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A brief review of the global and Indonesian diagnostic development for sexual transmitted diseases

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ABSTRACT

Sexually transmitted diseases (STDs) exhibit a high prevalence globally, with the World Health Organization (WHO) estimating that more than 1 million new cases are transmitted daily, including chlamydia, syphilis, trichomoniasis, gonorrhea, and viral infections such as hepatitis B virus (HBV), human immunodeficiency virus (HIV), human papillomavirus (HPV), and herpes simplex virus (HSV). Early and accurate diagnosis is imperative for effective disease management and control. Laboratory diagnostic methods play a significant role, contributing 40% to 60% of the diagnostic process. Timely detection not only aids in controlling the spread of STDs but also facilitates prompt treatment. However, Indonesia faces challenges in disease examination due to factors such as inadequate surveillance systems and limited diagnostic facilities, leading to a substantial number of undiagnosed cases. This review critically examines the development of STD diagnostics in Indonesia and globally. The field of global diagnostics is expansive and diverse, with numerous established techniques. Diagnostic methods have evolved rapidly from simple assays to multiplex and computerized assays. Similarly, Indonesia has made progress in diagnostic development, with locally-produced kits already available in the market, signaling a shift towards domestic production of diagnostics. This review provides a comprehensive analysis of these advancements and their implications for STD management.

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1. Introduction

Sexually transmitted diseases (STDs) represent a significant public health concern due to their high prevalence worldwide. The World Health Organization (WHO) has reported that more than 1 million new cases of STDs are transmitted daily (WHO, 2023b). STDs can be classified into two categories: curable STDs, such as chlamydia, gonorrhea, syphilis, and trichomoniasis; and incurable STDs caused by viral infections, including human papillomavirus (HPV) and chronic hepatitis B (WHO, 2023a; 2023b). In 2020, an estimated 374 million infections were attributed to the four curable STDs mentioned above (Garcia et al., 2023). Additionally, approximately 300 million women were affected by HPV, a leading cause of cervical and anal cancers, while 296 million individuals lived with chronic hepatitis B (WHO, 2023a; 2023b). Early examination and detection are crucial for the effective healing and control of diseases (WHO, 2023a). Furthermore, precise and accurate examination is essential to ensure correct diagnosis and appropriate therapy (Santacroce et al., 2021).

One of the key approaches for disease examination involves the use of laboratory diagnostic methods, which play a significant role, contributing approximately 40% to 60% of the disease diagnostic process. These methods enable health authorities to monitor and treat infections accurately and effectively, including screening asymptomatic sexually transmitted diseases (Muller, 2020; WHO, 2023a).

However, Indonesia encounters challenges in disease examination due to several factors, such as an inadequate surveillance system and limited examination facilities. Consequently, a substantial portion of the population remains undiagnosed, highlighting the need for innovative, portable, and point-of-care testing solutions (Muljono, 2017).

Therefore, this literature review aims to provide a comprehensive discussion on the development of diagnostic techniques for sexually transmitted diseases both in Indonesia and globally. The review will address the challenges faced by Indonesia and explore advancements and strategies in diagnostic technologies that can enhance disease detection and management.

A comprehensive literature review was undertaken to compile diagnostic advancements spanning from 2010 to the present, with a particular focus on developments from the last five years (2019-2024) on a global scale. The review specifically emphasized recent breakthroughs in diagnostic technologies. For the context of Indonesian diagnostic developments, a thorough search was conducted to gather information on all diagnostic innovations originating from Indonesia. Each identified article was individually

reviewed to ascertain the methods employed in these diagnostic techniques. Subsequently, the collected literature was categorized and sorted chronologically based on publication date. This systematic approach ensured a detailed examination of diagnostic progress both globally and within Indonesia.

2. Discussion

Sexually transmitted diseases (STDs) are infections transmitted through sexual contact and are categorized into curable and incurable types. Curable STDs include chlamydia, gonorrhoea, syphilis, and trichomoniasis, while incurable STDs due to viral infections include hepatitis B virus (HBV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), and human papillomavirus (HPV) (Garcia et al., 2023; WHO, 2023a; 2023b).

STDs can be transmitted through various routes, primarily via bodily secretions like saliva, mucous, and through wounds, particularly in oral, vulvar, anal, and urethral areas. Transmission can also occur through blood transfusion, contaminated needles, and tattoos, as well as from mother to child (Fu et al., 2022; Santacroce et al., 2021).

This discussion will be divided into two sections: global diagnostics development and Indonesian diagnostics development. The Indonesian diagnostics development section will focus on advancements in diagnostic technologies within the country, highlighting key innovations and progress in STD diagnostics on a local scale.

2.1. Global Diagnostics Development

The breadth of global advancements in diagnostics is vast and complex, rendering it unfeasible to comprehensively cover every aspect individually. Therefore, this section will highlight specific examples, with a particular emphasis on recent progress in diagnosing sexually transmitted diseases (STDs).

2.1.1. Hepatitis B Virus (HBV)

Table 1 presents a concise overview of recent advancements in the diagnosis of patients infected with the HBV.

The detection of hepatitis B typically relies on serological assays, including enzyme immunoassay (EIA), enzyme-linked immunosorbent assay (ELISA), chemiluminescent microparticle immunoassay (CMIA), electrochemiluminescence immunoassay (ECLIA), and molecular assays such as polymerase chain reaction (PCR). Serological detection of HBV involves identifying specific antigens or antibodies indicative of infection, thus characterizing the clinical phase as either acute or chronic. Detection methods are generally categorized as qualitative or quantitative. Qualitative assays determine infection status (positive or negative), while quantitative assays measure HBV DNA or protein levels, providing critical information for treatment monitoring (Abu et al., 2023).

Among the serological methods, ELISA is commonly employed. Recent developments include the use of antibody combinations for sandwich ELISA enhancement. In a study by Kim (2017), optimization was conducted to identify the optimal antibody pair for sandwich ELISA, demonstrating that specific combinations of capture and conjugate antibodies.

A novel approach for HBsAg detection involves the application of a photoelectrochemical immunosensor. The utilization of photoelectrochemical technology offers several advantages, including convenience, affordability, rapidity, and scalability. In this development, ZnAgInS quantum dots (QDs) integrated with gold nanoparticles (GNPs) were employed. The sensor operates based on the photocurrent response generated from the interaction between the target biomolecule and the sensor surface. The presence of GNPs enhances the photocurrent of ZnAgInS QDs under illumination from a white LED light source. The sensor specifically identifies HBsAg utilizing anti-HBsAg as the bio-recognition element. Experimental results demonstrate that the GNPs/ZnAgInS QDs-based biosensor exhibits favorable sensitivity, selectivity, stability, and reproducibility for HBsAg detection (Hu et al., 2018).

Table 1. Global Diagnostic Development on Hepatitis B Virus (HBV) and Current Diagnostic Technologies Summary Highlights

Diagnostic method	Highlights	Advantages	Disadvantages	Literature
Enzyme-Linked Immunosorbent Assay (ELISA)	Utilization of sandwich ELISA employing specific combinations of capture and conjugate antibodies to enhance the limit of detection.	Low limit of detection.	Labor-intensive.	Kim, 2017
Photoelectrochemical immunosensor	Utilization of photocurrent response for detecting biomolecule-sensor interactions.	Convenient, cost-effective, rapid, and amenable to miniaturization.	The selectivity, sensitivity, and stability of the immunosensor are highly influenced by the interaction affinity between anti-HBsAg and HBsAg.	Hu et al., 2018
Raman spectroscopy	Raman spectroscopy utilizes light scattering associated with the chemical structure and analysis of the target material.	This method offers the advantages of not requiring sample pre-treatment, providing non-destructive detection, achieving high-resolution fingerprinting, and offering simplicity and speed in analysis.	Raman effect may exhibit inherent weakness, necessitating rigorous optimization to enhance sensitivity and performance.	Tong et al., 2019
Nanoparticle-based lateral flow biosensors (LFB) combined with isothermal nucleic acid amplification	A point-of-care testing method involving sample amplification using a polymerase spiral reaction (PSR), followed by labelling and immobilization of the amplicon on the surface of colloidal gold nanoparticles.	Rapid, effective, accurate, and cost-effective.	Aerosol droplets may lead to false positive outcomes upon opening the reaction tube, attributable to the PSR assay's high sensitivity.	Lin et al., 2021
Support vector machines (SVMs)-based	Application of machine learning algorithms for disease prediction using routine blood tests.	Capable of integration into existing computer systems to create an intelligent in silico platform.	Required integration of routine pathology results with patient history and clinical notes, along with external validation of the model.	Ajuwon et al., 2023

Raman spectroscopy presents a viable method for HBV detection, leveraging scattering phenomena arising from the interaction between chemical structures and target molecules. The resultant scattering patterns are computationally analyzed to establish unique spectral fingerprints, facilitating the detection of biological molecule characteristics and alterations. Diagnosis of patient conditions can thereby be informed by physiological and molecular changes observed through this spectroscopic approach. Utilization of Raman spectroscopy demonstrates a sensitivity ranging from 80% to 87% and specificity from 79% to 92% in HBV detection (Tong et al., 2019).

Another advancement in diagnostic methodology involves the implementation of point-of-care (POC) testing utilizing nanoparticle-based lateral flow biosensors (LFB) and isothermal nucleic acid amplification, as detailed by Lin et al. (2021). In this approach, blood samples undergo initial amplification via isothermal polymerase spiral reaction (PSR), followed by labeling of the resultant products with FITC and biotin, as illustrated in Fig. 1. These labeled products are subsequently immobilized on the surface of colloidal gold nanoparticles to create hybrid DNA biosensors, allowing for visual detection. The test devised by Lin et al. can be completed within 60 minutes and boasts a detection capability of up to 5.4 copies/mL of HBV DNA.

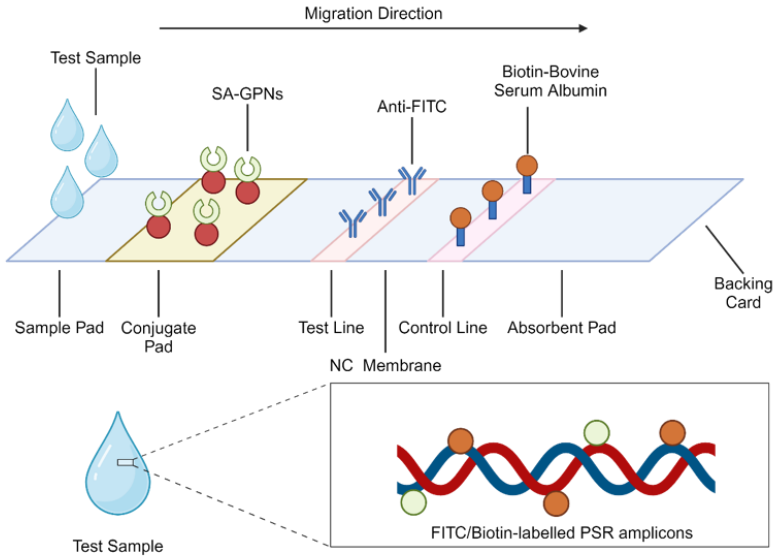

Fig. 1. Lateral flow biosensor with isothermal nucleic acid amplification (Created with BioRender.com) (Lin et al., 2021)

In addition to molecular advancements, diagnostic progress has been made through the application of machine learning algorithms using routine blood test samples, as described by Ajuwon et al. (2023). A support vector machines (SVMs)-based algorithm, supplemented by the random forest algorithm, was employed utilizing predictor variables derived from routine chemical and hematological markers prioritized by importance for distinguishing HBsAg-positive and -negative cases. Subsequently, a decision tree model was constructed based on this data. The outcomes of Ajuwon et al. (2023) algorithm yielded diagnostic accuracy of 85.4%, sensitivity of 91%, specificity of 72.6%, and precision of 88.2% in identifying patients with hepatitis B.

2.1.2. Human immunodeficiency virus (HIV)

The key developments in the diagnosis of HIV-infected patients are outlined in Table 2, summarizing recent advancements in this area.

The standard method for HIV diagnosis involves the use of a serum-based assay known as the HIV fourth-generation test, which combines antibody (Ab) and antigen (Ag) detection. This fourth-generation test is capable of detecting both HIV-1 and HIV-2, along with the p24 antigen. The presence of the p24 antigen can be identified as early as 14 days post-exposure. In cases where the antigen is positive, but the antibody is negative, confirmation through RNA testing is necessary to verify or refute the initial findings. RNA testing can also be employed to identify infection prior to p24 antigen formation (Huynh and Kahwaji, 2023).

Another screening method involves the use of rapid tests, which offer same-day results within approximately 30 minutes, making them cost-effective and user-friendly. Rapid tests commonly employ immunochromatography techniques. Various commercial rapid tests include Alere Determine HIV 1&2 (Alere Medical, Japan), DPP Rapid Test HIV 1/2 (Labtest, Brazil), DS Rapid Test HIV (Labtest, Brazil), Imunocrom HIV 1/2 (Mbiolog Diagnostico, Brazil), and HIV 1/2/O Tri-line (Abon Biopharm (Hangzhou) Co Ltd., China). An example of a lateral flow immunochromatography-based rapid test is Interkit HIV 1&2 (Intertek Katal Biotecnologica, Brazil). These rapid tests boast sensitivities exceeding 98.7% and specificities exceeding 99.7%, as per manufacturer specifications. However, it was observed that despite their utility, internal validation of rapid tests is imperative (Marinho et al., 2020).

As per the guidance provided by the Centers for Disease Control and Prevention (CDC), the utilization of point-of-care (POC) HIV testing is essential for advancing diagnostic methods into regions characterized by high-risk HIV prevalence but limited accessibility. POC testing is favored due to its simplicity, societal acceptance, and rapid result provision. Numerous tests have been developed to address this need, with notable progress seen in the creation of the OraQuick ADVANCE® Rapid HIV-1/2 test. This test employs a lateral flow assay and allows for independent sample collection, even in home settings. The OraQuick test is designed to detect both HIV-1 and HIV-2, utilizing a patient's gum swab sample inserted into a dedicated device, yielding results within 20 to 40 minutes.

Subsequent to the introduction of OraQuick, the Chembio DPP® HIV-1/2 test was developed, enabling sample analysis from oral fluid or whole blood. Additionally, the Determine™ HIV-1/2 Ag/Ab Combo and INSTI® HIV-1/HIV-2 Rapid Antibody Test utilize whole blood samples. A comparative study of POC methods highlighted that whole blood specimens exhibit higher sensitivity and specificity than oral fluid. Whole blood demonstrated sensitivity ranging from 95.53% to 97.21% and specificity from

98.84% to 99.42%, whereas oral fluid exhibited sensitivity of 89.94% to 92.18% and specificity of 93.06% to 95.38%.

Despite the observed differences, POC rapid tests remain viable options due to their commendable specificity and sensitivity levels (Chavez et al., 2020; FDA, 2012; Neuman et al., 2022).

In addition to rapid tests, several quantitative polymerase chain reaction (qPCR) assays have been developed to detect various aspects of HIV-1, including proviral DNA, RNA load, integration using Alu-PCR, and the long terminal repeat (LTR) region. Notably, Chung et al. (2022) contributed to this field by developing a droplet digital PCR (ddPCR) method. ddPCR offers improved accuracy, precision, and reproducibility compared to traditional qPCR, although it may not consistently exhibit greater sensitivity. Unlike standard PCR methods utilizing tubes, ddPCR utilizes a reaction mix that is randomly partitioned into droplets, each containing the target sequence, primers, dual quenched probes, and PCR master mix with enzyme. The employment of dual quenched probes serves to enhance the differentiation between signal and noise. According to Chung et al. (2022), ddPCR demonstrates the ability to detect low levels of virus that may go undetected by qPCR.

Table 2. Global diagnostic development on human immunodeficiency virus (HIV) and current diagnostic technologies summary highlights

Diagnostic method	Highlights	Advantages	Disadvantages	Literature
Antigen (Ag)-Antibody (Ab) combination test	Referred to as a fourth-generation test and considered the standard assay.	Capable of detecting HIV-1, HIV-2, and p24 antigen.	May fail to detect very early infections.	Huynh and Kahwaji, 2023
Lateral flow immunochromatography based rapid test	Enables same-day results, cost-effectiveness, and user-friendly operation. Commercialized kits: - Alere Determine HIV 1&2 (Alere Medical, Japan) - DPP Rapid Test HIV 1/2 (Labtest, Brazil) - DS Rapid Test HIV (Labtest, Brazil) - Imunocrom HIV 1/2 (Mbiolog Diagnostico, Brazil) - HIV 1/2/O Tri-line (Abon Biopharm (Hangzhou Co Ltda., China) - Interkit HIV 1&2 (Intertek Katal Biotecnologica, Brazil)	Can be utilized in settings lacking laboratory infrastructure and in remote or inaccessible regions. Offers affordability, rapid results, and simplicity of operation.	Internal validation is still necessary.	Marinho et al., 2020
	The table highlights the development of a point-of-care testing method characterized by its high specificity and sensitivity. Commercialized kits: Uses oral sample: OraQuick ADVANCE® Rapid HIV-1/2 Uses oral and whole blood: Chembio DPP® HIV-1/2 Uses whole blood: - Determine™ HIV-1/2 Ag/Ab Combo - INSTI® HIV-1/HIV-2 Rapid Antibody Test	Demonstrates high specificity and sensitivity.	using oral fluid for testing patients on PrEP could lead to false positive results, necessitating additional onsite or laboratory HIV testing. Additionally, this method exhibits lower sensitivity in identifying acute HIV infection (AHI).	Chavez et al., 2020; FDA, 2012; Neuman et al., 2022
Droplet digital Polymerase Chain Reaction (ddPCR)	This method involves the random distribution of a reaction mix into droplets, where each droplet contains the target sequence, primer, dual quenched probes, and PCR master mix with enzyme preloaded.	ddPCR demonstrates superior sensitivity compared to qPCR, enabling the detection of virus at low levels that are undetectable by qPCR.	Not consistently more sensitive than qPCR.	Chung et al., 2022

2.1.3. Herpes simplex virus (HSV)

Table 3 presents a summary of recent advances in the diagnosis of patients infected with HSV. This table outlines notable developments in HSV diagnostic techniques.

Traditionally, detection of the herpes virus has relied on microscopic imaging methods such as brightfield, confocal, or transmission electron microscopy (TEM). Additionally, viral glycoprotein detection has been achieved through agglutination and western blot techniques. One common agglutination assay utilized is the latex agglutination test, exemplified by the Virogen Herpes Slide Test (Wampole Laboratories, Cranbury, N.J.). In this test, the sample is mixed with a solution containing latex particles coated with HSV-specific antibodies in a test well. Positive samples exhibit observable agglutination clumps.

In western blot analysis, viral proteins are initially separated by gel electrophoresis based on their molecular weight. Subsequently, target proteins are transferred to a membrane and probed with specific antibodies labeled with fluorescent or radioactive isotopes. The position of the target protein on the gel, relative to a protein ladder, provides information about its molecular weight (Nath et al., 2021; Storch et al., 1988; Yoshida, 1994). Advancements in HSV detection have led to the adoption of polymerase chain reaction (PCR)-based diagnostic techniques and serology tests (Nath et al., 2021).

PCR testing involves the collection of tissue or blood samples via swabbing of cutaneous or mucosal tissue, followed by DNA extraction and amplification using PCR (de Montmollin et al., 2022; Madhavan et al., 1999; Schremser et al., 2020). In a separate investigation, ocular samples, particularly tears, were gathered and subjected to detection through a combination of DNA and serology tests. Real-time PCR targeting HSV DNA and HSV-sIgA ELISA were employed. The study demonstrated that HSV DNA testing achieved

a sensitivity of 55.8% and a specificity of 100%. Integration of ELISA results increased the positive predictive value to 90.9% and the negative predictive value to 61.3%, thereby enhancing test reliability (Shoji et al., 2016).

In another study, the IsoAmp HSV assay, a multiplex PCR test, was developed to provide results within 1 hour. This test utilized a two-step cycling probe technology (CPT) method to enhance sensitivity. The CPT method employed a DNA-RNA-DNA probe, which was cleaved by RNAse H when bound to the target sequence. The assay also used a portable fluorescence detector called FireFly, allowing PCR to be performed at the point of care (Tong et al., 2012).

Serological tests can be conducted using various methodologies including chemiluminescent immunoassay (CLIA), ELISA, and immunoblot techniques (de Ory et al., 2018). In the advancement of chemiluminescent technology for HSV detection, an investigation into the automation of chemiluminescent immunoassay (CLIA) was undertaken. Blood serum samples were utilized in this evaluation, where magnetic particles and antibody-isoluminol conjugates were employed for testing. The findings indicated that CLIA exhibited high sensitivity in detecting IgG anti-HSV-1 and HSV-2. Notably, the presence of elevated levels of hemoglobin, lipids, and bilirubin in the sample did not interfere with the accuracy of the results, thus affirming CLIA as a robust method for quantifying IgG HSV antibodies (Li et al., 2016).

ELISA, such as IgG-G2 Human® (Human Diagnostics, Germany), is utilized for IgG anti-HSV detection, with a testing duration of approximately 1.5 hours using TMB as the substrate. García-Cisneros et al. (2019) demonstrated that IgG-G2 Human® exhibited a sensitivity of 92% and specificity of 98% in their study.

Similarly, immunoblotting kits like Anti-HSV-1/HSV-2-gG-2 EUROLINE-WB (EUROIMMUN®, Germany) employ a nitrocellulose membrane containing HSV-1 extract and a membrane chip containing HSV-2 G2 protein. According to García-Cisneros et al. (2019), EUROLINE-WB demonstrated a sensitivity of 98.9% and specificity of 100%, affirming its reliability in detecting IgG antibodies against HSV.

Conclusively, both ELISA and immunoblotting techniques present robust options for IgG detection in HSV infections (García-Cisneros et al., 2019).

Table 3. Global diagnostic development on herpes simplex virus (HSV) and current diagnostic technologies summary highlights

Diagnostic method	Highlights	Advantages	Disadvantages	Literature
Latex agglutination test	Derived from the observed agglutination of latex particles coated with HSV-specific antibodies and HSV antigen. Commercial latex agglutination test: Virogen Herpes Slide Test (Wampole laboratories, Cranbury, N.J.)	Exhibits high sensitivity and specificity.	Could not differentiate between HSV type 1 and 2.	Nath et al., 2021; Storch et al., 1988; Yoshida, 1994
Western blot assay	The viral proteins were separated by molecular weight, transferred to a membrane, and then labeled with an antibody.	Accurate for detecting HSV antigens.	The test can produce false-negative outcomes for HSV-2 infection in individuals who have previously tested positive for HSV-1. Additionally, it is expensive and time consuming.	Nath et al., 2021; Storch et al., 1988; Yoshida, 1994
Real-time PCR combined with ELISA	Incorporating real-time PCR targeting HSV DNA alongside HSV-specific IgA ELISA with ocular samples enhances the overall robustness of the diagnostic testing methodology.	This approach enhances the reliability in diagnosing the various subgroups of herpes simplex keratitis (HSK).	The HSV DNA value is comparatively lower in disciform HSK than in dendritic or geographic HSK.	Shoji et al., 2016
Multiplex PCR	The development of a point-of-care assay known as the IsoAmp HSV assay involves the utilization of two-step cycling probe technology (CPT) in conjunction with a portable fluorescence detector known as FireFly.	Demonstrates sensitivities similar to those of FDA-cleared assays, offering portability, high throughput, and rapid results (within 1.5 hours).	Competitive inhibition of HSV-2 amplification can be observed with a tenfold excess of HSV-1, and similarly, competitive inhibition of HSV-1 amplification can be detected with a tenfold excess of HSV-2.	Tong et al., 2012
Chemiluminescent immunoassay (CLIA)	Utilization of magnetic particles and antibody-isoluminol conjugate enables the detection of antibodies against HSV-1 and HSV-2.	This method is less labor-intensive compared to ELISA, and it exhibits high sensitivity. Additionally, high concentrations of hemoglobin, lipids, and bilirubin in samples do not interfere with the test results.	High cost.	Li et al., 2016
ELISA	This assay detects IgG antibodies against HSV and is available commercially as the Human® kit from Human Diagnostics, Germany.	The method can utilize dried blood spot (DBS) as a sample with appropriate optimization.	The use of DBS samples exhibits very low specificity, necessitating further analysis with Western blotting for confirmation.	García-Cisneros et al., 2019
Immunoblot	This method employs a nitrocellulose membrane featuring HSV-1 extract and a membrane chip containing HSV-2 G2 protein. It is available commercially as the Anti-HSV-1/HSV-2-gG-2 EUROLINE-WB kit from EUROIMMUN®, Germany.	Demonstrates high sensitivity and specificity, with potential for optimization when using dried blood spot (DBS) samples.	Costly and requires significant time investment.	García-Cisneros et al., 2019

2.1.4. Human papillomavirus (HPV)

Table 4 presents a comprehensive overview of recent progress in diagnosing individuals with HPV infection.

The detection of HPV initially relied on cytology, particularly the Pap test, which analyzed cells obtained from the cervix. However, the Pap test has limitations, including low reproducibility and susceptibility to interference from blood and mucus (Chrysostomou & Kostrikis, 2020). Consequently, subsequent advancements in HPV diagnostics shifted towards virus identification. HPV examination primarily involves detecting HPV DNA. However, due to the transient nature of HPV DNA detection, ELISA-based testing was developed to measure HPV-specific immunity (Karem et al., 2002). Karem et al. (2002) developed an ELISA method for detecting HPV-specific antibodies using virus-like particles (VLPs) produced through a baculovirus expression system with SF21 cells. These VLPs were coated onto plates, and ELISA readings were performed at 405 nm using a phosphatase substrate. The optimized ELISA demonstrated a sensitivity of 93% and specificity of 98.5% (Karem et al., 2002).

Additionally, an EIA test combined with PCR, known as the GP5+/6+ PCR-based EIA kit HPV GP HR (EIA; Diassay, Rijswijk, Netherlands), was developed to amplify DNA samples using broad-spectrum primers. A specific cocktail probe for 14 high-risk HPV (hrHPV) genotypes was then hybridized to the amplicon in the EIA. Although this assay does not identify specific HPV genotypes, it exhibits high specificity for HPV diagnosis (Geraets et al., 2014; Hesselink et al., 2006).

Table 4. Global diagnostic development on human papillomavirus (HPV) and current diagnostic technologies summary highlights

Diagnostic method	Highlights	Advantages	Disadvantages	Literature
ELISA	Virus-like particles (VLPs) employed as plate coating exhibit high sensitivity and specificity.	Demonstrates reproducibility, along with high sensitivity and specificity.	To minimize the rates of false positives and false negatives, it is essential to employ multiple methods concurrently to ensure the consistency of cutoff value (COV) estimates.	Karem et al., 2002
Enzyme immunoassay (EIA) combined with PCR	DNA samples are initially amplified using broad-spectrum primers and subsequently hybridized in an EIA setup. This process is facilitated by the GP5+/6+ PCR-based EIA kit for high-risk HPV (hrHPV), commercially available from Diassay, Rijswijk, Netherlands.	Based on extensively clinically validated GP5+/6+ PCR, high-throughput and full genotyping capability, and could be verified using internal control.	Labor-intensive.	Geraets et al., 2014; Hesselink et al., 2006
ELISA	Pseudovirion (PsV)-based ELISA for the detection of HPV-specific IgG and IgM antibodies, facilitating the differentiation between IgG and IgM antibody responses.	Capable of distinguishing between IgG and IgM antibodies without the need for purification steps.	Detects both neutralizing and non-neutralizing antibodies, occasionally leading to an overestimation of the antibody response.	Toh et al., 2020
PCR	Detection of high-risk human papillomavirus (hrHPV) DNA, validated by the VALGENT, employs urine as the specimen, commercialized kit: Cobas® 4800 HPV Test (Roche).	Urine could be used as the specimen for this assay.	Further validation is required.	Wityawan et al., 2022
PCR Self-sampling	Suitable for self-sampling testing with commercially available kits: • Evalyn® Brush (Rovers® Medical Devices, Netherlands) • careHPV (Qiagen, Hilden, Germany)	Suitable for self-sampling with high acceptability and preference, characterized by ease of use, rapidity, accuracy, and safety.	More costly.	Fujita et al., 2023; Holme et al., 2020

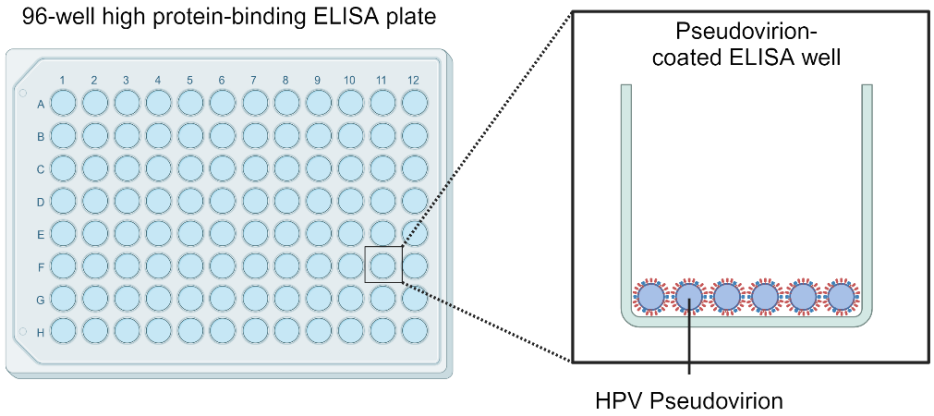

Fig. 2. Pseudovirion-coated 96-well ELISA plate by Toh et al. (2020)

The gold-standard method for measuring HPV antibodies is the pseudovirion-based neutralization assay (PBNA). However, due to its complexity and labor-intensive nature, PBNA lacks the ability to distinguish between different antibody isotypes and subclasses. To address this, a PsV-based ELISA protocol was developed to measure HPV-specific IgG and IgM antibodies. This involved transfecting HPV plasmid into HEK293TT cells with HPT16 plasmid DNA to produce PsV, which was then coated onto ELISA plates (Toh et al., 2020). This method successfully differentiated between IgG and IgM

antibodies, offering a viable alternative to PBNA for HPV antibody measurement.

To establish a standardized validation system, the Validation of HPV Genotyping Test (VALGENT) initiative was established with the aim of validating and comparing HPV genotyping tests, particularly nucleic acid-based tests (Arbyn et al., 2016; Chrysostomou and Kostrikis, 2020). Screening tests can generally be categorized into four groups based on their capabilities: HPV DNA tests that do not differentiate between genotypes, HPV DNA tests that partially differentiate genotypes, HPV DNA tests capable of distinguishing 12 oncogenic genotypes, and HPV mRNA tests capable of identifying individual genotypes (Cuschieri et al., 2023). Among the tests validated by VALGENT is the Cobas® 4800 HPV Test (Roche), which utilizes samples obtained from the cervix or urine. Following sample collection, polymerase chain reaction (PCR) is performed to detect hrHPV DNA. A study conducted on Indonesians revealed that this test exhibited a sensitivity of 87.5% and a specificity of 84%, indicating the potential for detecting hrHPV infection in the cervix using urine samples (Wityawan et al., 2022).

To broaden access to cervical cancer screening, investigations into self-sampling methods have been undertaken in various regions, including Japan and Central America. In Japan, the Accelerating Cervical Cancer Elimination by Self-Sampling (ACCESS) trial, a randomized controlled trial, evaluated the use of the Evalyn® Brush self-sampling kit (Rovers® Medical Devices, Netherlands). Meanwhile, in Central America, an assay known as careHPV (Qiagen, Hilden, Germany) was employed. This assay utilizes HPV DNA amplification to detect 14 types of hrHPV DNA. The outcomes of these studies demonstrated that self-sampling methods were well-received and could serve as effective strategies to promote broader participation in cervical cancer testing (Fujita et al., 2023; Holme et al., 2020).

2.1.5. Gonorrhoea, Chlamydia, and Trichomoniasis

The table presented in this review article outlines the key developments in diagnosing individuals with gonorrhea, chlamydia, and trichomoniasis, reflecting the recent advancements in this field.

Table 5. Global diagnostic development on gonorrhoea, chlamydia, and trichomoniasis and current diagnostic technologies summary highlights

Diagnostic method	Highlights	Advantages	Disadvantages	Literature
Multiplex PCR assay	Capable of simultaneous detection of gonorrhea, chlamydia, and trichomonas using a Taqman-based PCR assay employing quenchers and fluorophores. Commercialized assay: BD Max CT/GC/TV (MAX) assay	The method is capable of conducting multiple assays simultaneously and demonstrates high sensitivity and specificity when using vaginal, endocervical, and urine samples.	Further evaluation is required for anorectal and oropharyngeal sample types.	Van Der Pol et al., 2017; Van Der Pol et al., 2021
	FDA-approved point-of-care multiplex PCR testing capable of simultaneous detection of the three diseases. Commercialized kit: Visby Medical™	Compact, portable, scalable, and maintenance-free.	Further validation is required using samples from all genders and anatomical sites.	BioSpace, 2021; Morris et al., 2021
	Point-of-care testing for chlamydia and gonorrhea providing results within 30 minutes. Commercialized kit: binx health io®	The test provides prompt results.	Does not include a test for trichomoniasis.	binx, 2020; Van Der Pol et al., 2020; Van Der Pol and Gaydos, 2021
Lateral flow immunoassay	Point-of-care testing suitable for home use, capable of detecting *T. vaginalis* adhesin in trichomoniasis assays, utilizing immobilized capture antibody with blue particle dye. Commercialized kit: OSOM®	Straightforward to execute, does not require any specialized equipment, and can be completed within 15 minutes.	Limited to testing for trichomoniasis only.	Gaydos et al., 2017; Ibáñez-Escribano and Nogal-Ruiz, 2024

Several diagnostic methods are available for detecting gonorrhea, chlamydia, and trichomoniasis, encompassing morphological observation using a microscope, culture techniques, antigen detection, and nucleic acid amplification assays. Specimens used for testing typically include urine samples or vaginal swabs (Caruso et al., 2021). Notably, a multiplex nucleic acid assay has been developed to simultaneously identify chlamydia, gonorrhea, and trichomonas, utilizing endocervical and vaginal swabs as well as urine samples. This assay, known as the BD Max CT/GC/TV (MAX) assay, employs a TaqMan-based PCR method featuring specific target primers, with amplification incorporating quenchers and fluorophores. The testing process requires approximately 3 hours to complete. Evaluation of the assay's performance revealed a sensitivity ranging from 91.5% to 99.3% for chlamydia, varying by swab type, with vaginal swabs demonstrating the highest sensitivity. For gonorrhea, sensitivity ranged from 95.5% to 99.1%, with urine samples from men exhibiting the highest sensitivity. Regarding trichomoniasis, sensitivity ranged from 92.9% to 96.1%, with vaginal swabs also showing the highest sensitivity levels. These findings indicate that the BD Max CT/GC/TV assay is suitable for screening gonorrhea, chlamydia, and trichomoniasis in smaller laboratory settings (Van Der Pol et al., 2017).

Several point-of-care (POC) products have been developed for detecting gonorrhea, chlamydia, and trichomoniasis. One such product is Visby MedicalTM, which has received FDA approval. This test utilizes multiplex PCR technology for simultaneous detection of the three diseases and demonstrates a sensitivity ranging from 97.4% to 99.2%, along with a specificity between 96.9% and 99.4% (BioSpace, 2021; Morris et al., 2021).

Another POC testing option is the binx health io®, designed for chlamydia and gonorrhea detection. This test also employs nucleic acid amplification principles and yields results within 30 minutes. It boasts a sensitivity of 92.5% to 100% and a specificity of 99.1% to 100% (binx, 2020; Van Der Pol et al., 2020; Van Der Pol and Gaydos, 2021).

For trichomoniasis, the OSOM® test was developed, utilizing a lateral flow immunoassay to detect *T. vaginalis* adhesin. This test involves capture antibodies immobilized on nitrocellulose, with blue particles serving as the dye. Formation of an immune complex results in the appearance of a test line. The OSOM® test exhibits a sensitivity of 83% to 90% and can be performed by patients at home (Gaydos et al., 2017; Ibáñez-Escribano and Nogal-Ruiz, 2024).

2.1.6. Syphilis

Table 6 in this review article provides a concise overview of the latest advancements in diagnosing patients with syphilis.

Syphilis is caused by the bacterium *Treponema pallidum*. Direct detection of this pathogen can be achieved using microscopy, PCR (polymerase chain reaction), and direct fluorescent antibody testing specifically targeting *T. pallidum*. However, these methods are not widely available in clinical settings, leading most centers to rely on clinical signs and serological testing (Henao-Martínez and Johnson, 2014). The clinical manifestation of syphilis occurs in two stages. Primary syphilis develops at the initial exposure to an infected individual, characterized by an inflammatory response and the formation of a lesion approximately three weeks after infection. Without treatment, this lesion resolves spontaneously within two to three weeks, followed by the onset of secondary syphilis after four to eight weeks. PCR testing can detect a specific gene from *T. pallidum* DNA during both primary and secondary stages, particularly useful for oral lesions or other commensal treponemes. PCR can be conducted either quantitatively or qualitatively and typically requires about 40 minutes for completion. In addition to PCR, serological testing for syphilis involves two types of tests: treponemal and nontreponemal. Nontreponemal tests detect immunoglobulin (Ig) G and M antibodies against lipid antigens released by damaged cells and bacteria. Treponemal tests, on the other hand, detect IgG and IgM antibodies specifically targeting *T. pallidum*. Diagnosis of syphilis typically requires both nontreponemal and treponemal serological tests to confirm infection (Henao-Martínez and Johnson, 2014; Purwoko et al., 2021).

One of the developed diagnostic tests is the rapid syphilis treponemal (RST) test, specifically the Syphilis Health Check (SHC) manufactured by Diagnostics Direct. This rapid test identifies antibodies against *T. pallidum* antigen using recombinant treponemal antigen. The specimen utilized is a blood sample, with the concurrent nontreponemal test being the rapid plasma reagin (RPR) test, employed to detect antibodies against syphilis. The findings revealed a sensitivity of 76.9% and a specificity of 99%, indicating the test's suitability for screening purposes (Fakile et al., 2019b). Another noteworthy development is the qualitative RPR (Sure-Vue RPR; biokit/INOVA Diagnostics, Inv, San Diego, CA), a flocculation test, and Trep-Sure EIA (Trinity Biotech, Jamestown, NY). In an investigation where the Syphilis Health Check (SHC) was examined using whole blood obtained from fingersticks, the results demonstrated a sensitivity and specificity of 100% and 95.7%, respectively, when compared against consensus reference testing (CRT). However, the comparison with treponemal EIA yielded a sensitivity of 50% and a specificity of 95.9%. These outcomes affirm the utility of SHC in identifying potentially syphilis-infected patients when employing whole blood as the sample (Fakile et al., 2019a).

Table 6. Global diagnostic development on syphilis and current diagnostic technologies summary highlights

Diagnostic method	Highlights	Advantages	Disadvantages	Literature
Rapid immunochromato-graphic test Immunochromato-graphic test	Detects antibodies against *T. pallidum* antigen using recombinant treponemal antigen. Commercialized kit: Syphilis Health Check (SHC) by Diagnostics Direct	Demonstrates high sensitivity and can utilize whole blood as the specimen.	Proper training is necessary for individuals conducting the testing to ensure accurate results.	Fakile et al., 2019b
	Point-of-care testing that identifies treponemal antibodies using finger prick blood, capable of detecting syphilis in individuals living with HIV (PLWH). Commercialized kit: - SD Bioline Syphilis 3.0 (Standard Diagnostics Inc, Kyonggi-do, Korea) - Alere Determine Syphilis TP (Abbott Diagnostics Medical Co, Ltd)	Fast, suitable for use in low-resource settings, and yields rapid test results.	Additional training may impact sensitivity, potentially resulting in false negative syphilis results if sample volume is compromised.	Luna et al., 2023
Flocculation test	One commercially available standard RPR test is Sure-Vue RPR (Biokit/INOVA Diagnostics, Inc., San Diego, CA).	Cost-effective and straightforward to conduct.	Requires personnel with appropriate training.	Fakile et al., 2019a
EIA	EIA-based, Trep-Sure EIA (Trinity, Biotech, Jamestown, NY).	High sensitivity.	May potentially yield false positive EIA results, with concerning specificity results.	Fakile et al., 2019a
Treponema pallidum hemagglutination assay (TPHA)	One of the standardized commercial assay procedures is TPHA (Human Gesellschaft für Biochemica und Diagnostica mbH, Wiesbaden, Germany).	High accuracy, sensitivity, and specificity.	May exhibit cross-reactivity with other treponemal infections.	Luna et al., 2023
ELISA	One of the commercially available ELISA kits is the *T. pallidum* ELISA (Human Gesellschaft für Biochemica und Diagnostica mbH, Wiesbaden, Germany).	High sensitivity and specificity.	Requires instrumentation and skilled laboratory personnel.	Luna et al., 2023

Another diagnostic test developed targets syphilis screening specifically for individuals living with HIV (PLWH). This test utilized the SD Bioline Syphilis 3.0 (Standard Diagnostics Inc, Kyonggi-do, Korea) and Alere Determine Syphilis TP (Abbott Diagnostics Medical Co, Ltd), both of which are immunochromatographic assays indicating the presence or absence of treponemal antibodies through line visualization within 20 minutes. The rapid diagnostic testing (RDT) was conducted at the point of care using blood obtained via finger prick. The standard comparator in this assessment included TPHA (Human Gesellschaft für Biochemica und Diagnostica mbH, Wiesbaden, Germany) and *T. pallidum* ELISA (Human Gesellschaft für Biochemica und Diagnostica mbH, Wiesbaden, Germany). Based on the findings, the SD Bioline test demonstrated a sensitivity ranging from approximately 94.6% to 96.4%, while the Alere Determine test exhibited a sensitivity ranging from 87.5% to 99.1%. These results support the use of these rapid diagnostic tests for syphilis screening among individuals living with HIV (Luna et al., 2023).

2.2. Indonesian diagnostics development

Diagnostic development in Indonesia, particularly in the field of sexually transmitted diseases (STDs), has shown limited progress.

Nevertheless, here is an overview detailing the advancement of diagnostic kits and their utilization within Indonesia.

2.2.1. Development

A concise overview of the progress in diagnostic kit development in Indonesia is presented in Table 7.

2.2.1.1. Hepatitis B Virus (HBV)

One of the developed kits is the HBsAg and anti-HBsAg kit, created by the diagnostic team at the Institut Teknologi Bandung in collaboration with PT. Bio Farma (Persero). This kit utilizes an ELISA-based approach, incorporating independently developed components, including specific antibodies (Fadil, 2018; Lembaga Pengembangan Inovasi dan Kewirausahaan ITB, 2017; Permana, 2018). Additionally, a real-time PCR-based diagnostic test was developed at the Institut Teknologi Bandung (Rizkita and Fibriani, 2020). However, these kits are not yet commercially available.

As for commercialized kits, an immunochromatography test (ICT)-based diagnostic kit named HBsAg ENTEBE RPHA produced by PT. Hepatika Laboratory in Mataram Lombok, was developed for detecting HBsAg. This product exhibits a sensitivity of 90% and a specificity of 93.3% (Yuwono, 1988). Furthermore, Fokus Diagnostic developed an HBsAg strip based on immunoassay chromatography, known for its sensitivity of 94.11% and specificity of 100% (Kalma, 2014).

2.2.1.2. Human Immunodeficiency Virus (HIV)

To address the challenges associated with potential protein contamination and high costs inherent in western blotting, a recombinant immunoblot assay was pioneered at the Universitas Indonesia. This assay incorporates recombinant antigens representing the four subtypes of HIV-1, namely CRF01_AE, B, CRF02_AG, and C (Christian et al., 2017). Another innovative approach involves leveraging technology in the form of a multiassay algorithm (MAA) for HIV infection identification. This MAA utilizes data on CD4+ T cell count and plasma viral load (pVL) to construct a multiassay decision tree. Although effective in identifying 99.8% of chronic infections, the MAA does not detect recent infections that have occurred (Wulan et al., 2023).

2.2.1.3. Human Papillomavirus (HPV)

Nusantics developed a kit for HPV detection, known as CerviScan, which was subsequently distributed by Bio Farma. This kit utilizes polymerase chain reaction (PCR) technology and accepts urine and cervical swabs as specimen types. CerviScan is designed to identify hrHPV DNA and can specifically detect 14 hrHPV types, including the ability to genotype HPV types 16, 18, and 52. In one study utilizing this kit with urine samples, the test demonstrated high accuracy exceeding 95%, with a sensitivity of 68.6% and a specificity of 93.2%. Consequently, this domestically produced product, CerviScan, proves effective for detecting hrHPV subtypes (Andrijono et al., 2023).

Table 7. Indonesian diagnostic development on STDs and current diagnostic technologies summary highlights

Disease	Diagnostic method	Highlights	Advantages	Disadvantages	Literature
Hepatitis B Virus (HBV)	ELISA	HBsAg and Anti-HBsAg kits featuring independently developed components from Institut Teknologi Bandung.	Less costly.	Not yet available for commercial use.	Fadil, 2018; Lembaga Pengembangan Inovasi dan Kewirausahaan ITB, 2017; Permana, 2018
	real-time PCR	Developed by Institut Teknologi Bandung.	More sensitivity and specificity.	Not yet available for commercial use.	Rizkita and Fibriani, 2020
	Immunochromatography test (ICT)	A commercially available kit known as HBsAg ENTEBE RPHA, produced by PT. Hepatika Laboratory in Mataram Lombok.	High sensitivity and specificity.		Yuwono, 1988
	Immunoassasy chromatography strip	A commercially available HBsAg strip immunoassay chromatography kit, developed by Fokus Diagnostic.	High sensitivity and specificity, easy to use.	Unable to detect samples with low titers.	Kalma, 2014
Human Immunodeficiency Virus (HIV)	Recombinant immunoblot assay	Recombinant antigens derived from four subtypes of HIV-1, which were developed by researchers at Universitas Indonesia.	Has better reactivity than another commercial diagnostic kit test from M- company.	Not yet available for commercial use.	Christian et al., 2017
	Multiassay algorithm (MAA)	utilization of data concerning CD4+ T cell counts and plasma viral load (pVL) within a multiassay algorithm.	High-throughput, *in silico.*	necessity for a significant sample size that includes cases of seroconversion.	Wulan et al., 2023
Human Papillomavirus (HPV)	PCR	This assay detects the presence of high-risk HPV (hrHPV) DNA and can identify 14 hrHPV types. The commercialized kit, known as CerviScan, was developed by Nusantics and is distributed by Bio Farma.	High sensitivity and specificity.		Andrijono et al., 2023
Gonorrhoea, Chlamydia, and Trichomoniasis	Duplex PCR	A duplex PCR assay capable of detecting both chlamydia and gonorrhea, developed by Universitas Indonesia.	Capable of simultaneously detecting both chlamydia and gonorrhea.	Not yet available for commercial use.	Wardoyo et al., 2012

2.2.1.4. Gonorrhoea, Chlamydia, and Trichomoniasis

The current gold standard for detecting *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* remains culture cultivation. However, this method can be challenging due to the requirement for specialized equipment and the extended time it takes to obtain results (Adhata, 2022; Mamahit, 2000; Ratnasari et al., 2010; Reza and Tantari, 2015).

A notable advancement in this field was achieved at the Universitas Indonesia, involving the development of chlamydia and gonorrhea detection using duplex polymerase chain reaction (PCR) with genital fluid samples from patients. Analysis of PCR results from *N. gonorrhoeae* specimens collected from women's endocervix revealed a duplex PCR sensitivity of 100% and specificity of 61.9%. Similarly, in male urethral specimens, the duplex PCR exhibited a sensitivity of 75% and specificity of 40%. For chlamydia detection, the duplex PCR yielded more positive results compared to the antigen test, with a ratio of 10:3 for endocervix samples and 1:0 for urethral samples (Wardoyo et al., 2012).

2.3. Global vs. Indonesia: disparities in diagnostic kit development

Despite advancements in Indonesia, there remain notable disparities in diagnostic kit development compared to the global landscape, as shown in Table 8. Globally, a wider variety of advanced diagnostic technologies are developed and commercially available. In contrast, Indonesia primarily focuses on conventional methods, with limited or no commercial availability of these advanced diagnostics.

Table 8. Comparison of diagnostic kit commercially based on development in global vs. in Indonesia

		Diagnostic kit commercially based on development in global	**Diagnostic kit commercially based on development in Indonesia**
Hepatitis B	Under development	ELISA, Photoelectrochemical imunosensor, Raman, Nanoparticle-based lateral flow biosensors, Support vector machines (SVMs)-based	ELISA, PCR, Rapid test
	Commercially available	ELISA, CLIA, Rapid test, PCR	Rapid test
HIV	Under development	ddPCR, Rapid test	Recombinant immunoblot assay, Multiassay algorithm (MAA)
	Commercially available	Commercially available: Rapid test	Commercially available: NA
HSV	Under development	Latex agglutination test, Western blot assay, Real-time PCR combined with ELISA, Multiplex PCR, Chemiluminescent immunoassay (CLIA), ELISA, Immunoblot	NA
	Commercially available	Latex agglutination test, ELISA Immunoblot, rapid test	NA
HPV	Under development	ELISA, EIA-PCR, PCR	NA
	Commercially available	Cobas-PCR, PCR	PCR
Gonnorhea-Chlamidya	Under development		NA
	Commercially available	multiplex PCR assay, rapid test	NA
Syphilis	Under development		NA
	Commercially available	Rapid immunochromatographic test, Flocculation test EIA, Treponema pallidum hemagglutination assay (TPHA), ELISA	NA

Note: NA = not available

3. Conclusion

In summary, the advancement of diagnostic methods for sexually transmitted diseases (STDs) has evolved rapidly, transitioning from standard simplex PCR to multiplex PCR techniques. Furthermore, the development of ELISA assays capable of conducting multiple assays simultaneously has expanded diagnostic capabilities. Additionally, the integration of diagnostic techniques with computerization represents a promising breakthrough in diagnosing patients with potential recurrent STDs.

Diagnostic technology in Indonesia has also made significant progress, with several locally developed STD kits already available on the market. This trend underscores Indonesia's shift towards the production of indigenous diagnostic tools for sexually transmitted diseases.

Future perspectives

The development of diagnostic kits for hepatitis B and other sexually transmitted infections (STIs) by various Indonesian institutions showcases significant strides in local biomedical research and innovation. The HBsAg and anti-HBsAg kit developed by the Institut Teknologi Bandung in collaboration with PT. Bio Farma, using an ELISA-based approach and independently developed components, demonstrates the potential of local expertise in creating effective diagnostic tools (Fadil, 2018; Lembaga Pengembangan Inovasi dan Kewirausahaan ITB, 2017; Permana, 2018). Similarly, the real-time PCR-based diagnostic test from the same institution further highlights the progress in molecular diagnostic techniques (Rizkita and Fibriani, 2020). However, the fact that these kits are not yet commercially available indicates a gap in the transition from research to market-ready products, necessitating stronger industry-academia collaboration and streamlined regulatory processes.

The commercial availability of diagnostic kits like the HBsAg ENTEBE RPHA and the HBsAg strip developed by PT. Hepatika Laboratory and Fokus Diagnostic, respectively, illustrates successful examples of translating research into market-ready products. These kits demonstrate high sensitivity and specificity, showcasing the practical application of immunochromatography in diagnostic testing (Yuwono, 1988; Kalma, 2014).

Nusantics' development of the CerviScan kit for HPV detection, distributed by Bio Farma, marks another milestone in local diagnostic capabilities. Utilizing PCR technology, CerviScan can accurately detect and genotype high-risk HPV types from urine and cervical swab samples. With accuracy exceeding 95%, this kit is a testament to the efficacy of domestically produced diagnostic tools in addressing public health needs (Andrijono et al., 2023).

Despite these advancements, traditional methods like culture cultivation for detecting *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* remain challenging due to the need for specialized equipment and lengthy processing times (Adhata, 2022; Mamahit, 2000; Ratnasari et al., 2010; Reza and Tantari, 2015). Universitas Indonesia's development of duplex PCR for detecting chlamydia and gonorrhea using genital fluid samples represents a significant innovation. The duplex PCR technique, with its high sensitivity for *N. gonorrhoeae* in women and chlamydia in both sexes, underscores the potential for more efficient and accurate STI diagnostics (Wardoyo et al., 2012).

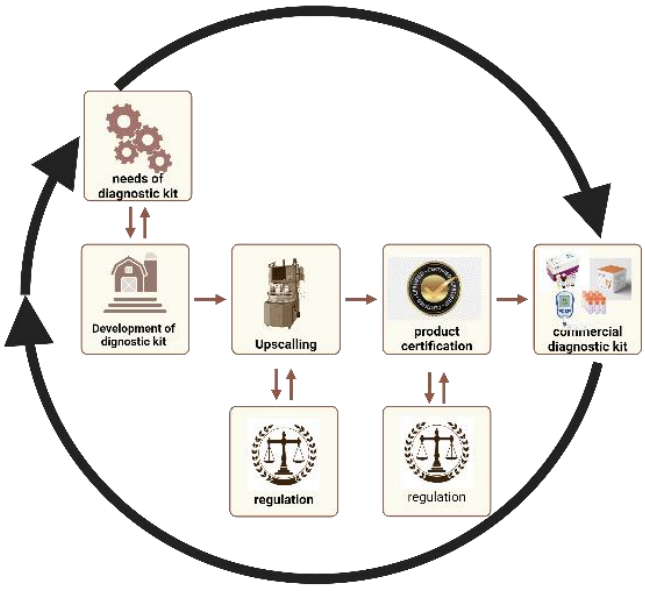

Fig. 3. Strategies for the Development of Diagnostic Kits in Indonesia (Created with BioRender.com)

As seen in Fig. 3, to bridge the gap between local and global diagnostic systems, Indonesia should adopt a strategic approach. In the short term, efforts should focus on commercializing locally developed kits through enhanced regulatory support and industry partnerships. Intermediate goals should aim at scaling production and distribution to ensure widespread availability. Long-term strategies should prioritize continuous research and innovation, integrating advanced diagnostic technologies to keep pace with global standards. By setting these goals, Indonesia can significantly enhance its diagnostic capabilities and public health outcomes, leveraging local innovations to address both domestic and global health challenges.

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Conflict of interest

The authors declare there is no conflict of interest in this research.

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