

Sexually Transmitted Infections (STIs): Moving Beyond Syndromic Care to Scalable, Timely Diagnosis

Sexually transmitted infections (STIs) remain an under-addressed public-health burden in many low- and middle-income countries (LMICs). The World Health Organization (WHO) estimates more than 1 million curable STIs are acquired every day worldwide. In 2020, approximately 374 million new infections occurred with one of four curable STIs: chlamydia (CT), gonorrhea (NG), syphilis, or trichomoniasis (TV) the majority of which are asymptomatic.¹ Limited access to timely, affordable diagnostics in primary-care and community settings continues to drive reliance on syndromic management, which enables same-visit treatment but is constrained by poor clinical specificity and sensitivity leading to missed infections and unnecessary overtreatment.² WHO evidence reviews have documented limited diagnostic accuracy of vaginal-discharge syndromic algorithms for detecting cervical infections such as CT and NG, underscoring the need for more accessible etiologic testing.³

These diagnostic gaps have particularly high consequences for STI control, antimicrobial stewardship, and maternal-newborn outcomes. *Neisseria gonorrhoea* (NG) is of growing concern in the context of antimicrobial resistance, and WHO surveillance continues to highlight urogenital NG as a priority pathogen within the global antimicrobial resistance agenda, reinforcing the importance of timely and accurate diagnosis to inform appropriate treatment.⁴ Studies have underscored the need for improved diagnostic approaches to support antimicrobial stewardship and emerging susceptibility-guided treatment strategies for NG.⁵ For syphilis in pregnancy, diagnostic access and rapid treatment remain central to prevention of congenital infection: WHO estimates that in 2022 there were approximately 700,000 cases of congenital syphilis and nearly 390,000 adverse birth outcomes, including stillbirths and neonatal deaths, that are largely preventable with early detection and treatment.⁶

Across curable STIs and high-risk human papillomavirus (hrHPV)-related disease, diagnostic needs vary by programmatic objective but share common constraints. For CT, NG, and TV, the priority is timely etiologic diagnosis that can replace or augment syndromic management, improve case detection among asymptomatic individuals, and support appropriate treatment while limiting unnecessary antibiotic use. For maternal and newborn health, rapid diagnosis of syphilis within antenatal care (ANC) is essential to prevent vertical transmission. For HPV, population-level screening and effective triage are required to sustain cervical cancer prevention programs as they scale.^{2,3,6}

For CT, NG, and TV, the dominant programmatic challenge is the continued reliance on syndromic management for genital discharge and related symptoms, particularly in primary-care, community, and HIV-integrated settings. These infections are frequently asymptomatic, especially among women, and symptom-based algorithms have limited sensitivity and specificity, resulting in substantial numbers of missed infections alongside widespread overtreatment. WHO guidelines acknowledge these limitations and recommend transitioning toward etiologic diagnosis where feasible, with same-day molecular testing for CT and NG preferred and rapid tests considered in more resource-constrained settings.^{2,3} Study evidence further demonstrates both the performance potential and the persistent implementation barriers associated with point-of-care (POC) testing for CT and NG, reinforcing the need for affordable, decentralized diagnostics to support this transition.^{4,5,7}

For syphilis, control is constrained not by a single diagnostic gap, but by multiple, distinct failures across the care pathway, each of which requires a different diagnostic approach. While dual HIV/syphilis treponemal rapid diagnostic tests (RDTs) have expanded initial screening coverage, particularly in antenatal care (ANC), they do not address the full set of programmatic needs for syphilis detection, treatment, and prevention of onward transmission.⁸ In primary and community care, individuals with early syphilis frequently present with genital ulcer disease. In the absence of an available diagnostic test at first presentation, care defaults to syndromic management, which lacks specificity and results in

either overtreatment with penicillin or undertreatment due to misclassification (e.g., herpes), sustaining ongoing community transmission.²

In ANC, dual HIV/syphilis treponemal RDTs used at the first ANC visit identify prior exposure but do not distinguish past treated infection from active disease. Confirmation of active infection often requires follow-up non-treponemal testing, which is frequently laboratory-based. Loss to follow-up between initial screening and confirmatory testing is common, leading to delayed or missed treatment and increasing risk of congenital syphilis.^{6,8} At birth and in the post-natal period, no single diagnostic test exists for congenital syphilis. Diagnosis relies on maternal infection history, paired serology, clinical findings, and radiologic evidence. In low-resource settings, limited laboratory and imaging capacity can necessitate presumptive treatment with long courses of intravenous penicillin or result in missed cases. Fragmented and inconsistent diagnostic pathways contribute to over- or under-treatment of infants.^{6,9}

Taken together, these gaps highlight that dual HIV/syphilis RDTs alone are insufficient to achieve syphilis control goals. Effective elimination will require a portfolio of solutions aligned to distinct programmatic decision points, including early adult detection to reduce transmission, POC confirmatory tests in ANC to prevent congenital infection, and diagnostics capable of definitively identifying congenital syphilis.^{6,8-10}

hrHPV infection adds a third major prevention priority. hrHPV is the cause of nearly all cervical cancers, and because cervical cancer develops over years through identifiable precancerous stages, effective screening programs can prevent progression when they enable timely detection and treatment.¹¹ WHO's 2021 cervical cancer screening guideline recommends hrHPV DNA testing as the preferred primary screening test.¹² A key operational barrier in many settings is loss to follow-up between screening and treatment, and same-day "screen-and-treat" pathways enabled by rapid HPV testing and immediate treatment when appropriate can substantially improve completion of care.¹³ Modelled and empirical studies from LMIC settings show that POC hrHPV testing, including self-collection strategies, can be both effective and cost-effective in reducing cervical cancer burden.^{14,15} In addition to primary screening, an important triage use case remains identifying which hrHPV-positive individuals are at highest risk of high-grade lesions and cancer progression.¹⁶

To guide innovation across these priorities, WHO has developed target product profiles (TPPs) and technology landscape analyses for POC STI diagnostics, including CT, NG TV, and syphilis; and hrHPV screening tests to detect cervical precancer and cancer.^{17,18} These TPPs emphasize that despite existing or emerging POC tests, gaps remain in achieving performance, operational feasibility, and affordability required for large-scale deployment in resource-limited settings.¹⁷ Importantly, the TPPs are technology-agnostic and define functional requirements rather than specific modalities, recognizing that different use cases may be served by different test characteristics and implementation pathways.^{17,18}

Addressing these gaps will require cost-disruptive, decentralized diagnostic solutions that can support high-coverage screening or same-visit diagnosis, integrate into primary-care and community platforms, and reliably link individuals to effective treatment and prevention services. Innovations of interest are those capable of shifting STI care away from reliance on syndromic management toward timely, etiologic diagnosis, while meeting the realities of scale: minimal infrastructure, simple workflows suitable for non-laboratory personnel, robustness in field conditions, and affordability compatible with population-level deployment. Sustained impact will depend not only on test performance, but on alignment with programmatic decision-making, health-system workflows, and equitable access at scale. Additional background and operational guidance are available through WHO's consolidated STI operational handbook.¹⁹

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