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NEW TECHNOLOGIES FOR CERVICAL CANCER SCREENING

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ABSTRACT

Cervical cancer is still a health worry around the world, especially in poorer countries. Traditional methods for detecting this disease are no longer as effective as they need to be. Many people cannot get to them; they are too expensive. Participation in cervical cancer screening remains low in many populations. Recent advances offer promising strategies to improve the accessibility and effectiveness of screening programs. Emerging technologies may enhance early detection and increase patient engagement, ultimately reducing cervical cancer incidence and mortality. Please, take a look at what is happening in a few key areas: studying the tiny components that make up our bodies, diagnosing problems at a molecular level using light to detect diseases, teaching computers to assist doctors, and analyzing the free-floating DNA in our blood. This report looks at all these emerging tools and technologies.

Researchers use metabolomics to study physiological processes by identifying small-molecule biomarkers, such as TMAO, which is a potential indicator of disease. Advances in spectroscopy, combined with machine learning, now enable non-invasive diagnostics. Recent innovations include rapid HPV tests and self-sampling kits. Doctors can analyze DNA fragments in blood as a non-surgical alternative to biopsies. With AI computers can interpret medical images to aid diagnosis and predict outcomes.

New technology has the potential to improve cervical cancer screening worldwide significantly. The ultimate goal is to catch early disease, reduce mortality, and work toward the elimination of cervical cancer. This marks a significant advance, and with effective strategies, the global health community can make substantial progress.

KEYWORDS

Human Papillomavirus, Cervical Cancer, Point-of-Care Diagnostics, Low-Resource Settings, Molecular Screening Tests, In Vivo Microscopy, Colposcopy, Decision Support, Machine Learning, Metabolites, Trimethylamine N-oxide, Cervical Automated Visual Evaluation, Digital Colposcope

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1. Introduction

Cervical cancer is a worldwide problem, and it is the main reason women die from cancer, especially in poorer countries. Just to put that into perspective, in 2018, over 570,000 women were diagnosed with cervical cancer, and sadly, about 311,000 of them lost their lives. The World Health Organization reported these numbers. A virus called Human papillomavirus, or HPV, causes most cases of cervical cancer (de Sanjosé et al., 2010). In fact, HPV infection causes all cases of cervical cancer, which makes it the main culprit behind this disease.

Cervical cancer is a threat, but there is an easy way to reduce the risk of dying from it: screening. It all comes down to spotting cell changes, called CIN, early, before they have the chance to develop into something more serious. When we identify these changes early, we can take action. Prevent the disease from spreading. The problem is that many screening programs have some flaws. For starters, they can be hard to access, expensive, and not always accurate. Even when we try to manage a problem for patients, it cannot be easy, especially in places with limited resources. Poor infrastructure, a shortage of female doctors, and conservative attitudes can make it hard for people to participate and get anything done. For many, simply needing to travel to a big city is already a significant barrier. All these factors combined can really hold things back.

Scientists are creating new technologies to overcome the limitations of current methods. The goal is to make cancer screening and treatment more efficient, affordable, and accurate. This change is necessary because the old ways have some significant flaws.

We are seeing progress in many areas. They vary widely and include:

Metabolomics enables the identification of novel biomarkers in biological fluids such as plasma. These biomarkers help distinguish between healthy individuals and patients with cervical cancer, and they also provide insights into disease progression (Zhou et al., 2019).

Spectroscopy, often combined with machine learning, offers the potential for rapid, non-invasive, or minimally invasive detection. It analyses tissue or biofluid samples. Researchers are exploring infrared and Raman spectroscopy as promising techniques for analysis.

Molecular diagnostics, which include affordable HPV tests and self-sampling options, make screening more accessible and easier for a wider range of people.

Circulating cell-free DNA (cfDNA) analysis, a minimally invasive "liquid biopsy" approach that can detect tumor-derived DNA and HPV cfDNA in plasma. It can offer potential for diagnosis, prognosis, and monitoring treatment response (Cao et al., 2020).

Deep learning and AI applications in digital cervicography and colposcopic analysis images to enhance the accuracy and efficiency of visual inspection (Hu et al., 2019). The World Health Organization has just recognized AI as a potential ally in combating cervical cancer.

New imaging tools, like mobile colposcopy, are making it easier to bring screening to people in remote or underserved areas.

This report will explore these new technologies for cervical cancer screening, examining their principles, status, potential benefits, and challenges in moving towards improved early detection and ultimately the elimination of cervical cancer as a public health problem.

2. Materials and Methods

We conducted a comprehensive literature search using PubMed to identify relevant publications about cervical cancer screening and HPV detection. We included only articles written in English. We made a preliminary selection of titles and abstracts, followed by a full-text review of the relevant publications. We used keywords such as human papillomavirus, cervical cancer, point-of-care diagnostics, low-resource settings, molecular screening tests, in vivo microscopy, colposcopy, decision support, machine learning, metabolites, trimethylamine N-oxide, cervical automated visual evaluation and digital colposcope to search in these databases. We set the time range of published articles to 2011-2025 and included some older publications if we considered them valuable for understanding the issue (Figure 1).

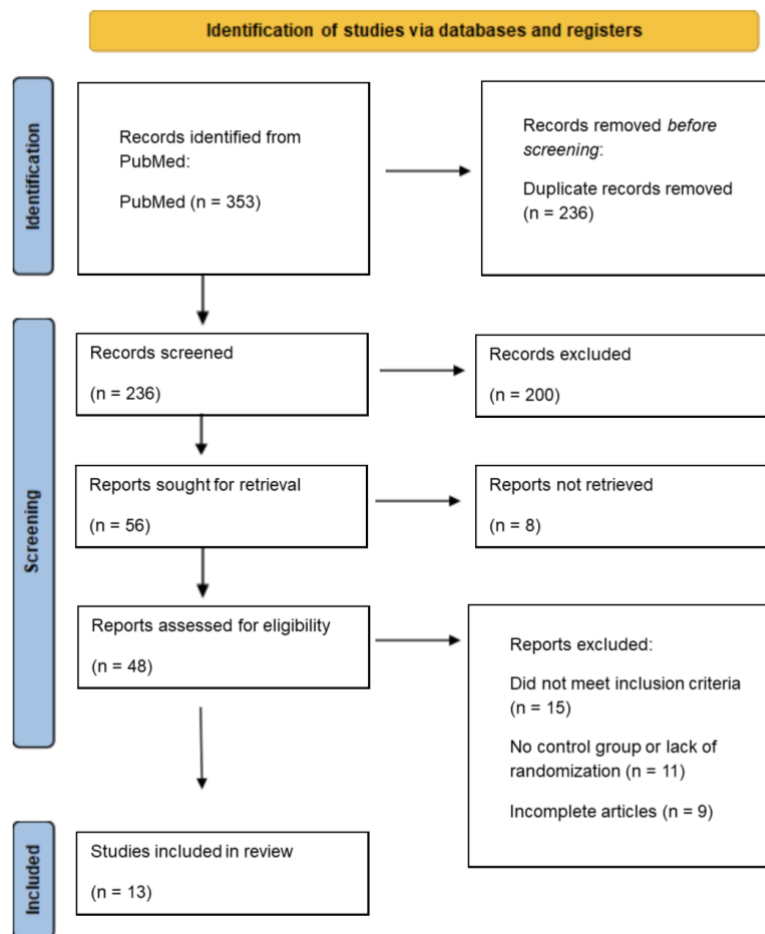


Fig. 1. Flow chart

3. Results

3.1 Metabolomics

3.1.1 Plasma Metabolic Profiling Reveals Distinct Metabolic Alterations in CC Patients

The study used LC-MS-based untargeted metabolomics to analyze blood plasma from 43 cervical cancer patients and 27 healthy people. The results showed noticeable differences in metabolism, especially in how the body processes carnitine, fats, and amino acids. When we combined the findings with gene expression data, they suggested that the metabolism of the tumor may have caused these changes.

3.1.2 A Panel of Five Metabolites as Potential CC Biomarkers

A LASSO model identified five metabolites — Cyclohexylamine, l-Carnitine, Val-

Thr, Sinigrin, and 5,6,7,8-tetrahydro-2-Naphthoic acid as potential biomarkers. This panel showed consistent results across various groups. It revealed significant plasma differences between women with cervical cancer and those without. Researchers found significantly elevated levels of Sinigrin — a compound with known anti-cancer properties — in the cervical cancer group (Matsui et al., 2018).

3.1.3 Multi-Omics Discrimination of I-IIA1 and IIA2-IV Substages in CC

Gene expression analysis combined with metabolomics effectively differentiated cervical cancer patients in FIGO stages I-IIA1 from those in stages IIA2-IV. Research has identified the MYC and Wnt/ β -catenin pathways as key influencers in tumor progression. In addition, tumor volume showed a correlation with metabolites such as TMAO and cancer biomarkers like CA125.

3.1.4 TMAO as a Biomarker for CC Progression

TMAO showed a strong link to the development of cervical cancer and was more effective than CA125 at identifying the difference between early (FIGO stages I-IIA1) and more advanced stages (IIA2-IV). Targeted metabolomics revealed that TMAO levels were higher in patients with later-stage cancer, while the levels of its building blocks — carnitine, choline, and TMA — remained unchanged.

3.1.5 TMAO Enhances Cancer Cell Proliferation In Vitro

TMAO promoted HeLa cell proliferation in a dose-dependent manner, with the most significant effect at 400 μ M, without any effects of increasing cell damage. TMAO appears to stimulate the growth of cancer cells in vitro.

3.2 New protein biomarkers

Compared with the control group, both the LSIL group and the HSIL group showed nine differentially expressed proteins. In the CC group, researchers identified five differentially expressed proteins. The proteins ORM2 and HPR exhibited obvious differential expressions in the LSIL and HSIL groups compared to the control group. These proteins may represent potential biomarkers for cervical cancer progression. The level of F9 increased steadily as cervical lesions developed from LSIL to HSIL and then to cervical cancer, which means that clinicians can use it to follow disease progression. The levels of CFI and AFM proteins were lower in patients after treatment compared to before treatment, which may help predict the effectiveness of the treatment. Analysis of protein functions showed that all these proteins are related to the complement system of the body and blood clotting processes.

3.3 Spectroscopy and machine learning

3.3.1 Biofluids

Research in this area primarily focuses on blood, specifically using Raman and infrared spectroscopy. Building on this, recent studies have shown promising initial results in distinguishing between healthy, precancerous, and cancerous states with machine learning models like CNNs and PCA-LDA, to make diagnosis less invasive (Baker et al., 2018).

3.3.2 Cytology

Researchers have used spectroscopy to study cervical cell samples, especially in early research. Infrared spectroscopy with principal component analysis and FTIR combined with support vector machines has demonstrated promising results. In one study, this approach proved to be even more accurate than Pap smear tests.

3.3.3 Breath, Urine, Saliva

Researchers are investigating the use of urine-based detection of HPV markers as a potential non-invasive method for screening. Still, precise and proven techniques for diagnosing cervical cancer directly from these fluids with spectroscopy and machine learning have not been described in the sources yet.

3.3.4 Tissues

Researchers have focused most on this area. Various spectroscopy techniques, especially Raman spectroscopy, combined with machine learning techniques like LDA, LR, SMLR, PLS-DA, ANN, and PCA-SVM (Kanter et al., 2009), worked well to separate normal, precancerous (CIN), and invasive cancer tissues, as well as different cancer types (Barik et al., 2022). Recent progress involves the use of confocal Raman micro-spectrometry and the combination of features to enhance diagnosis.

3.4 Molecular screening tests

3.4.1 Commercialized Tests (Condensed)

Several HPV tests are used in low- and middle-income countries, looking for DNA, RNA, or protein. They vary in the number of HPV types they can identify. This review focuses on tests that work well in low-resource areas. Some of them are subsidized and can be adapted for easy use at the point of care (e.g., tests based on isothermal amplification). We exclude high-infrastructure tests like Roche cobas because they are impractical for LMICs.

3.4.2 Hybrid Capture Tests

Hybrid capture assays detect HPV DNA by hybridizing it with RNA. They use ELISA for detection. Hybrid tests are usually not as sensitive as amplification methods but still work well enough for clinical use (Table 1).

Table 1. Comparison of Hybrid Capture HPV Tests

Feature	digene HC2 (Qiagen)	careHPV (Qiagen)
Genotyping	No	No
Equipment:	Specialized lab tools (plate reader, calibrated pipettes).	Bundled instruments (>US\$20,000) require power and trained staff.
Cost	High	~US\$5/test (ideal), ~US\$42/test (real-world)
Setting	Reference labs	In low-resource settings
Turn around	Standard lab workflow	Batch format → delayed results

3.4.3 PCR Tests

Nucleic acid amplification tests (NAATs), like PCR, offer higher sensitivity and specificity than hybrid capture methods but usually require more complex instrumentation. PCR minimizes cross-reactivity. Generally, research considers it the gold standard, but thermocycling increases equipment complexity and cost.

- GeneXpert HPV Assay (Cepheid):

It is Compatible with existing GeneXpert platforms already used for TB and HIV. It makes it a practical option in LMICs. The system automates sample prep, amplification, and detection via real-time PCR. It gives reliable results with little effort from the user. Results are delivered in about an hour (Hsiang et al., 2016).

- Detection: All high-risk HPV types with partial genotyping (HPV16 and HPV18/45).
- Ease of Use: The cassette-based format is simple and scalable, and GeneXpert already uses it.
- Performance: Validated in extensive studies with 89–100% sensitivity and 42.6–83% specificity, showing comparable results to Roche cobas and digene HC2. There was also a high level of concordance between patient-collected and clinician-collected samples.

3.4.4 Isothermal Nucleic Acid Amplification Tests

Isothermal NAATs are simpler than PCR. They allow amplifying nucleic acids at a constant temperature with the help of additional enzymes. It will enable reducing infrastructure demands and making them more suitable for use in low-resource settings. Although based on RNA assays, these methods can also detect DNA.

- Aptima HPV Assays (Hologic)
- Two TMA-based assays detect high-risk HPV; one includes partial genotyping (HPV16, 18, 45).
- Performance: Sensitivity 97.5%, specificity 90.2%.

- NucliSENS EasyQ (bioMérieux)
- Uses NASBA and molecular beacons to detect five high-risk types (16, 18, 31, 33, 45).
- Performance: Sensitivities and specificities range from 69–79.3% and 36–72.6% across studies.
- Pretest Proofer mRNA Test
- It also detects HPV types 16, 18, 31, 33, and 45 using NASBA, and processes samples in the lab with pre-loaded microtiter plates.
- Performance: Sensitivity 78.1%, specificity 75.5%.
- Efficiency: Runs 30 samples at a time, with low hands-on time.
- Comment: Expanding genotype coverage could improve sensitivity; combining RNA tests (high specificity) with DNA tests (high sensitivity) can optimize screening precision.

3.4.5 Protein Tests

Protein-based HPV tests, such as OncoE6, detect viral oncoproteins (E6) and typically have lower sensitivity but higher specificity than DNA tests (Table 2).

Table 2. Characteristics of Protein-Based HPV Test (OncoE6)

Feature	Details
Type	Lateral-flow test detecting HPV types 16, 18, and 45; designed for point-of-care use with separate lines for each type (partial genotyping).
Sensitivity	31.3–53.5% (up to 64.5% for patients with covered genotypes)
Specificity	98.9–99.4%
Sample preparation:	It takes over 45 minutes and involves multiple pipetting/centrifugation steps.
Limitations:	Limited genotype coverage restricts effectiveness.

3.5 Circulating Cell-Free DNA (cfDNA) Analysis

cfDNA analysis has shown a considerable potential for monitoring MRD in cervical cancer. A recent study found that patients with persistent HPV ctDNA after chemoradiation had worse progression-free survival (PFS). It suggests that they may have a higher risk of cancer recurrence and could require stronger treatment. A landmark analysis of MRD through cfDNA shortly after curative therapy closely correlates with recurrence risk (Siegel et al., 2024).

High-risk HPV causes most cervical cancers, and HPV-derived cell-free DNA (cfDNA) is a promising biomarker for diagnosis and monitoring. cfDNA enables non-invasive detection of HPV type and viral load, which may help guide immunotherapies targeting HPV oncoproteins (Recio et al., 2024).

3.6 Deep learning and artificial intelligence

3.6.1 AI in Pap Smear Analysis

Recent studies show that AI can help interpret Pap smears more effectively. One system, called AICCS, accurately graded cervical cell samples from a wide range of patients. In a prospective study, it reached an AUC of 0.947, a sensitivity of 0.946, a specificity of 0.890, and an overall accuracy of 0.892. Randomized trials also found that cytopathologists using AICCS improved their sensitivity by 13.3% and saw better AUC, specificity, and accuracy compared to those working without AI.

These findings demonstrate that AI can improve diagnostic accuracy and help doctors make decisions during cervical cancer screening with regular Pap tests. Cytology remains a costly and resource-intensive approach, especially for low- and middle-income countries (LMICs) (Egemen et al., 2024).

3.6.2 Deep Learning-based Automated Visual Evaluation

The integration of deep learning algorithms into portable colposcopes enables the development of cost-effective devices that provide real-time cervical cancer diagnoses. AVE algorithms analyse images from cervical exams to define stages of carcinogenesis. These methods rely on characteristics such as texture, colour, and edges. An AVE algorithm can adopt stages such as normal cervix, HPV infection, dysplasia, and invasive cancer. Researchers are currently testing the accuracy of AVE with smartphone images for cervical cancer

screening. The goal of developing automated visual evaluation is to apply deep learning for cervical cancer screening in real clinical settings.

3.6.3 AI for Dual-Stained Slide Analysis

New advances in automatically analyzing dual-stained slides (such as p16/Ki-67) use deep learning models that focus on biopsy data and could help to make complex lab setups less necessary and make cervical cancer screening more objective. An AI algorithm trained to read dual-stain slides showed the same sensitivity but much higher specificity than cytology and manual dual-stain analysis. In practice, AI-based dual-stain testing reduced the number of people sent for colposcopy by one-third compared to the Pap smear.

In 2024, the American Society of Colposcopy and Cervical Pathology (ASCCP) included dual-stain testing as a screening method for cervical cancer.

Doctors recommend a colposcopy for people who test positive with dual-stain (DS). Those who test DS-negative must return in one year for HPV-based testing, unless they are HPV16- or HPV18-positive, or have high-grade cytology results. In this case, patients need an immediate colposcopy. The guidelines also note that dual-stain testing reduces the number of colposcopies and enables the detection of high-grade dysplasia compared to cytology.

3.6.4 Deep Learning for HPV Screening

Researchers have created a DNA-based digital microholography platform for point-of-care HPV screening. This system provides automated results with the help of deep learning algorithms. This technology uses tiny beads that attach to high-risk HPV types 16 and 18. The beads form dimers, and their holographic patterns are analyzed to support cervical cancer diagnosis.

3.6.5 Comparison with Traditional Machine Learning

This study compares deep learning models, such as ResNet-50, with traditional machine learning models, including XGBoost, support vector machines, and random forests, for detecting cervical cancer from cervicography images. Deep learning models showed higher accuracy (Jusman et al., 2014). For example, ResNet-50 achieved an Area Under the Curve (AUC) of 0.97, which was higher than XGBoost (0.82), SVM (0.84), and Random Forest (0.79) (Alyafeai & Ghouti et al., 2020).

3.7 Advances in imaging technologies

3.7.1 Mobile Colposcopy

Several groups have designed mobile colposcopes to make this technology more affordable than traditional, stationary colposcopes. Researchers are already testing many of these new devices in clinics, and companies are preparing them for commercial use. Examples include the Pocket Colposcope, MobileODT, and Gynocular. Designers often make these devices portable and easy to use in different settings. Studies are comparing colposcopic impressions based on live colposcopy with the evaluation of static digital images obtained from such devices (Mendez et al., 2022).

3.7.2 High-Resolution Microendoscopy (HRME) and Other In Vivo Microscopy

HRME is another promising technology for examining cervical tissue in real time without the need for a biopsy. In rural Brazil, studies have used a mobile van equipped with in vivo microscopy to help detect cervical neoplasia on-site.

Research is developing tablet-connected and mobile phone-based HRME systems with automated image analysis to enable real-time evaluation (Grant et al., 2019). Other in vivo imaging technologies, such as probe-based confocal laser endomicroscopy and optical coherence tomography/microscopy, have shown promise in identifying neoplastic cervical tissue in lab samples. However, researchers still face challenges in applying these tools to real patients and in addressing their high cost.

3.7.3 Spectroscopy and Machine Learning for Image Analysis

Researchers are exploring spectroscopy techniques and machine learning for the diagnosis and screening of cervical cancer. These methods analyze the spectral properties of cervical tissues or cells to identify changes associated with cancer. For instance, infrared and Raman spectroscopy, paired with machine learning, have been used to analyze cervical cytology and tissue samples (Alajaji et al., 2025). Machine learning can help automatically interpret iodine cervigrams using Lugol solution captured by digital colposcopes.

4. Discussion

Cervical cancer is still a big world-spread problem, especially in areas with limited resources. Traditional methods of screening for it are no longer sufficient. They are often too expensive, complex to access, and not sensitive enough.

Molecular tests, especially HPV testing, are essential for cervical cancer screening. HPV DNA tests performed on-site are called point-of-care tests. For example, careHPV and GeneXpert help to make cervical cancer screening more accessible, although they cannot always identify all HPV types accurately. However, low-cost, quick HPV typing tests remain a key priority.

At the same time, emerging biomarkers — such as changes in host cell DNA methylation and HPV oncoproteins — must help to identify who most urgently needs follow-up care.

For example, careHPV and GeneXpert help to make cervical cancer screening more accessible, although they cannot always identify all HPV types accurately. Developing low-cost, rapid HPV typing tests remains a key priority. At the same time, emerging biomarkers— such as changes in host cell DNA methylation and HPV oncoproteins — could help identify who most urgently needs follow-up care.

Imaging technologies are also improving. Developers are working on mobile colposcopes to make screening more accessible. Adding AI for Automated Visual Evaluation (AVE) to these devices could provide real-time diagnosis. High-resolution microendoscopy and spectroscopy with machine learning are other promising ways to assess and diagnose without invasive procedures.

AI and deep learning are aiding in the reading of Pap smears and the examination of colposcopic images, thereby making screening faster, more accurate, and less prone to human error.

Rolling out these new technologies, especially in low-resource settings, requires careful consideration of feasibility, acceptability, adoption, and sustainability. The Proyecto Precancer case study uses the INSPIRE methodology, highlights the challenges, and what we can learn from them. This study demonstrated the successful adoption of HPV testing and thermal ablation in the Peruvian Amazon. Task-shifting management to primary care improved completion of care.

Metabolomics and transcriptomics analyses identified potential biomarkers, such as TMAO, for discriminating between cervical cancer stages. Proteomics studies have identified potential biomarkers, such as HPR, ORM2, F9, CFI, and AFM, that may indicate progression of cervical disease.

HPV vaccination is becoming more accessible. Now, WHO recommends just two or three doses, making it easier for people worldwide to gain protection.

5. Conclusions

New technologies are improving early detection of cervical cancer, giving hope that we can overcome many challenges of traditional screening.

Molecular tests, especially HPV testing, can help catch cervical changes earlier and identify who is at higher risk.

Imaging technologies, such as mobile colposcopy with automated visual evaluation (VA), in vivo microscopy, and spectroscopy, offer the possibility of faster, easier, and quicker diagnostics, especially in areas with limited resources.

Applying artificial intelligence and deep learning to image analysis and other aspects of screening could improve accuracy, efficiency, and support better decision-making. Cell-free DNA (cfDNA) analysis looks promising for monitoring and possibly detecting cervical cancer early, but more research is still needed, specifically for this disease.

Above all, the goal of these innovative approaches is to make cervical cancer screening more accessible, accurate, and affordable.

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