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Systematic Review: Diagnostic Accuracy of Hpv Dna Test as An Alternative to Visual Inspection with Acetic Acid (Via) For Early Cervical Cancer Screening

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Abstract

Cervical cancer is a major health issue globally, especially in low- and middle-income countries, where early detection is critical to reducing mortality. This systematic review aims to evaluate the diagnostic accuracy of HPV DNA testing compared to Visual Inspection with Acetic Acid (VIA) for early cervical cancer screening. The study reviewed literature published between 2020 and 2025 from multiple databases, selecting studies including women aged 18 and above from diverse settings. Data extraction utilized quality assessment through QUADAS-2 and focused on sensitivity, specificity, and predictive values. Four studies from Kenya, Africa, Italy, and Indonesia were analyzed. Results showed HPV DNA tests consistently demonstrate high sensitivity (94%–98%) and specificity (69%–100%), outperforming VIA in detecting high-risk HPV infections before morphological changes. The review concludes that HPV DNA testing is a promising alternative or complement to VIA, providing earlier and more accurate detection. However, challenges such as cost and resource availability remain. Effective integration strategies tailored to local infrastructure are essential to maximize benefits.

Keywords: Acetic Acid, Cervical Cancer Screening, Diagnostic Accuracy, Human Papillomavirus, HPV DNA Test.

INTRODUCTION

Cervical cancer remains a significant global health challenge, particularly among women in low- and middle-income countries (LMICs), where it is a leading cause of cancer mortality (WHO, 2021; Arbyn et al., 2022). This disease is strongly linked to persistent infection with high-risk human papillomavirus (HPV) types, which play a critical etiological role in the development of cervical intraepithelial neoplasia and invasive cervical cancer (CIN2+) (de Sanjose et al., 2023; Bruni et al., 2021). Effective early detection through routine screening programs is pivotal in reducing both the incidence and mortality rates of cervical cancer, as endorsed by international guidelines (WHO, 2021; Kelly et al., 2022).

Visual Inspection with Acetic Acid (VIA) has been widely adopted in resource-limited settings due to its simplicity, low cost, and ease of implementation in primary healthcare facilities (Smith et al., 2023; Ekawati et al., 2024). However, the accuracy of VIA relies heavily on the skill and experience of healthcare providers, leading to variability in diagnostic performance (Smith et al., 2023; James et al., 2021). On the other hand, molecular testing based on HPV DNA detection shows far greater sensitivity in identifying high-risk HPV infections before morphologic cervical changes develop, thereby offering superior diagnostic accuracy (Secretan, 2021; Utami et al., 2025). Nevertheless, HPV DNA testing demands more advanced laboratory infrastructure, higher costs, and complex logistics, which restrict its accessibility and widespread adoption in many LMICs (Zumrudah et al., 2023; Devine et al., 2021).

Among women living with HIV, who have an elevated risk for cervical cancer, studies consistently demonstrate that HPV DNA testing outperforms VIA with markedly higher sensitivity in detecting CIN2+ lesions (Kelly et al., 2022; Devine et al., 2021). Despite this

evidence, heterogeneity between studies and variations in specificity remain challenges, particularly in settings with limited resources and differing population characteristics (Kelly et al., 2022; Nwosu et al., 2022). In Indonesia and similar LMIC contexts, qualitative research highlights cost, service coverage, and national policy constraints as major barriers to HPV DNA test implementation, emphasizing the need for further evidence synthesis to guide policymaking (Ekawati et al., 2024; Zumrudah et al., 2023).

This systematic review aims to rigorously compare the diagnostic accuracy of HPV DNA testing with VIA for early cervical cancer screening and to explore contextual factors such as healthcare settings, reference standards, and examiner training that affect their performance. By synthesizing current international evidence, this study intends to provide an updated scientific basis to inform cervical cancer screening policies and programs in Indonesia and comparable countries. The review addresses the urgent need for practical, evidence-based strategies to optimize screening practices, with potential to promote HPV DNA testing as either a primary or complementary screening method to VIA, enhancing early detection outcomes (Utami et al., 2025; Rahma Kumala et al., 2024).

RESEARCH METHODS

This study utilized a systematic review design, aligning with established standards set forth by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement (Cresswell, 2022; Sugiyono, 2021). The primary objective was to compare the diagnostic accuracy of Human Papillomavirus (HPV) DNA testing and Visual Inspection with Acetic Acid (VIA) for early cervical cancer screening, synthesizing data from multiple research studies published within the five-year span of 2020–2025. This approach enables a rigorous aggregation and critical evaluation of evidence to inform screening policy and practice in contexts similar to Indonesia and other low- and middle-income countries (LMICs) (Ekawati et al., 2024; Sudaryono, 2024).

The data collection process employed a comprehensive literature search across four major electronic databases: PubMed, Scopus, ScienceDirect, and the Cochrane Library. Boolean operators AND and OR were systematically applied with keywords such as "HPV DNA test," "human papillomavirus DNA testing," "visual inspection with acetic acid," "VIA," "IVA," "cervical cancer screening," "early detection," "diagnostic accuracy," "sensitivity," and "specificity" to maximize retrieval of relevant studies (Emzir, 2022; Sugiyono, 2021). Selection criteria mandated inclusion of primary research articles published in English or Indonesian with full-text access, reported diagnostic accuracy outcomes, and comparative analyses between HPV DNA testing and VIA. Reviews, case reports, studies lacking explicit diagnostic data, or those applying only one diagnostic method without comparator were excluded to preserve methodological consistency and relevance (Kelly et al., 2022; Zumrudah et al., 2023).

Populations targeted across studies included women aged 18 years and older, encompassing both general and high-risk groups such as those living with HIV. Samples derived from primary and secondary healthcare settings allowed for assessment of diagnostic tools in real-world screening environments. The sample size varied per study but collectively represented diverse geographic and demographic cohorts from Kenya, sub-Saharan Africa, Italy, and Indonesia, enhancing the generalizability of findings (Utami et al., 2025; Reza Kumala et al., 2024). The comparator interventions examined were molecular HPV DNA assays capable of detecting high-risk HPV types versus VIA, which applies 3–5% acetic acid to cervix tissue for visual identification of acetowhite lesions indicative of precancerous changes.

The research protocol incorporated instrument quality assessments using established criteria consistent with QUADAS-2 to appraise study validity and risk of bias (Cresswell, 2022).

Extracted data elements included authorship, publication year, location, population details, HPV DNA test types, VIA procedure specifics, and key diagnostic accuracy measures—namely sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) (Sugiyono, 2021; Emzir, 2022). Data synthesis involved a detailed qualitative comparison and, where applicable, quantitative aggregation of diagnostic performance metrics with attention to heterogeneity among studies.

The research process unfolded from October 25 to November 25, 2025, encompassing identification, screening, eligibility determination, and final inclusion stages adhering strictly to PRISMA flow methodology (Cresswell, 2022). Through this layered approach, four studies met all criteria for inclusion in the analysis, representing sufficient methodological robustness to derive conclusions regarding comparative efficacy and applicability of HPV DNA testing relative to VIA in early cervical cancer screening.

RESULTS

A total of four studies from different countries were identified and analyzed in this systematic review to evaluate the diagnostic accuracy of HPV DNA tests in the early detection of cervical cancer. The four studies came from Western Kenya, Africa, Italy, and Indonesia, with diverse population characteristics and different HPV DNA detection methods.

Overall, the four studies showed that HPV DNA tests have very high sensitivity, with most studies reporting values above 94%, even reaching 98% in some populations. Specificity was also generally high, ranging from 69% to 100%, indicating the test's ability to accurately differentiate between individuals with and without high-risk HPV. However, variations were still found across populations and testing methods used.

In the general female population in Western Kenya, the use of Anyplex™ II HPV HR Detection showed a sensitivity of 94% and a specificity of 69%. The high sensitivity value indicates a good ability to detect high-risk HPV, although the lower specificity may indicate a possibility of false positive results, especially in populations with a high prevalence of HPV infection.

In the population of women with HIV in Africa, the use of the Care HPV Test resulted in a sensitivity of 97%, but specificity was not reported. The high sensitivity indicates the effectiveness of the Care HPV Test in detecting HPV infection in groups with low immunity, where conventional methods such as IVA often fail to detect precancerous lesions due to atypical cervical mucosal changes.

In women aged 25–64 years in Italy, studies using the HPV Self Test showed a sensitivity of 98% and a specificity of 100%. These results demonstrate very high diagnostic accuracy, with no false positive results reported. These findings also highlight the great potential of self-sampling methods in increasing cervical cancer screening coverage without compromising diagnostic accuracy. Meanwhile, in Indonesia, the use of the hrHPV ReadyMix qPCR Kit on 876 women undergoing health check-ups in Jakarta, Bandung, and Semarang showed a sensitivity of 96.55% and a specificity of 99.87%. These results reinforce that qPCR-based methods have excellent diagnostic performance and have the potential to be widely applied in population screening at healthcare facilities.

Overall, the results of these four studies indicate that the HPV DNA test has a high and consistent accuracy across various populations, making it a strong potential alternative to visual inspection with acetic acid (VIA) in early cervical cancer screening programs.

Table 2. Systematic Review of the sensitivity and specificity of HPV DNA types based on populations from various countries

Author	Country	populations	HPV DNA Type	Sensitivity	Specification
8	Western Kenya	701 women aged 18-64 years	Anyplex™ II HPV HR *Detection*	94%	69%
9	Afrika	554 women with HIV aged 31-41 years	*Care* HPV *Test*	97%	Not reported
10	Italia	889 cervical liquid-based cytology samples from women aged 25-64 years	HPV *Selfy Test*	98%	100%
11	Indonesia	876 samples from women visiting healthcare facilities in Jakarta, Bandung, and Semarang for a medical check-up	hrHPV ReadyMix qPCR Kit	96,55%	99,87%

DISCUSSION

The results of this systematic review indicate that the HPV DNA test has high diagnostic accuracy in detecting high-risk HPV infections that play a crucial role in the development of cervical cancer. From the four studies analyzed, the sensitivity of the HPV DNA test ranged from 94% to 98%, while its specificity ranged from 69% to 100%. These values demonstrate that the HPV DNA test can accurately detect the presence of HPV infection while distinguishing between positive and negative individuals with a low error rate.

These results show that the HPV DNA test is superior compared to the Visual Inspection with Acetic Acid (VIA) method, which is reported in various literature to have lower sensitivity and to be highly dependent on the examiner's expertise. The advantage of the HPV DNA test primarily lies in its ability to detect the presence of the virus before morphological changes appear on the cervix, making it more effective for early pre-cancer screening.

1. Variation in Sensitivity and Specificity Between Studies

The variation in sensitivity and specificity values between studies is mainly influenced by the type of testing method and the characteristics of the population. In a study conducted in Kenya, the Anyplex™ II HPV HR Detection method showed high sensitivity, at 94%, but its specificity was only 69%. This indicates that the test is very good at detecting positive cases, but it may potentially produce false-positive results, especially in populations with a high prevalence of HPV infection.

In the population of women with HIV in Africa, the Care HPV Test demonstrated a sensitivity of 97%, indicating high effectiveness in detecting HPV infections in groups with weakened immunity.

This method is beneficial because VIA often fails to detect pre-cancerous lesions in individuals with atypical cervical mucosal changes due to HIV infection.

Meanwhile, in Italy, the use of the HPV Self Test showed a sensitivity of 98% and a specificity of 100%, demonstrating excellent diagnostic performance. These findings also underscore the great potential of self-sampling methods in expanding the reach of cervical cancer screening without compromising result accuracy.

In Indonesia, the use of the truHPV ReadyMix qPCR Kit showed a sensitivity of 96.55% and a specificity of 99.87%. These values reinforce the evidence that qPCR-based methods have highly accurate detection capabilities and are suitable for widespread implementation in general population screening programs.

2. Advantages of HPV DNA Test Compared to IVA

HPV DNA testing has several main advantages compared to VIA. First, this test is more objective because the results do not depend on the examiner's visual interpretation, as with VIA. Second, HPV DNA testing can detect infections before cervical cell changes occur, making it more effective for detecting pre-cancer stages. Third, the self-sampling method available with some HPV DNA testing devices allows women to collect samples themselves, which can increase screening participation, especially in areas with limited medical staff. In addition, results from various studies show that HPV DNA testing has higher consistency among examiners compared to VIA, whose results can vary depending on the skills and experience of healthcare workers.

3. Implications for Cervical Cancer Screening Programs

Based on this review, the HPV DNA test has strong potential to become the primary screening method for early detection of cervical cancer, replacing or complementing the IVA method. With high sensitivity and more consistent results, the implementation of the HPV DNA test can improve the effectiveness of early detection and reduce the incidence of advanced-stage cervical cancer.

However, the main challenge in widely implementing this method is the relatively high cost of testing and the limited molecular laboratory facilities in some areas. Therefore, a feasible strategy is to combine IVA and HPV DNA, where IVA is used for initial screening, and HPV DNA serves as a confirmatory test for cases with positive IVA results.

CONCLUSION

The systematic review indicates that HPV DNA testing demonstrates superior diagnostic accuracy compared to visual inspection with acetic acid (VIA) for early cervical cancer screening. The pooled sensitivity ranges from 94% to 98%, and specificity varies between 69% and 100%, across diverse populations from Kenya, Africa, Italy, and Indonesia. These findings highlight the potential of HPV DNA testing as a reliable alternative or complement to VIA, especially given its ability to detect high-risk HPV infections prior to morphological changes, thereby facilitating earlier intervention and reducing cervical cancer burden. Nonetheless, the review underscores certain limitations, such as heterogeneity across studies regarding testing techniques, population characteristics, and the variability in specificity, which may influence the generalizability of results. Additionally, most HPV DNA tests require sophisticated laboratory infrastructure and higher costs, restricting their widespread adoption in low-resource settings. Future research should focus on standardizing testing protocols, evaluating cost-effectiveness in various contexts, and exploring integration strategies with existing screening programs, including primary HPV-based testing and triaging algorithms.

Practically, this evidence underscores the importance of adopting HPV DNA testing within national cervical cancer screening policies, particularly in settings where resources and technology permit. Such implementation could enhance early detection, bypass the limitations of visual-based methods dependent on examiner skill, and expand screening coverage through

self-sampling strategies. However, policymakers must address infrastructural and financial barriers to maximize benefits, potentially through phased integrations or subsidized programs. Overall, the findings advocate for a shift towards molecular testing as a primary screening modality, aligned with global efforts to reduce cervical cancer incidence, especially in LMICs. Further studies should evaluate long-term outcomes, feasibility, and acceptability to optimize implementation frameworks in different healthcare contexts.

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