JURNAL MANAJEMEN INFORMASI KESEHATAN
(HEALTH INFORMATION MANAGEMENT)
Volume 11, Issue 1, 2026 | Page 575-588
E-ISSN: 2622-0423 | P-ISSN: 2503-5118
https://ojs.stikessaptabakti.ac.id/jmis
https://doi.org/10.51851/jmis.v11i1.1103

Cost-Effectiveness of Human Papillomavirus (HPV) Testing for Cervical Cancer Screening: A Systematic Literature Review

Erni Anggraeni[1], Elismi Haryanti[2], Marilia de Jesus dos Reis[3], Paulina Fonseca de Carvalho[4], Firdaus Hafidz[5], Mufdlilah[6]

[1,2,3,4]Master of Midwifery Program, Faculty of Health Sciences, Universitas 'Aisyiyah Yogyakarta, Yogyakarta, Indonesia
[5]Department of Health Policy and Management, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia
[5]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, United Kingdom
[6]Department of Midwifery, Faculty of Health Sciences, Universitas 'Aisyiyah Yogyakarta, Yogyakarta, Indonesia

ernianggraeni588@gmail.com

ARTICLE INFO

Keywords:
Cervical cancer; Cost-effectiveness analysis; HPV testing; Screening; Systematic review.

Article History:
Received: 7/8/2026
Revised: 7/20/2026
Accepted: 8/13/2026

ABSTRACT

Background: Cervical cancer remains an important cause of morbidity and mortality, particularly in low- and middle-income countries (LMICs). HPV-based screening is recommended because of its higher sensitivity than conventional screening; however, evidence on the economic value of HPV screening strategies remains heterogeneous. This systematic review synthesized evidence on the clinical and economic effectiveness of HPV-based cervical cancer screening strategies.
Methods: A systematic review was conducted according to PRISMA guidelines and registered in PROSPERO (CRD420261442108). PubMed, Scopus, SpringerLink, RIS HTA, and NICE were searched for studies published from 2015 to 2026. Twenty-two studies met the eligibility criteria. Findings were synthesized narratively because heterogeneity in economic models, costing methods, outcome measures, and willingness-to-pay thresholds precluded meta-analysis.
Results: Twenty-one studies (95.5%) concluded that HPV-based screening was cost-effective, highly cost-effective, cost-saving, or dominant compared with conventional approaches, while one study (4.5%) reported that it was not cost-effective in its specific context. Primary HPV testing, HPV self-sampling, and strategies incorporating genotyping or risk-based triage improved detection of cervical intraepithelial neoplasia and reduced cervical cancer incidence and mortality. ICERs varied considerably across countries and strategies, from cost-saving to values below willingness-to-pay thresholds. HPV self-sampling was economically favorable in settings with low screening coverage, whereas primary HPV testing with genotyping or risk-based triage was more efficient in health systems with established infrastructure.
Conclusion: HPV-based screening provides clinical and economic value compared with conventional approaches. Implementation should be tailored to local health system capacity, healthcare costs, screening coverage, and population characteristics to maximize health benefits and efficiency.

How to cite this article:
Erni A, Elismi H, Marilia D, Paulina F, Firdaus H, Mufdlilah, (2026). Cost-Effectiveness of Human Papillomavirus (HPV) Testing for Cervical Cancer Screening: A Systematic Literature Review, 11(1). 575-588. https://doi.org/10.51851/jmis.v11i1.1103103

INTRODUCTION

Cervical cancer remains a major global public health challenge and is one of the leading causes of cancer-related morbidity and mortality among women. According to the World Health Organization (WHO), cervical cancer is the fourth most common cancer among women worldwide, with a disproportionate burden occurring in low- and middle-income countries (LMICs), where access to preventive screening, diagnosis, and treatment services remains limited (World Health Organization, 2023). In 2022, an estimated 660,000 new cases of cervical cancer and approximately 350,000 deaths were reported globally, highlighting the substantial health and economic burden associated with this preventable disease (Petersen et al., 2022).

Persistent infection with high-risk human papillomavirus (hr-HPV), particularly HPV types 16 and 18, is recognized as the necessary causal factor for nearly all cervical cancer cases (National Cancer Institute, 2024). Although most HPV infections are transient, persistent infection may progress from cervical intraepithelial neoplasia (CIN) to invasive cervical cancer if left undetected and untreated (Karimah et al., 2025). Consequently, effective cervical cancer screening plays a critical role in secondary prevention by enabling early detection and treatment of precancerous lesions, thereby reducing disease incidence and mortality.

For several decades, cytology-based screening using the Papanicolaou (Pap) smear has served as the standard approach for cervical cancer screening (Burd, 2003). However, advances in molecular diagnostics have demonstrated that HPV DNA testing offers substantially higher sensitivity for detecting high-grade cervical precancerous lesions than conventional cytology while allowing longer screening intervals because of its higher negative predictive value (Dasgupta, 2026). Based on accumulating evidence, the WHO now recommends HPV DNA testing as the preferred primary screening method for cervical cancer because of its superior clinical performance (World Health Organization, 2021).

In recent years, several HPV-based screening strategies have been developed to improve screening effectiveness and population coverage. These include primary HPV testing, HPV self-sampling, HPV genotyping, and HPV testing combined with risk-based triage. Each strategy has distinct clinical and operational characteristics that may influence screening participation, diagnostic accuracy, follow-up compliance, and healthcare resource utilization. For example, HPV self-sampling has the potential to increase participation among women who are reluctant or unable to attend facility-based screening, whereas HPV genotyping and risk-based triage may improve diagnostic precision and optimize referral pathways.

Despite their clinical advantages, HPV-based screening strategies generally require greater initial investment than conventional screening because they involve molecular diagnostic technologies, laboratory infrastructure, quality assurance systems, and follow-up management. Consequently, economic evaluation has become increasingly important for determining whether the additional costs associated with HPV-based screening are justified by improvements in health outcomes. Economic evaluations typically assess costs in relation to outcomes such as quality-adjusted life years (QALYs), life years gained (LYGs), disability-adjusted life years (DALYs), and incremental cost-effectiveness ratios (ICERs), thereby providing evidence to support efficient healthcare resource allocation (Kurniawan, 2025).

Numerous economic evaluation studies have compared HPV-based screening with conventional screening approaches, including Pap smear, liquid-based cytology (LBC), visual inspection with acetic acid (VIA), co-testing, or no screening. Overall, these studies suggest that HPV-based screening generally improves health outcomes while offering favorable economic value; however, the reported cost-effectiveness varies considerably across countries and healthcare systems because of differences in screening intervals, target populations, model assumptions, healthcare costs, screening participation rates, and willingness-to-pay (WTP) thresholds (Ang & Tay, 2025; Wibawa et al., 2024; Williams et al., 2022; Wong et al., 2021).

Although the number of economic evaluations has increased substantially over the past decade, their findings remain highly heterogeneous. Differences in screening strategies, economic perspectives,

costing methods, time horizons, healthcare system characteristics, and country-specific WTP thresholds make direct comparisons difficult and limit the generalizability of individual study findings. As a result, policymakers continue to face uncertainty regarding which HPV-based screening strategy provides the greatest economic value under different implementation contexts.

Previous systematic reviews have also presented important limitations. Most have focused on a single HPV-based intervention, particularly HPV self-sampling, or have restricted comparisons to HPV testing versus conventional cytology. In addition, many reviews have primarily emphasized clinical effectiveness while providing only limited synthesis of economic outcomes. Consequently, there remains a lack of comprehensive evidence that simultaneously compares multiple HPV-based screening strategies including primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage using standardized economic indicators such as ICERs, QALYs, LYGs, DALYs, and country-specific WTP thresholds. Furthermore, previous reviews have rarely examined how contextual factors, including healthcare system capacity, country income level, screening coverage, economic evaluation perspective, and model assumptions, influence the cost-effectiveness of HPV-based screening strategies across different settings.

The WHO Global Strategy to Accelerate the Elimination of Cervical Cancer, commonly referred to as the 90–70–90 strategy, recommends that 70% of women undergo screening using a high-performance HPV test by the ages of 35 and 45 years (Lee et al., 2023; Wang et al., 2023). Achieving this target requires screening programs that are not only clinically effective but also economically sustainable. However, because epidemiological characteristics, healthcare infrastructure, resource availability, and healthcare financing differ substantially between countries, the most economically efficient HPV-based screening strategy is unlikely to be universal. Therefore, synthesizing evidence across diverse economic settings is essential to support context-specific policy decisions.

This systematic review addresses these gaps by providing a comprehensive synthesis of economic evaluations across multiple HPV-based cervical cancer screening strategies rather than focusing on a single intervention. Unlike previous systematic reviews, this review simultaneously compares primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage across diverse healthcare settings while integrating both clinical effectiveness and economic outcomes. In addition, this review examines how contextual factors—including country income level, healthcare system characteristics, screening infrastructure, economic perspective, time horizon, and willingness-to-pay thresholds influence the cost-effectiveness of HPV-based screening strategies. By integrating these dimensions into a single comparative synthesis, this review provides a broader and more policy-relevant understanding of the economic value of HPV-based cervical cancer screening, thereby offering novel evidence to support decision-makers in selecting the most appropriate screening strategy according to local health system capacity and resource availability.

This systematic literature review aimed to synthesize the available evidence regarding the clinical effectiveness and cost-effectiveness of HPV-based cervical cancer screening strategies. Specifically, the review compared the economic value of primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage across different healthcare settings by evaluating ICERs, willingness-to-pay thresholds, and other economic outcomes to identify the most economically efficient strategies for cervical cancer screening.

METHOD

Study Design

This study was conducted as a systematic literature review (SLR) to identify, critically appraise, and synthesize the available evidence regarding the clinical effectiveness and cost-effectiveness of human papillomavirus (HPV)-based cervical cancer screening strategies. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines (Page et al., 2021), which provide internationally recognized standards for reporting systematic reviews. To enhance methodological transparency and minimize the risk of selective reporting bias, the review protocol

was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420261442108 before the literature search was initiated.

The review question was formulated using the Population, Intervention, Comparator, and Outcome (PICO) framework. The population comprised women eligible for cervical cancer screening. The interventions included HPV-based screening strategies, such as primary HPV DNA testing, clinician-collected HPV testing, HPV self-sampling, HPV genotyping, and other HPV-based screening approaches. These interventions were compared with conventional screening methods, including Papanicolaou (Pap) smear, liquid-based cytology (LBC), visual inspection with acetic acid (VIA), co-testing, or the absence of screening. The primary outcomes of interest were economic evaluation measures, including incremental cost-effectiveness ratios (ICERs), quality-adjusted life years (QALYs), disability-adjusted life years (DALYs), life years gained (LYGs), health-adjusted life years (HALYs), total program costs, and the overall economic conclusions reported by each study, such as cost-effective, highly cost-effective, cost-saving, or dominant.

Literature Search Strategy

A comprehensive literature search was conducted across five electronic databases, namely PubMed, Scopus, SpringerLink, the Health Technology Assessment Database (RIS HTA), and the National Institute for Health and Care Excellence (NICE). Studies published between January 2015 and May 2026 in either English or Indonesian were considered eligible. The search strategy combined Medical Subject Headings (MeSH) with free-text keywords related to cervical cancer, HPV screening, and economic evaluation using Boolean operators (AND and OR). The initial search strategy was developed for PubMed and subsequently adapted to the indexing system and search syntax of each database to maximize retrieval sensitivity. The primary search terms included combinations of "cervical cancer," "cervical neoplasm," "human papillomavirus," "HPV testing," "HPV DNA test," "primary HPV testing," "HPV self-sampling," "cervical cancer screening," "economic evaluation," "cost-effectiveness," "cost utility," "incremental cost-effectiveness ratio," and related terms. To ensure that no relevant studies were overlooked, the reference lists of all eligible articles and relevant review papers were manually screened to identify additional studies that met the inclusion criteria.

Eligibility Criteria

Studies were included if they were published as full-text articles in English or Indonesian between January 2015 and May 2026 and evaluated at least one HPV-based cervical cancer screening strategy, including clinician-collected HPV testing, primary HPV testing, HPV self-sampling, HPV genotyping, or HPV-based risk stratification approaches. Eligible studies were required to compare HPV-based screening with conventional screening methods, including Pap smear, liquid-based cytology, visual inspection with acetic acid, co-testing, or no screening, and to report economic outcomes such as ICERs, QALYs, DALYs, HALYs, life years gained, life years saved, program costs, or other recognized economic evaluation measures. Studies employing cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis, cost-minimization analysis, or health technology assessment methodologies were considered eligible. Studies focusing exclusively on cervical cancer treatment without evaluating screening interventions, studies that did not report economic outcomes, conference abstracts, editorials, letters to the editor, opinion articles, laboratory or animal studies, duplicate publications, and articles without accessible full-text versions were excluded from the review.

Study Selection

All retrieved records were imported into Rayyan.ai to facilitate reference management and duplicate removal. Duplicate records identified automatically by the software were verified manually before the screening process commenced. Two reviewers independently screened the titles and abstracts of all retrieved records according to the predefined eligibility criteria. Articles considered potentially relevant subsequently underwent full-text assessment by the same reviewers. Reasons for exclusion during the full-text review were documented in accordance with the PRISMA 2020 recommendations to ensure transparency throughout the selection process. Any disagreements between reviewers were resolved

through discussion until consensus was reached. When consensus could not be achieved, a third reviewer independently evaluated the study and made the final decision regarding its inclusion. The complete study selection process was summarized using a PRISMA 2020 flow diagram.

Quality Assessment

The methodological quality of the included studies was independently assessed by two reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Economic Evaluations, which consists of eleven domains evaluating key methodological aspects of economic evaluation studies (Gomersall et al., 2020). The checklist assesses the appropriateness of the study perspective, identification of alternatives, measurement of costs and outcomes, valuation methods, discounting procedures, incremental analysis, sensitivity analysis, and transparency of reporting. Quality assessment was performed independently, and any discrepancies between reviewers were resolved through discussion or consultation with a third reviewer when necessary.

Data Extraction

Data extraction was performed independently by two reviewers using a standardized data extraction form specifically developed for this review. Prior to formal data extraction, the form was piloted using several eligible studies to ensure consistency and completeness. The extracted information included the author, publication year, country, study design, study population, screening intervention, comparator, economic evaluation method, analytical perspective, decision model, time horizon, discount rate, currency, cost components, effectiveness measures, ICER values, willingness-to-pay thresholds, sensitivity analysis results, overall economic conclusions, and methodological quality scores based on the JBI checklist. After independent extraction, the results from both reviewers were compared to identify inconsistencies. Any discrepancies were resolved through discussion, and unresolved differences were adjudicated by a third reviewer to ensure data accuracy and reliability.

Data Synthesis

A quantitative meta-analysis was not performed because substantial methodological heterogeneity existed among the included studies. The studies differed considerably with respect to economic evaluation methodology, analytical perspective, decision-analytic models, screening strategies, screening intervals, target populations, healthcare system characteristics, costing methods, currencies, outcome measures, and country-specific willingness-to-pay thresholds. These differences precluded statistical pooling of results and would have limited the interpretability of summary effect estimates. Therefore, a narrative synthesis was considered the most appropriate approach to integrate the available evidence. The synthesis was conducted by grouping studies according to HPV-based screening strategy, including primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage, and comparing their clinical and economic outcomes across different healthcare settings. Additional comparisons were made based on country income classification, analytical perspective, implementation context, and economic outcomes, including ICERs, QALYs, DALYs, program costs, and willingness-to-pay thresholds. This approach enabled identification of consistent patterns in the economic performance of HPV-based screening strategies while considering differences in healthcare systems and resource availability across countries.

RESULTS AND DISCUSSION

Results

Study selection

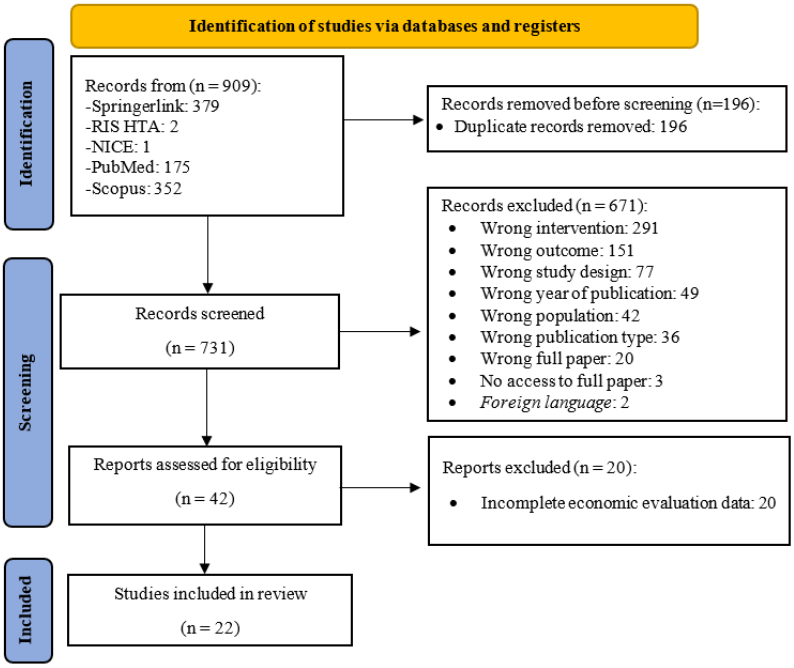

Figure 1. PRISMA 2020 flow diagram of the study selection process

A total of 909 records were found via database searches. Subsequent to the screening process, 671 publications were removed due to ineligible population (n=48), intervention (n=291), outcomes (n=151), study design (n=77), publication year (n=49), publication type (n=36), language (n=2), unavailability of full text (n=20), or inaccessibility of articles (n=3). Forty-two papers were subjected to full-text evaluation, resulting in the exclusion of 20 research that did not present economic evaluation outcomes. Ultimately, 22 research fulfilled the qualifying criteria and were incorporated into the narrative synthesis (Figure 1).

Characteristics of Included Studies

This review included 22 economic evaluation studies. Most studies employed cost-effectiveness analysis (CEA) (n = 19), while two used cost-utility analysis (CUA) and one applied cost-benefit analysis (CBA); several studies also incorporated budget impact analyses or trial-based economic evaluations. Markov and Policy1-Cervix were the most frequently used economic models, alongside microsimulation, hybrid, dynamic mathematical, and DICE simulation models. The studies were conducted across diverse settings, including Asia (n = 11), Europe (n = 4), North America (n = 3), Africa (n = 2), South America (n = 1), and one multicountry study involving 78 low- and middle-income countries. Most evaluated women aged 30–65 years using hypothetical or population-based screening cohorts. The interventions primarily consisted of primary HPV testing, HPV self-sampling, extended HPV genotyping, and HPV-based screening combined with triage or screen-and-treat strategies, which were compared with conventional screening methods, including Pap smear, liquid-based cytology (LBC), visual inspection with acetic acid (VIA), clinician-collected HPV testing, co-testing, or no screening. The studies commonly reported economic outcomes such as incremental cost-effectiveness ratios (ICERs), program costs, screening costs, and treatment costs, together with clinical outcomes including quality-adjusted life years (QALYs), life years gained (LYGs), disability-adjusted life years (DALYs), health-adjusted life years (HALYs), cervical cancer incidence and mortality, precancer detection rates, referral rates, and screening participation rates.

Quality Assessment

The methodological quality of the included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Economic Evaluations. Overall, the studies demonstrated high methodological quality, with scores ranging from 10 to 11 out of 11. Of the 22 studies, 20 (90.9%) achieved

the maximum score, indicating strong adherence to recommended standards for economic evaluation. The remaining two studies (9.1%) received a score of 10/11 because they did not adequately report adjustments for the differential timing of costs and outcomes. Nevertheless, no study was judged to have a high risk of methodological bias, and all 22 studies were considered sufficiently robust for inclusion in the final evidence synthesis.

Cost Characteristics of Included Studies

The studies presented significant variability in the parameters of economic evaluations (Table 1). Analytical views encompassed society (n=5), healthcare payer (n=5), healthcare system (n=3), provider or service provider (n=3), restricted societal (n=2), public health system (n=1), Ministry of Health (n=1), and two research that did not delineate the analytical perspective. The time horizons varied from 8 days to 100 years, with the majority of studies utilising lifetime or long-term perspectives to encompass the enduring costs and health implications of cervical cancer prevention.

Table 1. Cost characteristics of the included economic evaluation studies (n = 22)

Study	Perspective	Time Horizon	Currency	Cost Components	Intervention Cost	Comparator Cost
A1 Jansen et al. (2021)	Societal	Lifetime	Euro (€)	Screening test; diagnosis and treatment of precancerous lesions; cancer treatment; palliative care	€45 million (Primary HPV)	€57 million (No screening)
A2 Zhou et al. (2025)	Healthcare system	30 years	USD ($)	Screening; vaccination; cancer treatment	USD 10.35 (HPV)	USD 2.50 (VIA)
A3 Dimitrova et al. (2024)	Payer & Societal	5 years	Euro (€)	HPV/Pap test; physician visits; colposcopy; productivity loss	€43,580,902 (HPV DNA genotyping)	€83,590,104 (Pap smear)
A4 Hafidz et al. (2024)	Societal & Healthcare	5 years	USD ($)	Direct medical costs; indirect medical costs; cancer treatment	USD 201.23 (HPV DNA)	USD 90.62 (VIA); USD 105.44 (Pap smear)
A5 Nguyen et al. (2022)	Service provider	Lifetime	USD ($)	HPV/VIA testing; thermal ablation; biopsy; cancer treatment	USD 18 (HPV)	USD 6 (VIA)
A6 Choi et al. (2023)	Societal	Lifetime	USD ($)	Screening; precancer management; cancer treatment	USD 7.6–7.7 million (HPV DNA)	USD 7.9–8.0 million (Cytology)
A7 Meenan et al. (2023)	Healthcare system	12–18 months	USD ($)	Clinic visits; mailing; laboratory processing	USD 809,405 (HPV self-sampling)	USD 728,204 (Pap smear)
A8 Tran et al. (2024)	Ministry of Health	100 years	USD ($)	HPV vaccination; screening; triage; treatment of precancer, cancer, and HIV	USD 47.17 (HPV DNA)	USD 12.78 (Cytology)
A9 Keane et al. (2021a)	Government payer	2023–2100	USD ($)	Screening; digital registry; colposcopy; LEEP; cancer treatment	USD 111.77–115.38 per woman (HPV self-sampling)	USD 74.57–77.38 per woman (No screening)
A10 Keane et al. (2021b)	Government payer	Lifetime	USD ($)	Screening; diagnosis and treatment of precancer; cancer treatment	USD 16.72 (HPV DNA)	USD 12.11 (Cytology)

Study	Perspective	Time Horizon	Currency	Cost Components	Intervention Cost	Comparator Cost
A11 Hariprasad et al. (2024)	Disaggregated societal	8 days	Indian Rupee (₹)	Health system costs; out-of-pocket expenditure	₹1,271 (USD 15.3) (Home-based HPV self-sampling)	₹1,597 (USD 19.2) (VIA)
A12 Yusransyah et al. (2023)	Societal	Lifetime	USD ($)	Vaccination; screening; treatment of precancer and cancer	USD 10.52 (HPV)	USD 4.87 (VIA)
A13 Zhao et al. (2023)	Societal	Lifetime	USD ($)	Screening; HPV/CIN treatment; invasive cancer treatment	USD 358.2 (HPV)	USD 416.9 (Cytology triage)
A14 Pedersen et al. (2023)	Restricted societal	5 years	USD ($)	Screening and treatment; patient time; travel costs	USD 214 (HPV self-sampling)	USD 17 (Colposcopy)
A15 Shen et al. (2023)	Healthcare provider	5 years	USD ($)	Screening; disease management	USD 17,863,654 (HPV DNA)	USD 26,818,228 (Liquid-based cytology)
A16 Vale et al. (2021)	Public health system	Life expectancy	USD ($)	Screening; colposcopy; CIN and cancer treatment	USD 158.12 (hrHPV)	USD 181.64 (Cytology)
A17 Pedersen et al. (2022)	Restricted societal	Lifetime	USD ($)	Laboratory testing; patient time; travel costs	USD 1,850–1,900 (HPV self-sampling)	USD 1,750–1,800 (No screening)
A18 de Bondt et al. (2026)	Healthcare payer	Lifetime	USD ($)	Primary screening; follow-up management; precancer treatment	USD 121 (HPV)	USD 101 (Cytology)
A19 Lobin et al. (2024)	Not reported	65 cycles	Int$	VIA/HPV/Dual stain; cryotherapy; hysterectomy; chemoradiotherapy	Int$194.61 (HPV DNA)	Int$153.08 (VIA)
A20 Cromwell et al. (2021)	Healthcare payer	48 months	USD ($)	HPV and LBC testing; sampling; physician visits; colposcopy; biopsy; LEEP	USD 1,472,445 (HPV)	USD 1,581,750 (Liquid-based cytology)
A21 Chua et al. (2023)	Healthcare system	Lifetime	SGD / USD	Screening; physician visits; colposcopy; biopsy; treatment of precancer and cancer	SGD 150,396,871 (Extended HPV genotyping)	SGD 145,904,751 (Partial HPV genotyping + cytology triage)
A22 Simms et al. (2023)	Healthcare payer/provider	5 years	USD ($)	HPV/VIA testing; treatment of precancer; cancer treatment	USD 51 (HPV DNA)	USD 39 (VIA)

Cost components generally covered the complete cervical cancer screening pathway, including screening tests (HPV DNA testing, HPV self-sampling, cytology, LBC, and VIA), diagnostic follow-up procedures (colposcopy, biopsy, and triage), treatment of precancerous lesions (thermal ablation, cryotherapy, and LEEP), cervical cancer treatment, and palliative care. Studies conducted from a societal perspective additionally incorporated indirect costs, including productivity loss, transportation costs, and out-of-pocket expenditure.

Although HPV-based screening strategies generally required higher initial screening costs than conventional methods, several studies reported that these additional costs were offset by reductions in long-term diagnostic and treatment expenditures through earlier detection of precancerous lesions, fewer

invasive cancer cases, and reduced need for repeated screening. Differences in reported costs were primarily attributable to variations in analytical perspective, time horizon, healthcare financing systems, local service prices, and model assumptions.

Clinical Effectiveness of HPV-Based Cervical Cancer Screening Strategies

Twenty-two studies evaluated the clinical effectiveness of HPV-based cervical cancer screening using outcomes including HPV infection detection, precancerous lesion detection, cervical cancer incidence and mortality, quality-adjusted life years (QALYs), life years gained (LYGs), disability-adjusted life years (DALYs), screening participation, and follow-up procedures. Overall, HPV-based screening consistently demonstrated superior clinical performance compared with conventional screening methods, including cytology, Pap smear, visual inspection with acetic acid (VIA), and no screening (Table 2).

Table 2. Summary of the clinical effectiveness of HPV-based cervical cancer screening strategies (n = 22)

Clinical Outcome	Study Code	Key Finding
Detection of HPV infection and precancerous lesions	A1, A3, A7, A20, A21	Improved detection of HPV infection, CIN2+, and CIN3+ compared with conventional screening.
Cervical cancer incidence	A2, A4, A5, A8, A10, A18, A19, A22	Reduced cervical cancer incidence and accelerated progress toward elimination targets.
Cervical cancer mortality	A1, A3, A4, A5, A8, A12, A18, A19	Reduced cervical cancer mortality compared with conventional screening.
Health outcomes (QALYs, LYG, DALYs, HALYs)	A1, A2, A4, A6, A8, A9, A11–A17, A19, A21, A22	Improved health outcomes through increased QALYs and life years while reducing disease burden.
Screening participation	A7, A11, A20	HPV self-sampling increased screening participation and population coverage.
Referral and treatment efficiency	A1, A13, A18, A20, A21, A22	Risk-based triage improved referral efficiency, reduced unnecessary colposcopies and overtreatment, and optimized resource utilization.
Cervical cancer elimination	A2, A9, A10	HPV-based screening supported progress toward the WHO cervical cancer elimination targets.

Primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage consistently improved the detection of HPV infection and high-grade precancerous lesions while reducing cervical cancer incidence and mortality. Most studies also reported improvements in health outcomes, including increased QALYs, LYGs, and HALYs, together with reductions in DALYs. HPV self-sampling substantially increased screening participation and coverage, particularly among underserved populations, whereas HPV genotyping and risk-based triage improved referral efficiency by reducing unnecessary colposcopies and overtreatment without compromising lesion detection. Collectively, these findings indicate that HPV-based screening strategies provide greater clinical effectiveness than conventional screening and support their wider implementation in cervical cancer prevention programs.

Cost-Effectiveness of HPV-Based Cervical Cancer Screening Strategies

Twenty-two studies evaluated the economic value of HPV-based cervical cancer screening using outcomes such as incremental cost-effectiveness ratios (ICERs), quality-adjusted life years (QALYs), life years gained (LYGs), disability-adjusted life years (DALYs), and health-adjusted life years (HALYs). Overall, 21 of the 22 studies (95.5%) concluded that HPV-based screening was cost-effective, highly cost-effective, cost-saving, or economically dominant compared with conventional screening methods, whereas only one study (4.5%) reported that HPV DNA testing was not cost-effective because the ICER exceeded the national willingness-to-pay (WTP) threshold (Table 3).

Table 3. Summary of the economic evaluation findings of HPV-based cervical cancer screening strategies

Economic Outcome	Study Code	Key Finding
Primary HPV testing is cost-effective	A1, A3, A6, A9, A10, A18, A20, A22	ICERs were generally below national WTP thresholds and improved health outcomes compared with conventional screening.
HPV-based strategies are cost-saving or dominant	A3, A11, A13, A16, A20	Produced better health outcomes at equal or lower costs than comparator strategies.
HPV self-sampling improves economic efficiency	A5, A7, A11, A14	Increased screening participation and reduced service delivery costs while remaining cost-effective.
HPV genotyping and risk-based triage improve cost-effectiveness	A6, A10, A19, A21	Improved referral efficiency and reduced unnecessary follow-up procedures.
HPV screening provides long-term economic benefits	A8, A12	Reduced disease burden and generated favorable long-term economic outcomes.
HPV vaccination combined with screening is highly cost-effective	A2	Produced favorable ICERs and greater reductions in cervical cancer risk.
Cost-effectiveness depends on implementation context	A4, A17	Influenced by screening costs, adherence, healthcare capacity, and WTP thresholds.
Emerging technologies show economic potential	A15	AI-assisted cytology demonstrated favorable cost-effectiveness in appropriate settings.

Primary HPV testing was the most frequently evaluated strategy and consistently demonstrated favorable economic performance across diverse healthcare settings by improving health outcomes while remaining below country-specific WTP thresholds in most studies. HPV self-sampling also showed substantial economic benefits, particularly in settings with low screening coverage, by increasing participation and reducing service delivery costs. In addition, HPV genotyping and risk-based triage further improved program efficiency by optimizing referral pathways and reducing unnecessary follow-up procedures. Several studies also reported that combining HPV screening with preventive interventions, particularly HPV vaccination, generated additional long-term health benefits and represented a highly cost-effective strategy.

Although the overall findings strongly supported the economic value of HPV-based screening, cost-effectiveness varied according to implementation context. Factors such as screening adherence, test costs, healthcare system capacity, and country-specific WTP thresholds influenced economic performance, indicating that the optimal screening strategy should be tailored to local healthcare and economic conditions.

Discussion

This systematic review demonstrates that HPV-based cervical cancer screening strategies provide superior clinical effectiveness and economic value compared with conventional screening methods, including Pap smear and visual inspection with acetic acid (VIA). Across the **22 included economic** evaluation studies, primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage consistently improved the detection of precancerous lesions, reduced cervical cancer incidence and mortality, and generated better health outcomes measured by quality-adjusted life years (QALYs), life years gained (LYGs), and disability-adjusted life years (DALYs). Most studies also reported incremental cost-effectiveness ratios (ICERs) below national willingness-to-pay (WTP) thresholds, with several identifying

HPV-based strategies as cost-saving or economically dominant (Armijo et al., 2026; Dimitrova et al., 2024; Nguyen et al., 2022; Pan et al., 2025; Vale et al., 2021).

The superior economic performance of HPV-based screening is primarily attributable to its higher sensitivity for detecting high-risk HPV infection and cervical precancer, enabling earlier treatment and reducing the long-term burden and costs of invasive cervical cancer (Boon et al., 2022; Hakim et al., 2025; Mayasari, 2025). These findings support the World Health Organization recommendation to adopt HPV DNA testing as the preferred primary screening method and reinforce its central role in achieving the WHO cervical cancer elimination targets (World Health Organization, 2021; Wilailak et al., 2025; Zhou et al., 2025).

This review also highlights the complementary roles of HPV self-sampling and HPV genotyping with risk-based triage. Self-sampling improved screening participation, particularly among underserved populations, while reducing barriers to access and indirect healthcare costs (Foley et al., 2025; Otieno et al., 2024). Meanwhile, HPV16/18 genotyping and dual-stain triage improved referral efficiency by reducing unnecessary colposcopies without compromising the detection of clinically significant precancerous lesions (Garay et al., 2021; Jung et al., 2025; Keane et al., 2021).

In addition, emerging digital health technologies, including digital registries, reminder systems, and artificial intelligence-assisted cytology, have the potential to enhance screening adherence, diagnostic accuracy, and service efficiency, particularly in resource-constrained settings (T. Wu et al., 2024; Y. Wu & Wang, 2025). However, the economic performance of HPV-based screening remains context-dependent and is influenced by factors such as vaccination coverage, screening adherence, healthcare infrastructure, screening intervals, and country-specific resource availability. Accordingly, cervical cancer prevention programs should integrate HPV vaccination with risk-based HPV screening while adapting implementation strategies to local epidemiological and healthcare system characteristics to maximize both health outcomes and economic efficiency.

IMPLICATIONS

The findings support the adoption of HPV-based screening as the preferred strategy for cervical cancer prevention because of its demonstrated clinical effectiveness and economic value. Primary HPV testing should be prioritized where resources permit, while HPV self-sampling offers a practical alternative to improve screening coverage in underserved populations. Integrating HPV genotyping, risk-based triage, and digital health technologies may further enhance program efficiency. In Indonesia, expanding HPV DNA testing and self-sampling through the Ministry of Health's Free Health Check Program (CKG) could strengthen early detection and equitable access to cervical cancer screening.

RESEARCH CONTRIBUTION

This systematic review extends previous evidence by comparing multiple HPV-based cervical cancer screening strategies including primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage within a single economic synthesis. By integrating findings across different healthcare settings, economic perspectives, willingness-to-pay thresholds, and implementation contexts, this review provides comprehensive evidence to support context-specific and evidence-informed cervical cancer screening policies.

LIMITATIONS

This review has several limitations. First, substantial heterogeneity in study designs, economic models, analytical perspectives, and willingness-to-pay thresholds precluded quantitative meta-analysis. Second, most included studies were simulation-based, and their findings depended on assumptions regarding disease progression, screening adherence, and healthcare costs, which may differ from real-world implementation. Third, only two studies used trial-based economic evaluations, limiting the generalizability of the findings. Therefore, the cost-effectiveness of HPV-based screening should be interpreted in the context of local healthcare systems, implementation capacity, and population characteristics.

SUGGESTIONS

Future research should prioritize real-world economic evaluations, particularly in low- and middle-income countries, to validate model-based findings. Standardized economic evaluation methods are also needed to improve comparability across studies. In addition, further research should assess the long-term economic impact of integrating HPV self-sampling, HPV vaccination, and digital health technologies, including artificial intelligence, into national cervical cancer screening programs.

CONCLUSION

This systematic review demonstrates that HPV-based cervical cancer screening strategies, including primary HPV testing, HPV self-sampling, HPV genotyping, and risk-based triage, provide superior clinical effectiveness and economic value compared with conventional screening methods. Most included studies found these strategies to be cost-effective, highly cost-effective, cost-saving, or economically dominant across diverse healthcare settings. Primary HPV testing offered the greatest overall value in established screening programs, whereas HPV self-sampling was particularly beneficial for improving screening coverage in underserved populations. These findings support the wider implementation of HPV-based screening while emphasizing the need to adapt screening strategies to local healthcare capacity, economic resources, and population characteristics.

ACKNOWLEDGEMENTS

The authors like to convey their profound appreciation to the contributors of the primary studies used in this systematic review for supplying the evidence synthesised in this research. The authors express gratitude to the Master's Program in Midwifery, Faculty of Health Sciences, Universitas 'Aisyiyah Yogyakarta, Indonesia, for its academic assistance during the paper production.

REFERENCES

Ang, J. X., & Tay, S. K. (2025). Comparison of Clinical Efficacy of Liquid-Based Cytology and High-Risk Human Papillomavirus Testing With Partial Genotyping in Cervical Screening of Women Below 30 Years Old. *Cancer Control*, *32*. https://doi.org/10.1177/10732748251336414

Armijo, N., Espinoza, M. A., Contreras-Montiel, P., Vera, M., & Balmaceda, C. (2026). Cost-effectiveness of primary HPV genotyping and dual-stain or cytology reflex testing versus cytology-based screening for cervical cancer in Chile. *PLOS One*, *21*(3), e0332010. https://doi.org/10.1371/journal.pone.0332010

Boon, S. S., Luk, H. Y., Xiao, C., Chen, Z., & Chan, P. K. S. (2022). Review of the Standard and Advanced Screening, Staging Systems and Treatment Modalities for Cervical Cancer. *Cancers*, *14*(12), 2913. https://doi.org/10.3390/cancers14122913

Brisson, M., Kim, J. J., Canfell, K., Drolet, M., Gingras, G., Burger, E. A., Martin, D., Simms, K. T., Bénard, É., Boily, M.-C., Sy, S., Regan, C., Keane, A., Caruana, M., Nguyen, D. T. N., Smith, M. A., Laprise, J.-F., Jit, M., Alary, M., … Hutubessy, R. (2020). Impact of HPV vaccination and cervical screening on cervical cancer elimination: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *The Lancet*, *395*(10224), 575–590. https://doi.org/10.1016/S0140-6736(20)30068-4

Burd, E. M. (2003). Human Papillomavirus and Cervical Cancer. *Clinical Microbiology Reviews*, *16*(1), 1–17. https://doi.org/10.1128/CMR.16.1.1-17.2003

Dasgupta, S. (2026). Efficiency of Human Papillomavirus (HPV) Testing in Cervical Cancer Screening and Vaccination: A Review. *Cureus*, *18*(1). https://doi.org/10.7759/cureus.102126

Dimitrova, M., Petrov, M., Petrova, G., & Mitkova, Z. (2024). Economic consequences of the implementation of primary DNA-HPV genotype testing in Bulgaria. *Biotechnology & Biotechnological Equipment*, *38*(1). https://doi.org/10.1080/13102818.2024.2358134

Foley, S., Flowers, A., Isher-Witt, J., Crawford, K., Nkonga, J., Burcin, M., & Gaglioti, A. H. (2025). "It really is HPV that's pulling us down": Findings from a health plan quality improvement learning collaborative targeting the HEDIS IMA measure. *Human Vaccines & Immunotherapeutics*, *21*(1). https://doi.org/10.1080/21645515.2025.2569760

Garay, O. U., Maritano Furcada, J., Ayerbe, F., Pena Requejo Rave, R. A., & Tatti, S. A. (2021). Cost-Effectiveness and Budget Impact Analysis of Primary Screening With Human Papillomavirus Test With Genotyping in Argentina. *Value in Health Regional Issues*, *26*, 160–168. https://doi.org/10.1016/j.vhri.2021.07.004

Gomersall, J. S., Jadotte, Y. T., Xue, Y., Lockwood, S., Riddle, D., & Preda, A. (2020). Conducting systematic reviews of economic evaluations. *International Journal of Evidence-Based Healthcare*, *13*(3), 170–178. https://doi.org/10.1097/XEB.0000000000000063

Hakim, R. U., Amin, T., & Ul Islam, S. M. B. (2025). Advances and Challenges in Cervical Cancer: From

Molecular Mechanisms and Global Epidemiology to Innovative Therapies and Prevention Strategies. *Cancer Control*, *32*. https://doi.org/10.1177/10732748251336415

Huh, W. K., Ault, K. A., Chelmow, D., Davey, D. D., Goulart, R. A., Garcia, F. A. R., Kinney, W. K., Massad, L. S., Mayeaux, E. J., Saslow, D., Schiffman, M., Wentzensen, N., Lawson, H. W., & Einstein, M. H. (2022). Use of Primary High-Risk Human Papillomavirus Testing for Cervical Cancer Screening. *Obstetrics & Gynecology*, *125*(2), 330–337. https://doi.org/10.1097/AOG.0000000000000669

Jung, L., Klamminger, G. G., Nigdelis, M. P., & Eltze, E. (2025). Impact of HPV Testing Based on the 2020 Update of the German Cervical Cancer Screening Program—Data from a Retrospective Monocentric Study. *Cancers*, *17*(12), 2024. https://doi.org/10.3390/cancers17122024

Karimah, R., Indriastuti, E., Eljatin, D. S., Soraya, F., Fitriani, F. N., Haykal, M. N., Hidayah, R. N., Sari, D. W., Rangkuti, R. Y., Nurhayati, L., Syulthoni, Z. B., & Fadli, S. (2025). Peningkatan Deteksi Dini Kanker Serviks melalui Skrining HPV DNA kepada Masyarakat di Institut Teknologi Sepuluh Nopember. *Sewagati*, *9*(6), 1637–1646. https://doi.org/10.12962/j26139960.v9i6.9141

Keane, A., Shi, J.-F., Simms, K. T., Liu, Y.-J., Lew, J.-B., Mazariego, C., Yuill, S., Wu, R.-F., Liu, Z.-H., Zhao, F.-H., Jeronimo, J., Canfell, K., & Qiao, Y.-L. (2021). Health economic evaluation of primary human papillomavirus screening in urban populations in China. *Cancer Epidemiology*, *70*, 101861. https://doi.org/10.1016/j.canep.2020.101861

Kurniawan, M. F. (2025). *Economic evaluation of health and related care interventions: Costs, Outcomes and Cost Effectiveness Methods*. Kebijakan Kesehatan Indonesia. https://kebijakankesehatanindonesia.net/economic-evaluation-of-health-and-related-care-interventions/

Lee, J., Ismail-Pratt, I., Machalek, D. A., Kumarasamy, S., & Garland, S. M. (2023). The recovery strategies to support cervical cancer elimination in lower-and middle-income countries (LMICs) following COVID-19 disruptions. *Preventive Medicine Reports*, *35*, 102291. https://doi.org/10.1016/j.pmedr.2023.102291

Mayasari, S. P. (2025). Komparasi Efikasi Skrining Kanker Serviks Menggunakan HPV DNA Testing, Pap Smear, Dan Liquid Biopsy: Tinjauan Sistematis. *Indonesian Journal of Health Community*, *6*(1), 33. https://doi.org/10.31331/ijheco.v6i1.3893

National Cancer Institute. (2024). *Cervical Cancer Causes, Risk Factors, and Prevention*. National Cancer Institute. https://www.cancer.gov/types/cervical/causes-risk-prevention

Nguyen, D. T. N., Simms, K. T., Keane, A., Mola, G., Bolnga, J. W., Kuk, J., Toliman, P. J., Badman, S. G., Saville, M., Kaldor, J., Vallely, A., & Canfell, K. (2022). Towards the elimination of cervical cancer in low-income and lower-middle-income countries: modelled evaluation of the effectiveness and cost-effectiveness of point-of-care HPV self-collected screening and treatment in Papua New Guinea. *BMJ Global Health*, *7*(3), e007380. https://doi.org/10.1136/bmjgh-2021-007380

Otieno, J. A., Were, L., Nyanchoka, M., Olwanda, E., Mulaku, M., Sem, X., Kohli, M., Markby, J., Muriuki, A., & Ochodo, E. (2024). Human papillomavirus self-sampling versus provider-sampling in low- and middle-income countries: a scoping review of accuracy, acceptability, cost, uptake, and equity. *Frontiers in Public Health*, *12*. https://doi.org/10.3389/fpubh.2024.1439164

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Systematic Reviews*, *10*(1), 89. https://doi.org/10.1186/s13643-021-01626-4

Pan, F., van der Schans, J., Nazrul, N., Koot, J. A. R., Beltman, J., Greuter, M. J. W., & de Bock, G. H. (2025). The effect of hrHPV prevalence on cervical cancer screening strategies: a cost-effectiveness study of Bangladesh. *BMC Public Health*, *25*(1), 561. https://doi.org/10.1186/s12889-025-21756-x

Petersen, Z., Jaca, A., Ginindza, T. G., Maseko, G., Takatshana, S., Ndlovu, P., Zondi, N., Zungu, N., Varghese, C., Hunting, G., Parham, G., Simelela, P., & Moyo, S. (2022). Barriers to uptake of cervical cancer screening services in low-and-middle-income countries: a systematic review. *BMC Women's Health*, *22*(1), 486. https://doi.org/10.1186/s12905-022-02043-y

Vale, D. B., Silva, M. T., Discacciati, M. G., Polegatto, I., Teixeira, J. C., & Zeferino, L. C. (2021). Is the HPV-test more cost-effective than cytology in cervical cancer screening? An economic analysis from a middle-income country. *PLOS ONE*, *16*(5), e0251688. https://doi.org/10.1371/journal.pone.0251688

Wang, M., Jin, Y., & Zheng, Z.-J. (2023). The association of cervical cancer screening and quality of care: A systematic analysis of the Global Burden of Disease Study 2019. *Journal of Global Health*, *13*, 04090. https://doi.org/10.7189/jogh.13.04090

Wibawa, B. W., Lestari, R. H., & Prasetyo, D. S. (2024). Perbandingan HPV DNA Test Hybrid Capture dan Pap Smear untuk Diagnosis Dini Karsinoma Serviks. *EJournal Kedokteran Indonesia*, *12*(2), 187. https://doi.org/10.23886/ejki.12.643.187

Wilailak, S., Kengsakul, M., & Kehoe, S. (2025). Strategic approaches for global cervical cancer elimination: An update review and call for national action. *International Journal of Gynecology & Obstetrics*, *171*(S1), 120–128. https://doi.org/10.1002/ijgo.70276

Williams, J., Kostiuk, M., & Biron, V. L. (2022). Molecular Detection Methods in HPV-Related Cancers. *Frontiers in Oncology*, *12*. https://doi.org/10.3389/fonc.2022.864820

Wong, J. Z. Y., Chai, J. H., Yeoh, Y. S., Mohamed Riza, N. K., Liu, J., Teo, Y.-Y., Wee, H. L., & Hartman, M. (2021). Cost effectiveness analysis of a polygenic risk tailored breast cancer screening programme in Singapore. *BMC Health Services Research*, *21*(1), 379. https://doi.org/10.1186/s12913-021-06396-2

World Health Organization. (2021). *WHO recommends DNA testing as a first-choice screening method for cervical cancer prevention*. World Health Organization. https://www.who.int/europe/news/item/11-09-2021-who-recommends-dna-testing-as-a-first-choice-screening-method-for-cervical-cancer-prevention

World Health Organization. (2023). *Cervical cancer*. World Health Organization. https://www.who.int/health-topics/cervical-cancer#tab=tab_1

Wu, T., Lucas, E., Zhao, F., Basu, P., & Qiao, Y. (2024). Artificial intelligence strengthenes cervical cancer screening – present and future. *Cancer Biology & Medicine*, 1–16. https://doi.org/10.20892/j.issn.2095-3941.2024.0198

Wu, Y., & Wang, A. (2025). A Review on the Applications of Artificial Intelligence for Diagnosing and Treating Cervical Cancer. *International Journal of Women's Health*, *Volume 17*, 3955–3970. https://doi.org/10.2147/IJWH.S551976

Zhou, L., Li, Y., Wang, H., Qin, R., Han, Z., & Li, R. (2025). Global cervical cancer elimination: quantifying the status, progress, and gaps. *BMC Medicine*, *23*(1), 67. https://doi.org/10.1186/s12916-025-03897-3