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REVIEW

Scaling HPV Self-Sampling in Low-Resource Settings: From Evidence to Sustainable Implementation

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Abstract: Profound global inequities in cervical cancer burden persist, with nearly 90% of deaths occurring in low- and middle-income countries (LMICs). High-performance human papillomavirus (HPV) testing is the recommended primary screening method, but its scale-up remains constrained by resource and infrastructure limitations. HPV self-sampling optimizes health system resources by eliminating universal speculum examinations during primary screening, yet a critical implementation gap remains regarding how programs transition from pilot projects to routine national practice. To examine this transition, a literature search was conducted through May 2026, focusing on implementation of cervical screening using vaginal self-sampling and molecular DNA amplification techniques within resource-limited settings. While policy endorsement in LMICs expanded from 10 countries in 2020 to 29 in 2026—with 23 recommending self-sampling for all women—real-world implementation lags significantly, as reflected in an estimated five-year HPV-based screening coverage of only 2% in LMICs in 2022. Selected country case studies illustrate diverse delivery models and varying stages of implementation scale, ranging from localized research projects and regional campaigns to scaled national programs: community health worker home visits increased screening uptake four-fold in Argentina, digital health platforms and electronic registries are supporting national scale-up in Malaysia and Rwanda, and single-day near-point-of-care projects achieved very high follow-up rates in remote Amazonian populations. Beyond these country experiences, the review evaluates key considerations along the clinical care cascade, highlighting the importance of triage and treatment capacity, active tracing strategies to minimize loss to follow-up, and supply chain management. Ultimately, self-sampling serves as a promising equity strategy whose success relies on sustained political, financial, and structural commitment across the full clinical pathway.

Keywords: cervical cancer screening, HPV testing, self-sampling, LMIC, implementation, health systems strengthening

Introduction

In 2022, an estimated 662,000 women were diagnosed with cervical cancer and 350,000 women died from the disease worldwide, with nearly 90% of deaths occurring in low- and middle-income countries (LMICs). Age-standardized mortality rates are more than four times higher in low-resource settings —18.5 deaths per 100,000 women in low-income countries, 10.3 in lower-middle-income countries, 5.5 in upper-middle-income countries, and 2.4 in high-income countries[1] — reflecting profound inequities in access to cervical cancer prevention, early detection, and treatment services.

These inequities have contributed to persistently high incidence and mortality rates in these settings.[1] Prior to current human papillomavirus (HPV)-based screening frameworks, traditional prevention strategies relied primarily on cytology or visual inspection with acetic acid (VIA), both of which have achieved limited population-level impact in lower-resource settings. While cytology has long served as a primary screening tool in higher-resource contexts and some LMICs, its reach is heavily dependent on specialized personnel and laboratory infrastructure. Free of laboratory requirements, VIA has been widely adopted across many LMICs, but remains highly examiner-dependent and demands

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continuous clinical training and quality assurance.[2] Although LMICs represent a highly heterogeneous group with substantial variations in health infrastructure, laboratory capacity, and financing mechanisms, both traditional screening methods have broadly struggled to achieve high population coverage across these diverse resource-constrained environments. As a result, screening coverage remains low, with an estimated 5-year coverage with any screening method (ie, cytology, HPV testing, VIA, or combinations of these methods) of about 26% in LMICs compared to 74% in high-income countries.[3] Coverage gaps are particularly pronounced among underserved populations, including women living with human immunodeficiency virus (women living with HIV, WLWH), who face an elevated risk of cervical cancer and often encounter additional barriers to accessing care.[4]

In response, there has been a paradigm shift toward more accessible, scalable and user-centered approaches, most notably through self-sampling of cervical and vaginal cells for the detection of HPV.[5,6] By enabling women to collect their own specimens, self-sampling moves the primary entry point from health facilities into communities and even households, overcoming structural and sociocultural barriers. This approach is aligned with the World Health Organization (WHO) Global strategy to accelerate the elimination of cervical cancer, which calls for screening 70% of women with a high-performance test by 2030.[6] In this context, WHO recommends HPV testing as the preferred primary screening method and recognizes self-sampling as an additional strategy to expand coverage, particularly where traditional screening approaches have failed to reach underserved populations.[5,7]

In health systems facing severe workforce and infrastructure constraints, reliance on provider-based screening and universal speculum examinations is neither feasible nor resource-efficient (Figure 1). Self-sampling offers a pragmatic alternative by eliminating the need for clinic visits among women who test HPV-negative while concentrating scarce clinical resources on the management of screen-positive individuals.

Numerous randomized trials and implementation studies across diverse settings have examined the range of available collection tools—including swabs, brushes, and lavage devices— with current practice converging on high-performance HPV deoxyribonucleic acid (DNA) amplification assays paired with validated sampling devices, such as FLOQSwabs or Evalyn brushes. These combinations have demonstrated high analytical sensitivity and specificity, as well as practical advantages for implementation, including sample stability during transport and reduced dependence on strict cold-chain requirements. Meta-analyses confirm that HPV DNA testing on self-collected samples can achieve accuracy comparable to provider-collected specimens when highly sensitive polymerase chain reaction (PCR)-based methods are used.[10,11] Importantly, more recent post-implementation experience has highlighted that performance depends not only on the collection device itself, but also on the pairing with the HPV test on the laboratory workflow, and the quality assurance systems supporting the testing process.[12]

Beyond feasibility, user acceptability has emerged as a critical driver of the success of self-sampling approaches.[13] Women across diverse contexts consistently report a preference for self-collection due to increased privacy, autonomy, and convenience, particularly in settings where cultural norms or prior negative experiences may discourage gynecological pelvic examinations. While barriers persist−including fear of procedure error, doubts about test reliability, and the absence of direct contact with the healthcare provider[14] −addressing these concerns through clear instructions, community engagement, and supportive communication is essential to maximize uptake.

Although extensive literature has established the diagnostic accuracy, device performance, and acceptability of HPV self-sampling, a critical knowledge gap remains regarding how health systems transition from isolated pilot projects to sustainable, routine national programs. Successfully closing this implementation gap requires moving beyond technical aspects of the self-sampling device to analyze complex realities across the full clinical cascade. Accordingly, this review synthesizes real-world implementation experiences across diverse low-resource settings, highlighting examples of countries or projects that have successfully expanded screening implementation. It further examines critical health-system components along the longitudinal care pathway—specifically triage and treatment capacity, loss to follow-up, digital tracking, and supply chain governance—to outline the frameworks required for sustainable national scale-up. This review focuses on HPV screening with vaginal self-sampling using DNA amplification techniques—either PCR-based or isothermal—within low-resource health system contexts.

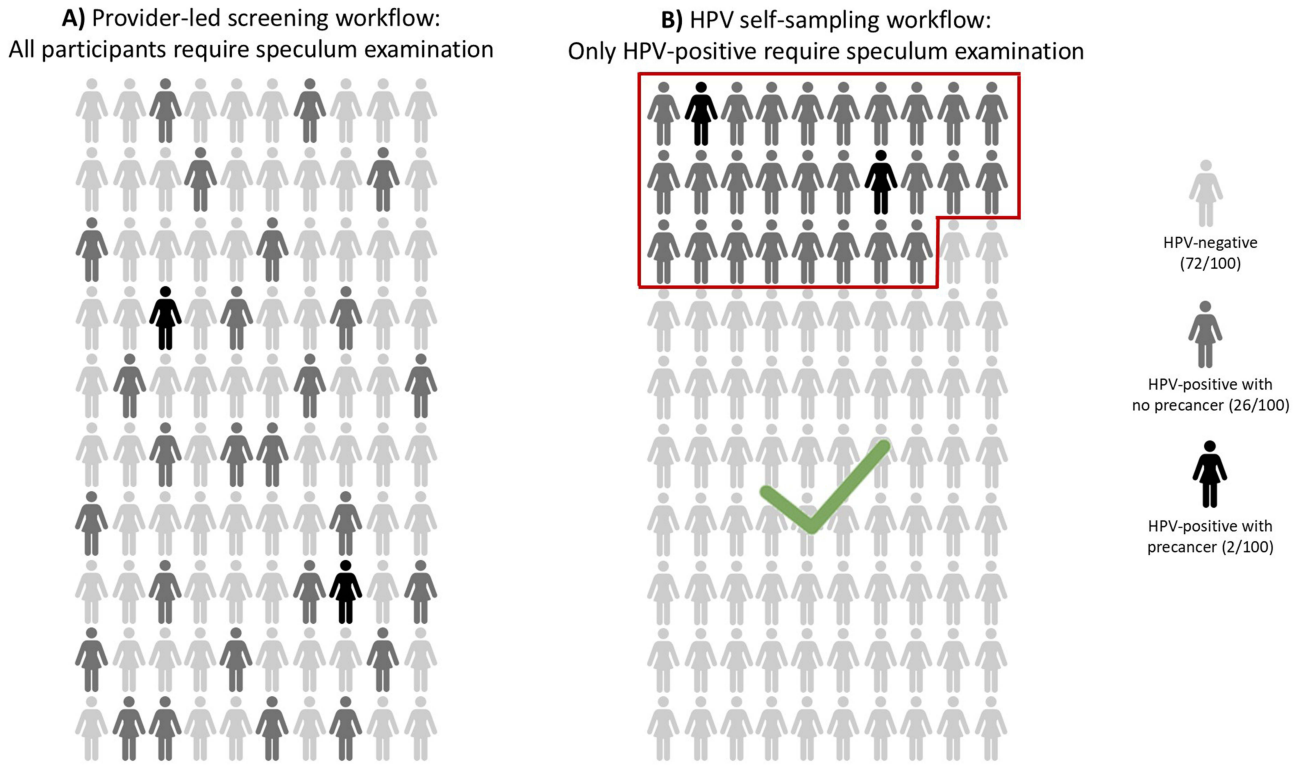

Figure 1 Optimizing clinical resource allocation via HPV self-sampling. (**A**) Provider-led screening workflow (VIA, cytology or provider-collected HPV testing): all screening participants require a speculum examination. (**B**) HPV self-sampling workflow: only women with a positive HPV result require a speculum examination. Based on the multi-country PAVE study, in which overall HPV prevalence was 28.5%, this approach would reduce the speculum examination burden to approximately 28% of screened women, allowing the remaining 72% with a negative HPV result to be reassured without pelvic examination. Among HPV-positive women, the precancer/cancer risk (CIN3+) was 7.1%.[8,9]
Abbreviations: CIN3+, cervical intraepithelial neoplasia grade 3 or worse; HPV, human papillomavirus; PAVE, HPV-automated visual evaluation; VIA, visual inspection with acetic acid.

Methods

This review applies a dual-framework approach: a structured synthesis of national policy and coverage data, combined with a narrative review strategy and thematic evaluation of the clinical care cascade. The foundational literature search strategy was conducted across major biomedical databases (PubMed, Web of Science, and Scopus) for peer-reviewed studies published up to April 2026. Search terms included combinations of keywords related to cervical screening using HPV self-sampling ("cervical screening", "cervical cancer screening", "HPV self-sampling", "self-collection", "vaginal self-sampling") paired with implementation and resource concepts ("low-resource settings", "LMIC", "implementation", "scale-up"). Country case studies were purposefully selected to reflect diverse delivery strategies (eg, community outreach, facility-based, door-to-door, and single-day approaches), broad geographic representation across Latin America, Africa, Asia, and the Pacific, and varying stages of policy transition from research pilots to national programs. Information on national policy recommendations and screening coverage were derived from the updated WHO cervical cancer screening coverage estimates for 2022, which compiled program and coverage data for 194 WHO Member States and 8 associated countries and territories using an established methodology, including review of scientific literature, official documents, government websites, input from country experts, and a formal WHO country consultation conducted in April-May 2024, with additional responses received through July 2025.[3] The detailed methodology and country-level data sources have been described elsewhere.[3] For the present review, these baseline data were complemented with updated national policy reports and country-level programmatic updates available up to May 2026 to capture recent developments in HPV self-sampling recommendations. To ensure a comprehensive overview of real-world implementation, this review was further enriched with findings from recently completed country experiences presented at international conferences and manuscripts currently in preparation. Following this methodology, the synthesized evidence is presented in two sequential parts: an empirical mapping of national HPV self-sampling recommendations, real-world

implementation models and country case studies, followed by an analytical discussion of health-system barriers across the clinical care cascade.

Real-World Implementation Models and Country Case Studies

Following the search strategy and selection framework described above, this section synthesizes evidence on the global policy landscape and country-specific implementation models for HPV self-sampling. A comprehensive overview of national recommendations and implementation initiatives involving HPV self-sampling is provided in Figure 2 and Supplementary Tables S1 and S2.

HPV self-sampling has progressively expanded in LMICs, increasing from 10 countries before the launch of the WHO cervical cancer elimination initiative in 2020 to 29 of 133 (22%) LMICs recommending HPV self-sampling by 2026—14 upper-middle-income, 11 lower-middle-income, and 4 low-income countries. Among these, 23 countries recommend self-sampling as the primary screening option for all women in the target population, while 6 restrict its use to under-screened populations. In most settings (21/29; 72%), HPV self-sampling was introduced alongside the adoption of HPV-based screening (Figure 2).[3]

However, policy endorsement does not necessarily translate into effective implementation. Although HPV testing and self-sampling are increasingly included in national cervical cancer screening recommendations, their translation into routine practice has been uneven, particularly in LMICs where financing, infrastructure, workforce, and service-delivery constraints limit scale-up. This implementation gap is reflected in the persistently low coverage of HPV-based screening

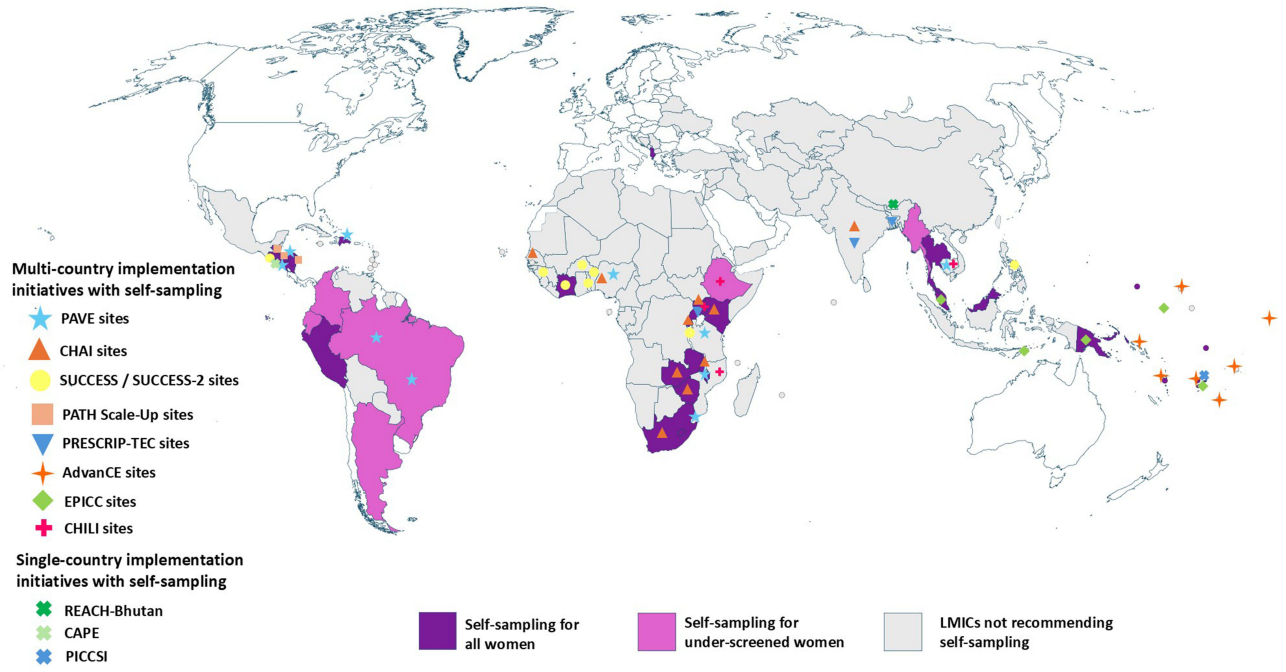

Figure 2 National recommendations and implementation initiatives involving HPV self-sampling for cervical cancer screening in LMICs, up to May 2026. Country colors indicate whether national recommendations include HPV self-sampling as a primary screening option for all screening-eligible women or specifically for under-screened populations. Symbols indicate selected multi-country and single-country implementation initiatives involving HPV self-sampling. For EPICC, only countries with explicitly documented use of HPV self-sampling were mapped. National recommendation classifications were based on the updated WHO cervical cancer screening coverage estimates for 2022,[3] supplemented by national policy documents, program information, and country-level updates available up to May 2026. The sources supporting each national recommendation and target-population classification are provided in Supplementary Table S1. The implementation initiatives, with their participating countries and supporting references are listed in Supplementary Table S2. This figure summarizes official recommendations on HPV self-sampling for cervical cancer screening and does not reflect the existence, organization, or implementation of screening programs within each country. The presence of a recommendation does not imply nationwide or homogeneous implementation.implementation.The boundaries shown and the designations used on this map do not imply the expression of any opinion whatsoever concerning the legal status of any country, territory, city or area or its authorities, or concerning the delimitation of its frontiers or boundaries.

Abbreviations: AdvanCE, Advancing Cervical Cancer Elimination in the Pacific; CAPE, Cervical Cancer Prevention in El Salvador; CHAI, Clinton Health Access Initiative; CHILI, Community-based HPV Screening Implementation in Low-Income countries; EPICC, Elimination Partnership in the Indo-Pacific for Cervical Cancer; HPV, human papillomavirus; LMICs, low- and middle-income countries; PAVE, HPV-Automated Visual Evaluation; PRESCRIP-TEC, Prevention and Screening Innovation Project Toward Elimination of Cervical Cancer; SUCCESS, Scale Up Cervical Cancer Elimination with Secondary Prevention Strategy.

in LMICs—estimated at only 2% in the previous 5 years in 2022—and the almost negligible coverage observed in low-income countries.[3] As a result, many programs continue to rely predominantly on cytology or VIA, despite their known performance limitations.

The remainder of this section focuses on selected country experiences and single-country and multi-country initiatives that illustrate different pathways for introducing HPV self-sampling into real-world service delivery, ranging from implementation research and demonstration projects to subnational and national programs. Additional initiatives represented in Figure 2, including Clinton Health Access Initiative (CHAI), Scale Up Cervical Cancer Elimination with Secondary Prevention Strategy (SUCCESS), Prevention and Screening Innovation Project Toward Elimination of Cervical Cancer (PRESCRIP-TEC), Community-based HPV Screening Implementation in Low-Income countries (CHILI), and PICCSI, are summarized in Supplementary Table S2, together with their participating countries and supporting references.

Although several LMICs now recommend HPV self-sampling, only a small number have progressed from pilot initiatives to routine implementation within national screening strategies. Argentina represents one of the clearest examples of real-world implementation. The strategy was first introduced in 2011 through the Jujuy Demonstration Project (the EMA study), in which self-sampling offered during home visits by community health workers (CHWs) increased screening uptake four-fold compared with referral for provider-based sampling (86% vs 20%).[15] Since 2014, self-sampling has been integrated into the National Cervical Cancer Prevention Program (PNPCC) as a complementary strategy to reach under-screened women, and has been progressively scaled up across the country, reaching 19 of 24 jurisdictions by 2023.[16,17] Implementation relies on trained CHWs offering self-sampling kits during household or community visits, with referral pathways for triage and treatment. This sustained integration within a national program, supported by routine program data, positions Argentina as an important proof of concept for self-sampling at scale in LMICs. However, recent financing and governance challenges highlight the vulnerability of such gains in the absence of sustained health-system support.[16,17]

Other programmatic experiences illustrate complementary pathways for implementing HPV self-sampling beyond pilot studies. The Cervical Cancer Prevention in El Salvador (CAPE) project provided early programmatic experience with HPV-based screening and self-sampling among women who had not attended cervical cancer screening for at least three years. Self-sampling was acceptable to non-attenders and helped identify access, knowledge, procedure-related, and confidentiality barriers.[18,19] CAPE was piloted and scaled up between 2012 and 2017, supporting adoption of HPV screen-and-treat within the national cervical cancer screening program.[20] In parallel, the Scale-Up project run by PATH in collaboration with national institutions in Nicaragua, Guatemala and Honduras saw a successful introduction of self-sampling and HPV DNA detection,[21] although regulatory barriers subsequently limited broader implementation.

More recently, a global initiative−the HPV-Automated Visual Evaluation (PAVE) study−used HPV self-sampling as a primary screening method across nine countries (Dominican Republic, El Salvador, Honduras, Brazil, Nigeria, Tanzania, Malawi, Eswatini, and Cambodia), paving the way for member nations to transition these research frameworks into real-world practice.[8,9,22] Part of this initiative was the Cervical Cancer Risk Management (MARCO) project in Brazil that piloted a decentralized model specifically designed to overcome geographic barriers in remote regions where the cytology-based national screening program was difficult to access. In two areas of the Brazilian Amazon, the project evaluated a single-day strategy utilizing self-sampling and near point-of-care (POC) HPV testing. By delivering rapid HPV results directly within the community, the proof-of-concept demonstrated that it is possible to screen a high volume of women daily and achieve high follow-up and treatment.[23] This experience underscores how single-day HPV self-sampling models can help bridge coverage gaps in hard-to-reach populations left underserved by traditional, multi-visit health facility networks.

In sub-Saharan Africa, Rwanda provides an example of self-sampling being embedded within a broader national HPV-based screening and treatment pathway.[24] Early experience from the Screen, Notify, See, and Treat program demonstrated the feasibility of HPV-based screening in public health facilities, while also highlighting challenges related to recruitment, loss to follow-up, confidentiality, and efficient use of resources.[25] Rwanda subsequently developed a national cervical cancer elimination strategy and operational guidelines for screening and treatment of precancerous lesions, with WHO support. In 2020, the country adopted HPV DNA testing, with national scale-up starting in 2021,[24,26]

supported by an electronic medical record system designed to track women across screening, triage, treatment, referral, and follow-up.[27] Program reports describe Rwanda's current model as integrating community-level education, self-sampling, HPV testing, portable treatment devices, digital patient tracking, and follow-up within the national health system.[28]

In Malawi, Médecins Sans Frontières (MSF), in partnership with local health authorities, has supported screening services across two southern districts since 2017 and is now building directly upon the PAVE study results. During the PAVE-Malawi project, self-sampling was offered both at established MSF-supported Ministry of Health facilities and through community strategies.[22] This experience demonstrated the high acceptability of self-sampling, reaching more than 6100 women during the study period and maintaining a 72% follow-up rate through targeted tracing and active follow-up strategies.[9] Following these positive outcomes, in 2025 the program officially transitioned to HPV testing with self-sampling as the routine standard of care under MSF.[29]

In Nigeria, implementation efforts under the PAVE framework focused on a highly structured, proactive outreach strategy designed to bring screening directly to the population.[22] Deployed as a door-to-door campaign, community mobilization teams first conducted a local population census and household mapping within target areas in the Osun State before directly offering self-sampling kits to eligible women. This micro-planned, census-driven strategy allowed the program to systematically maximize geographic reach to nearly 8000 women during the study period and actively identify underserved women, providing a robust operational model that has informed subsequent national elimination strategies led by the National Taskforce on Cervical Cancer Elimination.[30]

In Asia, Bhutan, Thailand and Malaysia illustrate different pathways from implementation research to program adoption. In Bhutan, the REACH-Bhutan study demonstrated the feasibility and acceptability of community-based screening using self-collected samples for HPV testing in rural settings,[31] supporting the subsequent transition to primary HPV DNA screening under the national Health Flagship Program. The program includes HPV self-sampling and has achieved a reported 77% ever-screened coverage among the target population.[32] Thailand has transitioned from cytology to HPV-based screening and introduced self-sampling options, in 2023, within its national screening program.[33] Malaysia's Program Removing Obstacles to cervical ScrEening (ROSE) targets women eligible for cervical cancer screening, particularly under-screened and underserved populations, through a user-centered model that combines self-sampling for primary HPV testing, centralized laboratory processing, and an e-health platform for results communication and follow-up.[34]

Across the Pacific Islands, regional initiatives are increasingly embedding self-sampling within HPV-based screen-and-treat models, often using POC HPV testing and same-day treatment to address geographic dispersion and limited access to specialist services.[35,36] The regional Advancing Cervical Cancer Elimination in the Pacific (AdvanCE) program will support HPV-based screening and treatment for 130,000 women in Fiji, Kiribati, the Republic of the Marshall Islands, Samoa, Solomon Islands, Tonga, and Vanuatu, using a screen-and-treat model based on self-sampling, POC HPV testing with Xpert HPV assay, and same-day treatment or referral to the specialist services when indicated.[36] Early national and subnational experiences in Papua New Guinea, Tuvalu, Fiji, and Vanuatu further illustrate how self-collection, rapid HPV testing, and decentralized same-day care are being used to overcome access barriers across island settings; notably, Tuvalu has already reached the WHO 70% screening target, with 76% of eligible women screened.[37–42]

Together, these selected experiences illustrate how the transition from implementation research to routine service delivery is shaped by the target population, delivery model, follow-up and treatment capacity, and the broader health-system context.

Health System Barriers and Considerations Along the Care Cascade

Building upon the country implementation models presented above, this section provides an analytical discussion of the operational bottlenecks, health-system requirements, and considerations along the multi-step clinical care cascade.

The evidence synthesized in this review underscores the potential of self-sampling to close the screening gap for the most vulnerable populations. However, the transition from research pilots to national-scale intervention is rarely seamless. Self-sampling does offer a critical opportunity for equity, but this opportunity can only be realized if the act of sampling is viewed not as a standalone event, but as the entry point to a multi-step clinical cascade.[43,44] In resource-

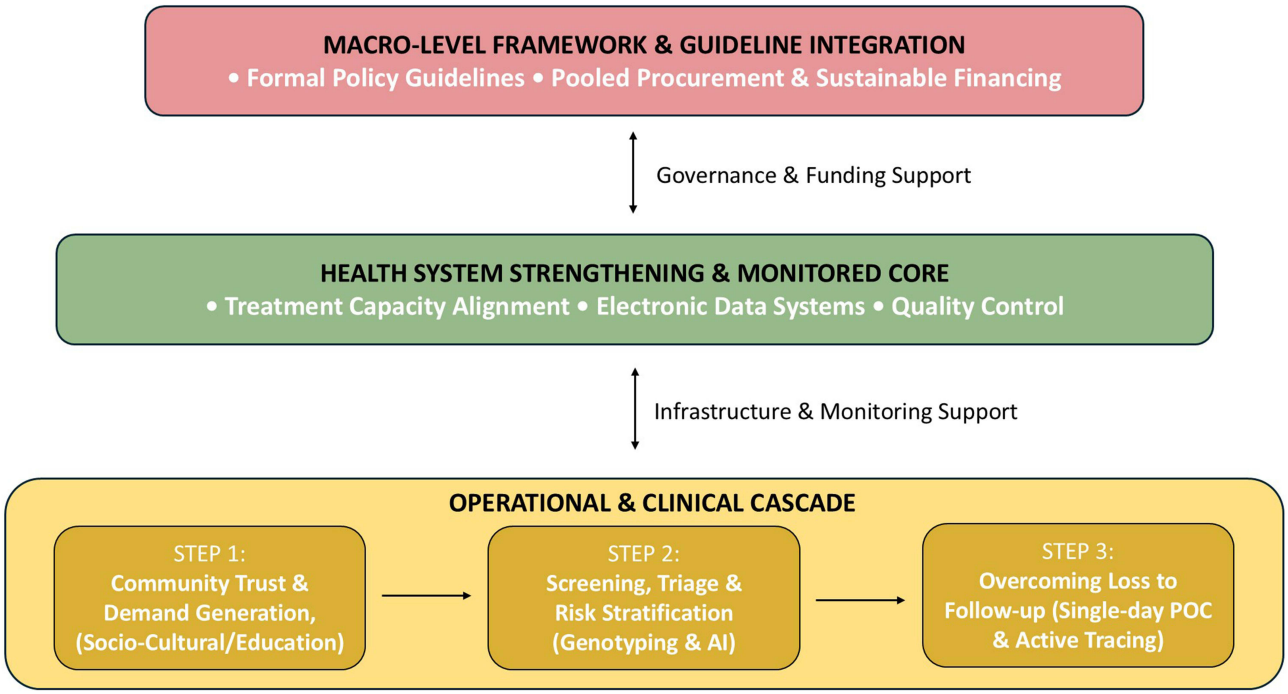

Figure 3 Conceptual framework for scaling HPV self-sampling from research pilots to national health system integration. The multi-level model illustrates the dynamic interaction between the horizontal operational and clinical cascade (steps 1–3: patient engagement, triage/risk stratification, and active loss-to-follow-up reduction) and the supporting vertical infrastructure. The patient care pathway relies on continuous support from the health system core (treatment capacity, digital data registries, and quality monitoring) and the overarching macro-level framework (national policy guidelines, financing, and pooled procurement). Bidirectional arrows denote ongoing operational and policy feedback required for sustainable program implementation.
Abbreviations: AI, artificial intelligence; POC, point-of-care (HPV testing).

limited settings, introducing self-sampling can increase screening enrollment, consequently demanding increased health system capacity to absorb and manage a larger volume of screen-positive individuals.

Stakeholders must move beyond the distribution of kits and address the operational requirements needed to prevent the screening process from stalling after the initial sample is collected. A conceptual framework presented in Figure 3 illustrates how the horizontal clinical care cascade (community trust, triage/risk stratification, and active loss-to-follow-up reduction) depends on continuous bidirectional support from core health-system infrastructure (treatment capacity, digital tracking, quality control) and macro-level governance (national guidelines, pooled procurement, and sustainable financing). Without a comprehensive plan to address these systemic requirements, the gains in screening coverage achieved through self-sampling may not translate into a measurable reduction in cervical cancer incidence and mortality.

Addressing Educational and Socio-Cultural Needs

Successful implementation of HPV self-sampling requires bridging the gap between technological availability and community trust through community engagement and targeted demand generation (Figure 3, Cascade - Step 1). A key challenge is adapting educational materials to reflect the shift from visual-based methods to molecular testing. Unlike VIA, which provides immediate visual feedback, educational materials must clearly explain why a positive HPV result is meaningful even if the cervix looks "normal" on visual examination and why management may differ according to the HPV type detected, the woman's underlying risk, and the screening algorithm used.

Education must also address the fear of "doing it wrong", as some women may have greater confidence in samples collected by a healthcare provider than in samples collected by themselves.[14] High-quality, culturally tailored instructions are essential to reassure users of the high accuracy of self-collection. Evidence shows that when self-sampling is offered as the primary, standard screening method, it achieves high acceptability among the population.[13] However, when programs instead offer a choice between provider-collected sample and self-sampling, some women may prefer the direct

interaction and relationship with a healthcare provider.[45,46] Education should frame self-sampling as an accurate and safe primary screening option while making clear that sampling is only the first step in a longitudinal care pathway.

Beyond individual education, HPV self-sampling programs must be adapted to local sociocultural realities. In sub-Saharan Africa, qualitative evidence points to social stigma, misinformation, and the influence of cultural norms and religion as recurring community-level barriers to acceptability and uptake of self-sampling and cervical screening.[47] In focus groups studies, husband disapproval is often identified as a key barrier to self-sampling.[45,46] For these reasons, implementation strategies should engage trusted community leaders and involve men to reduce stigma and create a supportive environment for both initial uptake and adherence to the full care cascade.

Navigating the Triage and Treatment Bottleneck

The effectiveness of any self-sampling program is ultimately determined by the efficiency of the clinical cascade that follows a positive HPV result.[48] WHO guidelines include "screen-and-treat" algorithms in which treatment eligibility is assessed following a positive HPV screening result without an additional triage test, as well as "screen-triage-treat" algorithms that use an additional test to determine management.[7,49] In regions with high HPV prevalence, such as many LMICs and particularly in sub-Saharan Africa, managing all eligible HPV-positive women through a screen-and-treat approach often demands a level of treatment capacity that health systems cannot realistically sustain. Consequently, the reality for many LMIC programs is reliance on "screen-triage-treat" algorithms to prioritize treatment while reducing unnecessary procedures. Triage methods commonly used in high-income countries—such as cytology, colposcopy, and dual staining—may be feasible only in some middle-income economies and typically only effective in urban areas. In contrast, in most low-income settings, the most common triage method is VIA, either alone for all HPV-positive women or in combination with limited HPV genotyping, where immediate treatment is prioritized for women positive for HPV16/18 and VIA is reserved for women positive for other high-risk types. However, VIA has important limitations even as a triage test, including subjectivity and low performance,[2] which can result in both overtreatment and missing high-grade lesions.

Recent WHO guidelines recommend moving toward extended genotyping,[49] shifting the focus from limited genotyping (HPV16/18) to a more nuanced risk stratification (also from triage only to a primary and triage in one test result), allowing the primary HPV result itself to inform both screening and triage decisions (Figure 3, Cascade - Step 2). By grouping HPV types according to their oncogenic risk (group 1a: HPV16; group 1b: HPV18/45; group 1c: alpha-9 types HPV31/33/35/52/58; group 1d: HPV39/51/56/59), immediate treatment resources can be directed to those at highest risk. The PAVE study has already reported successful risk stratification using this approach, with cervical intraepithelial neoplasia grade 3 or worse (CIN3+) risks ranging from 2% to 20%, providing a template for how molecular data can optimize clinical management in LMICs.[8,9]

Parallel to these molecular advances, artificial intelligence (AI)-assisted triage is being evaluated as a strategy to reduce the subjectivity of visual evaluation. When a speculum examination is required after an HPV positive result to perform triage or assess eligibility for treatment, a digital image of the cervix can be captured simultaneously at virtually no extra cost and processed using an AI algorithm. Algorithms trained on robust histopathological endpoints could provide a more objective and scalable triage approach in settings where traditional colposcopy and pathology are rarely available. Findings from the PAVE study suggest that AI can add a powerful layer of risk stratification when combined with HPV extended genotyping.[8,9] Several AI algorithms are currently undergoing development and validation, including initiatives led by the International Agency for Research on Cancer (IARC) and CHAI, when added to self-sampling and HPV testing.[50–52] External validation remains a critical prerequisite before different algorithms can be robustly compared or regulated and incorporated into routine program decision-making. The performance of AI-assisted visual triage among women without a visible squamo-columnar junction drops and clinical management is unclear.[9] In these situations, endocervical sampling to exclude hidden lesion would be indicated provided that pathology is available.

Overcoming the "Loss to Follow-Up" Challenge

Loss to follow-up (LTFU) is a major barrier to the effectiveness of HPV self-sampling programs. It may occur at any point in the care cascade when individuals with a positive screening result do not complete the recommended triage,

diagnostic assessment, or treatment. Here we will focus specifically on the LTFU after a positive HPV result on a self-collected sample, particularly the failure to complete the recommended triage or treatment.

One promising strategy for reducing LTFU is the implementation of POC or near POC HPV testing technologies combined with single-day strategies, which aim to minimize the number of required clinical encounters ensuring that the majority of HPV-positive women receive care on the same day (Figure 3, Cascade - Step 3). Technological advancements are rapidly moving toward decentralized molecular diagnostics, with platforms such as Xpert HPV and the ScreenFire HPV risk stratification (RS) assay already showing high performance in field settings.[8,9,37,53,54] Recent evidence from a proof-of-concept part of the MARCO project study using the ScreenFire HPV RS assay as a near-POC solution in the Brazilian Amazon demonstrated the feasibility of screening approximately 100 women per day with a follow-up rate exceeding 99%, illustrating the transformative power of single-day strategies in remote areas.[23]

Furthermore, innovative simplified assays are being developed to bridge the access gap in the most remote settings. Recently developed paper-based hybrid capture assay[55] or isothermal amplification POC tests[56,57] offer promising solutions requiring minimal instrumentation and few simple steps, though they currently focus on HPV16/18 rather than extended genotyping. The urgent need for accurate, rapid, and affordable genotyping assays is emphasized by the WHO Target Product Profiles (TPP) for HPV screening tests,[58] which provide clear requirements for the private sector by listing the essential characteristics required for tests to be fit-for-purpose in low-resource environments.

Until full POC becomes available, interventions continue to rely on multi-day strategies and the success of follow-up depends on robust human-resource frameworks and active tracing activities (Figure 3, Cascade - Step 3). Dedicated teams, including targeted call centers and CHWs, are crucial for maintaining high follow-up rates by providing personalized navigation through the health system. Here, extended genotyping can also serve as a prioritization tool, issuing a high-priority "order" for immediate recall (HPV16 as most urgent, followed by HPV18/45, group 1c, and lastly group 1d). This risk-stratified approach ensures that women at highest risk are followed and are not lost along the cascade.

Furthermore, in settings with a high burden of HIV, the integration of cervical screening with HIV services offers a powerful mechanism to reduce the gaps in screening, follow-up and treatment. Since WLWH are regularly followed within antiretroviral therapy clinics, these regular touchpoints provide an ideal opportunity to offer integrated cervical cancer screening and care. The US President's Emergency Plan for AIDS Relief (PEPFAR)-supported Go Further partnership, launched in 2018, provides an example of this model, integrating cervical cancer screening and treatment services within existing HIV treatment and women's health services in 12 countries with a high HIV burden in sub-Saharan Africa.[59] By embedding self-sampling and immediate follow-up into routine HIV visits, programs can leverage existing clinical infrastructure to ensure these high-risk women are screened and treated without the need for additional, separate appointments, thereby maximizing both clinical resources and patient retention.[60–62]

Strengthening System Readiness: Treatment Capacity and Program Monitoring

Beyond the technicalities of collection and triage lies the foundational challenge of health system readiness. While self-sampling effectively increases the volume of women screened, it simultaneously risks exposing—and overwhelming—pre-existing gaps in treatment capacity. Implementation must therefore begin with a pragmatic assessment of available treatment resources, both ablative and surgical. In fragile healthcare systems, a sudden surge in screen-positive cases without a corresponding increase in treatment infrastructure can lead to system strain, long waiting lists and LTFU at the treatment stage. To prevent the collapse of these services, scaling up screening must be synchronized with planned expansion of the clinical workforce, equipment and referral capacity, using phased implementation where appropriate.[63]

A "ready system" requires robust data systems, quality control, and program monitoring (Figure 3, Health System Core). A dedicated electronic data collection tool is key to track each woman from sample collection and laboratory testing through communication of results, triage, referral, and confirmation of treatment. Monitoring must go beyond simple uptake numbers; it requires the tracking of key performance indicators to measure the efficiency of the entire cascade, such as the proportion of HPV-positive women who successfully complete triage and treatment within defined timeframes. Continuous quality control of laboratory assays and digital tracking of clinical follow-up

is needed to identify bottlenecks in real-time. Without effective electronic tracking systems and clearly defined performance indicators, self-sampling risks remaining a fragmented research intervention rather than a cohesive, scalable and sustainable public health strategy.

These are inherently complex tasks for implementers, and while specific operational manuals and technical recommendations exist to guide these efforts—such as those published by the WHO[63–65] —their application requires adaptation to the local context, sustained human and financial resources and long-term political and health system commitment.

Navigating Cost-Effectiveness, Scalability, and Policy Integration

Successfully scaling HPV self-sampling from research projects to a sustainable national program relies heavily on its formal integration into national guidelines (Figure 3, Macro-Level Framework). Rather being treated as a secondary auxiliary option, national frameworks must officially recognize self-sampling as a primary entry point for screening. Formal policy integration is essential to secure long-term political commitment, anchor health infrastructure, and align multi-sectoral stakeholders. Robust evidence from health-economic studies supports that HPV testing on self-collected samples is cost-effective and often the only viable way to achieve widespread screening coverage in low-resource environments.[66–69]

Achieving cost-effective implementation at scale also requires overcoming regulatory and supply-chain barriers. National programs must ensure that validated collection devices and HPV assays are legally registered for import and use within the country. Once cleared, health ministries and international procurement agencies must establish robust procurement processes and are encouraged to utilize large joint tenders and pooled purchasing agreements to disrupt high retail unit prices. Aggregating demand across multiple jurisdictions (eg, regions, states, or even multi-country coalitions) creates the market volume necessary to pressure manufacturers into lowering costs, making wide-scale procurement economically feasible.[70–72] Finally, sustainable implementation requires moving from short-term donor-funded research or demonstration projects towards long-term national budget lines. This transition should be supported by transparent private-public coordination with health ministries, procurement agencies, manufacturers, distributors, laboratories, service providers, and resilient supply chains.

Conclusions and Synthesis of the Path Forward

HPV self-sampling offers a promising approach to transform cervical cancer screening into an active, community-centered tool that optimizes health system resources by reducing reliance on primary speculum examinations. By expanding access among under-screened populations while improving the service delivery efficiency, self-sampling has driven substantial global momentum across Latin America, sub-Saharan Africa, and the Asia-Pacific region as programs transition from localized demonstration projects toward routine national practice. However, self-sampling cannot act as a standalone intervention; its success depends on integration within a broader health-system framework that supports a longitudinal clinical cascade through robust risk-based management, digital data networks, active patient tracking, and matched treatment capacity. While current evidence relies primarily on observational pilots and emerging programmatic reports, these real-world experiences demonstrate that with sustained political, financial, and structural commitment, HPV self-sampling provides a pragmatic, scalable pathway toward global cervical cancer elimination.

AI Declaration

During the preparation of this work the authors used artificial intelligence tools—Gemini (Google, version 3.5), ChatGPT (OpenAI, version 5.5), and Copilot (Microsoft, version Smart)—to improve the readability and language of the manuscript. After using those tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Author Contributions

All authors (FI, BS, and SdS) made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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