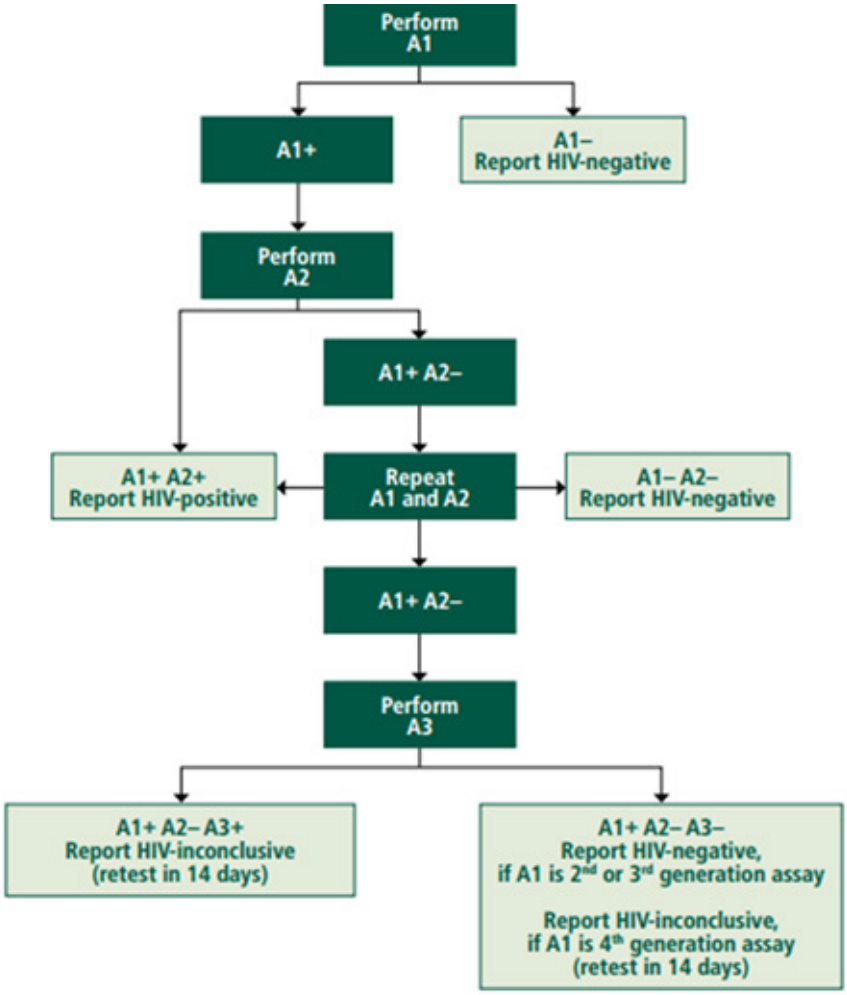
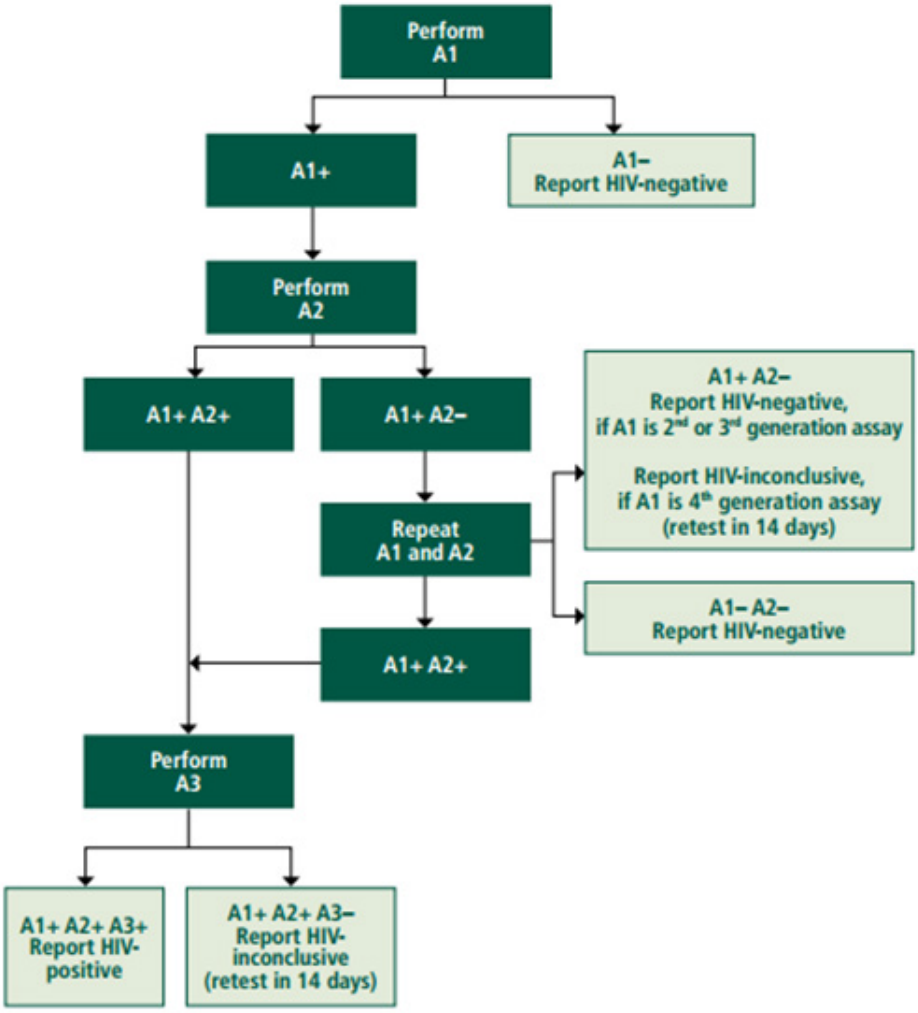


Figure 2: WHO recommended HIV testing strategy for low prevalence settings (below 5%)



WHO is in the process of adapting their recommended standardised testing strategies to include multiplex assays which are consistent with the performance standards defined by the WHO prequalification assessment. In the interim, countries can begin to use the dual HIV/syphilis RDTs. Methodologies for users to perform verification or testing algorithm performance evaluation versus pre-established performance claims prior to introducing an IVD into routine use are available from Clinical & Laboratory Standards Institute (CSLI) [13]. Performance of a verification study before changing national testing algorithms should be considered in addition to ensuring access, increasing screening and treatment coverage of seroreactive individuals, cost, and feasibility analyses.

Figure 3: WHO interim recommended syphilis testing and treatment strategy for low syphilis prevalence settings (below 5%)

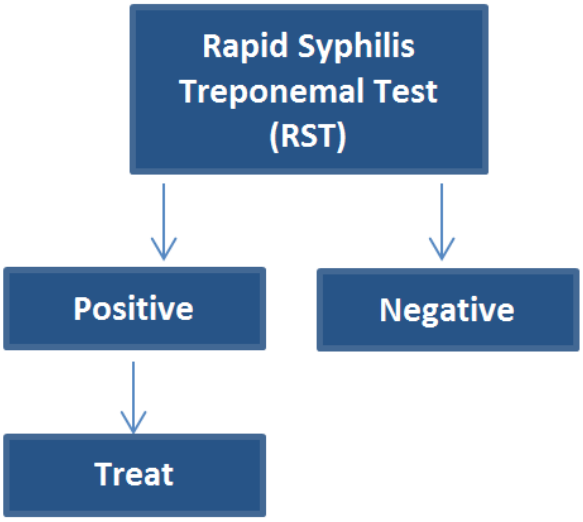
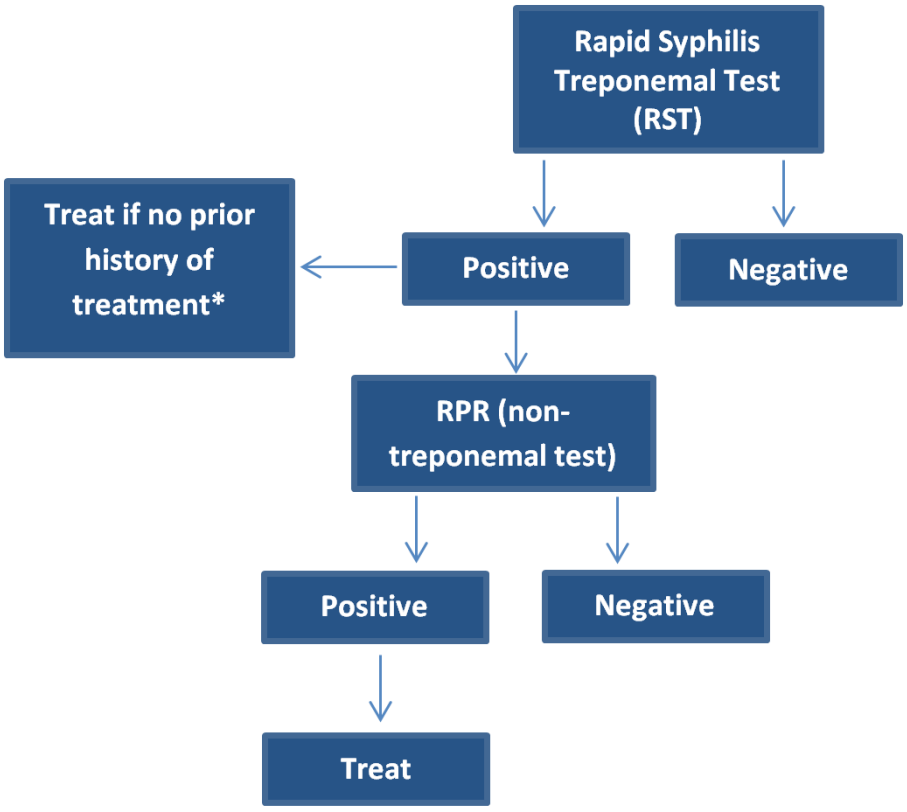


Figure 4: WHO interim recommended syphilis testing and treatment strategy for high syphilis prevalence settings (above 5%)



** Pregnant women who have tested positive and received treatment during a previous pregnancy should be considered for re-treatment upon receiving a positive syphilis test result in subsequent pregnancies.*

Background Information

Approximately 1.5 million pregnant women are seropositive for HIV, and 900,000 are infected with syphilis annually [14–15]. Mother-to-child transmission (MTCT) of HIV and syphilis remain significant causes of perinatal morbidity and mortality [16]. HIV MTCT can occur during pregnancy, delivery, or breastfeeding. Without any intervention, MTCT rates vary between 20% and 35% in breastfed infants or 15% and 20% for non-breastfed infants [17]. However, these MTCT rates can be reduced to less than 5% upon provision of effective interventions [12]. Untreated maternal syphilis results in significant adverse pregnancy outcomes, such as spontaneous abortion, stillbirth, foetal death, preterm birth, low birth weight, neonatal death and congenital syphilis [18]. In addition, maternal syphilis has been shown to increase the risk of MTCT of HIV [19]. Prenatal syphilis screening followed by treatment early in pregnancy effectively treats the pregnant woman and prevents congenital syphilis. In collaboration with WHO regions, WHO has prioritized the elimination of mother to child transmission (EMTCT) of HI [11–12]. Several countries have now achieved validation of EMTCT for HIV and/or syphilis [20].

Screening all pregnant women for HIV and syphilis at the first antenatal care visit is recommended by WHO and in nearly all countries of the world. In countries committed to eliminating mother-to-child transmission (EMTCT) of HIV and syphilis, services are being scaled up rapidly. While the testing of pregnant women for HIV is relatively well-resourced, syphilis-infected pregnant women often go undiagnosed and untreated. While many countries have antenatal syphilis screening policies, more than 350,000 adverse pregnancy outcomes occur annually due to untreated maternal syphilis, despite the low cost of treatment [21]. In order to meet current targets, efforts have been made to accelerate the dual EMTCT of syphilis and HIV [22]. Early diagnosis and treatment of both HIV and syphilis in pregnant women has been proven as an effective strategy in the prevention of both adverse outcomes of pregnancy and MTCT. Key populations, such as men who have sex with men (MSM), transgender people, injecting drug users and sex workers would also benefit from improved HIV and syphilis screening coverage [23–25].

Recent advances in the development of dual HIV/syphilis rapid tests means that there are new testing options to add to the historical set of screening tools such as laboratory-based non-treponemal tests (e.g. RPR and VDRL) and treponemal tests (e.g. TPPA, TPHA) for syphilis, enzyme immunoassays (EIA) and confirmatory assays for HIV, and single pathogen RDTs for either HIV or for treponema pallidum. Additional guidance for the use and interpretation of single rapid HIV and syphilis tests are available [26–27]. Anticipated benefits and advantages of dual HIV/syphilis RDTs may include: streamlined procurement; minimized storage space; simplified training of healthcare personnel; only a single finger-prick required; receipt of test results and treatment in a shorter time period; and reduced unit cost for the reagents compared with two single RDTs for HIV and syphilis.

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