Syphilis Elimination in Indonesia by 2030: Keeping in the Right Track

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ABSTRACT

Syphilis is still a global significant public health issue, including in Indonesia. World Health Organization estimated there were 7 million new syphilis infections in 2020 globally. Ministry of Health Republik Indonesia (RI) reported a total of 76,923 new cases in 2020. World Health Organization has set an ambitious target to reduce the incidence by 90% before 2030, in spite of slow global response. Syphilis elimination target in 2030 can be achieved through good cooperation between ministry of health and relevant institutions at central, provincial, and district/city levels; increasing and expanding public access to screening, diagnosis, and treatment; intensification sexually transmitted infection (STI) prevention such as health promotion, transmission prevention, surveillance, and case management; strengthening partnership and participation across sectors; increasing research and development regarding STI; and strengthening program management through monitoring, evaluation, and follow-up.

Keywords: Elimination, sexually transmitted infection, syphilis.

ABSTRAK

Sifilis masih menjadi masalah kesehatan publik dunia yang signifikan, termasuk di Indonesia. World Health Organization memperkirakan di dunia terdapat 7 juta kasus sifilis baru tahun 2020. Kementerian Kesehatan Republik Indonesia (Kemenkes RI) mencatat 76.923 kasus baru di tahun 2020. WHO telah menargetkan pengurangan insiden sebanyak 90% sebelum tahun 2030, meskipun respons global masih terbilang lambat. Target eliminasi sifilis tahun 2030 dapat dicapai melalui kerja sama yang baik antara Kemenkes RI dan institusi yang relevan di tingkat pusat, provinsi, dan kota/kabupaten; meningkatkan dan memperluas akses publik ke skrining, diagnosis, dan tata laksana; intensifikasi pencegahan IMS melalui promosi kesehatan, pencegahan transmisi, surveilans, dan manajemen kasus; memperkuat kerja sama dan partisipasi lintas sektoral; meningkatkan penelitian dan perkembangan terkait IMS; serta memperkuat manajemen program melalui *monitoring*, evaluasi, dan *follow up*.
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Kata kunci: Eliminasi, infeksi menular seksual, sifilis.

INTRODUCTION

Syphilis is still a significant global public health issue, including in Indonesia. World Health Organization estimated that there were 7 million new syphilis infection in 2020 globally.[1] Ministry of Health Republik Indonesia (RI) reported a total of 76,923 new cases in 2020.[2] WHO has set an ambitious target to reduce the incidence by 90% before 2030,[1] in spite of slow global response.[1] Congenital syphilis cases has decreased as the result of massive interventions in antenatal care, including screening and treatment for pregnant women.[1] However, there are still a lot of work to achieve the target. The major challenge lies in high risk population, particularly in low- and middle-income countries.[1]

Syphilis is a sexually transmitted infection (STI) caused by *Treponema pallidum sub. pallidum*. Like other STI, syphilis can spread through direct contact during vaginal, anal, or oral sex. Syphilis can also be transmitted from a pregnant woman to her baby, whether in utero or direct contact with the lesion during or after delivery. Untreated or delayed treatment of syphilis in pregnancy can cause abortion, prematurity, low birthweight, stillbirth, and congenital syphilis.[3-5]

Stages of Syphilis

Syphilis has distinct stages of disease, each is associated with different clinical manifestations. The first stage is primary syphilis, occurs 10-90 days after contact and is characterized by the appearance of one or more chancres. The chancre, or *ulcus durum*, ranges in diameter from a few millimeters to 2 cm, sharply demarcated with regular, raised indurated borders and clean base. The chancre is classically painless. Secondary syphilis, the second stage, is a disseminated, systemic form

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of infection. Rashes usually erupt 3-12 weeks after chancre appearance, usually nonpruritic. Various types of rashes can be present; erythematous macule or maculopapules are commonly present symmetrically in trunk, extremities including palm and soles. Other dermatologic manifestations include a patchy nonscarring alopecia (moth-eaten), annular papule or plagues around mouth and nose or genital, and the highly infectious condyloma lata.[3,4]

Symptoms of secondary syphilis will subside even without treatment, but the disease will progress to the third stage, or the latent stage; it is a period with no visible signs or symptoms. Seroreactivity is the only evidence of the infection. Asymptomatic patients who acquired syphilis within the last year are classified as early latent infection. If the infection has been acquired for more than 1 year, it is classified as late latent syphilis. About 15% untreated latent syphilis will progress to tertiary stage, the rest will remain latent indefinitely. Tertiary syphilis may affect many different organ systems, such as heart, ocular, and brain and may cause death.[3,4]

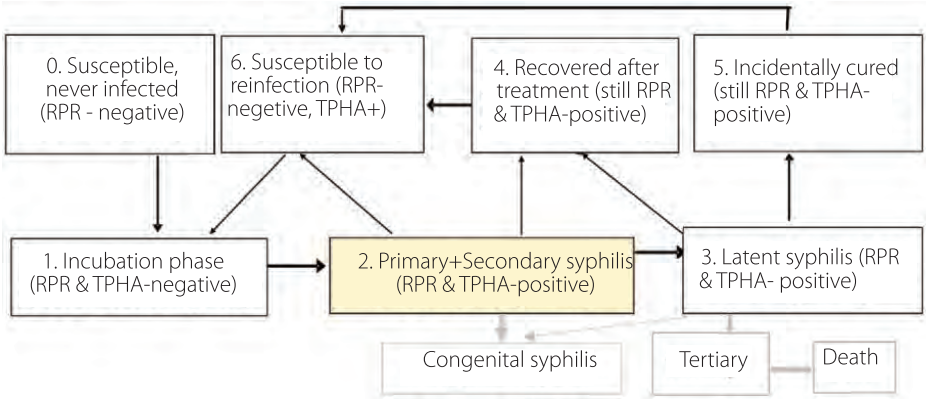
SYPHILIS IN INDONESIA

Like many countries in the world, the incidence and prevalence of sexually transmitted infections in Indonesia are not fully reported. However, the burden is presumably high due to suspected asymptomatic cases, high risk population, limited diagnostic facility and therapy. The latest report showed that STI service is only available in 20% primary health care facility in Indonesia, and only few STI patients looking for treatment,[2] making the actual STI burden is still unknown.

Populations at-risk of contracting syphilis are called key populations. It consist of female sex workers (FSW), men who have sex with men (MSM), transgender, people who inject drugs (PWID), as well as correctional inmates and FSW customers.[2,5–7] Until 2017, syphilis screening in Indonesia, including screening for pregnant women, was targeted to key populations.[2] In 2017, the Ministry of Health issued a regulation on triple elimination (HIV, syphilis, hepatitis B) from mother to child through Peraturan Menteri Kesehatan no 52 tahun 2017,[8] which later was replaced by Peraturan Menteri Kesehatan no 23 tahun 2022.[6] Thus, syphilis screening is more widely implemented. This regulation encourages the expansion of access to syphilis screening to cover lower risk areas and populations, especially pregnant women.[2,5]

Syphilis Regulation in Indonesia

Management of syphilis in Indonesia is now regulated in Peraturan Menteri Kesehatan Republik Indonesia no 23 tahun 2022[6] on the countermeasure of human immunodeficiency virus, acquired immunodeficiency syndrome, and sexually transmitted infections. This regulation set an elimination target of syphilis: (1) incidence in men 6 per 100,000 uninfected population (>15 years old), (2) incidence in women 5 per 100,000 uninfected population (>15 years old), and (3) incidence of congenital syphilis less than 50 per 100,000 live births. These targets are to achieve through good cooperation between ministry of health and relevant institutions at central, provincial, and district/city levels; increasing and expanding public access to screening, diagnosis, and treatment; intensification STI prevention such as health promotion, transmission prevention, surveillance, and case management; strengthening partnership and participation across sectors; increasing research and development regarding STI; and strengthening program management through monitoring, evaluation, and follow-up.[6]



Abbreviations: RPR = Rapid Plasma Reagin test; TPHA =Treponema pallidum hemagglutination assay
Figure 1. Syphilis natural history: flow between modelled infection stages.[9]

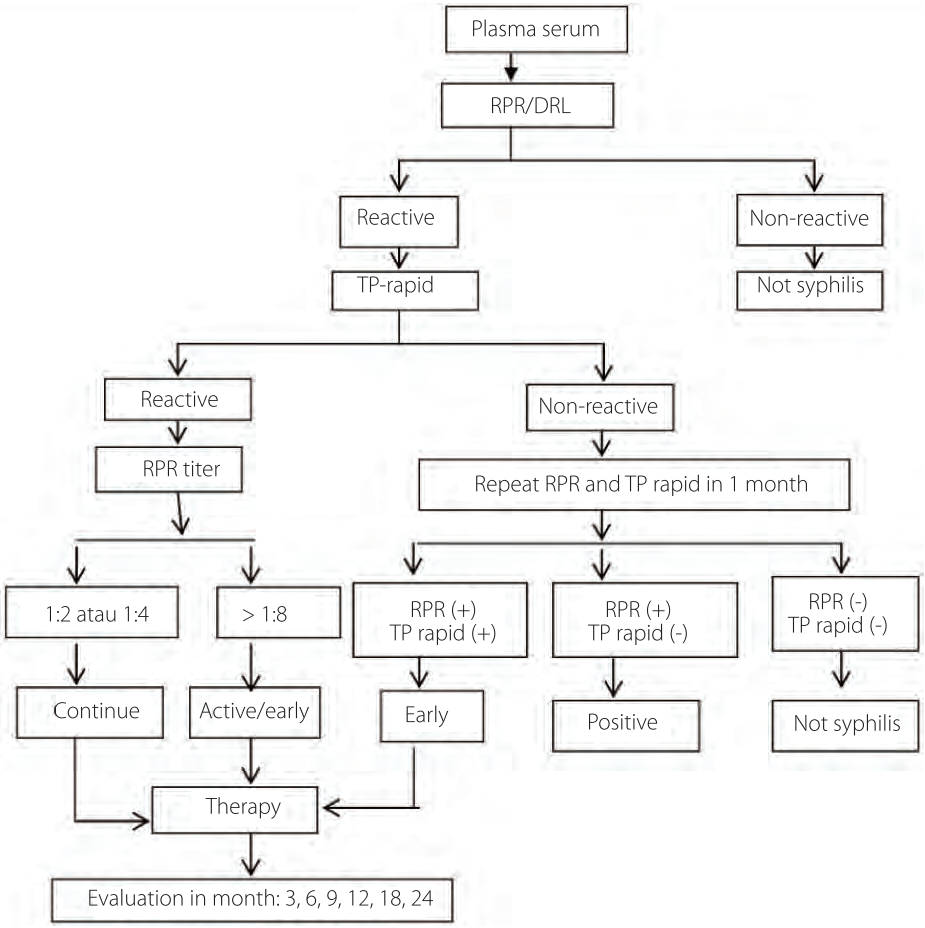
National estimate of prevalence and incidence of STI as well as trend data are important in program planning, resource mobilization, logistic management and supply chain and advocate for investment in STI prevention and treatment and to allocate available resources. According to the *Country Review* Indonesia in 2020,[2] STI burden estimation has to be conducted with estimation tools. For syphilis, the tools are SITE (syphilis interventions towards elimination),[9,10] and WHO congenital syphilis (CS) instrument.[11] SITE was developed as an instrument to simulate syphilis transmission in adults, study impact, service cost, and effectivity of syphilis prevention intervention cost, screening and treatment intervention, as well as intervention/scenario program. While WHO CS instrument was developed by WHO to help countries in aligning number of cases of congenital syphilis with WHO elimination target.[5]

SITE model distinguishes 6 stages of infection: (0) individual at risk of infection, the sum depends on the possibility of transmission per sexual contact, number of sexual partners, number of sexual activities per couple, use of condom and the possibility of meeting infected partner. If left untreated, infected individual will progress to stage (1) incubation period, (2) primary/secondary syphilis, and (3) latent syphilis. The movement rate between stages reflects the assumed duration of stages in untreated infection and the scope of treatment and screening at each stage. (4) Treatment (cured) is assumed only by symptom-based or screening.[2] Individual at latent stage can be cured (5) accidentally while receiving effective antibiotics treatment for other infections. This model also assumes that all treated individual become (6) susceptible to reinfection, same as those who were never infected.[2,9]

The model is used to simulate interventions, including screening followed by treatment for positive result; notification, test, and therapy for the partner of the treated patient; and the use of condom.

Serologic diagnosis of syphilis in Indonesia

Early screening is part of the elimination strategy planned by the Ministry of Health[6]. Serologic tests are needed to confirm clinical diagnosis. Syphilis serologic tests consist of nontreponemal and treponemal test.[5] Nontreponemal tests, such as RPR (Rapid Plasma Reagent) and VDRL (Venereal Diseases Research Laboratory), detect immunoglobulin which is the antibody to the lipid of destroyed *T. pallidum* cells. This antibody can also occur in other condition, such as acute viral infection and autoimmune chronic disease.[5] Therefore, this test is nonspecific and can give false positive result. This test is used to detect infection and active-reinfection, as well as to monitor the therapy. Because this test cost less than the treponemal test, this test usually becomes the screening tool.



Abbreviations: RPR = Rapid Plasma Reagin test; DRL: Disease Research Laboratory
Figure 2. Syphilis serologic tests flowchart if treponemal and nontreponemal tests are available.[5]

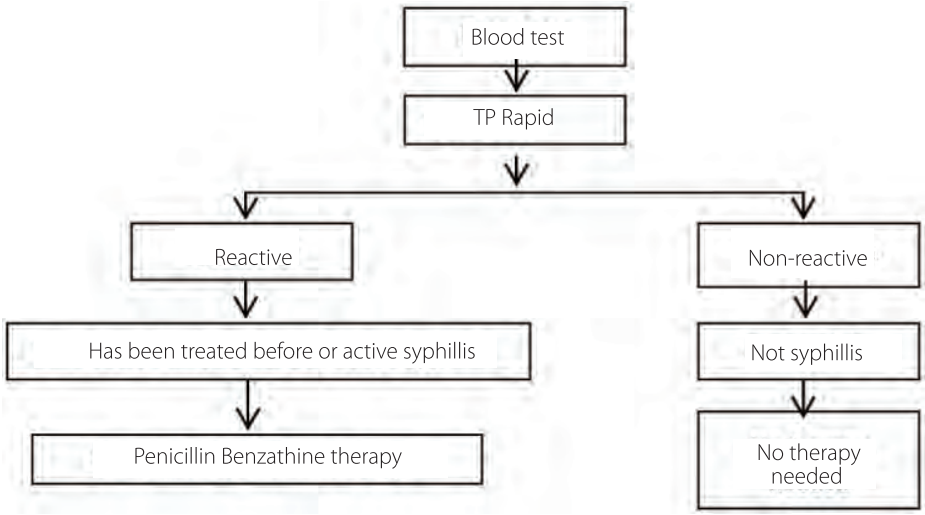


Figure 3. Syphilis serologic tests flowchart when only TP-rapid available.[5]

Treponemal tests, such as TPHA (*Treponema Pallidum* Haemagglutination Assay), TP-PA (*Treponema Pallidum* Particle Agglutination Assay), FTA-ABS (Fluorescent Treponemal Antibody Absorption), can detect antibody specific to Treponema, thus rarely gives false positive result. This test can show reactive/positive result for a lifetime, even if the syphilis therapy has succeeded. Treponemal test only shows that someone has been infected by Treponema, this test cannot distinguish between active infection and adequately treated infection.[5]

Syphilis rapid test (*Treponema pallidum*/TP rapid) is a modest and faster treponemal test method. The kit do not need any specific storage; can use whole blood, and only requires little training to analyse. The use is easy and gives result in a relatively fast time (10-15 minutes). Compared to the other treponemal tests, the sensitivity of this rapid test is around 85%-87% and the specificity is around 93%-98%.[5] TP rapid is not only used as a confirmatory test, but can also be used in syphilis screening; the test cannot be used to monitor therapy or to determine whether this is an active or past infection, just like the other treponemal tests.[5]

Ideally, nontreponemal test has to be followed by the treponemal test. A positive treponemal test only, without nontreponemal test cannot tell whether the patient was having an active syphilis infection now, or a past infection, because treponemal test will always come out positive once a person has been infected. Therefore, nontreponemal test is needed to distinguish the infection, as well as evaluating the treatment by assessing the titers.[5]

However, not all of these tests are available in the healthcare facilities. In limited resources area with high number of cases of syphilis, if RPR or TPHA is not available, TP rapid can be used as syphilis screening, as the test is fast, convenient, and easy to use. If the test is reactive, the patient should be referred to a more complete laboratory for RPR titers, to

make sure it is an active infection. But if titer test is not available as well, Benzathine Penicillin of 2.4 million units intramuscular with adjusted dose according to which stage of syphilis, can be given immediately regarding to high risk possibility.[5]

CONCLUSION

Strategies of syphilis elimination have been well-planned. The burden lies on the implementation of the strategies. The syphilis elimination by 2030 may be achieved with good cooperation between the Ministry of Health and relevant institutions at central, provincial, and district/city levels; an easier access to screening, diagnosis, and treatment; as well as health promotion, transmission prevention, surveillance, and case management.

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