Review

Improving Accessibility of Cervical Cancer Screening: A Global Perspective on Self-Sampling and Digital Innovation

Michelle Gomes , Elena Provaggi , Andrea Pembe , Adeola Olaitan , Aleksandra Gentry-Maharaj [*]

Review

Improving Accessibility of Cervical Cancer Screening: A Global Perspective on Self-Sampling and Digital Innovation

Michelle Gomes [1,2], **Elena Provaggi** [2], **Andrea B. Pembe** [3], **Adeola Olaitan** [4,*] **and Aleksandra Gentry-Maharaj** [4,5,*]

[1] The London School of Hygiene and Tropical Medicine (LSHTM); London, IL

[2] Daye, UK

[3] Muhimbili University of Health and Allied Sciences (MUHAS), Tanzania;

[4] Department of Women's Cancer, EGA Institute for Women's Health, University College London, London, UK

[5] MRC Clinical Trials Unit at UCL, Institute of Clinical Trials and Methodology, University College London, London, UK

* Correspondence: a.gentry-maharaj@ucl.ac.uk,

Abstract: Cervical cancer causes 350,000 deaths annually, with 90% occurring in low and middle-income countries (LMICs), despite being largely preventable through vaccination and screening. This review examines innovative approaches to address screening coverage gaps worldwide, analysing both established programmes in high-income countries and implementation strategies for LMICs. Self-sampling technologies demonstrate significant potential to increase cervical cancer prevention compared to traditional methods, particularly benefiting underserved populations across all healthcare settings. Among self-collection devices, vaginal brushes achieve sensitivity of 94.6% (95% CI: 92.4-96.8) for HPV detection, while novel approaches like the tampon show promising results (sensitivity 82.9-100%, specificity 91.6-96.8%) with high user acceptability. Implementation strategies vary by healthcare context, with high-income countries achieving success through integrated screening programmes and digital solutions, while LMICs demonstrate effective adaptation through community-based distribution (20-35% uptake) and innovative delivery methods. In resource-limited settings, self-sampling increases participation through enhanced patient comfort and cultural acceptability, while reducing costs by 32-48%. Progress toward the WHO's cervical cancer elimination goals require careful consideration of local healthcare infrastructure, cultural contexts, and sustainable financing mechanisms. Future research priorities include optimising self-sampling technologies for sustainability and scalability, developing context-specific implementation strategies, and validating artificial intelligence applications to enhance screening efficiency across diverse healthcare settings.

Keywords: cervical cancer (CC); human papillomavirus (HPV); screening; self-sampling; low- and middle-income countries (LMICs); FemTech

1. Introduction

FemTech represents a rapidly evolving sector of technology-driven solutions transforming cervical cancer prevention through Artificial Intelligence (AI) enabled diagnostics, smart self-sampling devices, and integrated digital platforms [1,2]. This review evaluates emerging self-sampling technologies and FemTech solutions for cervical cancer screening, analysing innovations and performance metrics, implementation strategies, and cost-effectiveness considerations for resource-limited settings.

Human Papillomavirus (HPV) infection is extremely common, with an estimated 80% of sexually active people acquiring at least one HPV type during their lifetime [3,4]. While most infections clear naturally within two years, persistent infection with high-risk HPV types causes 99.7% of cervical cancer cases, making HPV detection an important screening strategy [5,6]. In 2022, there were 660,000 new diagnoses and 350,000 from cervical cancer deaths globally [7,8].

This preventable disease disproportionately affects LMICs, which account for 90% of cervical cancer mortality [9–11]. The burden varies significantly by region, with age-standardised incidence rates ranging from 75 cases per 100,000 women in some African countries to less than 10 per 100,000 in many high-income countries [11]. The risk of persistent infection and progression to cancer is higher in people with compromised immune systems, particularly those living with HIV who are 6 times more likely to develop cervical cancer [12]. These disparities reflect inequitable access to both HPV vaccination and screening programmes [13,14].

The United Kingdom's experience illustrates both progress and persistent challenges in cervical cancer control. While comprehensive screening programs contributed to a 25% decrease in incidence rates since the early 1990s, recent data show a 4% increase over the past decade suggesting evolving risk factors and potential gaps in screening coverage [15,16]. This trend has been exacerbated by the COVID-19 disruptions, with screening participation declining significantly. Some areas of London now report screening uptake rates as low as 48%, reflecting widespread disengagement with screening services [17,18].

Screening detects asymptomatic precancerous lesions which if undetected and untreated, can put women at risk of developing cervical cancer. In 2023, the NHS announced a plan for cervical cancer elimination by 2040 (defined as fewer than 4 cases per 100,000 women) which aligns with the World Health Organization (WHO) global 90-70-90 initiative, which aims for 90% HPV vaccination coverage, 70% screening coverage, and 90% treatment of precancerous lesions by 2030 [9,19]. Achieving this goal requires enhanced HPV vaccination coverage, increased screening participation, and innovative solutions adaptable to diverse healthcare settings [20–24]. Scotland demonstrates the potential success of comprehensive prevention strategies, achieving near elimination through high vaccination uptake and effective screening programmes [25]. The prevention of cervical cancer stands at a critical transition point. While HPV vaccination programmes are widespread in high income countries, their full impact on mortality rates will take decades to realise due to the extended latency between infection and cancer development [26,27]. Meanwhile, the evolution from traditional cytology to HPV-based screening (see Figure 1) offers enhanced detection capabilities, though implementation challenges persist, especially in resource-limited settings [28,29].
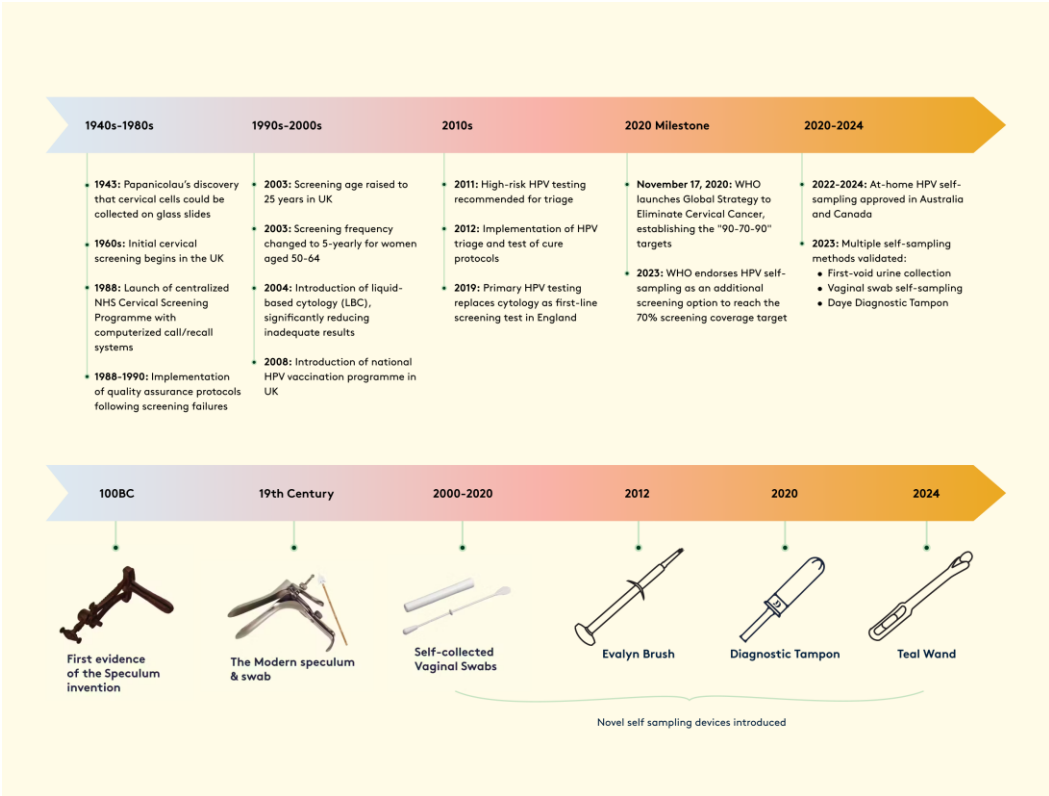
Figure 1. Timeline of cervical cancer screening evolution, 1940s-2024. The upper panel shows key policy and technological developments in cervical screening programs, highlighting major milestones in the UK and globally. The lower panel illustrates the progression of screening devices from ancient speculums to modern self-sampling methods, demonstrating the advancement toward patient-centered screening approaches.

1.1. Prevention Strategies

1.1.1. Primary Prevention

HPV vaccination demonstrates exceptional efficacy, with the Swedish nationwide study (1.7 million women) showing a 90% reduction in cervical cancer incidence among girls vaccinated before age 17 over 2006-2017 [30]. Norwegian registry data showed 82% reduction in CIN2+ in girls vaccinated at an early age [31]. Effectiveness significantly decreases when vaccination is given after age 17 [32]. A systematic review from 2023 demonstrated vaccine effectiveness ranging from 74-93% for ages 9-14 versus 12-90% for ages 15-18, highlighting the critical importance of vaccination at an early age [33]. The implementation of WHO's 90% vaccination coverage strategy poses significant challenges in LMICs due to infrastructure limitations and cost barriers [34,35]. Historical controversies surrounding vaccine trials and implementation programmes have created enduring trust issues in some regions, particularly in India and Sub-Saharan Africa [36]. These challenges underscore the importance of ethical implementation practices, community engagement, and cultural sensitivity in vaccination programmes.

1.1.2. Secondary Prevention

The evolution of screening methods marks a significant advancement in cervical cancer prevention, transitioning from traditional cytology to HPV-based approaches [37,38]. While high-income countries maintain screening coverage above 60%, LMICs struggle with rates as low as 20%, highlighting the need for resource-appropriate solutions [39]. Secondary prevention through HPV testing has emerged as superior to cytology for cervical screening; extensive research demonstrates enhanced sensitivity compared to cytology-based approaches [40,41].

1.1.3. Emerging Technologies

WHO's 2021 guidelines recommended HPV DNA testing as the preferred screening method for women aged 30-49 years, with 5–10-year intervals [42]. Implementation success varies globally, requiring careful consideration of local healthcare infrastructure, resource availability, population-specific needs and healthcare system capacity [6,43].

Self-sampling represents a transformative approach to cervical cancer screening, particularly for underserved populations at elevated risk of HPV infection [44,45]. This review examines how innovative technologies and implementation strategies can bridge disparities in screening access. We analyse the potential of self-sampling and FemTech solutions to overcome traditional barriers, with particular focus on their application in resource-limited settings where conventional screening methods remain challenging to implement.

2. Understanding HPV and Cervical Carcinogenesis: A Foundation for Prevention

Understanding the relationship between HPV infection and cervical cancer development is crucial for developing effective prevention strategies and implementing appropriate screening programs [6,46,47]. Persistent infection with high-risk HPV is the primary causative agent of cervical cancer, with high-risk types 16 and 18 responsible for approximately 70% of cases globally, while types 31, 33, 45, 52, and 58 contribute another 20% [48,49]. The global prevalence of HPV16 and HPV18 in women with normal cytology is 3.2% and 1.4%, respectively [50,51].

HPV causes cervical cancer through persistent infection of epithelial cells, where continued expression of the viral oncoproteins E6 and E7 disrupt cell cycle regulation, leading to genomic instability and malignant transformation [52,53]. This process can result in precancerous lesions, graded as Cervical Intraepithelial Neoplasia (CIN1-3), with CIN2/3 requiring treatment to prevent progression to cancer [54,55]. Early detection through screening and colposcopy examination is crucial for identifying and managing CIN [56].

2.1. HPV Vaccination

Prophylactic HPV vaccines have demonstrated efficacy, achieving up to 90% reduction in vaccine-type HPV infections and 85% reduction in high-grade cervical lesions among vaccinated cohorts aged 13-24 years [57]. Evidence suggests extending screening intervals for vaccinated populations, with recommendations to start screening at age 30 instead of 25 for vaccinated women [58]. However, even the broadest 9-valent vaccine does not protect against all oncogenic HPV types, necessitating continued screening programs [59,60].While vaccination coverage is increasing globally, uptake remains suboptimal in many regions, and women aged 35 and older, who were not eligible for vaccination programs, remain at risk and require regular screening [61,62].

Recent evidence supports WHO's simplified HPV vaccination schedules: one dose for ages 9-14 years, one or two doses for ages 15-20 years, and two doses for those over 21 years. This optimisation reduces costs by 30% while maintaining efficacy in younger age groups [63,64].

Global vaccination rates declined significantly, with studies showing coverage reductions of 42% in Italy and decreased uptake from 89.92% to 69.59% during the pandemic in US border communities [65]. These disruptions are projected to increase cases of cervical cancer and precancerous lesions over the coming decades, necessitating urgent recovery strategies [66].

2.2. Evolution of Cervical Cancer Screening Methods

The transition from traditional cytology to HPV-based screening represents a significant advancement in cervical cancer detection. HPV testing demonstrates superior detection of precancerous lesions with 98.1% sensitivity (95% CI: 96.3-96.7) for CIN3+, compared to cytology's 48.5% sensitivity (95% CI: 44.0-53.0) [67]. While HPV testing shows slightly lower specificity (94.4%, 95% CI: 94.1-94.7) than cytology (97.9%, 95% CI: 97.8-98.1), new molecular technologies offer improved specificity without compromising sensitivity [67].

Emerging molecular approaches such as mRNA-based tests specifically detect active HPV infections by identifying viral oncogene expression, reducing false positives from transient infections [68]. Next-generation sequencing platforms enable simultaneous detection of multiple biomarkers, allowing better risk stratification of HPV-positive women. These innovations help identify women most at risk of disease progression while reducing unnecessary referrals [69].

2.4. Innovative Vaccination and Screening Approaches in High-Income Countries

High-income countries have pioneered different approaches to implementing HPV-based screening and self-sampling programs, providing valuable insights for global cervical cancer prevention strategies. Australia and the UK demonstrate successful integration of vaccination and screening programs. Australia's comprehensive approach, achieving 80% vaccination coverage and implementing primary HPV screening, projects cervical cancer elimination by 2028, with 92% reduction in high-grade abnormalities among women vaccinated before age 15 [26,70]. The UK's strategy complements its screening programme, contributing to a 25% decrease in cervical cancer incidence since the 1990s [71].

European countries have led self-sampling innovations. The opt-in model in the Netherlands achieved 16% self-sampling uptake by 2020, while Sweden's direct-mailing approach during COVID-19 increased coverage from 54% to 60% in one year, reaching Europe's highest rate of 83% [72,73]. Both countries maintain sustained screening coverage above 70% through automated testing platforms and standardised protocols, particularly benefiting under-screened populations [72,73].

2.5. Prevention Strategies in Middle and Low-Income Countries

Middle-income countries have developed effective hybrid approaches to cervical cancer prevention, exemplified by Malaysia and Thailand's integration of national vaccination programs with phased HPV-based screening implementation [74]. These programs achieve 85-90% vaccination coverage through school-based delivery systems while expanding screening access via public-private partnerships [75].

WHO's pragmatic approach for LMICs focuses on high-precision HPV testing with two lifetime screens at ages 35 and 45, balancing effective coverage against resource constraints [76]. Rwanda's successful implementation demonstrates the potential of this approach, achieving 93% HPV vaccination coverage among girls aged 11-12 and screening 329,000 women between 2013-2016, resulting in a 50% reduction in cervical cancer mortality [77].

Successful programs utilise community health worker networks, mobile clinics, and partnerships with local religious leaders while integrating self-sampling options to optimise resource utilisation [78]. This comprehensive approach enables LMICs to maximise precancerous lesion detection during peak risk periods while maintaining cost-effectiveness within resource-limited healthcare systems [74].

3. Implementation Barriers and Economic Impact of Cervical Screening in LMICs

The implementation of cervical cancer prevention programs in low- and middle-income countries faces significant systemic challenges that impact both healthcare delivery and economic outcomes. A WHO analysis (2022) of 45 African countries revealed only 15% have universal health coverage schemes for cervical cancer screening, resulting in significant out-of-pocket expenditure for families [79]. Screening rates in LMICs remain critically low at 5%, exemplified by Nigeria where only 8.7% of 60.9 million at-risk women undergo screening, with even lower rates in rural areas [80].

The economic implications are substantial yet promising: every dollar invested in cervical cancer prevention yields a $3.20 return through improved health outcomes and productivity gains [81]. HPV-based screening programs demonstrate high cost-effectiveness, with an incremental cost-effectiveness ratio of $569 per quality-adjusted life year gained [82].

3.1. Innovative Implementation Strategies in LMICs

Several countries have developed effective solutions to increase screening coverage through innovative integration with existing healthcare services and novel delivery approaches. Rwanda has successfully integrated cervical screening with HIV/AIDS care services, with studies showing increased screening rates among HIV-positive women through integrated services [77]. Ethiopia's screening coverage remains very low at less than 2% nationally, while Zambia has achieved about 26% population-level coverage through HIV program integration [83,84]. Mobile screening units and task-shifting strategies have been implemented in Rwanda to reach women in remote areas, with the country screening nearly 95,000 women and achieving 91% treatment rates for those testing positive [85].

International support has been crucial, with Gavi, The Vaccine Alliance committing $600 million for HPV vaccination and the Global Fund reaching over 1 million women through integrated HIV-screening programmes [86]. While many LMICs currently rely on visual inspection methods – direct inspection of the cervix to identify macroscopic morphological abnormalities, with typically low specificity - (Visual inspection with acetic acid ((VIA))/Visual inspection with Lugol's Iodine ((VILI))) due to resource constraints, these approaches offer advantages of immediate results and same-day treatment [87]. The emergence of HPV self-sampling technologies presents an opportunity to implement more sensitive molecular testing while maintaining community-based screening benefits, which in some setting will be followed up by VIA/VILI and in some contexts referral to colposcopy (depending on the infrastructure available, based on country).

4. Enhancing Screening Participation Through Self-Sampling: Evidence and Implementation

Self-sampling represents a transformative approach to cervical cancer screening, addressing traditional barriers while improving accessibility for underserved populations through patient-centred collection methods. Cervical screening coverage in England has declined, with only 69.9-71.2% of eligible women screened within the recommended interval [88,89]. Barriers to screening include discomfort, embarrassment, time constraints, and procedure-related anxiety [90]. Lower uptake is associated with younger age, ethnic minority background, and socioeconomic deprivation [91]. Women who have experienced sexual abuse are less likely to attend screening [92]. Studies show that transgender men and non-binary people have significantly lower cervical screening uptake, with only 58% of those eligible having been screened [93]. Research indicates that transgender men are 37% less likely to be current with cervical screening compared to cisgender patients, and are ten times more likely to have inadequate test results [94].

The YouScreen trial in London (n=8338) validated self-sampling's effectiveness in increasing participation, achieving 56% uptake through GP practices compared to 13% via direct mailing. The approach showed particular success among ethnic minorities (64% coverage) and socioeconomically deprived populations (60% coverage)[95].

Implementation strategies for self-sampling vary in effectiveness, with community-based distribution through pharmacies and health centres achieving higher uptake (20-35%) compared to direct mailing methods (8-25%) [95]. The UK HPValidate study validated multiple device-test combinations (3 different collection devices: Evalyn Brush (Rovers Medical), Self-Vaginal Floqswabs (Copan) and Aptima Multitest (Hologic), demonstrating strong user preference (85%) for having self-sampling as an option alongside traditional screening [96].

Economic analyses demonstrate cost-effectiveness of self-sampling in low-resource settings. A 2023 study in Sikkim, India found that HPV self-testing cost US$15.3 per woman screened compared to US$19.2 for traditional screening, representing a significant cost reduction [97].

Successful implementation in LMICs requires tailored delivery approaches combining clinic-based and home-based methods. Community health workers facilitate education and sample collection through door-to-door visits, while trusted community leaders address health literacy through visual instructions [97]. Sample transport systems using swabs remain stable at room temperature for up to two weeks, eliminating cold-chain requirements [98]. Digital platforms enable

result communication where infrastructure permits, as demonstrated by the PRESCRIP-TEC project across Bangladesh, India, Uganda and Slovakia [99].

Self-sampling is endorsed by WHO because of its potential to increase screening coverage among underserved populations, though success depends on standardised procedures, comprehensive follow-up protocols, and context-specific implementation strategies that consider local healthcare infrastructure and economic conditions [45].

5. Evolution and Performance of Self-Sampling Technologies in Cervical Screening

The development of self-sampling technologies represents a significant advancement in cervical cancer screening, with various collection methods demonstrating increasing accuracy and accessibility while addressing traditional barriers to participation [100]. Collection approaches have evolved to encompass vaginal swabs with soft, flexible tips made of cotton, polyester, or nylon fibres; brushes designed with flexible low-density polyethylene (LDPE) bristles for standardised sampling; and diagnostic tampons utilising absorbent materials to collect vaginal secretions [101,102]. Additional innovations include urine collection devices targeting first-void samples and menstrual fluid collection systems like Qvin-pad and the Papcup [103,104]. These diverse sampling methods offer specific advantages and performance characteristics suited to different healthcare settings and patient populations, enabling more inclusive screening options across varied contexts.

Performance metrics from meta-analyses show that self-collected samples have slightly lower detection rates compared to clinician collection, with sensitivity reduced by 14% (95% CI: 9-20%) and specificity by 11% (95% CI: 8-15%) [105]. However, newer PCR-based assays demonstrate comparable accuracy, particularly with lavage devices and brushes [105].

The integration of AI enhances screening precision through advanced image analysis capabilities. Recent studies demonstrate AI algorithms achieving sensitivity and specificity ranges of 0.22-0.93 and 0.67-0.95 respectively in classifying visual inspection images [106,107]. Wu et al. (2024) highlight how AI-assisted digital microscopy platforms like CytoBrain can analyse digitised cervical samples with up to 78% efficiency in cell classification, reducing reliance on specialised personnel while maintaining diagnostic accuracy [108]. While these technologies show particular promise for resource-limited settings, large-scale validation in real-world conditions remains crucial for establishing clinical feasibility.

Recent advancements in point-of-care (POC) HPV testing offer promising solutions for cervical cancer screening in resource-limited settings. These tests aim to provide rapid results with high sensitivity and specificity, addressing barriers in traditional cytology-based screening [109,110]. The careHPV test demonstrates good performance, with sensitivity and specificity around 88% and 84% for CIN2+ detection [111]. New technologies like isothermal amplification and lateral flow detection enable low-cost, sample-to-answer HPV testing suitable for decentralised screening [20]. HPV-based screen-and-treat approaches have shown effectiveness in reducing cervical disease and over-treatment compared to visual inspection methods [112]. A study in Papua New Guinea found high acceptability and safety of an integrated POC HPV self-sampling and same-day treatment strategy. POC innovations are transforming screening accessibility in resource-limited settings [113]. The Hemex Health Gazelle platform demonstrates the potential for rapid, affordable testing with high accuracy, achieving results within 8 minutes while maintaining laboratory-grade standards [114].

WHO has recently launched updated target product profiles for POC tests, emphasising the need for affordable, user-friendly devices suitable for low-resource settings [115]. These profiles aim to guide manufacturers in developing tests that meet specific performance and operational characteristics crucial for effective cervical cancer screening in diverse healthcare contexts [115].

5.1. Device Types and Clinical Performance

The Evalyn® Brush and FLOQSwabs™ (Copan) represent extensively validated self-sampling methods, with the Evalyn® Brush achieving 97% user acceptability through innovative features like depth indicators and click mechanisms [121,128]. FLOQSwabs™ use short nylon fibres arranged on a solid plastic shaft. The fibres are positioned perpendicularly to promote strong capillary action,

allowing for rapid absorption of liquid samples. Also because it lacks an internal core, more than 90% of the collected sample can be easily released into testing media. While urine-based testing offers minimal invasiveness and potential integration with other screening programs, it demonstrates lower sensitivity (51-63%) compared to other self-sampling methods, limiting its current utility as a primary screening approach [129].

Table 1. provides a comprehensive comparison of current self-sampling devices, highlighting key features: [92,116–127].

The Daye Diagnostic Tampon (DT) shows promising performance with 82.9% sensitivity and 91.6% specificity, achieving the highest valid result rates (99.2%) compared to vaginal self-swabs (95.4%) and clinician-collected samples (90.8%) [123]. User acceptance is high, with 78.3% reporting high comfort pre-sampling and 74.5% finding it "very easy" to use [123,130]. When collected first in the sampling sequence, the DT achieves optimal performance (100% sensitivity, 96.8% specificity), with 70.5% of participants preferring this method [123].

Teal Health was granted Breakthrough Device Designation by FDA in 2024 [131]. It has integrated digital features, including visualisation capabilities and automated sample verification, achieving 94% sample adequacy rates and higher user satisfaction (Stanford Medicine Innovation Report, 2023). The Papcup system offers HPV detection from menstrual blood samples, providing results within 15 minutes and improving accessibility for younger women while maintaining functionality for post-menopausal women through traditional swab collection [132]. A novel approach using a modified menstrual pad (Q-Pad) for passive HPV sample collection showed high concordance (95-100%) with clinician-collected samples among HPV-positive women, offering potential for integration into cervical cancer prevention programs [125].

A collection of studies examined the effectiveness of self-sampling methods for HPV testing compared to clinician-taken cervical samples. Vaginal self-sampling using dry flocked swabs, wet dacron swabs, and urine samples showed similar sensitivity and specificity to clinician-taken samples for detecting high-grade cervical lesions [92,133,134]. Self-sampling methods were generally well-accepted by women, with urine collection being the easiest and most preferred option [92].

Digital health solutions demonstrate significant benefits in cervical cancer screening programmes, with electronic health interventions improving screening participation rates by 46% compared to usual care, with particularly strong impact in LMIC settings [135]. However, a critical limitation is the requirement for additional cytology visits following HPV-positive results, leading to 35-45% patient dropout rates during follow-up [136]. While newer devices attempt dual sample collection for both HPV and cytology testing, cytological examination from self-collected samples shows lower adequacy rates compared to clinician collection, primarily due to their inability to sample the cervical transformation zone where precancerous lesions typically originate [137]. Studies comparing self-sampling cytology to clinician collection show sensitivity ranges of 64.7-71.9% and specificity of 81.0-86.6% for detecting intraepithelial lesions [138]. Current self-sampling devices cannot access the endocervical cells in the transformation zone - a capability that requires speculum examination in a clinical setting - limiting their utility for comprehensive cervical screening [138,139].

5.2. Advancements in DNA Methylation Testing

Recent advancements in DNA methylation testing represent a significant breakthrough in cervical cancer screening strategies. Meta-analyses demonstrate that DNA methylation markers achieve 63% sensitivity and 76% specificity for CIN2+, and 71% sensitivity and 75% specificity for CIN3+ [140]. This approach effectively identifies women at higher risk of progression to cancer while reducing unnecessary referrals. The WID-qCIN test, which assesses methylation of DPP6, RALYL, and GSX1 genes, demonstrated improved performance over cytology in a large real-world cohort [141]. While methylation assays initially require higher investment in molecular infrastructure, their superior sensitivity (63-71% for CIN2+/CIN3+) and reduced need for specialised cytology expertise make them potentially cost-effective for LMICs in the long term [142]. There is the potential to repurpose Covid testing PCR equipment which is universally available, reducing investment costs in

DNA methylationSelf-sampling in combination with DNA methylation testing presents a promising pathway for cervical cancer screening evolution, potentially streamlining the screening process by eliminating separate cytology testing and reducing reliance on clinical infrastructure while maintaining high diagnostic standards.

HPV genotyping provides another effective triage strategy, already implemented in countries like the Netherlands. This approach allows risk stratification of HPV-positive self-samples based on type-specific risk, though implementation in LMICs requires consideration of cost and laboratory infrastructure. Studies show that genotyping can effectively identify women requiring immediate colposcopy versus those suitable for routine screening intervals [143,144].

Successful implementation requires careful consideration of quality assurance, healthcare integration, and cost analysis. This innovative combination of self-sampling, methylation testing, and POC analysis represents a potentially transformative approach to cervical cancer screening, aligned with WH**O'**s elimination goals, and could significantly improve screening accessibility and effectiveness in low-resource settings while maintaining high diagnostic standards.

6. Conclusions

The landscape of cervical cancer prevention is transforming through emerging technologies and evolving healthcare strategies. While progress has been made, substantial disparities persist between high-income countries and LMICs, necessitating innovative solutions.

Self-sampling technologies, including novel approaches like the Diagnostic Tampon, and the Teal Wand, show promise for increasing screening accessibility. Meta-analyses demonstrate that self-sampling can increase participation by 1.5 to 2.5 times compared to traditional methods, particularly impacting underserved populations [145,146].

The integration of AI and molecular testing enhances screening precision, with AI algorithms demonstrating 95% accuracy in identifying cervical abnormalities **[**147**]**. POC testing, showing 93% sensitivity and 91% specificity, offers potential solutions for resource-limited settings [148].

Cost-effectiveness analyses indicate that integrated digital health solutions can reduce screening costs by 46% in low-resource settings while improving follow-up rates [135]. However, successful implementation requires careful consideration of quality assurance, follow-up pathways, healthcare infrastructure integration, and cultural acceptability.

As HPV vaccination coverage increases globally, screening protocols will require adjustment, with evidence suggesting extended intervals for vaccinated populations [58]. Critical knowledge gaps require focused research, including standardised quality metrics for sample adequacy and evidence-based risk-stratification algorithms. Research priorities vary by healthcare setting, with high-income countries focusing on AI integration and multi-cancer detection platforms, while LMICs require cost-effective sample transport systems and POC testing validation.

The goal of cervical cancer elimination appears increasingly achievable through these innovative approaches, but success depends on addressing implementation challenges, particularly in resource-limited settings.

References

1. Chandra Sekar PK, Thomas SM, Veerabathiran R. The future of cervical cancer prevention: advances in research and technology. Explor Med. 2024 May 22;384–400.

2. Accelerating the impact of technology and innovation for global cervical cancer prevention (Conference Presentation) | Semantic Scholar [Internet]. [cited 2024 Dec 11]. Available from: https://www.semanticscholar.org/paper/Accelerating-the-impact-of-technology-and-for-Ramanujam/28f74703b3992f143b2156d4aa9a994ff14f0b2d

3. Epidemiology and natural history of HPV. | Semantic Scholar [Internet]. [cited 2024 Dec 11]. Available from: https://www.semanticscholar.org/paper/Epidemiology-and-natural-history-of-HPV.-Cox/28f52ed799891e264adeafb6afb09823fa2c29e3

4. Jensen JE, Becker GL, Jackson JB, Rysavy MB. Human Papillomavirus and Associated Cancers: A Review. Viruses. 2024 Apr 26;16(5):680.

5. Towards elimination of cervical cancer – human papillomavirus (HPV) vaccination and cervical cancer screening in Asian National Cancer Centers Alliance (ANCCA) member countries - PMC [Internet]. [cited 2024 Oct 7]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10415801/

6. Okunade KS. Human papillomavirus and cervical cancer. J Obstet Gynaecol. 2020 Jul 3;40(5):602–8.

7. Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, et al. Global estimates of incidence and mortality of cervical cancer in 2020: a baseline analysis of the WHO Global Cervical Cancer Elimination Initiative. Lancet Glob Health. 2022 Dec 14;11(2):e197–206.

8. Viveros-Carreño D, Fernandes A, Pareja R. Updates on cervical cancer prevention. Int J Gynecol Cancer. 2023 Mar;33(3):394–402.

9. Cervical Cancer Elimination Initiative [Internet]. [cited 2024 Dec 11]. Available from: https://www.who.int/initiatives/cervical-cancer-elimination-initiative

10. Vaccarella S, Laversanne M, Ferlay J, Bray F. Cervical cancer in A frica, L atin A merica and the C aribbean and A sia: Regional inequalities and changing trends. Int J Cancer. 2017 Nov 15;141(10):1997–2001.

11. Hull R, Mbele M, Makhafola T, Hicks C, Wang SM, Reis RM, et al. Cervical cancer in low and middle-income countries. Oncol Lett. 2020 Sep;20(3):2058–74.

12. Cervical cancer [Internet]. [cited 2024 Dec 11]. Available from: https://www.who.int/news-room/fact-sheets/detail/cervical-cancer

13. Spencer JC, Brewer NT, Coyne-Beasley T, Trogdon JG, Weinberger M, Wheeler SB. Reducing Poverty-related Disparities in Cervical Cancer: The Role of HPV Vaccination. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2021 Oct;30(10):1895–903.

14. Falcaro M, Soldan K, Ndlela B, Sasieni P. Effect of the HPV vaccination programme on incidence of cervical cancer and grade 3 cervical intraepithelial neoplasia by socioeconomic deprivation in England: population based observational study. BMJ. 2024 May 15;385:e077341.

15. GOV.UK [Internet]. [cited 2024 Dec 11]. NHS Cervical Screening Programme Audit of invasive cervical cancer: national report 1 April 2016 to 31 March 2019. Available from: https://www.gov.uk/government/publications/cervical-screening-invasive-cervical-cancer-audit-2016-to-

2019/nhs-cervical-screening-programme-audit-of-invasive-cervical-cancer-national-report-1-april-2016-to-31-march-2019

16. Choi S, Ismail A, Pappas-Gogos G, Boussios S. HPV and Cervical Cancer: A Review of Epidemiology and Screening Uptake in the UK. Pathogens. 2023 Feb 11;12(2):298.

17. Rajwinder K Hira, George Akomfrah.

18. GOV.UK [Internet]. [cited 2024 Dec 18]. Cervical screening standards data report 2022 to 2023. Available from: https://www.gov.uk/government/publications/cervical-screening-standards-data-report-2022-to-2023/cervical-screening-standards-data-report-2022-to-2023

19. England NHS. NHS England » NHS sets ambition to eliminate cervical cancer by 2040 [Internet]. 2023 [cited 2024 Dec 11]. Available from: https://www.england.nhs.uk/2023/11/nhs-sets-ambition-to-eliminate-cervical-cancer-by-2040/

20. Kundrod KA, Jeronimo J, Vetter B, Maza M, Murenzi G, Phoolcharoen N, et al. Toward 70% cervical cancer screening coverage: Technical challenges and opportunities to increase access to human papillomavirus (HPV) testing. Brault MA, editor. PLOS Glob Public Health. 2023 Aug 16;3(8):e0001982.

21. Gravitt PE, Silver MI, Hussey HM, Arrossi S, Huchko M, Jeronimo J, et al. Achieving equity in cervical cancer screening in low- and middle-income countries (LMICs): Strengthening health systems using a systems thinking approach. Prev Med. 2021 Mar;144:106322.

22. eClinicalMedicine. Global strategy to eliminate cervical cancer as a public health problem: are we on track? eClinicalMedicine. 2023 Jan;55:101842.

23. Allanson ER, Schmeler KM. Preventing Cervical Cancer Globally: Are We Making Progress? Cancer Prev Res (Phila Pa). 2021 Dec 1;14(12):1055–60.

24. Canfell K. Towards the global elimination of cervical cancer. Papillomavirus Res. 2019 Dec;8:100170.

25. Palmer TJ, Kavanagh K, Cuschieri K, Cameron R, Graham C, Wilson A, et al. Invasive cervical cancer incidence following bivalent human papillomavirus vaccination: a population-based observational study of age at immunization, dose, and deprivation. J Natl Cancer Inst. 2024 Jun 7;116(6):857–65.

26. Hall MT, Simms KT, Lew JB, Smith MA, Saville M, Canfell K. Projected future impact of HPV vaccination and primary HPV screening on cervical cancer rates from 2017–2035: Example from Australia. Consolaro MEL, editor. PLOS ONE. 2018 Feb 14;13(2):e0185332.

27. Luckett R, Feldman S. Impact of 2-, 4- and 9-valent HPV vaccines on morbidity and mortality from cervical cancer. Hum Vaccines Immunother. 2016 Jun 2;12(6):1332–42.

28. Maver PJ, Poljak M. Primary HPV-based cervical cancer screening in Europe: implementation status, challenges, and future plans. Clin Microbiol Infect. 2020 May;26(5):579–83.

29. Wentzensen N, Arbyn M. HPV-based cervical cancer screening- facts, fiction, and misperceptions. Prev Med. 2017 May;98:33–5.

30. Lei J, Ploner A, Elfström KM, Wang J, Roth A, Fang F, et al. HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med. 2020 Oct;383(14):1340–8.

31. Orumaa M, Lahlum EJ, Gulla M, Tota JE, Nygård M, Nygård S. Quadrivalent HPV Vaccine Effectiveness Against Cervical Intraepithelial Lesion Grade 2 or Worse in Norway: A Registry-Based Study of 0.9 Million Norwegian Women. J Infect Dis. 2024 Apr 25;jiae209.

32. Mikalsen MP, Simonsen GS, Sørbye SW. Impact of HPV Vaccination on the Incidence of High-Grade Cervical Intraepithelial Neoplasia (CIN2+) in Women Aged 20–25 in the Northern Part of Norway: A 15-Year Study. Vaccines. 2024 Apr 16;12(4):421.

33. Ellingson MK, Sheikha H, Nyhan K, Oliveira CR, Niccolai LM. Human papillomavirus vaccine effectiveness by age at vaccination: A systematic review. Hum Vaccines Immunother. 19(2):2239085.

34. Tsu VD, LaMontagne DS, Atuhebwe P, Bloem PN, Ndiaye C. National implementation of HPV vaccination programs in low-resource countries: Lessons, challenges, and future prospects. Prev Med. 2021 Mar;144:106335.

35. Guignard A, Praet N, Jusot V, Bakker M, Baril L. Introducing new vaccines in low- and middle-income countries: challenges and approaches. Expert Rev Vaccines. 2019 Feb 1;18(2):119–31.

36. Kumar S, Butler D. Calls in India for legal action against US charity. Nature [Internet]. 2013 Sep 9 [cited 2024 Dec 18]; Available from: https://www.nature.com/articles/nature.2013.13700

37. Swanson AA, Pantanowitz L. The evolution of cervical cancer screening. J Am Soc Cytopathol. 2024 Jan;13(1):10–5.

38. Chatterjee PB, Hingway SR, Hiwale KM. Evolution of Pathological Techniques for the Screening of Cervical Cancer: A Comprehensive Review. Cureus [Internet]. 2024 May 21 [cited 2024 Dec 13]; Available from: https://www.cureus.com/articles/248905-evolution-of-pathological-techniques-for-the-screening-of-cervical-cancer-a-comprehensive-review

39. Sharma J, Yennapu M, Priyanka Y. Screening Guidelines and Programs for Cervical Cancer Control in Countries of Different Economic Groups: A Narrative Review. Cureus [Internet]. 2023 Jun 28 [cited 2024 Dec 13]; Available from: https://www.cureus.com/articles/156265-screening-guidelines-and-programs-for-cervical-cancer-control-in-countries-of-different-economic-groups-a-narrative-review

40. Arbyn M, Ronco G, Anttila A, Meijer CJLM, Poljak M, Ogilvie G, et al. Evidence Regarding Human Papillomavirus Testing in Secondary Prevention of Cervical Cancer. Vaccine. 2012 Nov;30:F88–99.

41. Ogilvie G, Nakisige C, Huh WK, Mehrotra R, Franco EL, Jeronimo J. Optimizing secondary prevention of cervical cancer: Recent advances and future challenges. Int J Gynecol Obstet. 2017 Jul;138(S1):15–9.

42. WHO recommends DNA testing as a first-choice screening method for cervical cancer prevention [Internet]. [cited 2024 Dec 13]. Available from: https://www.who.int/europe/news-room/11-09-2021-who-recommends-dna-testing-as-a-first-choice-screening-method-for-cervical-cancer-prevention

43. Murewanhema G, Dzobo M, Moyo E, Moyo P, Mhizha T, Dzinamarira T. Implementing HPV-DNA screening as primary cervical cancer screening modality in Zimbabwe: Challenges and recommendations. Sci Afr. 2023 Sep;21:e01889.

44. Lozar T, Nagvekar R, Rohrer C, Dube Mandishora RS, Ivanus U, Fitzpatrick MB. Cervical Cancer Screening Postpandemic: Self-Sampling Opportunities to Accelerate the Elimination of Cervical Cancer. Int J Womens Health. 2021 Sep 18;13:841–59.

45. Serrano B, Ibáñez R, Robles C, Peremiquel-Trillas P, De Sanjosé S, Bruni L. Worldwide use of HPV self-sampling for cervical cancer screening. Prev Med. 2022 Jan;154:106900.

46. Subramanya D, Grivas PD. HPV and Cervical Cancer: Updates on an Established Relationship. Postgrad Med. 2008 Jan;120(4):7–13.

47. Barukčić I. Human Papillomavirus—The Cause of Human Cervical Cancer. J Biosci Med. 2018;06(04):106–25.

48. Cervical Cancer Causes, Risk Factors, and Prevention - NCI [Internet]. 2022 [cited 2024 Dec 13]. Available from: https://www.cancer.gov/types/cervical/causes-risk-prevention

49. Lowy DR, Solomon D, Hildesheim A, Schiller JT, Schiffman M. Human papillomavirus infection and the primary and secondary prevention of cervical cancer. Cancer. 2008 Sep 17;113(S7):1980–93.

50. Bruni L, Diaz M, Barrionuevo-Rosas L, Herrero R, Bray F, Bosch FX, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. Lancet Glob Health. 2016 Jul;4(7):e453-463.

51. References Human papillomavirus vaccines: WHO position paper, May 2017 (References with abstracts cited in the position paper in the order of appearance.) SAGE guidance for the development of evidence-based vaccine-related recommendations. In 2017 [cited 2024 Dec 13]. Available from: https://www.semanticscholar.org/paper/References-Human-papillomavirus-vaccines%3A-WHO-May/7dc6c6b55657f911c80ea0427208cb1ff5aa913c

52. Chen JJ, Department of Medicine, University of Massachusetts Medical School, Worcester, MA. Genomic Instability Induced By Human Papillomavirus Oncogenes. Am Chin J Med Sci. 2010;3(2):043.

53. Korzeniewski N, Spardy N, Duensing A, Duensing S. Genomic instability and cancer: Lessons learned from human papillomaviruses. Cancer Lett. 2011 Jun;305(2):113–22.

54. Balasubramaniam SD, Balakrishnan V, Oon CE, Kaur G. Key Molecular Events in Cervical Cancer Development. Medicina (Mex). 2019 Jul 17;55(7):384.

55. Mello V, Sundstrom RK. Cervical Intraepithelial Neoplasia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Dec 13]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK544371/

13

56.   Cooper DB, Dunton CJ. Colposcopy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Dec 13]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK564514/

57.   Arbyn M, Xu L. Efficacy and safety of prophylactic HPV vaccines. A Cochrane review of randomized trials. Expert Rev Vaccines. 2018 Dec 2;17(12):1085–91.

58.   Giorgi Rossi P, Carozzi F, Federici A, Ronco G, Zappa M, Franceschi S, et al. Cervical cancer screening in women vaccinated against human papillomavirus infection: Recommendations from a consensus conference. Prev Med. 2017 May;98:21–30.

59.   Zhai L, Tumban E. Gardasil-9: A global survey of projected efficacy. Antiviral Res. 2016 Jun;130:101–9.

60.   Signorelli C, Odone A, Ciorba V, Cella P, Audisio RA, Lombardi A, et al. Human papillomavirus 9-valent vaccine for cancer prevention: a systematic review of the available evidence. Epidemiol Infect. 2017 Jul;145(10):1962–82.

61.   Silver MI, Kobrin S. Exacerbating disparities?: Cervical cancer screening and HPV vaccination. Prev Med. 2020 Jan 1;130:105902.

62.   Staley H, Shiraz A, Shreeve N, Bryant A, Martin-Hirsch PP, Gajjar K. Interventions targeted at women to encourage the uptake of cervical screening. Cochrane Gynaecological, Neuro-oncology and Orphan Cancer Group, editor. Cochrane Database Syst Rev [Internet]. 2021 Sep 6 [cited 2024 Dec 15];2021(9). Available from: http://doi.wiley.com/10.1002/14651858.CD002834.pub3

63.   Stanley M, Schuind A, Muralidharan KK, Guillaume D, Willens V, Borda H, et al. Evidence for an HPV one-dose schedule. Vaccine. 2024 Jul 11;42:S16–21.

64.   PRIMAVERA Immunobridging Trial - NCI [Internet]. 2020 [cited 2024 Dec 15]. Available from: https://dceg.cancer.gov/research/cancer-types/cervix/primavera

65.   Rosa AD. Impact of the COVID-19 pandemic on HPV vaccination coverage in the general population and in PLWHs [Internet]. European Review. 2022 [cited 2024 Dec 18]. Available from: https://www.europeanreview.org/article/29922

66.   Castanon A, Rebolj M, Pesola F, Pearmain P, Stubbs R. COVID-19 disruption to cervical cancer screening in England. J Med Screen. 2022 Sep;29(3):203–8.

67.   Ramírez AT, Valls J, Baena A, Rojas FD, Ramírez K, Álvarez R, et al. Performance of cervical cytology and HPV testing for primary cervical cancer screening in Latin America: an analysis within the ESTAMPA study. Lancet Reg Health Am. 2023 Oct;26:100593.

68.   Cuschieri K, Wentzensen N. Human Papillomavirus mRNA and p16 Detection as Biomarkers for the Improved Diagnosis of Cervical Neoplasia. Cancer Epidemiol Biomarkers Prev. 2008 Oct 1;17(10):2536–45.

69.   Cuschieri K, Ronco G, Lorincz A, Smith L, Ogilvie G, Mirabello L, et al. Eurogin roadmap 2017: Triage strategies for the management of HPV -positive women in cervical screening programs. Int J Cancer. 2018 Aug 15;143(4):735–45.

70.   Hall MT, Simms KT, Lew JB, Smith MA, Brotherton JM, Saville M, et al. The projected timeframe until cervical cancer elimination in Australia: a modelling study. Lancet Public Health. 2019 Jan 1;4(1):e19–27.

71.   Bryant E. The impact of policy and screening on cervical cancer in England. Br J Nurs. 2012 Feb 21;21(Sup4):S4–10.

72.   Arbyn M, Costa S, Latsuzbaia A, Kellen E, Girogi Rossi P, Cocuzza CE, et al. HPV-based Cervical Cancer Screening on Self-samples in the Netherlands: Challenges to Reach Women and Test Performance Questions. Cancer Epidemiol Biomarkers Prev. 2023 Feb 6;32(2):159–63.

73.   Elfström M, Gray PG, Dillner J. Cervical cancer screening improvements with self-sampling during the COVID-19 pandemic. eLife. 2023 Dec 12;12:e80905.

74.   Integrating HPV vaccination programs with enhanced cervical cancer screening and treatment, a systematic review. | Semantic Scholar [Internet]. [cited 2024 Dec 19]. Available from: https://www.semanticscholar.org/paper/Integrating-HPV-vaccination-programs-with-enhanced-Wirtz-Mohamed/cea64a5bb058a357a4f17750bd4326202fdb9fcd

75.   Ebrahimi N, Yousefi Z, Khosravi G, Malayeri FE, Golabi M, Askarzadeh M, et al. Human papillomavirus vaccination in low- and middle-income countries: progression, barriers, and future prospective. Front Immunol. 2023 May 12;14:1150238.

76.   Sankaranarayanan R, Qiao Y lin, Keita N. The Next Steps in Cervical Screening. Womens Health. 2015 Mar;11(2):201–12.

77.   Binagwaho A, Wagner C, Gatera M, Karema C, Nutt C, Ngaboa F. Achieving high coverage in Rwanda's national human papillomavirus vaccination programme. Bull World Health Organ. 2012 Aug 1;90(8):623–8.

78.   Poli UR, Muwonge R, Bhoopal T, Lucas E, Basu P. Feasibility, Acceptability, and Efficacy of a Community Health Worker–Driven Approach to Screen Hard-to-Reach Periurban Women Using Self-Sampled HPV Detection Test in India. JCO Glob Oncol. 2020 Nov;(6):658–66.

79.   Tracking Universal Health Coverage in the WHO African Region, 2022.

80.   Okolie EA, Aluga D, Anjorin S, Ike FN, Ani EM, Nwadike BI. Addressing missed opportunities for cervical cancer screening in Nigeria: a nursing workforce approach. ecancermedicalscience. 2022 Apr 11;16:1373.

81.   WHO CERVICAL CANCER ELIMINATION INITIATIVE: FROM CALL TO ACTION TO GLOBAL MOVEMENT.

82.   Goldhaber-Fiebert JD, Stout NK, Salomon JA, Kuntz KM, Goldie SJ. Cost-Effectiveness of Cervical Cancer Screening With Human Papillomavirus DNA Testing and HPV-16,18 Vaccination. JNCI J Natl Cancer Inst. 2008 Mar 5;100(5):308–20.

83.   Zambia steps up cervical cancer screening with HPV testing | WHO | Regional Office for Africa [Internet]. 2024 [cited 2024 Dec 19]. Available from: https://www.afro.who.int/countries/zambia/news/zambia-steps-cervical-cancer-screening-hpv-testing

84.   Desta AA, Alemu FT, Gudeta MB, Dirirsa DE, Kebede AG. Willingness to utilize cervical cancer screening among Ethiopian women aged 30–65 years. Front Glob Womens Health [Internet]. 2022 Aug 30 [cited 2024 Dec 19];3. Available from: https://www.frontiersin.org/journals/global-womens-health/articles/10.3389/fgwh.2022.939639/full

85.   Miller S. Clinton Health Access Initiative. 2023 [cited 2024 Dec 19]. Scaling up an effective model of care to prevent and treat cervical cancer in Rwanda. Available from: https://www.clintonhealthaccess.org/blog/scaling-up-an-effective-model-of-care-to-prevent-and-treat-cervical-cancer-in-rwanda/

86.   Wave of new commitments marks historic step towards the elimination of cervical cancer [Internet]. [cited 2024 Dec 19]. Available from: https://www.gavi.org/news/media-room/wave-new-commitments-marks-historic-step-towards-elimination-cervical-cancer

87.   Innovative approaches to cervical cancer screening in low- and middle-income countries | Semantic Scholar [Internet]. [cited 2024 Dec 19]. Available from: https://www.semanticscholar.org/paper/Innovative-approaches-to-cervical-cancer-screening-Toliman-Kaldor/12d6a2a977b943b7da0eb4a2322846ecb0ed2a33

88.   Davies-Oliveira JC, Smith MA, Grover S, Canfell K, Crosbie EJ. Eliminating Cervical Cancer: Progress and Challenges for High-income Countries. Clin Oncol. 2021 Sep;33(9):550–9.

89.   Ibrahim A, Simeen N. 32P Cervical cancer: Barriers and smears to prevention. ESMO Open. 2024 Jun;9:103532.

90.   Waller J, Bartoszek M, Marlow L, Wardle J. Barriers to cervical cancer screening attendance in England: a population-based survey. J Med Screen. 2009 Dec;16(4):199–204.

91.   Marlow L, McBride E, Varnes L, Waller J. Barriers to cervical screening among older women from hard-to-reach groups: a qualitative study in England. BMC Womens Health. 2019 Dec;19(1):38.

92.   Cadman L, Waller J, Ashdown-Barr L, Szarewski A. Barriers to cervical screening in women who have experienced sexual abuse: an exploratory study: Table 1. J Fam Plann Reprod Health Care. 2012 Oct;38(4):214–20.

93.   Berner AM, Connolly DJ, Pinnell I, Wolton A, MacNaughton A, Challen C, et al. Attitudes of transgender men and non-binary people to cervical screening: a cross-sectional mixed-methods study in the UK. Br J Gen Pract J R Coll Gen Pract. 2021 Aug;71(709):e614–25.

94.   Dhillon N, Oliffe JL, Kelly MT, Krist J. Bridging Barriers to Cervical Cancer Screening in Transgender Men: A Scoping Review. Am J Mens Health. 2020 Jun 3;14(3):1557988320925691.

95.   Lim AWW, Deats K, Gambell J, Lawrence A, Lei J, Lyons M, et al. Opportunistic offering of self-sampling to non-attenders within the English cervical screening programme: a pragmatic, multicentre, implementation feasibility trial with randomly allocated cluster intervention start dates (YouScreen). eClinicalMedicine. 2024 Jul 16;73:102672.

96.   HPValidate: clinical validation of hrHPV test system using self-collected vaginal samples in NHS England commissioned laboratories providing cervical screening services.

97.   Hariprasad R, John A, Abdulkader RS. Challenges in the Implementation of Human Papillomavirus Self-Sampling for Cervical Cancer Screening in India: A Systematic Review. JCO Glob Oncol. 2023 Mar;(9):e2200401.

98.   Woo YL, Gravitt P, Khor SK, Ng CW, Saville M. Accelerating action on cervical screening in lower- and middle-income countries (LMICs) post COVID-19 era. Prev Med. 2021 Mar;144:106294.

99.   Feasibility of the WHO strategy to eliminate cervical cancer as a public health problem, lessons learned from the PRESCRIP-TEC project | Knowledge Action Portal on NCDs [Internet]. [cited 2024 Dec 19]. Available from: https://www.knowledge-action-portal.com/en/content/feasibility-who-strategy-eliminate-cervical-cancer-public-health-problem-lessons-learned

100.   Gupta S, Palmer C, Bik EM, Cardenas JP, Nuñez H, Kraal L, et al. Self-Sampling for Human Papillomavirus Testing: Increased Cervical Cancer Screening Participation and Incorporation in International Screening Programs. Front Public Health. 2018 Apr 9;6:77.

101.   Viviano M, Willame A, Cohen M, Benski AC, Catarino R, Wuillemin C, et al. A comparison of cotton and flocked swabs for vaginal self-sample collection. Int J Womens Health. 2018 May 15;10:229–36.

102.   Daye [Internet]. [cited 2024 Dec 22]. At-Home HPV Screen | Test Your Gynae Health. Available from: https://www.yourdaye.com/products/at-home-hpv-screening

103.   Papcup [Internet]. [cited 2024 Dec 22]. Papcup | Cervical Screening. Available from: https://www.papcup.co.uk

104.   BioSpace [Internet]. 2024 [cited 2024 Dec 22]. Qvin™ Introduces Q-Pad™: Transforming Women's Health with FDA-Cleared Lab Testing using Menstrual Blood. Available from: https://www.biospace.com/qvin-introduces-q-pad-transforming-women-s-health-with-fda-cleared-lab-testing-using-menstrual-blood

105.   Arbyn M, Smith SB, Temin S, Sultana F, Castle P. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. BMJ. 2018 Dec 5;363:k4823.

106.   Viñals R, Jonnalagedda M, Petignat P, Thiran JP, Vassilakos P. Artificial Intelligence-Based Cervical Cancer Screening on Images Taken during Visual Inspection with Acetic Acid: A Systematic Review. Diagnostics. 2023 Feb 22;13(5):836.

107.   Gupta R, Sarwar A, Sharma V. Screening of Cervical Cancer by Artificial Intelligence based Analysis of Digitized Papanicolaou-Smear Images. In 2017 [cited 2024 Dec 19]. Available from: https://www.semanticscholar.org/paper/Screening-of-Cervical-Cancer-by-Artificial-based-of-Gupta-Sarwar/44acfd2e0a27500a100cf31ad9c9f5d018997bac

108.   Wu T, Lucas E, Zhao F, Basu P, Qiao Y. Artificial intelligence strengthens cervical cancer screening – present and future. Cancer Biol Med. 2024 Oct 15;21(10):864–79.

109.   Gupta R, Gupta S. Point-of-care tests for human papillomavirus detection in uterine cervical samples: A review of advances in resource-constrained settings. Indian J Med Res. 2023 Nov;158(5 & 6):509–21.

110.   Seely S, Zingg JM, Joshi P, Slomovitz B, Schlumbrecht M, Kobetz E, et al. Point-of-Care Molecular Test for the Detection of 14 High-Risk Genotypes of Human Papillomavirus in a Single Tube. Anal Chem. 2023 Sep 12;95(36):13488–96.

111.   Kelly H, Mayaud P, Segondy M, Pant Pai N, Peeling RW. A systematic review and meta-analysis of studies evaluating the performance of point-of-care tests for human papillomavirus screening. Sex Transm Infect. 2017 Dec;93(S4):S36–45.

112.   Kuhn L, Denny L. The time is now to implement HPV testing for primary screening in low resource settings. Prev Med. 2017 May;98:42–4.

113. Vallely AJB, Saville M, Badman SG, Gabuzzi J, Bolnga J, Mola GDL, et al. Point-of-care HPV DNA testing of self-collected specimens and same-day thermal ablation for the early detection and treatment of cervical pre-cancer in women in Papua New Guinea: a prospective, single-arm intervention trial (HPV-STAT). Lancet Glob Health. 2022 Sep;10(9):e1336–46.

114. Shrivas S, Patel M, Kumar R, Gwal A, Uikey R, Tiwari SK, et al. Evaluation of Microchip-Based Point-Of-Care Device "Gazelle" for Diagnosis of Sickle Cell Disease in India. Front Med. 2021 Oct 13;8:639208.

115. Target product profiles for human papillomavirus screening tests to detect cervical pre-cancer and cancer [Internet]. [cited 2024 Dec 19]. Available from: https://www.who.int/publications/i/item/9789240100275

116. Agency for Drugs and Technologies in Health. (2017). Health Technology Update: Issue 18. https://www.cda-amc.ca/sites/default/files/pdf/Health_Technology_Update_Issue_18.pdf   8/1055-9965.EPI-20-1226.

117. Chakravarti P, Maheshwari A, Tahlan S, Kadam P, Bagal S, Gore S, et al. Diagnostic accuracy of menstrual blood for human papillomavirus detection in cervical cancer screening: a systematic review. ecancermedicalscience. 2022 Jul 14;16:1427.

118. Arias M, Jang D, Gilchrist J, Luinstra K, Li J, Smieja M, et al. Ease, Comfort, and Performance of the HerSwab Vaginal Self-Sampling Device for the Detection of Chlamydia trachomatis and Neisseria gonorrhoeae. Sex Transm Dis. 2016 Feb;43(2):125–9.

119. Davies JC, Sargent A, Pinggera E, Carter S, Gilham C, Sasieni P, 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. BJOG Int J Obstet Gynaecol. 2024 Oct;131(11):1456–64.

120. Jentschke M, Chen K, Arbyn M, Hertel B, Noskowicz M, Soergel P, et al. Direct comparison of two vaginal self-sampling devices for the detection of human papillomavirus infections. J Clin Virol Off Publ Pan Am Soc Clin Virol. 2016 Sep;82:46–50.

121. Leinonen MK, Schee K, Jonassen CM, Lie AK, Nystrand CF, Rangberg A, et al. Safety and acceptability of human papillomavirus testing of self-collected specimens: A methodologic study of the impact of collection devices and HPV assays on sensitivity for cervical cancer and high-grade lesions. J Clin Virol. 2018 Feb;99–100:22–30.

122. Martinelli M, Giubbi C, Di Meo ML, Perdoni F, Musumeci R, Leone BE, et al. Accuracy of Human Papillomavirus (HPV) Testing on Urine and Vaginal Self-Samples Compared to Clinician-Collected Cervical Sample in Women Referred to Colposcopy. Viruses. 2023 Sep 7;15(9):1889.

123. Milanova V, Gomes M, Mihaylova K, Twelves JL, Multmeier J, McMahon H, et al. Diagnostic Accuracy of the Daye Diagnostic Tampon Compared to Clinician-Collected and Self-Collected Vaginal Swabs for Detecting HPV: A Comparative Study [Internet]. medRxiv; 2024 [cited 2024 Dec 20]. p. 2024.12.02.24318200. Available from: https://www.medrxiv.org/content/10.1101/2024.12.02.24318200v1

124. National Institute for Health and Care Excellence (NICE). The technology [Internet]. Available from: https://www.nice.org.uk/advice/mib273/chapter/The-technology.

125. Naseri S, Young S, Cruz G, Blumenthal PD. Screening for High-Risk Human Papillomavirus Using Passive, Self-Collected Menstrual Blood. Obstet Gynecol. 2022 Sep 1;140(3):470–6.

126. Nilyanimit P, Chaithongwongwatthana S, Oranratanaphan S, Poudyal N, Excler JL, Lynch J, et al. Comparable detection of HPV using real-time PCR in paired cervical samples and concentrated first-stream urine collected with Colli-Pee device. Diagn Microbiol Infect Dis. 2024 Mar;108(3):116160.

127. Sechi I, Muresu N, Puci MV, Saderi L, Del Rio A, Cossu A, et al. Preliminary Results of Feasibility and Acceptability of Self-Collection for Cervical Screening in Italian Women. Pathogens. 2023 Sep;12(9):1169.

128. Lorenzi NPC, Termini L, Longatto Filho A, Tacla M, De Aguiar LM, Beldi MC, et al. Age-related acceptability of vaginal self-sampling in cervical cancer screening at two university hospitals: a pilot cross-sectional study. BMC Public Health. 2019 Dec;19(1):963.

129. Sabeena S, Kuriakose S, Binesh D, Abdulmajeed J, Dsouza G, Ramachandran A, et al. The Utility of Urine-Based Sampling for Cervical Cancer Screening in Low-Resource Settings. Asian Pac J Cancer Prev. 2019 Aug 1;20(8):2409–13.

130. Turner F, Drury J, Hapangama DK, Tempest N. Menstrual Tampons Are Reliable and Acceptable Tools to Self-Collect Vaginal Microbiome Samples. Int J Mol Sci. 2023 Jan;24(18):14121.

131. FDA Puts Teal Health on an Accelerated Path to Market for our At-Home Cervical Cancer Screening [Internet]. [cited 2024 Dec 20]. Available from: https://www.getteal.com/post/fda-puts-teal-health-on-an-accelerated-path-to-market-for-our-at-home-cervical-cancer-screening

132. Shafaghmotlagh S. Cancer Research UK - Cancer News. 2024 [cited 2024 Dec 20]. Papcup: Could this at-home HPV test make cervical screening easier? Available from: https://news.cancerresearchuk.org/2024/09/04/papcup-at-home-hpv-test-to-make-cervical-screening-smear-test-easier/

133. Vaginal and Urine Self-sampling Compared to Cervical Sampling for HPV-testing with the Cobas 4800 HPV Test. Anticancer Res [Internet]. 2017 Jul 20 [cited 2024 Dec 19];37(8). Available from: http://ar.iiarjournals.org/content/37/8/4183.abstract

134. [PDF] Clinical performance and acceptability of self-collected vaginal and urine samples compared with clinician-taken cervical samples for HPV testing among women referred for colposcopy. A cross-sectional study | Semantic Scholar [Internet]. [cited 2024 Dec 19]. Available from: https://www.semanticscholar.org/paper/Clinical-performance-and-acceptability-of-vaginal-A-%C3%98rnskov-Jochumsen/08d58fd35f8974135928df67f200fbf3fb39aa99

135. Liu X, Ning L, Fan W, Jia C, Ge L. Electronic Health Interventions and Cervical Cancer Screening: Systematic Review and Meta-Analysis. J Med Internet Res. 2024 Oct 31;26:e58066.

136. Olthof EMG, Aitken CA, Siebers AG, Van Kemenade FJ, De Kok IMCM. The impact of loss to follow-up in the Dutch organised HPV-based cervical cancer screening programme. Int J Cancer. 2024 Jun 15;154(12):2132–41.

137. Manley K, Patel A, Pawade J, Glew S, Hunt K, Villeneuve N, et al. The use of biomarkers and HPV genotyping to improve diagnostic accuracy in women with a transformation zone type 3. Br J Cancer. 2022 Jan 1;126(1):91–9.

138. Gibert MJ, Sánchez-Contador C, Artigues G. Validity and acceptance of self vs conventional sampling for the analysis of human papillomavirus and Pap smear. Sci Rep. 2023 Feb 16;13(1):2809.

139. Othman NH, Zaki FHM, Hussain NHN, Yusoff WZW, Ismail P. SelfSampling Versus Physicians' Sampling for Cervical Cancer Screening Agreement of Cytological Diagnoses. Asian Pac J Cancer Prev APJCP. 2016;17(7):3489–94.

140. Kelly H, Benavente Y, Pavon MA, De Sanjose S, Mayaud P, Lorincz AT. Performance of DNA methylation assays for detection of high-grade cervical intraepithelial neoplasia (CIN2+): a systematic review and meta-analysis. Br J Cancer. 2019 Nov;121(11):954–65.

141. Schreiberhuber L, Barrett JE, Wang J, Redl E, Herzog C, Vavourakis CD, et al. Cervical cancer screening using DNA methylation triage in a real-world population. Nat Med. 2024 Aug;30(8):2251–7.

142. Zhang L, Tan W, Yang H, Zhang S, Dai Y. Detection of Host Cell Gene/HPV DNA Methylation Markers: A Promising Triage Approach for Cervical Cancer. Front Oncol. 2022 Mar 25;12:831949.

143. Chatzistamatiou K, Tsertanidou A, Moysiadis T, Mouchtaropoulou E, Pasentsis K, Skenderi A, et al. Comparison of different strategies for the triage to colposcopy of women tested high-risk HPV positive on self-collected cervicovaginal samples. Gynecol Oncol. 2021 Sep;162(3):560–8.

144. Song F, Du H, Wang C, Huang X, Wu R, CHIMUST team. The effectiveness of HPV16 and HPV18 genotyping and cytology with different thresholds for the triage of human papillomavirus-based screening on self-collected samples. Meyers C, editor. PLOS ONE. 2020 Jun 11;15(6):e0234518.

145. Verdoodt F, Dehlendorff C, Kjaer SK. Dose-related Effectiveness of Quadrivalent Human Papillomavirus Vaccine Against Cervical Intraepithelial Neoplasia: A Danish Nationwide Cohort Study. Clin Infect Dis Off Publ Infect Dis Soc Am. 2020 Feb 3;70(4):608–14.

146. Yeh PT, Kennedy CE, De Vuyst H, Narasimhan M. Self-sampling for human papillomavirus (HPV) testing: a systematic review and meta-analysis. BMJ Glob Health. 2019 May;4(3):e001351.

18

147. Ouh YT, Kim TJ, Ju W, Kim SW, Jeon S, Kim SN, et al. Development and validation of artificial intelligence-based analysis software to support screening system of cervical intraepithelial neoplasia. Sci Rep. 2024 Jan 23;14(1):1957.

148. Holmström O, Linder N, Kaingu H, Mbuuko N, Mbete J, Kinyua F, et al. Point-of-care digital cytology with artificial intelligence for cervical cancer screening at a peripheral clinic in Kenya. 2020 Aug 14 [cited 2024 Dec 20]; Available from: http://medrxiv.org/lookup/doi/10.1101/2020.08.12.20172346