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Comparative analysis of diagnostic methods for high-risk HPV detection: A scoping review and meta-analysis

Rahmi Amtha^{1*}, Monica Dwi Hartanti^{2,3†}, Nadira Putri Fedin¹, Indrayadi Gunardi^{1†}, Christopher Andrew Teguh², Ilham Hizbulloh², Muhammad Ihsan Rizal⁴, Yani Kurniawan², Didik Tulus Subekti³, and Christina Safira Whinie Lestari³

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Abstract

Introduction: High-risk (HR) human papillomavirus (HPV) is the main cause of cervical cancer and a substantial proportion of oropharyngeal cancers, making early and accurate detection critical for effective screening and prevention, particularly in low-resource settings.

Objective: This study aims to compare the diagnostic accuracy of point-of-care and rapid testing methods for HR-HPV detection.

Methods: We conducted a scoping review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews framework. PubMed/MEDLINE, ScienceDirect, and Scopus were searched for English-language studies published from 2010 through July 2025. Fifteen studies met the inclusion criteria, with eight included in the meta-analysis.

Results: Recombinase polymerase amplification combined with clustered regularly interspaced short palindromic repeats/Cas12a achieved the highest pooled diagnostic performance, with a sensitivity of 0.94 and specificity of 0.97. Polymerase chain reaction-based analyses also showed high accuracy (sensitivity = 0.85; specificity = 0.97) but exhibited considerable heterogeneity across platforms and sample types. Loop-mediated isothermal amplification demonstrated moderate performance (sensitivity = 0.60; specificity = 0.91), while p16 immunohistochemistry offered good sensitivity (0.91) but lower specificity (0.73), supporting its use as a confirmatory rather than primary screening tool. In situ hybridization and next-generation sequencing provided broader genotyping capability but were limited by higher cost and technical complexity.

Conclusion: Polymerase chain reaction remains the clinical gold standard for HR-HPV detection, whereas recombinase polymerase amplification/clustered regularly interspaced short palindromic repeats–Cas12a emerges as a promising alternative for decentralized, low-resource screening. Future multi-center studies should standardize reporting, expand genotype coverage beyond HPV-16 and HPV-18, and assess cost, turnaround time, and operational feasibility to ensure that advances in

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HR-HPV diagnostics translate effectively into public health benefit.

Keywords: Diagnostic; Human papillomavirus; Point of care; Rapid diagnostic

1. Introduction

Human papillomavirus (HPV) infection is a major cause of cervical cancer in women, with subtypes 16 and 18 accounting for more than 70% of cases worldwide.^{1,2} Beyond cervical disease, HPV contributes to over 60–90% of anal, vaginal, oropharyngeal, and penile cancers. More than 150 HPV genotypes have been identified and are classified as either high-risk (HR) or low-risk (LR) based on their potential to drive cervical carcinogenesis. Common HR types include 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 58, 59, 68, and 82, whereas LR types include 6, 11, 32, 40, 42, 43, 44, 54, 61, 70, 72, 81, 84, and 87.³

Over the past decade, HPV infection has also been linked to a rising incidence of oropharyngeal squamous cell carcinoma (OPSCC), particularly in the tonsils and base of the tongue, and notably among younger men.⁴ Oral HPV infection increases the risk of malignant transformation by roughly 50-fold, and HPV-driven OPSCCs are dominated by HR-HPV-16, which is detected in approximately 90% of cases.^{5–9}

Most HPV infections clear spontaneously within one to two years, a process known as viral clearance, which substantially reduces the likelihood of cancer progression.^{6,10} Persistent infection, however, promotes carcinogenesis through overexpression of the viral E6 and E7 oncoproteins, which suppress the tumor suppressor genes p53 and Rb and drive uncontrolled cell proliferation.^{6,11} Given the significant health burden posed by HPV-related cancers, early and accurate detection of HR-HPV types is essential for effective screening and prevention.

Detection strategies generally fall into two categories: direct identification of the viral genome, typically by nucleic acid amplification tests such as polymerase chain reaction (PCR), and the recognition of HPV-induced morphological changes in patient cells or tissues that indicate precancerous or malignant transformation.¹² Nucleic acid testing, which offers high sensitivity and specificity, is now central to the diagnosis of many pathogens.¹³ HPV DNA detection remains the gold standard because viral integration into host DNA strongly

correlates with the development of invasive carcinoma.¹⁴ Yet in many low-resource settings, where HPV-related disease is most prevalent, these molecular tests are often inaccessible due to limited funding, infrastructure, and trained personnel. This underscores the need for affordable, point-of-care diagnostic tools to help reduce the burden of HPV disease.¹³

Understanding the range of available detection methods is crucial because the choice of assay directly affects diagnostic accuracy, the ability to distinguish transient from persistent infection, and the clinical decisions surrounding screening and patient management. Accurate detection not only differentiates infections that will clear spontaneously from those likely to progress to cancer but also enables earlier intervention, particularly where resources are scarce. Against this backdrop, the present study aims to comprehensively evaluate diagnostic methods for HR-HPV by mapping existing evidence through a scoping review and quantitatively summarizing diagnostic accuracy via meta-analysis to inform both clinical practice and future research.

2. Methodology

2.1. Eligibility criteria

This scoping review was conducted following the methodological framework of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist 2018. Studies were eligible if they met the following conditions: the target population comprised human subjects infected with HPV. The review focused on point-of-care testing methods for HPV detection, including loop-mediated isothermal amplification (LAMP), clustered regularly interspaced short palindromic repeats (CRISPR)-based assays, immunohistochemistry (IHC), p16 protein detection, and recombinase polymerase amplification (RPA). We considered only studies in which point-of-care testing was implemented or formally evaluated. Acceptable designs included observational and cohort studies, clinical investigations, and laboratory-based studies. Only articles published in English between 2010 and July 2025 were

included. We specifically sought clinical studies that compared at least two diagnostic methods. Narrative reviews, editorials, letters, and studies confined solely to laboratory-based methods without a point-of-care application were excluded.

2.2. Information sources

A comprehensive literature search was performed across three electronic databases—PubMed/MEDLINE, ScienceDirect, and Scopus. Two investigators (IG and NPF) independently conducted the search, screened records, and removed duplicates before data extraction. Titles and abstracts were screened independently by the same two investigators, and any disagreements were resolved by a third investigator (RA).

2.3. Search strategy

The core search terms included “LAMP” or “Loop-mediated Isothermal Amplification,” “CRISPR,” “IHC” or “Immunohistochemistry,” “P16,” “HPV” or “human papillomavirus,” “RPA” or “Recombinase polymerase amplification,” and “point of care.” The complete database-specific strategies are provided in Table S1.

All records identified were imported into Microsoft Excel 2019 for reference management, and duplicates were removed. Titles and abstracts were screened independently by two reviewers (IG and NPF) based on the predefined eligibility criteria. Full texts of potentially relevant studies were then assessed, with any discrepancies resolved through discussion or, when necessary, adjudication by a third reviewer (RA and MDH).

2.4. Statistical analysis

The extracted data were summarized descriptively. Summary tables captured the distribution of point-of-care testing approaches, targeted HPV genotypes, study settings, and diagnostic performance, and were used to highlight temporal trends and evidence gaps. When studies demonstrated sufficient homogeneity in design, diagnostic targets, and reported outcomes, a quantitative synthesis was undertaken.

Meta-analyses used a random-effects model (DerSimonian–Laird method) to account for expected heterogeneity. For diagnostic accuracy outcomes, pooled sensitivity, specificity, positive predictive value, negative predictive value, and corresponding 95% confidence intervals (CIs) were calculated using a bivariate random-effects model. Heterogeneity was assessed with the I^2 statistic, with thresholds of 25%, 50%, and 75% interpreted as low, moderate, and high, respectively. Subgroup analyses explored potential sources of heterogeneity by assay type

(IHC, LAMP, PCR, and RPA) and by genotype (HPV-16 and HPV-18). All analyses were performed with OpenMeta v12.11.14 (Brown University, <http://www.cebm.brown.edu/openmeta/>). Publication bias was not assessed.

3. Results

3.1. Study selection

Figure 1 shows that database searches identified 3,543 records. After removing 14 duplicates, 3,529 titles and abstracts were screened. Of these, 2,991 articles were excluded for not meeting the inclusion criteria. The remaining 538 full-text articles were assessed for eligibility, and 523 were subsequently excluded. In total, 15 studies were included in the qualitative synthesis, of which eight contributed data to the meta-analysis.

3.2. Subgroup analysis

As shown in Table S2 and Figure 2, multiple assay platforms were used for HPV-16 detection, including RPA, PCR-based methods, LAMP, and sequencing approaches. RPA combined with CRISPR/Cas12a consistently demonstrated excellent diagnostic performance, achieving 100% sensitivity, specificity, and accuracy. PCR assays also performed strongly, with sensitivity ranging from 87.65% to 100% and specificity from 96.67% to 100%. In contrast, isothermal amplification using LAMP assays yielded only moderate results, with a sensitivity of 90.9% and a specificity of 88.9%, while sequencing-based next-generation sequencing of plasma showed lower diagnostic accuracy, with a sensitivity of 57.14% and a specificity of 37.5%.

For HPV-18, a similar pattern was observed. RPA with CRISPR/Cas12a again achieved 100% sensitivity, specificity, and accuracy (Table S2 and Figure 2). PCR platforms such as Onclarity and TaqMan also produced high diagnostic values, with specificity exceeding 98% and accuracy approaching 99%. By comparison, isothermal amplification using LAMP assays showed markedly weaker performance, with specificity dropping to 22.2% and accuracy around 36.05%.

For other HR-HPV genotypes, in situ hybridization (ISH) assays demonstrated variable diagnostic power (Table S2 and Figure 2). DNA ISH achieved high sensitivity (86.3%) and specificity (95.3%), whereas RNA scope and other ISH formats showed more variable performance, with sensitivity ranging from 53.5% to 93.4%.

3.3. Heterogeneity

For isothermal amplification assays (Figure 3A), both sensitivity and specificity analyses under a fixed-effect model revealed no significant heterogeneity ($I^2 = 0$; $p =$

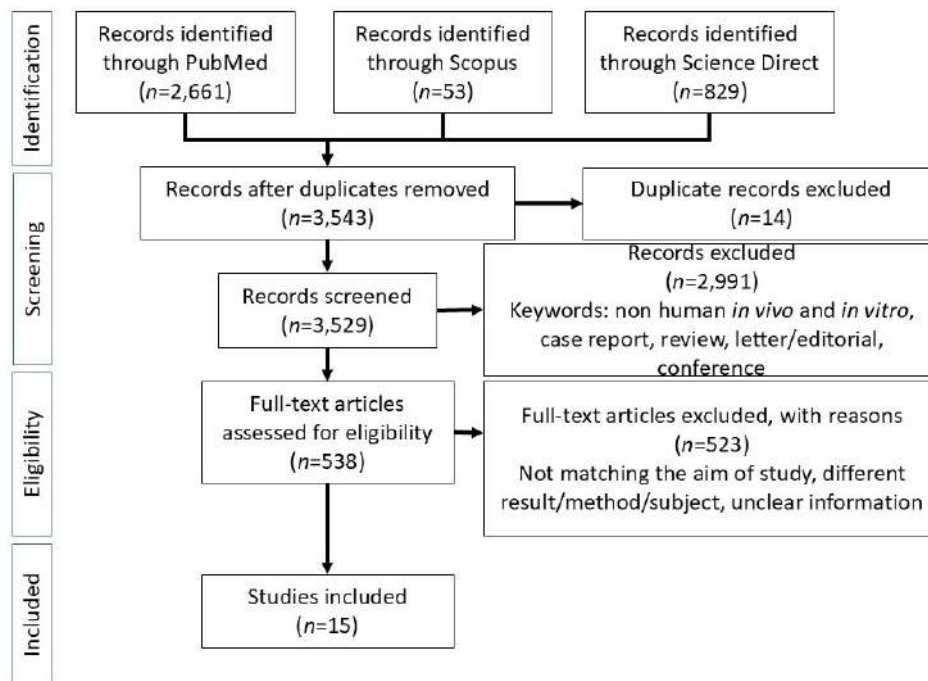


Figure 1. Flow chart of the 2018 Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

0.826 and $p = 0.639$, respectively), indicating that diagnostic performance estimates were consistent across studies. IHC assays also showed homogeneity for sensitivity ($I^2 = 0$; $p = 0.445$), but specificity demonstrated significant heterogeneity ($\tau^2 = 0.843$; $I^2 = 90.47$; $p = 0.001$), suggesting considerable variability in the ability of immunostaining markers to rule out non-HPV cases in different settings.

In contrast, RPA assays (Figure 3B) displayed moderate-to-substantial heterogeneity for sensitivity ($\tau^2 = 3.252$; $I^2 = 69.88$), whereas specificity remained homogeneous ($I^2 = 0$; $p = 0.550$). The variation in sensitivity likely reflects differences in primer-probe design, reaction conditions, or target gene selection across studies. PCR-based assays (Figure 3C) exhibited the highest overall heterogeneity. Sensitivity showed substantial variation ($\tau^2 = 0.585$; $I^2 = 75.34$; $p < 0.001$), and specificity was even more heterogeneous ($\tau^2 = 6.727$; $I^2 = 96.27$; $p < 0.001$). Such variability may stem from differences in PCR platforms, sample sources (e.g., tissue, plasma, or oral rinse), viral load thresholds, and operator-dependent factors that influence diagnostic accuracy.

When results were stratified by genotype, HPV-16 detection (Figure 3E) demonstrated high heterogeneity for both sensitivity ($\tau^2 = 1.769$; $I^2 = 73.23$; $p < 0.001$) and specificity ($\tau^2 = 6.506$; $I^2 = 96.18$; $p < 0.001$). Despite HPV-

16 being the most extensively studied genotype, these findings indicate persistent methodological variation, possibly related to assay chemistry, sample preparation, and population-level viral prevalence. For HPV-18 (Figure 3F), sensitivity showed moderate heterogeneity ($\tau^2 = 1.492$; $I^2 = 61.39$; $p = 0.051$), while specificity revealed substantial heterogeneity ($\tau^2 = 2.082$; $I^2 = 66.98$; $p = 0.028$). The narrower evidence base for HPV-18 compared with HPV-16 may further contribute to variability in performance outcomes.

3.4. Meta-analysis

When stratified by assay type (Figure 3), diagnostic performance differed across platforms. Isothermal assays (Figure 3A) showed a modest pooled sensitivity of 0.599 but relatively high specificity of 0.907, indicating that although false negatives remain a concern, these assays are reliable for ruling out HPV infection when results are negative. In contrast, RPA assays (Figure 3B) demonstrated excellent overall performance, with a sensitivity of 0.942 and a specificity of 0.974, suggesting strong diagnostic utility and consistent accuracy despite moderate heterogeneity in sensitivity estimates. PCR-based assays (Figure 3C) also achieved high pooled sensitivity (0.846) and specificity (0.971).

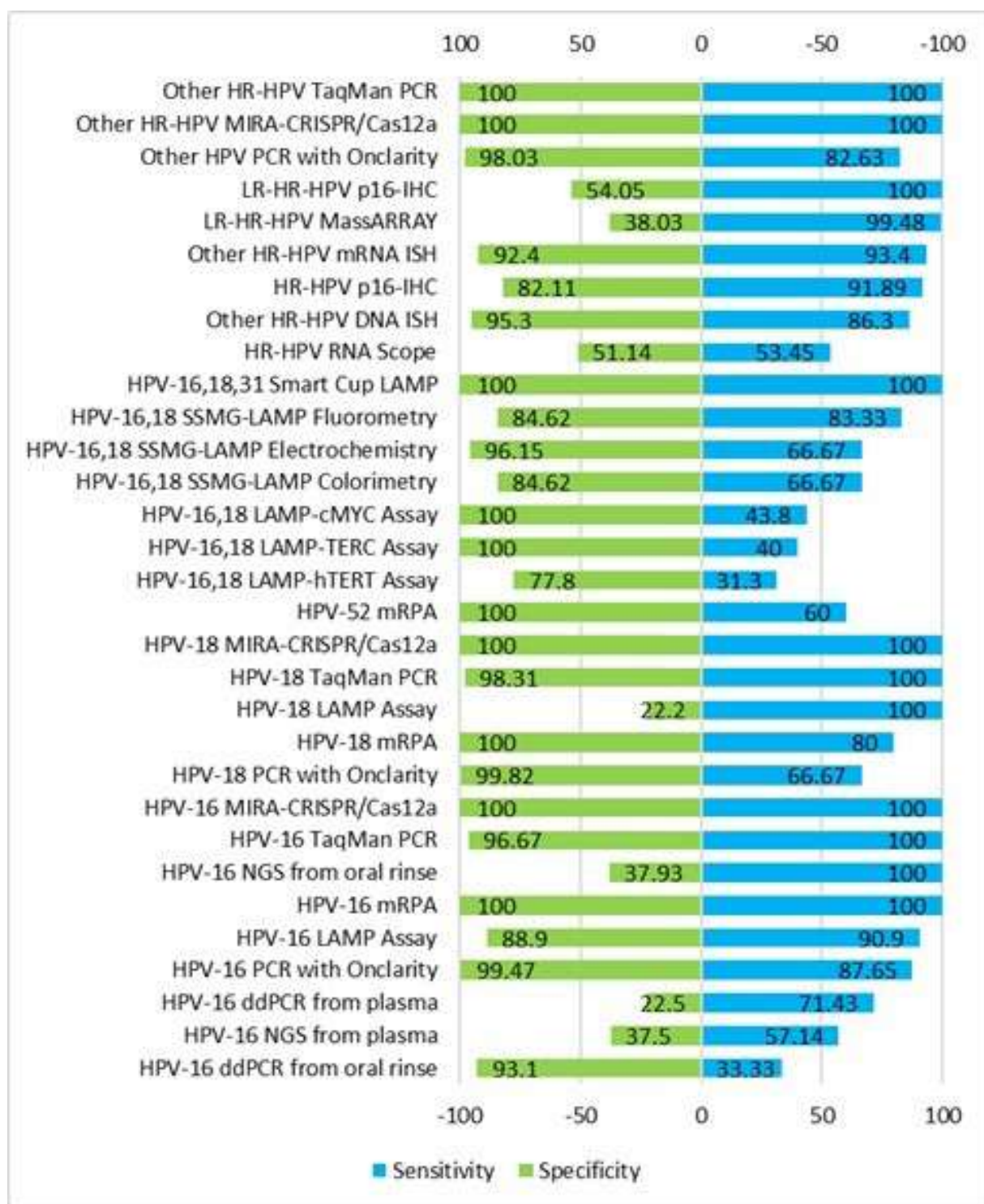


Figure 2. Sensitivity and specificity score for each type of assay based on HPV genotype

Abbreviations: ddPCR: Droplet digital polymerase chain reaction; HR-HPV: High risk human papillomavirus; hTERT: Human telomerase reverse transcriptase; IHC: Immunohistochemistry; ISH: In situ hybridization; LAMP: Loop-mediated isothermal amplification; LR-HPV: Low risk human papillomavirus; MIRA: Multienzyme isothermal rapid amplification; MIRA-CRISPR: Multienzyme isothermal rapid amplification-clustered regularly interspaced short palindromic repeats; mRPA: Multiplex recombinase polymerase amplification; NGS: Next generation sequencing; PCR: Polymerase chain reaction; SSMG: Sequence specific magnetic gel.



Figure 3. Sensitivity and specificity meta-analysis of assay types and HPV genotypes. (A) Isothermal assays. (B) Recombinase polymerase amplification assays. (C) Polymerase chain reaction assays. (D) Immunohistochemistry assays. (E) HPV-16. (F) HPV-18. Abbreviations: CI: Confidence interval; FN: False negative; FP: False positive; HPV: Human papillomavirus; TN: True negative; TP: True positive.

However, the substantial heterogeneity across studies indicates that the reliability of these estimates depends heavily on methodological standardization, including the choice of target genomic regions and amplification conditions. IHC assays (Figure 3D) showed high sensitivity (0.906) but lower specificity (0.726), reflecting a tendency to over-diagnose HPV-related disease. This finding aligns

with the heterogeneity observed in specificity analyses, likely driven by differences in antibody clones, staining protocols, and interpretation criteria.

Genotype-specific analyses revealed similarly strong results. HPV-16 detection (Figure 3E) reached a sensitivity of 0.870 and specificity of 0.868, while HPV-18 detection (Figure 3F) demonstrated comparable sensitivity (0.874)

but markedly higher specificity (0.989). Despite these favorable pooled accuracy metrics, both genotypes exhibited substantial heterogeneity, particularly in specificity, suggesting that variations in primer and probe design as well as differences in population-level HPV prevalence may influence diagnostic performance.

4. Discussion

4.1. Study design

Based on Table S2, the most common study designs were observational retrospective¹⁵⁻¹⁹ and experimental laboratory investigations,²⁰⁻²³ followed by observational prospective,²⁴⁻²⁶ cohort,^{27,28} and a single cross-sectional diagnostic accuracy study.²⁹ These designs allowed direct head-to-head comparisons between novel assays and established reference methods, but also introduced heterogeneity in patient selection and reference standards. Retrospective studies are frequently used in HPV diagnostics because archived cervical cytology samples and biobank materials enable parallel testing of multiple assays on identical aliquots without the cost or time required for new recruitment.¹² In parallel, experimental laboratory designs remain essential for establishing analytical validity, such as limit of detection, reproducibility, and genotype inclusivity/exclusivity, before large-scale clinical implementation. Their flexibility and cost-effectiveness make them particularly suited to rapidly evolving technologies such as extended genotyping, isothermal amplification, and point-of-care molecular assays.³⁰

4.2. Analysis of heterogeneity

This scoping review and meta-analysis provides a comparative overview of diagnostic methods for detecting HR-HPV, examining study design, sample type, diagnostic performance, and future directions. Our findings reaffirm that PCR remains the clinical gold standard for HR-HPV detection, while emerging technologies such as RPA combined with CRISPR show considerable promise for rapid testing in low-resource settings.

The highest heterogeneity of PCR indicates that the performance of PCR-based assays varies widely across studies, likely due to differences in assay protocols, primer sets, target genes, sample collection methods, and laboratory workflows. Such variability makes PCR outcomes highly sensitive to methodological preferences and operational conditions. This wide dispersion also reflects the diverse clinical settings, populations, and specimen types included in the studies, all of which can influence the diagnostic accuracy of PCR.

4.3. Sample origin

Cervical specimens predominated across studies,^{16,20-25,28,29} with additional work in oropharyngeal and head-and-neck tissues,^{15,18,19,27,28} oral rinse or saliva,^{15,23,27} plasma,^{15,28} formalin-fixed paraffin-embedded/biopsy tissue,²⁸ and a small number of urine samples. Although overlap of sample matrices within individual studies was common, the evidence base remains anchored in cervical screening, with a meaningful subset focused on HPV-driven OPSCC. Globally, HPV-16 and HPV-18 account for over 70% of cervical cancer cases, with HPV-16 responsible for more than half,² and HPV-16 similarly dominates HPV-positive OPSCC.⁶ Consequently, diagnostic performance varied by sample type: cervical swabs consistently yielded the most robust data, whereas plasma, saliva/oral rinse, and formalin-fixed paraffin-embedded tissue produced more variable results. This highlights the need for matrix-specific validation before clinical adoption.

4.4. Human papillomavirus detection methods

Polymerase chain reaction-based assays were the most frequently evaluated approaches,^{15,18,20,28,29} followed by p16 IHC,^{16,17,28} LAMP/isothermal assays,^{21,23,25} and RPA-/CRISPR-derived methods.^{20,22,24} ISH^{16,28} and next-generation sequencing^{15,18} appeared less often, and MassARRAY/genotyping was reported in only one study.²⁷ Reference standards most commonly involved PCR-based comparators^{19-25,29} and p16-IHC,^{15,18,19,27,28} with ISH used in several studies,^{15,19} and a single study employing histopathology or magnetic resonance imaging as an explicit comparator. This landscape underscores PCR's role as the de facto benchmark, while p16-IHC is frequently applied in head-and-neck disease.

Protein-based markers such as p16-IHC offer excellent sensitivity for detecting HPV-driven oncogenesis, with reported rates of 91.89–100%. However, their relatively limited specificity (54.05–82.11%), subjective interpretation, and site-dependent variability reduce their robustness across settings.¹⁷ Nucleic acid-based tissue methods, particularly ISH, provide higher specificity and allow direct visualization of viral nucleic acids in a histological context, yet tend to be less sensitive than PCR, are labor-intensive, and require access to tissue samples.²⁸

Moreover, PCR-based assays—including ddPCR, TaqMan, and Onclarity—remain the most established molecular methods, offering high specificity and broad genotype coverage. Their reliability, however, depends on thermocycling infrastructure and strict workflow conditions, and they may detect transient infections of uncertain

clinical significance, complicating interpretation.^{15,29} More recently, isothermal techniques such as RPA and multienzyme isothermal rapid amplification–CRISPR have emerged as promising alternatives. These assays are rapid and instrument-light, making them attractive for use in resource-limited settings.^{24,29} LAMP represents another cost-effective and rapid option requiring only a simple heat source and allowing visual readouts, but its diagnostic performance remains inconsistent across target regions and is challenged by complex primer design and the risk of carryover contamination.²¹ At the other end of the spectrum, sequencing and MassARRAY platforms provide unparalleled genotyping depth and multiplexing capability. Despite these advantages, their clinical adoption is limited by lower specificity in certain sample types, such as liquid biopsies or oral rinses, as well as by high costs and technical complexity.²⁷

Programmatic screening requires diagnostic methods that combine high accuracy with practical feasibility. PCR platforms such as Cobas, Onclarity, and TaqMan offer established workflows, reliable supply chains, and consistently strong specificity (96.67–100%), making them dependable anchors for population-based screening and triage. Isothermal strategies, including RPA and LAMP, reduce equipment requirements and shorten time-to-result. Evidence from Table S2 shows that RPA/CRISPR can match or even exceed PCR accuracy in small studies (75–100%), underscoring their potential for decentralized testing and use in resource-limited settings. By contrast, p16 IHC and ISH remain valuable for tissue-based confirmation, especially in OPSCC, but are less suited as primary screening tools.

4.5. Accuracy in detecting human papillomavirus

Across method-level analyses, HPV-18 showed the highest central tendency, with sensitivity ranging from 31.3% to 100% and specificity from 22.2% to 100%, while HPV-16 also performed strongly (sensitivity = 31.3–100%; specificity = 22.5–100%). Other HR-HPV genotypes yielded pooled sensitivities of 53.45–100% and specificities of 38.03–100%, though sample sizes were smaller and methodologies more variable. The wide specificity range (22.2–100%) observed in certain LAMP or liquid-biopsy contexts highlights the strong influence of sample matrix and implementation on diagnostic performance. Four studies reported results at the broader HR-HPV or LR-HPV + HR-HPV category level rather than genotype-specific, and several involved mixed cervical and oropharyngeal settings. Such inconsistent stratification by risk group and anatomical site limits cross-study comparability and may inflate or deflate pooled metrics when low-risk types or

non-cervical matrices are not clearly distinguished.

4.6. Limitations and future research

This study has several limitations. First, substantial heterogeneity was observed across included studies, particularly in PCR- and genotype-specific analyses, reflecting differences in assay platforms, sample sources, and patient populations. Second, many studies reported only sensitivity and specificity, restricting the application of advanced meta-analytic models. Third, risk of bias was not systematically assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 or the Standards for Reporting of Diagnostic Accuracy guidelines, and publication bias was not formally analyzed. Finally, only a small number of studies evaluated RPA/CRISPR; while pooled results are highly encouraging, larger prospective trials are needed to confirm their utility across diverse clinical contexts.

Future research should prioritize standardization of reporting in HPV diagnostic studies, including the use of flow diagrams, and adherence to established reporting guidelines such as the Standards for Reporting of Diagnostic Accuracy, alongside systematic risk-of-bias assessment using tools such as the Quality Assessment of Diagnostic Accuracy Studies-2. Comparator selection should also be clearly defined and anchored to recognized gold standards appropriate for the clinical context, avoiding composite or algorithmic comparators, unless explicitly specified. Assay validation should be matrix-specific, covering cervical screening specimens, OPSCC tissues, oral rinse or saliva, plasma/ctDNA, and self-collected samples, with pre-specified thresholds to ensure reproducibility and comparability.

The further development and scaling of isothermal platforms, particularly RPA- and CRISPR-based assays, represent a key opportunity given their strong diagnostic performance and operational advantages. Diagnostic panels should also expand genotype coverage beyond HPV-16 and HPV-18 to include other HR-HPV types such as 31, 33, 45, 52, and 58, reflecting regional epidemiology and evolving patterns in the post-vaccination era.³⁰ Finally, future studies should extend their scope beyond diagnostic accuracy to incorporate key implementation outcomes, turnaround time, assay failure or indeterminate rates, hands-on time, staffing requirements, and total cost of ownership, while considering equity and access. Prospective evaluation of self-collection strategies and decentralized workflows in low-resource settings will be critical to ensure that advances in HPV diagnostics translate into meaningful public health benefits across diverse populations.³¹

5. Conclusion

This scoping review and meta-analysis demonstrates that diagnostic methods for HR-HPV show considerable variation in accuracy. RPA/CRISPR assays consistently achieved the highest diagnostic performance, with pooled sensitivity of 0.94 and specificity of 0.97, indicating strong potential for low-resource and point-of-care applications. PCR-based methods also showed high pooled sensitivity (0.85) and specificity (0.97), but substantial heterogeneity across platforms and sample types limits generalizability. LAMP assays provided moderate and variable performance (sensitivity = 0.60; specificity = 0.91), while p16-IHC yielded good sensitivity (0.91) but limited specificity (0.73), restricting its role to confirmatory rather than primary screening. Taken together, PCR remains the gold standard for clinical HPV detection, whereas RPA/CRISPR offers a promising alternative for decentralized testing, and tissue-based assays retain value in histopathological contexts. Future research should prioritize large-scale, multi-center validation of isothermal platforms and expand genotype coverage beyond HPV-16 and HPV-18 to reflect shifting epidemiology.

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Conflict of interest

The authors have no conflicts of interest associated with the material presented in this paper.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data is available from the corresponding author upon reasonable request.

Further disclosure

A comprehensive literature search was performed across three electronic databases—PubMed/MEDLINE, ScienceDirect, and Scopus. Two investigators (IG and NPF) independently conducted the search, screened records, and removed duplicates before data extraction. Titles and abstracts were screened independently by the same two investigators, and any disagreements were resolved by a third investigator (RA).

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ORIGINAL RESEARCH ARTICLE

Comparative analysis of diagnostic methods for high-risk HPV detection: A scoping review and meta-analysis

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Abstract

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Introduction: High-risk (HR) human papillomavirus (HPV) is the main cause of cervical cancer and a substantial proportion of oropharyngeal cancers, making early and accurate detection critical for effective screening and prevention, particularly in low-resource settings.

Objective: This study aims to compare the diagnostic accuracy of point-of-care and rapid testing methods for HR-HPV detection.

Methods: We conducted a scoping review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews framework. PubMed/MEDLINE, ScienceDirect, and Scopus were searched for English-language studies published from 2010 through July 2025. Fifteen studies met the inclusion criteria, with eight included in the meta-analysis.

Results: Recombinase polymerase amplification combined with clustered regularly interspaced short palindromic repeats/Cas12a achieved the highest pooled diagnostic performance, with a sensitivity of 0.94 and specificity of 0.97. Polymerase chain reaction-based analyses also showed high accuracy (sensitivity = 0.85; specificity = 0.97) but exhibited considerable heterogeneity across platforms and sample types. Loop-mediated isothermal amplification demonstrated moderate performance (sensitivity = 0.60; specificity = 0.91), while p16 immunohistochemistry offered good sensitivity (0.91) but lower specificity (0.73), supporting its use as a confirmatory rather than primary screening tool. In situ hybridization and next-generation sequencing provided broader genotyping capability but were limited by higher cost and technical complexity.

Conclusion: Polymerase chain reaction remains the clinical gold standard for HR-HPV detection, whereas recombinase polymerase amplification/clustered regularly interspaced short palindromic repeats–Cas12a emerges as a promising alternative for decentralized, low-resource screening. Future multi-center studies should standardize reporting, expand genotype coverage beyond HPV-16 and HPV-18, and assess cost, turnaround time, and operational feasibility to ensure that advances in

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HR-HPV diagnostics translate effectively into public health benefit.

Keywords: Diagnostic; Human papillomavirus; Point of care; Rapid diagnostic

1. Introduction

Human papillomavirus (HPV) infection is a major cause of cervical cancer in women, with subtypes 16 and 18 accounting for more than 70% of cases worldwide.^{1,2} Beyond cervical disease, HPV contributes to over 60–90% of anal, vaginal, oropharyngeal, and penile cancers. More than 150 HPV genotypes have been identified and are classified as either high-risk (HR) or low-risk (LR) based on their potential to drive cervical carcinogenesis. Common HR types include 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 58, 59, 68, and 82, whereas LR types include 6, 11, 32, 40, 42, 43, 44, 54, 61, 70, 72, 81, 84, and 87.³

Over the past decade, HPV infection has also been linked to a rising incidence of oropharyngeal squamous cell carcinoma (OPSCC), particularly in the tonsils and base of the tongue, and notably among younger men.⁴ Oral HPV infection increases the risk of malignant transformation by roughly 50-fold, and HPV-driven OPSCCs are dominated by HR-HPV-16, which is detected in approximately 90% of cases.^{5–9}

Most HPV infections clear spontaneously within one to two years, a process known as viral clearance, which substantially reduces the likelihood of cancer progression.^{6,10} Persistent infection, however, promotes carcinogenesis through overexpression of the viral E6 and E7 oncoproteins, which suppress the tumor suppressor genes p53 and Rb and drive uncontrolled cell proliferation.^{6,11} Given the significant health burden posed by HPV-related cancers, early and accurate detection of HR-HPV types is essential for effective screening and prevention.

Detection strategies generally fall into two categories: direct identification of the viral genome, typically by nucleic acid amplification tests such as polymerase chain reaction (PCR), and the recognition of HPV-induced morphological changes in patient cells or tissues that indicate precancerous or malignant transformation.¹² Nucleic acid testing, which offers high sensitivity and specificity, is now central to the diagnosis of many pathogens.¹³ HPV DNA detection remains the gold standard because viral integration into host DNA strongly

correlates with the development of invasive carcinoma.¹⁴ Yet in many low-resource settings, where HPV-related disease is most prevalent, these molecular tests are often inaccessible due to limited funding, infrastructure, and trained personnel. This underscores the need for affordable, point-of-care diagnostic tools to help reduce the burden of HPV disease.¹³

Understanding the range of available detection methods is crucial because the choice of assay directly affects diagnostic accuracy, the ability to distinguish transient from persistent infection, and the clinical decisions surrounding screening and patient management. Accurate detection not only differentiates infections that will clear spontaneously from those likely to progress to cancer but also enables earlier intervention, particularly where resources are scarce. Against this backdrop, the present study aims to comprehensively evaluate diagnostic methods for HR-HPV by mapping existing evidence through a scoping review and quantitatively summarizing diagnostic accuracy via meta-analysis to inform both clinical practice and future research.

2. Methodology

2.1. Eligibility criteria

This scoping review was conducted following the methodological framework of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist 2018. Studies were eligible if they met the following conditions: the target population comprised human subjects infected with HPV. The review focused on point-of-care testing methods for HPV detection, including loop-mediated isothermal amplification (LAMP), clustered regularly interspaced short palindromic repeats (CRISPR)-based assays, immunohistochemistry (IHC), p16 protein detection, and recombinase polymerase amplification (RPA). We considered only studies in which point-of-care testing was implemented or formally evaluated. Acceptable designs included observational and cohort studies, clinical investigations, and laboratory-based studies. Only articles published in English between 2010 and July 2025 were

included. We specifically sought clinical studies that compared at least two diagnostic methods. Narrative reviews, editorials, letters, and studies confined solely to laboratory-based methods without a point-of-care application were excluded.

2.2. Information sources

A comprehensive literature search was performed across three electronic databases—PubMed/MEDLINE, ScienceDirect, and Scopus. Two investigators (IG and NPF) independently conducted the search, screened records, and removed duplicates before data extraction. Titles and abstracts were screened independently by the same two investigators, and any disagreements were resolved by a third investigator (RA).

2.3. Search strategy

The core search terms included “LAMP” or “Loop-mediated Isothermal Amplification,” “CRISPR,” “IHC” or “Immunohistochemistry,” “P16,” “HPV” or “human papillomavirus,” “RPA” or “Recombinase polymerase amplification,” and “point of care.” The complete database-specific strategies are provided in Table S1.

All records identified were imported into Microsoft Excel 2019 for reference management, and duplicates were removed. Titles and abstracts were screened independently by two reviewers (IG and NPF) based on the predefined eligibility criteria. Full texts of potentially relevant studies were then assessed, with any discrepancies resolved through discussion or, when necessary, adjudication by a third reviewer (RA and MDH).

2.4. Statistical analysis

The extracted data were summarized descriptively. Summary tables captured the distribution of point-of-care testing approaches, targeted HPV genotypes, study settings, and diagnostic performance, and were used to highlight temporal trends and evidence gaps. When studies demonstrated sufficient homogeneity in design, diagnostic targets, and reported outcomes, a quantitative synthesis was undertaken.

Meta-analyses used a random-effects model (DerSimonian–Laird method) to account for expected heterogeneity. For diagnostic accuracy outcomes, pooled sensitivity, specificity, positive predictive value, negative predictive value, and corresponding 95% confidence intervals (CIs) were calculated using a bivariate random-effects model. Heterogeneity was assessed with the I^2 statistic, with thresholds of 25%, 50%, and 75% interpreted as low, moderate, and high, respectively. Subgroup analyses explored potential sources of heterogeneity by assay type

(IHC, LAMP, PCR, and RPA) and by genotype (HPV-16 and HPV-18). All analyses were performed with OpenMeta v12.11.14 (Brown University, <http://www.cebm.brown.edu/openmeta/>). Publication bias was not assessed.

3. Results

3.1. Study selection

Figure 1 shows that database searches identified 3,543 records. After removing 14 duplicates, 3,529 titles and abstracts were screened. Of these, 2,991 articles were excluded for not meeting the inclusion criteria. The remaining 538 full-text articles were assessed for eligibility, and 523 were subsequently excluded. In total, 15 studies were included in the qualitative synthesis, of which eight contributed data to the meta-analysis.

3.2. Subgroup analysis

As shown in Table S2 and Figure 2, multiple assay platforms were used for HPV-16 detection, including RPA, PCR-based methods, LAMP, and sequencing approaches. RPA combined with CRISPR/Cas12a consistently demonstrated excellent diagnostic performance, achieving 100% sensitivity, specificity, and accuracy. PCR assays also performed strongly, with sensitivity ranging from 87.65% to 100% and specificity from 96.67% to 100%. In contrast, isothermal amplification using LAMP assays yielded only moderate results, with a sensitivity of 90.9% and a specificity of 88.9%, while sequencing-based next-generation sequencing of plasma showed lower diagnostic accuracy, with a sensitivity of 57.14% and a specificity of 37.5%.

For HPV-18, a similar pattern was observed. RPA with CRISPR/Cas12a again achieved 100% sensitivity, specificity, and accuracy (Table S2 and Figure 2). PCR platforms such as Onclarity and TaqMan also produced high diagnostic values, with specificity exceeding 98% and accuracy approaching 99%. By comparison, isothermal amplification using LAMP assays showed markedly weaker performance, with specificity dropping to 22.2% and accuracy around 36.05%.

For other HR-HPV genotypes, in situ hybridization (ISH) assays demonstrated variable diagnostic power (Table S2 and Figure 2). DNA ISH achieved high sensitivity (86.3%) and specificity (95.3%), whereas RNA scope and other ISH formats showed more variable performance, with sensitivity ranging from 53.5% to 93.4%.

3.3. Heterogeneity

For isothermal amplification assays (Figure 3A), both sensitivity and specificity analyses under a fixed-effect model revealed no significant heterogeneity ($I^2 = 0$; $p =$

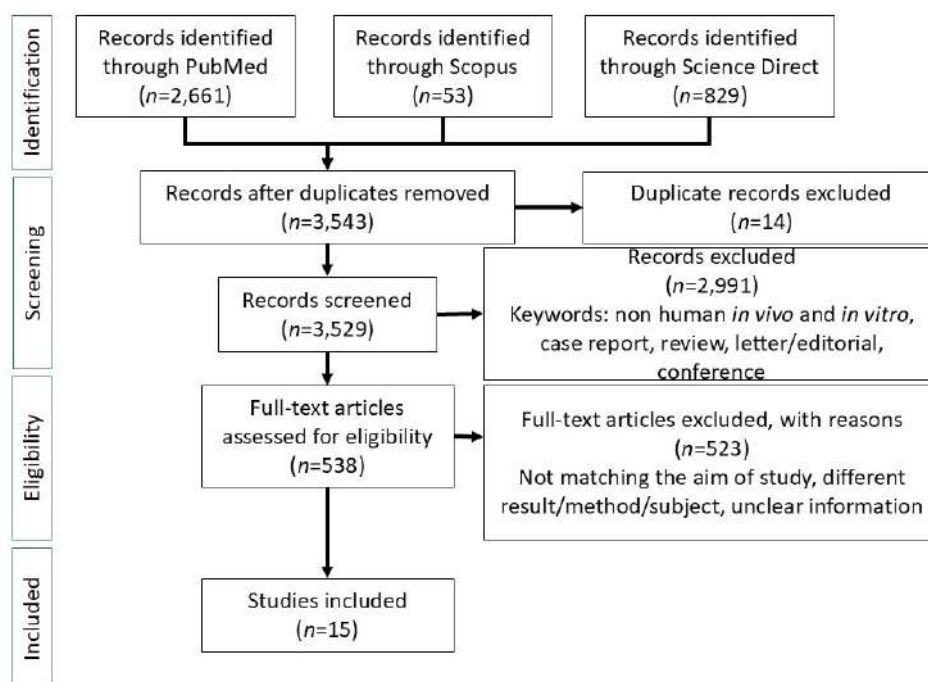


Figure 1. Flow chart of the 2018 Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

0.826 and $p = 0.639$, respectively), indicating that diagnostic performance estimates were consistent across studies. IHC assays also showed homogeneity for sensitivity ($I^2 = 0$; $p = 0.445$), but specificity demonstrated significant heterogeneity ($\tau^2 = 0.843$; $I^2 = 90.47$; $p = 0.001$), suggesting considerable variability in the ability of immunostaining markers to rule out non-HPV cases in different settings.

In contrast, RPA assays (Figure 3B) displayed moderate-to-substantial heterogeneity for sensitivity ($\tau^2 = 3.252$; $I^2 = 69.88$), whereas specificity remained homogeneous ($I^2 = 0$; $p = 0.550$). The variation in sensitivity likely reflects differences in primer–probe design, reaction conditions, or target gene selection across studies. PCR-based assays (Figure 3C) exhibited the highest overall heterogeneity. Sensitivity showed substantial variation ($\tau^2 = 0.585$; $I^2 = 75.34$; $p < 0.001$), and specificity was even more heterogeneous ($\tau^2 = 6.727$; $I^2 = 96.27$; $p < 0.001$). Such variability may stem from differences in PCR platforms, sample sources (e.g., tissue, plasma, or oral rinse), viral load thresholds, and operator-dependent factors that influence diagnostic accuracy.

When results were stratified by genotype, HPV-16 detection (Figure 3E) demonstrated high heterogeneity for both sensitivity ($\tau^2 = 1.769$; $I^2 = 73.23$; $p < 0.001$) and specificity ($\tau^2 = 6.506$; $I^2 = 96.18$; $p < 0.001$). Despite HPV-

16 being the most extensively studied genotype, these findings indicate persistent methodological variation, possibly related to assay chemistry, sample preparation, and population-level viral prevalence. For HPV-18 (Figure 3F), sensitivity showed moderate heterogeneity ($\tau^2 = 1.492$; $I^2 = 61.39$; $p = 0.051$), while specificity revealed substantial heterogeneity ($\tau^2 = 2.082$; $I^2 = 66.98$; $p = 0.028$). The narrower evidence base for HPV-18 compared with HPV-16 may further contribute to variability in performance outcomes.

3.4. Meta-analysis

When stratified by assay type (Figure 3), diagnostic performance differed across platforms. Isothermal assays (Figure 3A) showed a modest pooled sensitivity of 0.599 but relatively high specificity of 0.907, indicating that although false negatives remain a concern, these assays are reliable for ruling out HPV infection when results are negative. In contrast, RPA assays (Figure 3B) demonstrated excellent overall performance, with a sensitivity of 0.942 and a specificity of 0.974, suggesting strong diagnostic utility and consistent accuracy despite moderate heterogeneity in sensitivity estimates. PCR-based assays (Figure 3C) also achieved high pooled sensitivity (0.846) and specificity (0.971).

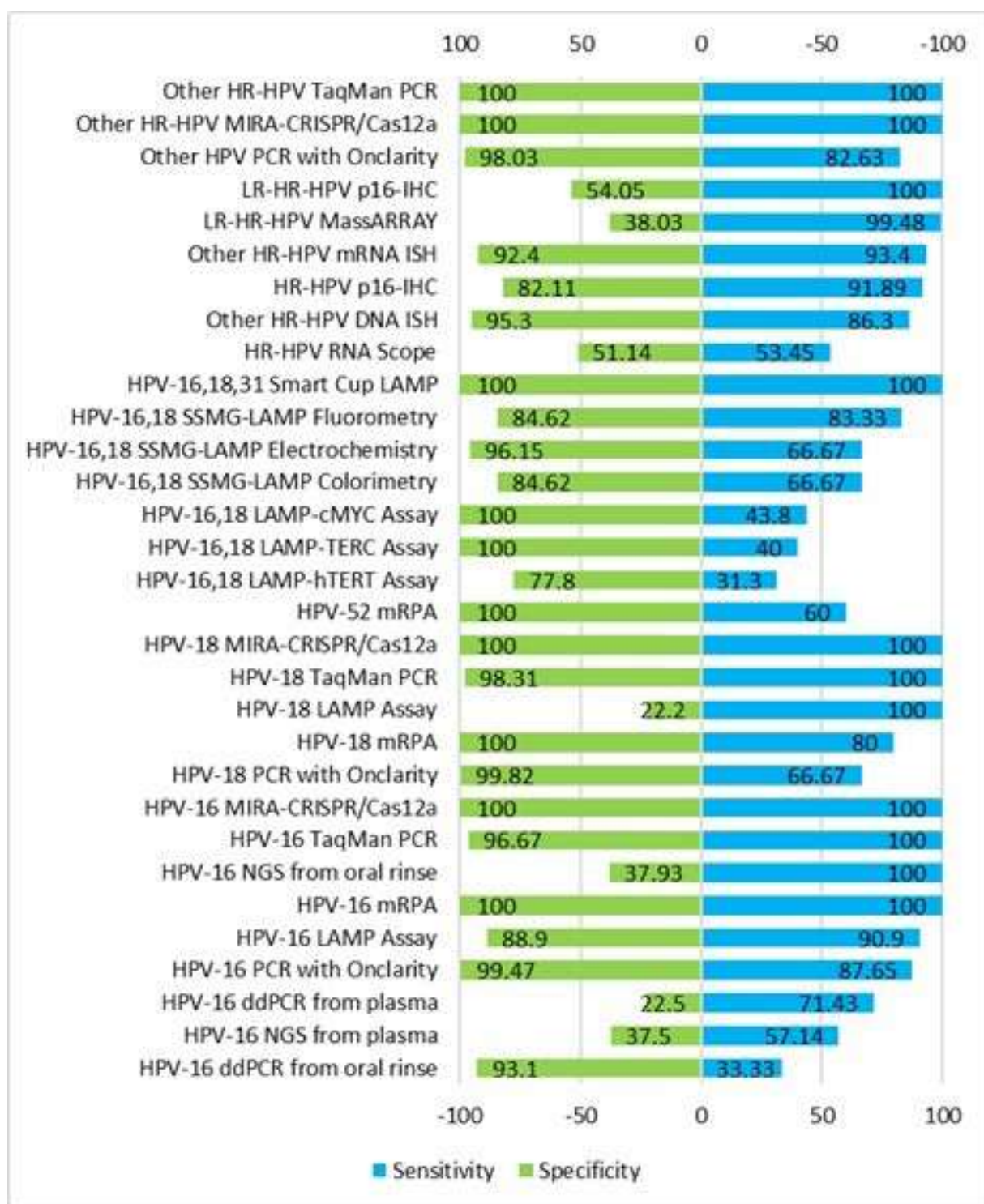


Figure 2. Sensitivity and specificity score for each type of assay based on HPV genotype

Abbreviations: ddPCR: Droplet digital polymerase chain reaction; HR-HPV: High risk human papillomavirus; hTERT: Human telomerase reverse transcriptase; IHC: Immunohistochemistry; ISH: In situ hybridization; LAMP: Loop-mediated isothermal amplification; LR-HPV: Low risk human papillomavirus; MIRA: Multienzyme isothermal rapid amplification; MIRA-CRISPR: Multienzyme isothermal rapid amplification-clustered regularly interspaced short palindromic repeats; mRPA: Multiplex recombinase polymerase amplification; NGS: Next generation sequencing; PCR: Polymerase chain reaction; SSMG: Sequence specific magnetic gel.



Figure 3. Sensitivity and specificity meta-analysis of assay types and HPV genotypes. (A) Isothermal assays. (B) Recombinase polymerase amplification assays. (C) Polymerase chain reaction assays. (D) Immunohistochemistry assays. (E) HPV-16. (F) HPV-18.

Abbreviations: CI: Confidence interval; FN: False negative; FP: False positive; HPV: Human papillomavirus; TN: True negative; TP: True positive.

However, the substantial heterogeneity across studies indicates that the reliability of these estimates depends heavily on methodological standardization, including the choice of target genomic regions and amplification conditions. IHC assays (Figure 3D) showed high sensitivity (0.906) but lower specificity (0.726), reflecting a tendency to over-diagnose HPV-related disease. This finding aligns

with the heterogeneity observed in specificity analyses, likely driven by differences in antibody clones, staining protocols, and interpretation criteria.

Genotype-specific analyses revealed similarly strong results. HPV-16 detection (Figure 3E) reached a sensitivity of 0.870 and specificity of 0.868, while HPV-18 detection (Figure 3F) demonstrated comparable sensitivity (0.874)

but markedly higher specificity (0.989). Despite these favorable pooled accuracy metrics, both genotypes exhibited substantial heterogeneity, particularly in specificity, suggesting that variations in primer and probe design as well as differences in population-level HPV prevalence may influence diagnostic performance.

4. Discussion

4.1. Study design

Based on Table S2, the most common study designs were observational retrospective¹⁵⁻¹⁹ and experimental laboratory investigations,²⁰⁻²³ followed by observational prospective,²⁴⁻²⁶ cohort,^{27,28} and a single cross-sectional diagnostic accuracy study.²⁹ These designs allowed direct head-to-head comparisons between novel assays and established reference methods, but also introduced heterogeneity in patient selection and reference standards. Retrospective studies are frequently used in HPV diagnostics because archived cervical cytology samples and biobank materials enable parallel testing of multiple assays on identical aliquots without the cost or time required for new recruitment.¹² In parallel, experimental laboratory designs remain essential for establishing analytical validity, such as limit of detection, reproducibility, and genotype inclusivity/exclusivity, before large-scale clinical implementation. Their flexibility and cost-effectiveness make them particularly suited to rapidly evolving technologies such as extended genotyping, isothermal amplification, and point-of-care molecular assays.³⁰

4.2. Analysis of heterogeneity

This scoping review and meta-analysis provides a comparative overview of diagnostic methods for detecting HR-HPV, examining study design, sample type, diagnostic performance, and future directions. Our findings reaffirm that PCR remains the clinical gold standard for HR-HPV detection, while emerging technologies such as RPA combined with CRISPR show considerable promise for rapid testing in low-resource settings.

The highest heterogeneity of PCR indicates that the performance of PCR-based assays varies widely across studies, likely due to differences in assay protocols, primer sets, target genes, sample collection methods, and laboratory workflows. Such variability makes PCR outcomes highly sensitive to methodological preferences and operational conditions. This wide dispersion also reflects the diverse clinical settings, populations, and specimen types included in the studies, all of which can influence the diagnostic accuracy of PCR.

4.3. Sample origin

Cervical specimens predominated across studies,^{16,20-25,28,29} with additional work in oropharyngeal and head-and-neck tissues,^{15,18,19,27,28} oral rinse or saliva,^{15,23,27} plasma,^{15,28} formalin-fixed paraffin-embedded/biopsy tissue,²⁸ and a small number of urine samples. Although overlap of sample matrices within individual studies was common, the evidence base remains anchored in cervical screening, with a meaningful subset focused on HPV-driven OPSCC. Globally, HPV-16 and HPV-18 account for over 70% of cervical cancer cases, with HPV-16 responsible for more than half,² and HPV-16 similarly dominates HPV-positive OPSCC.⁶ Consequently, diagnostic performance varied by sample type: cervical swabs consistently yielded the most robust data, whereas plasma, saliva/oral rinse, and formalin-fixed paraffin-embedded tissue produced more variable results. This highlights the need for matrix-specific validation before clinical adoption.

4.4. Human papillomavirus detection methods

Polymerase chain reaction-based assays were the most frequently evaluated approaches,^{15,18,20,28,29} followed by p16 IHC,^{16,17,28} LAMP/isothermal assays,^{21,23,25} and RPA-/CRISPR-derived methods.^{20,22,24} ISH^{16,28} and next-generation sequencing^{15,18} appeared less often, and MassARRAY/genotyping was reported in only one study.²⁷ Reference standards most commonly involved PCR-based comparators^{19-25,29} and p16-IHC,^{15,18,19,27,28} with ISH used in several studies,^{15,19} and a single study employing histopathology or magnetic resonance imaging as an explicit comparator. This landscape underscores PCR's role as the de facto benchmark, while p16-IHC is frequently applied in head-and-neck disease.

Protein-based markers such as p16-IHC offer excellent sensitivity for detecting HPV-driven oncogenesis, with reported rates of 91.89–100%. However, their relatively limited specificity (54.05–82.11%), subjective interpretation, and site-dependent variability reduce their robustness across settings.¹⁷ Nucleic acid-based tissue methods, particularly ISH, provide higher specificity and allow direct visualization of viral nucleic acids in a histological context, yet tend to be less sensitive than PCR, are labor-intensive, and require access to tissue samples.²⁸

Moreover, PCR-based assays—including ddPCR, TaqMan, and Onclarity—remain the most established molecular methods, offering high specificity and broad genotype coverage. Their reliability, however, depends on thermocycling infrastructure and strict workflow conditions, and they may detect transient infections of uncertain

clinical significance, complicating interpretation.^{15,29} More recently, isothermal techniques such as RPA and multienzyme isothermal rapid amplification–CRISPR have emerged as promising alternatives. These assays are rapid and instrument-light, making them attractive for use in resource-limited settings.^{24,29} LAMP represents another cost-effective and rapid option requiring only a simple heat source and allowing visual readouts, but its diagnostic performance remains inconsistent across target regions and is challenged by complex primer design and the risk of carryover contamination.²¹ At the other end of the spectrum, sequencing and MassARRAY platforms provide unparalleled genotyping depth and multiplexing capability. Despite these advantages, their clinical adoption is limited by lower specificity in certain sample types, such as liquid biopsies or oral rinses, as well as by high costs and technical complexity.²⁷

Programmatic screening requires diagnostic methods that combine high accuracy with practical feasibility. PCR platforms such as Cobas, Onclarity, and TaqMan offer established workflows, reliable supply chains, and consistently strong specificity (96.67–100%), making them dependable anchors for population-based screening and triage. Isothermal strategies, including RPA and LAMP, reduce equipment requirements and shorten time-to-result. Evidence from Table S2 shows that RPA/CRISPR can match or even exceed PCR accuracy in small studies (75–100%), underscoring their potential for decentralized testing and use in resource-limited settings. By contrast, p16 IHC and ISH remain valuable for tissue-based confirmation, especially in OPSCC, but are less suited as primary screening tools.

4.5. Accuracy in detecting human papillomavirus

Across method-level analyses, HPV-18 showed the highest central tendency, with sensitivity ranging from 31.3% to 100% and specificity from 22.2% to 100%, while HPV-16 also performed strongly (sensitivity = 31.3–100%; specificity = 22.5–100%). Other HR-HPV genotypes yielded pooled sensitivities of 53.45–100% and specificities of 38.03–100%, though sample sizes were smaller and methodologies more variable. The wide specificity range (22.2–100%) observed in certain LAMP or liquid-biopsy contexts highlights the strong influence of sample matrix and implementation on diagnostic performance. Four studies reported results at the broader HR-HPV or LR-HPV + HR-HPV category level rather than genotype-specific, and several involved mixed cervical and oropharyngeal settings. Such inconsistent stratification by risk group and anatomical site limits cross-study comparability and may inflate or deflate pooled metrics when low-risk types or

non-cervical matrices are not clearly distinguished.

4.6. Limitations and future research

This study has several limitations. First, substantial heterogeneity was observed across included studies, particularly in PCR- and genotype-specific analyses, reflecting differences in assay platforms, sample sources, and patient populations. Second, many studies reported only sensitivity and specificity, restricting the application of advanced meta-analytic models. Third, risk of bias was not systematically assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 or the Standards for Reporting of Diagnostic Accuracy guidelines, and publication bias was not formally analyzed. Finally, only a small number of studies evaluated RPA/CRISPR; while pooled results are highly encouraging, larger prospective trials are needed to confirm their utility across diverse clinical contexts.

Future research should prioritize standardization of reporting in HPV diagnostic studies, including the use of flow diagrams, and adherence to established reporting guidelines such as the Standards for Reporting of Diagnostic Accuracy, alongside systematic risk-of-bias assessment using tools such as the Quality Assessment of Diagnostic Accuracy Studies-2. Comparator selection should also be clearly defined and anchored to recognized gold standards appropriate for the clinical context, avoiding composite or algorithmic comparators, unless explicitly specified. Assay validation should be matrix-specific, covering cervical screening specimens, OPSCC tissues, oral rinse or saliva, plasma/ctDNA, and self-collected samples, with pre-specified thresholds to ensure reproducibility and comparability.

The further development and scaling of isothermal platforms, particularly RPA- and CRISPR-based assays, represent a key opportunity given their strong diagnostic performance and operational advantages. Diagnostic panels should also expand genotype coverage beyond HPV-16 and HPV-18 to include other HR-HPV types such as 31, 33, 45, 52, and 58, reflecting regional epidemiology and evolving patterns in the post-vaccination era.³⁰ Finally, future studies should extend their scope beyond diagnostic accuracy to incorporate key implementation outcomes, turnaround time, assay failure or indeterminate rates, hands-on time, staffing requirements, and total cost of ownership, while considering equity and access. Prospective evaluation of self-collection strategies and decentralized workflows in low-resource settings will be critical to ensure that advances in HPV diagnostics translate into meaningful public health benefits across diverse populations.³¹

5. Conclusion

This scoping review and meta-analysis demonstrates that diagnostic methods for HR-HPV show considerable variation in accuracy. RPA/CRISPR assays consistently achieved the highest diagnostic performance, with pooled sensitivity of 0.94 and specificity of 0.97, indicating strong potential for low-resource and point-of-care applications. PCR-based methods also showed high pooled sensitivity (0.85) and specificity (0.97), but substantial heterogeneity across platforms and sample types limits generalizability. LAMP assays provided moderate and variable performance (sensitivity = 0.60; specificity = 0.91), while p16-IHC yielded good sensitivity (0.91) but limited specificity (0.73), restricting its role to confirmatory rather than primary screening. Taken together, PCR remains the gold standard for clinical HPV detection, whereas RPA/CRISPR offers a promising alternative for decentralized testing, and tissue-based assays retain value in histopathological contexts. Future research should prioritize large-scale, multi-center validation of isothermal platforms and expand genotype coverage beyond HPV-16 and HPV-18 to reflect shifting epidemiology.

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Conflict of interest

The authors have no conflicts of interest associated with the material presented in this paper.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Data is available from the corresponding author upon reasonable request.

Further disclosure

A comprehensive literature search was performed across three electronic databases—PubMed/MEDLINE, ScienceDirect, and Scopus. Two investigators (IG and NPF) independently conducted the search, screened records, and removed duplicates before data extraction. Titles and abstracts were screened independently by the same two investigators, and any disagreements were resolved by a third investigator (RA).

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