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Recent Advances in Human Papillomavirus Testing Technologies

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SUMMARY: *Human papillomavirus (HPV) examination has made cervical cancer screening change from observation which based on morphology to molecular risk classification, hence clinically useful progress is not balanced among targets, platforms and sampling work procedures. This review synthesized the latest proof from PubMed, Web of Science, Scopus, and WHO guidance documents, with stress on English language comparative research and guides issued from 2023 to 2025. Newest data indicate that authenticated DNA tests are still the main support of first-step checking because they bring together high sensitivity, automatic operation, and expandable genotyping, therefore E6/E7 mRNA, p16/Ki-67 double staining, and E6/E7 oncoprotein tests enhance triage specificity through concentrating on biologically active infection or transformation. Self-collection, urine examination, CRISPR-rooted on-site detection platforms, long-read combination analysis, and AI-supported cytology enlarge access or deepen risk classification, but standardization and forward-looking verification still lack enough for overall substitution of mature working procedures. On the whole, this research area is advancing in the direction of a step-by-step model, in which the first step is primary HPV nucleic acid examination, after which there comes genotype-conscious and activity-based classification, with sampling simplification and testing close to patient being utilized to promote coverage and shorten turnaround time. This framework can give support to more accurate and more easy-to-reach cervical cancer prevention work.*

KEYWORDS: *human papillomavirus; cervical cancer screening; molecular diagnostics; genotyping; self-sampling; triage*

1 Introduction

Long-duration sustained infection by high-risk human papillomavirus (HR-HPV) is the necessary etiologic factor that propels nearly all cervical cancers, but the clinical significance of this statement lies in its public health context, and not in virology on its own. Cervical cancer still is one of the most able-to-be-prevented malignant tumors in women, for this illness usually develops through can-be-recognized pre-cancer stages and for the cause-carrying pathogen is already known. Even thus, the load is still very heavy and divided in an uneven way. Recent global calculation results show that disease occurrence and death still gather in environments where screening range, follow-up ability and treatment obtaining are not complete, not in places where the biological action of HPV is essentially different. In the identical time, global attribute studies continuously show that HPV16 and HPV18 hold the

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largest share of invasive cervical cancer, hence proving that the path from persistent infection to malignant transformation is biologically specific and epidemiologically consistent in all regions [1-3]. The disease has the nature that can be prevented, this makes the continuation of this burden especially have important results: different from many malignant tumors, cervical cancer frequently can be blocked by repeated examination, classification disposal that aims at problems, and therapy of pre-cancer damage before the condition of invasion happens. Therefore, the current variation of burden reflects not only the virologic exposure, but also the sufficiency of testing paths, memory systems, and treatment connection. It also indicates that screening policy holds uncommon strategic importance: when the causal route is understood and precursor harm spots can be found, mistakes in test choosing or coverage change more directly into avoidable sickness and death.

This epidemic rule explains why cervical cancer examination has step by step shifted from morphology-focused observation toward direct examination of virus risk. Traditional cytology in past time had changing influence because it cut down cancer occurrence when organized plans got repeated joining and high-quality glass slide explanation. However, cytology can only discover the shape changes which show up after infection has kept going for a time long enough to cause unusual situations in cells. HPV tests deal with a different position on the cause chain: they find infection or tumor-causing activity before shape change development is completely set up. The actual outcome is higher analytic and clinical sensitivity for early risk catching, but also a more complex specificity issue, therefore a positive HPV result may stand for temporary infection, continuous cancer-causing infection, or already changing illness. That contradiction between early finding and excessive referral is now the core of the construction of current screening calculation procedures [4]. In other words, therefore, the transformation toward molecular checking has not removed the uncertainty of diagnosis; it has already caused this relocation to be done. The core difficult problem is no longer whether the virus can be discovered, but how the positive result of HPV should be explained in a method that balances early handling against unnecessary operation processes. That is the cause for why the choosing of assay has become unable to be separated from the design of clinical pathway.

Hence, the phrase “HPV testing”, no longer has the reference to a single technology category. It contains experiments which are different in analyte kind, genome target, amplification chemical, output detail, processing amount, and planned clinical work. Certain experiments have been optimized for wide preliminary screening and great sensitivity; other tools are planned to perfect management after HPV positive result through finding genotype-corresponding risk or through checking living oncogene expression which has biological function. DNA examinations that aim at L1 regions, examinations which are oriented to E6/E7 genes, mRNA examinations, dual-color method plans, cancer protein checks, integration analysis, and AI-supported shape observation all work in the big HPV testing field, but they reply to different clinical questions. A method which gives good performance as an entry checking experiment is not certainly the optimal triage biomarker, and a platform which has outstanding biological particularity may still not have enough expandable degree for population level usage [5]. The object of analysis is important because viral genome breakage, copy quantity, and expression condition all can affect what a positive outcome means in biological terms. The form of reporting is important because gathered high-risk positive results, incomplete gene analysis, and expanded gene analysis bring about different following-hand processing choices. Throughput has importance because screening programs rely on stable, expandable working flows instead of on separated analysis excellent performance. To clinical workers and program layout personnel, these differences are not technique details but they are the factors which decide what actions will be taken afterwards.

This differentiation has gotten more and more important when screening projects go forward to risk-centered management. A modern program is not only in need of a test which has analytic validity; it requires a testing procedure which is suitable for the predetermined decision node. The main first-step screening must have the property of being reproducible, can be done by machines, and be sufficiently sensitive for application on a big scale. Reflex triage needs must cut unnecessary colposcopy, therefore it must not let clinically meaningful precancerous lesions escape away. Methods of taking samples must maintain performance levels while boosting participation rates, especially in groups that lack screening enough. The platform construction also must match the ability of the health system, because a very good laboratory test method may have program failure if it relies on facilities that do not exist in the place where care is given. Practical guides for cytopathology and molecular selection sorting more and more emphasize this layered logic, in which the selection of assay, information of genotype, specificity of biomarker, and design of work flow are all considered together, not as isolated technical characteristics [6]. The target product outlines that are put forward for HPV examination emphasize exactly these demands through connecting test effect to cost that people can bear, sample processing, and the environment of intended use instead of connecting only to laboratory measurement indexes. This system-based angle of view therefore can help make explanation that why in recent academic papers more and more researchers evaluate detecting experiments not only via sensitivity and specificity, but also via transportation stability, suitability with materials collected by oneself, automation work load, and adaptability for distributed projects.

A second reason why we need newly to do synthesis is that recent progress have not taken place on only one technology axial line. A number of innovations make efforts to promote biological distinction, for instance E6/E7 mRNA test methods, double-color cell checks, and integration-focused analyses which pay attention to changing infection instead of mere existence of virus. Other new creations mainly solve the problems of access and implementation, including self-sampling, urine gathering, cartridge-based amplification, and CRISPR-supported near-patient testing. Still other people raise the efficiency of interpretation by means of the artificial intelligence assisted cytology method or colposcopy method. These development situations are frequently discussed just like they compete for the identical position, but in actual practice they take up different places in the screening route. The clinical problem already is not any longer if HPV testing is more good than morphology in a general meaning; it is which kind of test, on which kind of sample, at which stage of medical care, that best promotes detection, triage, coverage, and timeliness under the constraints of real world. This role difference is especially concerned in low-resource and broken-care settings, where the best-performing test on document may not bring the best population result if it cuts down participation, puts off follow-up, or relies on repeated clinic coming.

Under this background, the current article sums up recent progress in HPV detection technologies via a clinically organized framework. Instead of listing platforms one by one separately, it makes comparison among morphology-based screening, DNA-based pathogen examination, transformation-connected biomarkers, and newly appeared access-focused or precision-focused technologies on the basis of what they give to the screening route. This review gives especial focus to the difference between first-step screening and after-positive selection, to the mutual compromise between sensibility and particularity, and to the working influences of sample-taking and platform designing. The goal is not merely to find out newer technologies, but to make clear which technologies are ripe enough for daily combination, which are best placed as additional tools, and which still have hope but not yet enough standardization for wide carrying out. Through reorganizing the documents in this manner, this review has the objective to assist a more accurate comprehension of technological

maturation, clinical arrangement, and probable future orientation in cervical cancer screening. Hence, this article regards HPV testing as one integrated screening architecture, not as a simple list of testing items. This frame is constructed for making the review can be directly used by people to screen pathway design.

2 Material and Methods

This article has been revised into a structured narration review, not a protocol-registered system review. PubMed, Web of Science, Scopus, and WHO publication databases have been searched up to 10 April 2026 through combinations of the terms “human papillomavirus” or “HPV” together with “cervical screening”, “molecular detection”, “DNA”, “mRNA”, “genotyping”, “dual stain”, “self-sampling”, “urine”, “CRISPR”, “integration”, and “artificial intelligence”.

The eligible sources that conform to requirements are English language comparative clinical studies, meta-analyses, assay verification studies, practice implementation studies, and authoritative guiding documents which are directly connected with HPV testing in cervical screening. We gave priority to publications that were published between 2023 and 2025, therefore the recent platforms and management suggestions could be emphasized by us. Studies that only discuss vaccines, individual case reports, editorials that do not carry original research data, and papers that do not focus on the performance of cervical screening or the design of molecular tests, all of these are excluded.

Data were extracted on analyte target, detection principle, sample type, genotyping capacity, reported CIN2+/CIN3+ performance when available, operational requirements, and proposed clinical role. The final synthesis emphasized 25 references and was organized into four analytic domains: morphology-based screening, DNA-based pathogen detection, activity-based triage markers, and emerging access or precision technologies. Because no new human participants or samples were involved, ethics review was not required.

3 Results

3.1 Morphology-based screening remains clinically relevant but biologically indirect

To clarify why morphology-based screening was gradually supplemented by molecular assays, Figure 1 contrasts the workflow logic of conventional Pap smear preparation and liquid-based cytology.

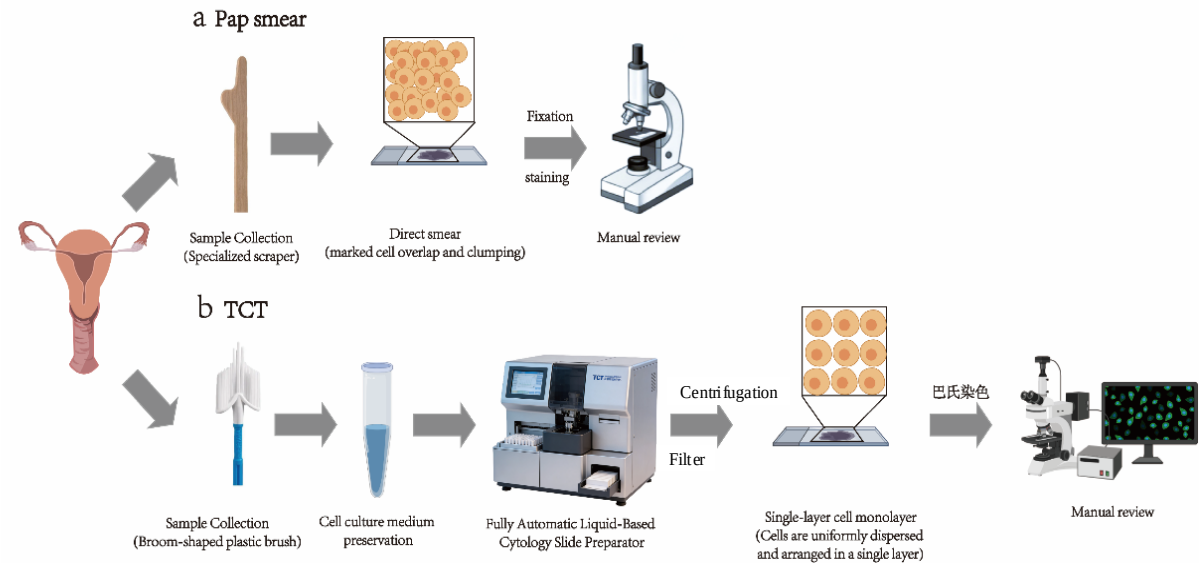

Figure 1: *Workflow comparison between conventional Pap smear and liquid-based cytology.*

Figure 1 demonstrates that liquid-based cytology, it is mainly promoted specimen preparation—cell dispersion, background decrease, and slide uniformity—instead of altering the biological endpoint that is being interrogated. Morphology-based methods still have use because they expose structure and cell abnormities that can direct instant microscope analysis, but they still find a result that comes after infection, not the infecting or changing process itself. From the practical perspective, the method informs the clinician whether cellular harm already can be seen, it does not tell whether carcinogenic HPV action exists before morphology turns into clear abnormality.

This biological interval from the starting incident therefore helps give explanation for the performance situation that has been reported in the recent comparative research results. In one meta-analysis that concentrates on screening tools applied in low and middle income countries, Pap examination obtained a combined sensitivity of 60.3% and a specificity of 96.7% for CIN2+, hence primary HPV testing obtained a higher combined sensitivity of 79.5% but a lower specificity of 72.6%. This comparison has the meaning of disclosure in clinical aspect. Cytology still keeps relatively high specificity because morphological abnormality is a later and more selective occurrence, but this same logic restricts sensitivity for early or tiny diseases. On the contrary, HPV examination methods can catch risk earlier and in a wider range, this makes the finding of cases better but increases the quantity of women that need classification processing after obtaining a positive result. Owing to this cause, cytology has not any longer been able to be best comprehended as an independent competitor to HPV examination; it may be more appropriately placed as one context-related or reflection tool inside a wider risk-relying approach.

The recent research about automation shows that a part of the historical burden of cytology can be decreased, hence its biological restrictions still exist. The research group led by Xue have given the report that an independent AI system achieved 89.4% sensitivity and 66.4% specificity on abnormal squamous-cell examination, and hence a strategy that puts cytologist into the working loop made manual work burden decrease by 37.5%, and thus it did not miss any abnormal squamous cases [8, 9]. These outcomes have importance in practice because they indicate that digital assistance can enhance throughput and stability in morphology-centered working processes. Nevertheless, this promotion is mainly on the procedure side: AI promotes efficiency when people read slides, but it does not change the

fact that the interpretation which is based on slides relies on the performance of morphology. Therefore, artificial intelligence-improved cytology can enhance triage work, quality management, and work team efficiency, hence it is not probable to replace verified molecule access tests in environments where primary HPV examination is already possible to carry out.

3.2 DNA-based pathogen detection remains the backbone of primary screening

Because the clinical behavior of an HPV assay is strongly influenced by target selection, Figure 2 summarizes the genomic regions most commonly used in molecular testing.

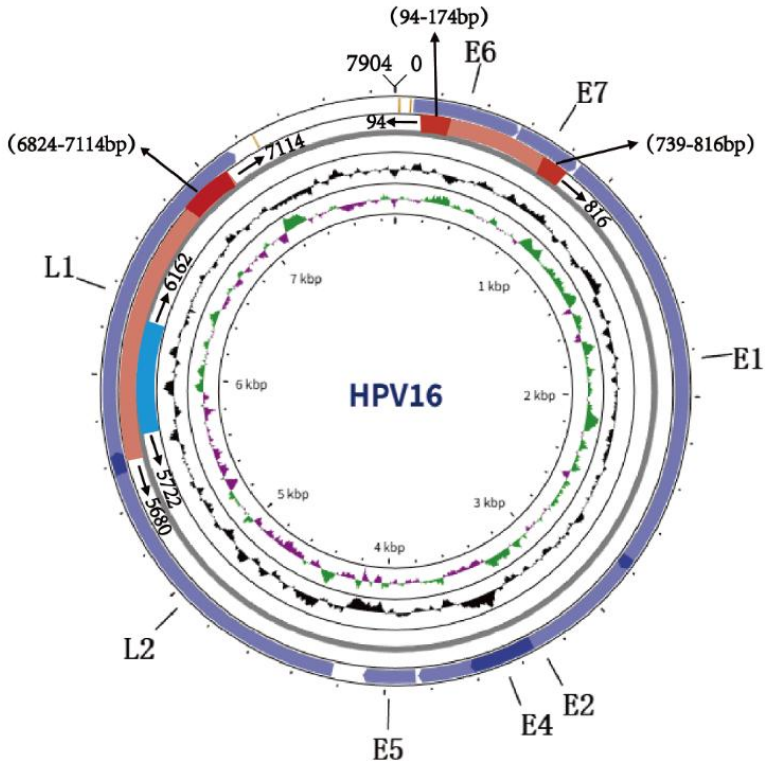

Figure 2: Common genomic regions used as targets in HPV molecular testing.

Figure 2 makes clear that target choice is a biological design decision rather than a merely analytical convenience. L1-directed assays generally maximize broad viral detection and genotype coverage because the region is sufficiently conserved for robust amplification across multiple high-risk types. Assays directed toward E6 and E7, in contrast, are more tightly linked to oncogenic function and can better reflect the relevance of a positive result in lesions where carcinogenic progression is biologically active. A pooled high-risk result, a partial-genotyping result, and an extended-genotyping result are not interchangeable outputs, even when all are generated from DNA-based platforms.

The already verified DNA examination methods still are the core of first-step screening, therefore they supply the most advantageous combination of sensitivity, automation, handling ability, and repeatable stability. The real-world proof regarding the cobas platform has reported that the sensitivity is 98.66% and the specificity is 87.15% for CIN2+, hence it supports that this platform acts as a mature screening tool, not only is it just an analytically sensitive assay. That maturity has importance on the program level. Primary early-stage screening needs stable group-wise handling, uniform result explanation, and quality guarantee for large groups of people, and verified PCR-based DNA systems at present meet these needs

better than newer but not yet uniform technologies. Their operation advantages can also explain why DNA examination has become the core part of organized screening routes in both high-resource and more and more middle-resource environments.

Within the DNA category, however, the field has moved beyond simple pooled positivity. The core development is that the risk information which is carried by the first test result, it gets constantly enriched step by step. Data got from the baseline stage of the Onclarity trial demonstrated that lengthened genotyping is able to stratify HPV-positive women with more precision than the traditional HPV16/18 versus "other high-risk" two-part division only. The clinical usefulness of this extra detail level is very big. When the entry inspection differentiates risk-related gene type groups, the following inspection can be more selective, colposcopy recommendation can be better put in order of importance, hence low immediate risk positive cases can be processed with fewer unnecessary processing measures. From this angle, DNA examination has already not been merely a screening doorkeeper; it increasingly becomes the first layer of risk modeling which people use.

The value of this strategy has obtained reinforcement from concordance analyses which are completed across different platforms. De Marco and other persons indicated that the output of BD Onclarity extended genotyping had clinically significant consistency with other screening tests, triage biological markers, and histopathological results, hence it supports that this method can be used as a component with rich information in integrated management algorithms, hence not as an independent typing work[11]. Even so, higher information content cannot wipe out the difference which exists between different platforms. A 2024 comparison work of four HPV genotyping methods discovered method-specified differences in detection range, subtype consistency, and actual report behavior, hence this shows that platform replacement should not be assumed only because assays in name aim at overlapping high-risk types. The more wide meaning is that analytical equal relation, gene type resolution, and clinical decision support must all together get evaluation [12, 13]. For conventional examination, DNA detection methods still are the most powerful entry technique, but their best use more and more relies on the way genotype information is changed into follow-up classification and repeat examination decisions.

3.3 Activity-based and transformation-related markers improve post-HPV-positive triage

A positive consequence from DNA testing does not inevitably mean persistence which has biological significance. Numerous infectious conditions are temporary, and the clinical issue which exists after a positive first screening is not purely whether HPV can be found, but whether the infection which has been detected possesses sufficient activity to make immediate stepped-up evaluation be justified. Due to this cause, triage technologies more and more put focus on transcription activity or host-cell change after HR-HPV positive result is confirmed. Among these labeled molecules, E6/E7 mRNA examination has the most distinct mechanism-based reason, therefore it measures the expression of virus cancer-causing genes which are directly taking part in malignant change instead of only the existence of virus.

In the CERVIVA primary screening study, HPV mRNA showed equivalent sensitivity to HPV DNA for detection of CIN2+ (93.2% vs. 92.8%) and CIN3+ (94.6% vs. 94.6%), while offering higher specificity for CIN2+ (84.0% vs. 80.8%) and CIN3+ (88.44% vs. 85.62%) [13]. This kind of mode is clinically of great importance, therefore it indicates that strategies based on mRNA can maintain the detection of lesions, thus it also reduces the quantity of HPV-positive women who go through unneeded reflex procedures. From the perspective of work flow, the additional value of mRNA does not lie more in substituting for every DNA test, but lies in making post-positive risk resolution clearer. Where program architecture

already depends on a highly sensitive DNA entry test, an activity-based second step can materially improve the balance between detection and referral burden.

Other biological downstream markers have hopeful prospects but are not as mature in a unified way. One 2024 system review and total analysis has verified that E6/E7 oncoprotein tests possess clinic related correctness for finding high-grade lesions, but also has shown obvious difference between different platforms, populations, and study designs [14]. That such heterogeneity possesses direct implementation-related consequences: oncoprotein detection tests still stay attractive because in concept they are closer to transforming infection than DNA positivity, yet the evidence base of them is not as operationally standardized as that of authenticated DNA or mRNA working procedures. By comparison, the p16/Ki-67 dual staining has already gone more toward the practical application adoption. Nowadays existing guiding opinions hold that it can be used for handling HPV-positive persons, because it gives stronger post-positive risk distinguishing ability compared with only cytology, and it suits well with risk-based screening arrangement paths [15]. Put all together, these data point out that the main specificity improvements in current screening at present are obtained from transformation-conscious markers instead of from gradual alterations in cytology itself.

3.4 Sampling and platform innovations broaden access and improve timeliness

Coverage gaps have become a central limiting factor in cervical cancer prevention, which means that sampling logistics are now nearly as important as assay chemistry. Self-sampling is attractive not because it changes HPV biology, but because it changes who can realistically enter the screening pathway. An updated meta-analysis showed that offering self-sampling kits directly to women markedly increases participation compared with standard invitation alone, with relative risk estimates reaching 11.0 for direct-mail strategies and 6.3 for opt-in approaches [16]. These figures indicate that self-sampling should be interpreted primarily as an implementation intervention with diagnostic implications, not merely as an alternative collection technique.

Acceptability findings strengthen that interpretation. A systematic review from Latin America documented favorable user acceptance of vaginal self-sampling, particularly where embarrassment, travel burden, or reluctance to undergo pelvic examination reduces participation in clinician-based screening [17]. The relevant benchmark is therefore not only analytical agreement, but also whether self-collection increases real coverage without breaking recall and follow-up.

Near-term verification researches give forward the idea that this goal can be reached when the self-collect instruments, conveyance culture medium and experiment methods are carefully matched with each other. The research of HPValidate discovered that the relative sensibility of authenticated DNA and mRNA working flows on self-gathered vaginal samples was near to that of the samples gathered by doctors on many kinds of self-sampling apparatuses [18]. This gives support to the viewpoint that materials which are self-collected can have clinical credibility when the entire pre-analytical chain is got to be optimized.

Urine examination provides one more non-invasive path, especially for women who refuse vaginal or cervical sample collection completely. In a random comparison diagnostic research, first-voided urine gathered with a special device had better effect than common-pot urine gathering and presented hopeful detection sensitivity for CIN2+, therefore stressing that the importance of pre-analysis standardization but not urine as a single type [19]. A 2023 colposcopy-based comparison similarly discovered that good consistency exists between urine or vagina self-collecting samples and clinician-gathered neck of uterus samples,

although positive or inconsistent results still needed combination with traditional diagnosis following check[20]. These research works indicate that urine examination possesses true starting-point significance, but that its clinical function still is dependent on perfect gathering systems and clear rearward verification channels.

On the opposite side of the innovation scope, novel platforms are making efforts to promote the speed of problem settlement or the profundity of analysis. One multi-channel RPA-CRISPR/Cas12a testing method has reached a detection boundary of around 1 copy/μL for six high-risk gene types within about 40 minutes, hence it demonstrates the potential of decentralized spot care molecule screening in places where lab basic facilities are not enough. By contrast, the integration analysis of long reads can disclose the complex architecture of HPV-host breakpoints, and thus may deepen risk stratification through the distinguishing of biologically advanced patterns of viral-host interaction[21, 22]. These methods solve different questions: CRISPR-supported POCT pursues fast acquisition and moving convenience, hence combined analysis pursues mechanism-related depth. At present, neither one replaces the already verified conventional screening experiments, but both two show the directions in which this domain is developing.

The auxiliary imaging that is helped by AI therefore adds one more layer of innovation to working flow. Recently, systematic review evidences show that artificial intelligence which is applied in colposcopy can reach clinically meaningful diagnostic accuracy for cervical intraepithelial neoplasia and the detection of cancer, hence the generalizability on different devices, populations, and image obtaining conditions is still a problem that has not been solved [23]. The probable near-term function of AI is supporting not substituting: case sorting priority giving, biopsy position selecting, quality checking, and work load decreasing are more possible ways than complete replacing of expert evaluation.

To consolidate the above comparisons, Table 1 summarizes the major targets, representative findings, and current clinical roles of the principal technologies.

Table 1: *Comparative summary of major HPV testing technologies and their current clinical roles.*

Technology	Primary target	Representative findings	Strengths	Current role
Morphology-based cytology	Cell morphology	Pap testing: pooled sensitivity 60.3% and specificity 96.7% for CIN2+; LBC improves specimen quality but remains reader-dependent	Morphological context; familiar workflow	Triage or confirmation, but suboptimal as a stand-alone primary test
HC2 DNA hybridization	Pooled HR-HPV DNA	Historically validated benchmark assay, but no genotype-level resolution	Robust clinical validation	Legacy/reference role; less informative for risk-based management
Real-time PCR DNA (cobas-type)	L1 or E6/E7 DNA	Representative real-world study: sensitivity 98.66%, specificity 87.15% for CIN2+	High sensitivity; automation; partial genotyping	Mature primary screening option
Extended-genotyping PCR (Onclarity-type)	Grouped E6/E7 DNA targets	Adds risk discrimination beyond HPV16/18 and supports more selective triage	Genotype-aware management	Primary screening plus risk stratification
HPV E6/E7 mRNA	Oncogene transcripts	CIN2+ sensitivity 93.2% vs. 92.8% for DNA; specificity 84.0% vs. 80.8%	Higher biological specificity	Triage or selected primary-screening workflows
p16/Ki-67 dual stain	Host transformation markers	Better post-HPV-positive risk stratification than cytology alone in current guidance	High triage value	Reflex triage after positive HPV
E6/E7 oncoprotein assays	Viral oncoproteins	Clinically relevant for high-grade lesion detection, but evidence remains heterogeneous	Direct link to oncogenic activity	Adjunct triage rather than universal first-line testing
Self-sampling HPV testing	DNA or mRNA on vaginal self-samples	Participation RR up to 11.0 with direct-mail kits; relative sensitivity close to clinician samples	Improves coverage and acceptability	Population outreach and under-screened groups
Urine HPV testing	DNA in first-void urine	Promising non-invasive option; dedicated collection devices outperform standard urine collection	Highest patient acceptability	Alternative entry test with confirmatory follow-up
RPA-CRISPR/Cas12a POCT	HR-HPV DNA	Detection limit about 1 copy/μL for 6 HR types in ~40 min	Fast; portable; low-infrastructure potential	Emerging point-of-care screening
AI-assisted cytology/colposcopy	Image-derived features	Cytology AI: 89.4% sensitivity, 66.4% specificity; 37.5% workload reduction	Improves workflow efficiency	Decision support rather than assay replacement
Integration analysis (NGS/long-read)	HPV-host breakpoints	High-resolution mapping of integration patterns and heterogeneity	Progression insight; mechanistic depth	High-risk stratification and research use

Note: Representative findings are drawn from selected contemporary studies and are not fully head-to-head across identical populations.

From Table 1, three big types of situations come out. First, the DNA assays which have been validated still are the most mature choice for primary screening on population scale, therefore they supply the most reliable balance among sensitivity, automation and implementation that can be scaled. Second, the main increases in post-positive particularity are more and more produced by biologically downstream marking things such as mRNA, double dyeing, and chosen oncoprotein examinations hence not by further perfecting of shape study only. Thirdly, the newly emerged things including self-sampling, urine gathering, movable amplification platforms, and AI, they mainly promote the obtaining convenience, result feedback time, or work flow efficiency.

4 Discussion

This domain is gradually departing from the supposition that a single assay ought to respond to all clinical questions which exist in cervical screening. A relatively consistent model has layers: a verified high-effectiveness HPV nucleic acid examination serves as the initial test, and more particular biological markers are therefore used to optimize processing among females who obtain positive results. Recent WHO direction gives support to this orientation through acknowledging the function of mRNA-based HPV examination in screening policy and through making formal the utilization of dual-stain cytology as one triage selection after a positive HPV outcome [24, 25].

Within that layered model, the meaning of assay innovation depends on where the assay is positioned. Broad DNA-based platforms are strongest when the goal is population-level sensitivity and standardized throughput. Biomarkers which can notice transformation have more value when the clinical work is to cut needless colposcopy without giving up the check of clinically important lesions. The innovations on sampling have the greatest importance when participation becomes the main bottleneck. This function difference, therefore, is having more usefulness than the situation that we treat all new technologies as if they all compete for the same position on the path.

The current review also puts emphasis on an implementation enlightenment. A test with strong technology does not automatically bring better population results unless it is connected with recall, triage and treatment. Self-sampling, urine examination, POCT, and AI can possess quite diverse analytical characteristics, but all of them achieve success or encounter failure in actual application based on if they promote finishing of the complete screening route. Hence, future evaluation ought to compare not only the performance of assays, but also the consequences in program terms such as participation, turnaround time, referral efficiency, and loss in follow-up.

The present review possesses certain limitations. It gives first priority to newly published English literature and clinical-direction comparison evidences, hence some earlier foundation researches have not been discussed in detailed way. Furthermore, not all the reported performance estimates come from populations that are the same, or from direct one-to-one comparison designs. Even so, this synthesis is enough to display an explicit moving direction: primary HPV examination is gradually getting more informative, post-positive classification is step by step getting more biologically specific, and implementation techniques are more and more crucial for real-world screening effects.

5 Conclusion

HPV examination technologies are developing from simple yes-no detection toward

biologically informed, access-directional, and risk-graded screening. At current stage, the validated DNA detection methods which have genotype-related analysis still are the strongest foundation for primary cervical cancer screening, therefore E6/E7 mRNA, p16/Ki-67 double staining, and some selected oncoprotein examinations thus provide the clearest pathway for more specific classification processing.

Self-sampling, urine gathering, on-site molecular platforms, and AI ought to be comprehended as implementation amplifiers or accuracy auxiliary tools instead of isolated substitutes for all already established working processes. Future advancement will rely not so much on creating one single better assay as on matching target, sample kind, and triage route with the expected clinical environment.

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References

[1] Li Z, Liu P, Yin A, et al. Global landscape of cervical cancer incidence and mortality in 2022 and predictions to 2030: The urgent need to address inequalities in cervical cancer[J]. International Journal of Cancer, 2025, 157(2): 288-297.

[2] Wei F, Georges D, Man I, et al. Causal attribution of human papillomavirus genotypes to invasive cervical cancer worldwide: A systematic analysis of the global literature[J]. The Lancet, 2024, 404(10451): 435-444.

[3] World Health Organization. Cervical cancer[EB/OL]. Geneva: World Health Organization, 2025.

[4] World Health Organization. Target product profiles for human papillomavirus screening tests to detect cervical pre-cancer and cancer[R]. Geneva: World Health Organization, 2024.

[5] He Z, Zheng X, Liu R, et al. Recent advances in HPV detection: From traditional methods to nanotechnology and the application of quantum dots[J]. International Journal of Nanomedicine, 2025, 20: 6333-6356.

[6] Goulart R A, Nayar R, Lorey T, et al. Extended HPV genotyping and dual stain for the triage of primary HPV screen-positive cases: Practical guidance for the cytopathology laboratory[J]. Cancer Cytopathology, 2025, 133(4): e70006.

[7] Smith S K, Nwosu O, Edwards A, et al. Performance of screening tools for cervical neoplasia among women in low- and middle-income countries: A systematic review and meta-analysis[J]. PLOS Global Public Health, 2023, 3(2): e0001598.

[8] Xue P, Xu H M, Tang H P, et al. Improving the accuracy and efficiency of abnormal cervical squamous cell detection with cytologist-in-the-loop artificial intelligence[J]. Modern Pathology, 2023, 36(8): 100186.

[9] Fleider L A, Tinnirello M L A, Gomez Cherey F, et al. High sensitivity and specificity rates of cobas® HPV test as a primary screening test for cervical intraepithelial lesions in a real-world setting[J]. PLOS ONE, 2023, 18(2): e0279728.

[10] Stoler M H, Parvu V, Yanson K, et al. Risk stratification of HPV-positive results using extended genotyping and cytology: Data from the baseline phase of the Onclarity trial[J]. Gynecologic Oncology, 2023, 174: 68-75.

[11] De Marco L, Bisanzi S, Ronco G, et al. Extended HPV genotyping by the BD Onclarity assay: Concordance with screening HPV-DNA assays, triage biomarkers, and histopathology in women from the NTCC2 study[J]. Microbiology Spectrum, 2025, 13(1): e00897-24.

[12] Siqueira J D, Alves B M, Castelo Branco A B C, et al. Comparison of four different human papillomavirus genotyping methods in cervical samples: Addressing method-specific advantages and limitations[J]. Heliyon, 2024, 10(3): e25474.

[13] White C, Reynolds S, Murphy K, et al. Performance of the HPV E6/E7 mRNA Aptima HPV assay combined with partial genotyping compared with the HPV DNA Cobas 4800 HPV test for use in primary screening: Results from the CERVIVA HPV primary screening study in Ireland[J]. International Journal of Cancer, 2024, 154(1): 53-64.

[14] Downham L, Jaafar I, Rol M L, et al. Accuracy of HPV E6/E7 oncoprotein tests to detect high-grade cervical lesions: A systematic literature review and meta-analysis[J]. British Journal of Cancer, 2024, 130(4): 517-525.

[15] Clarke M A, Wentzensen N, Perkins R B, et al. Recommendations for use of p16/Ki67 dual stain for management of individuals testing positive for human papillomavirus[J]. Journal of Lower Genital Tract Disease, 2024, 28(2): 124-130.

[16] Costa S, Verberckmoes B, Castle P E, et al. Offering HPV self-sampling kits: An updated meta-analysis of the effectiveness of strategies to increase participation in cervical cancer screening[J]. British Journal of Cancer, 2023, 128(5): 805-813.

[17] Narvaez L, Viviano M, Dickson C, et al. The acceptability of HPV vaginal self-sampling for cervical cancer screening in Latin America: A systematic review[J]. Public Health in Practice, 2023, 6: 100417.

[18] Mathews C S, Sargent A, Cuschieri K, et al. HPValidate-human papillomavirus testing with DNA and mRNA assays on self-collected samples in cervical screening: Comparison of test characteristics on three self-sampling devices[J]. British Journal of Cancer, 2025, 133(5): 665-673.

[19] Davies J C, Sargent A, Pinggera E, et al. Urine high-risk human papillomavirus testing as an alternative to routine cervical screening: A comparative diagnostic accuracy study of two urine collection devices using a randomised study design trial[J]. BJOG: An International Journal of Obstetrics & Gynaecology, 2024, 131(11): 1456-1464.

[20] Martinelli M, Giubbi C, Di Meo M L, et al. Accuracy of human papillomavirus testing on urine and vaginal self-samples compared to clinician-collected cervical sample in women referred to colposcopy[J]. Viruses, 2023, 15(9): 1889.

[21] Liu Y, Chao Z, Ding W, et al. A multiplex RPA-CRISPR/Cas12a-based POCT technique and its application in human papillomavirus typing assay[J]. Cellular & Molecular Biology Letters, 2024, 29: 34.

[22] Cui X, Li Y, Zhang C, et al. Multiple HPV integration mode in the cell lines based on long-reads sequencing[J]. Frontiers in Microbiology, 2023, 14: 1294146.

[23] Takahashi T, Kobayashi Y, Sakurai R, et al. A systematic review of the application of artificial intelligence in colposcopy: Diagnostic accuracy for cervical intraepithelial neoplasia and cervical cancer[J]. Clinical Medicine Insights: Oncology, 2025, 19: 11795549251374908.

[24] World Health Organization. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition: Use of mRNA tests for human papillomavirus (HPV)[R]. Geneva: World Health Organization, 2021.

[25] World Health Organization. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention: Use of dual-stain cytology to triage women after a positive test for human papillomavirus (HPV)[R]. Geneva: World Health Organization, 2024.