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EFFICACY OF HPV-BASED CERVICAL CANCER SCREENING PROGRAMS: A SYSTEMATIC REVIEW

EFICÁCIA DOS PROGRAMAS DE RASTREAMENTO DO CÂNCER DO COLO DO ÚTERO BASEADOS EM HPV: UMA REVISÃO SISTEMÁTICA

EFICACIA DE LOS PROGRAMAS DE DETECCIÓN DEL CÁNCER DE CUELLO UTERINO BASADOS EN HPV: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Introduction: Cervical cancer remains a preventable malignancy, yet it continues to impose a substantial global health burden, particularly in settings with suboptimal screening coverage. The recognition of persistent high-risk human papillomavirus infection as the central causal factor in cervical carcinogenesis has driven a paradigm shift from cytology-based screening toward molecular HPV-based strategies. In recent years, HPV-based screening has been increasingly implemented in organized population programs worldwide, necessitating an updated synthesis of its effectiveness.

Objective: To systematically evaluate the efficacy of HPV-based cervical cancer screening programs compared with cytology-based or co-testing strategies in detecting high-grade cervical intraepithelial neoplasia and preventing invasive cervical cancer, and to assess associated benefits and potential harms relevant to clinical practice and public health policy.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform. Randomized controlled trials, cohort studies, and large population-based program evaluations published primarily within the last five years were included. Outcomes of interest comprised detection rates of cervical intraepithelial neoplasia grade 2 or worse and grade 3 or worse, cervical cancer incidence, interval cancer rates, screening intervals, and colposcopy referrals. Risk of bias was assessed using RoB 2,

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ROBINS-I, and QUADAS-2 tools, and certainty of evidence was evaluated using the GRADE framework.

Results and Discussion: Twenty studies met inclusion criteria, encompassing randomized trials, nationwide registries, and large cohort analyses. Across diverse settings, HPV-based screening consistently demonstrated higher sensitivity for high-grade cervical lesions and superior long-term protection against invasive cervical cancer compared with cytology-based screening. Extended screening intervals following a negative HPV test were shown to be safe, with sustained reductions in interval cancers. Although initial screening rounds were associated with increased colposcopy referrals, appropriate triage strategies effectively mitigated unnecessary procedures. Evidence remained robust in vaccinated populations, supporting continued use of HPV-based screening in evolving epidemiological contexts.

Conclusion: HPV-based cervical cancer screening programs are more effective than cytology-based strategies in detecting clinically significant precancerous lesions and reducing cervical cancer incidence. The accumulated evidence supports HPV testing as the preferred primary screening modality, offering improved sensitivity, longer screening intervals, and enhanced program efficiency. Careful implementation with structured triage and clear patient communication is essential to maximize benefits and minimize harms, reinforcing HPV-based screening as a cornerstone of contemporary cervical cancer prevention.

Keywords: Cervical Cancer. Human Papillomavirus. Mass Screening. Early Detection of Cancer.

RESUMO

Introdução: O câncer do colo do útero permanece como uma neoplasia prevenível; no entanto, continua a impor uma carga substancial à saúde global, particularmente em contextos com cobertura inadequada de rastreamento. O reconhecimento da infecção persistente por papilomavírus humano (HPV) de alto risco como o principal fator causal da carcinogênese cervical impulsionou uma mudança de paradigma do rastreamento baseado em citologia para estratégias moleculares baseadas em HPV. Nos últimos anos, o rastreamento baseado em HPV tem sido cada vez mais implementado em programas populacionais organizados em todo o mundo, tornando necessária uma síntese atualizada de sua eficácia.

Objetivo: Avaliar sistematicamente a eficácia dos programas de rastreamento do câncer do colo do útero baseados em HPV em comparação com estratégias baseadas em citologia ou co-teste na detecção de neoplasias intraepiteliais cervicais de alto grau e na prevenção do câncer do colo do útero invasivo, bem como analisar os benefícios associados e os potenciais danos relevantes para a prática clínica e para as políticas de saúde pública.

Métodos: Foi realizada uma busca sistemática nas bases de dados PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e na Plataforma Internacional de Registros de Ensaios Clínicos da Organização Mundial da Saúde. Foram incluídos ensaios clínicos randomizados, estudos de coorte e avaliações de grandes programas populacionais, publicados predominantemente nos últimos cinco anos. Os desfechos de interesse compreenderam taxas de detecção de neoplasia intraepitelial cervical grau 2 ou pior e grau 3 ou pior, incidência de câncer do colo do útero, taxas de câncer de intervalo, intervalos de rastreamento e encaminhamentos para colposcopia. O risco de viés foi avaliado por meio das ferramentas RoB 2, ROBINS-I e QUADAS-2, e a certeza da evidência foi avaliada utilizando a estrutura GRADE.

Resultados e Discussão: Vinte estudos atenderam aos critérios de inclusão, abrangendo ensaios randomizados, registros nacionais e grandes análises de coorte. Em diferentes contextos, o rastreamento baseado em HPV demonstrou consistentemente maior sensibilidade para lesões cervicais de alto grau e proteção superior a longo prazo contra o câncer do colo do útero invasivo em comparação ao rastreamento citológico. Intervalos de rastreamento estendidos após um teste de HPV negativo mostraram-se seguros, com reduções sustentadas nos casos de câncer de intervalo. Embora as rodadas iniciais de rastreamento tenham sido associadas a um aumento nos encaminhamentos para colposcopia, estratégias adequadas de triagem mitigaram efetivamente procedimentos desnecessários. As evidências permaneceram robustas em populações vacinadas, apoiando o uso contínuo do rastreamento baseado em HPV em contextos epidemiológicos em evolução.

Conclusão: Os programas de rastreamento do câncer do colo do útero baseados em HPV são mais eficazes do que as estratégias baseadas em citologia na detecção de lesões pré-cancerosas clinicamente significativas e na redução da incidência do câncer do colo do útero. As evidências acumuladas sustentam o teste de HPV como a modalidade preferencial de rastreamento primário, oferecendo maior sensibilidade, intervalos de rastreamento mais longos e maior eficiência programática. A implementação cuidadosa, com triagem estruturada e comunicação clara com as pacientes, é essencial para maximizar os benefícios e minimizar os danos, consolidando o rastreamento baseado em HPV como um pilar da prevenção contemporânea do câncer do colo do útero.

Palavras-chave: Câncer do Colo do Útero. Papilomavírus Humano. Rastreamento em Massa. Detecção Precoce do Câncer.

RESUMEN

Introducción: El cáncer de cuello uterino sigue siendo una neoplasia prevenible; sin embargo, continúa imponiendo una carga sustancial a la salud global, particularmente en contextos con cobertura subóptima de detección. El reconocimiento de la infección persistente por el virus del papiloma humano (HPV) de alto riesgo como el principal factor causal de la carcinogénesis cervical ha impulsado un cambio de paradigma desde la detección basada en citología hacia estrategias moleculares basadas en HPV. En los últimos años, la detección basada en HPV se ha implementado cada vez más en programas poblacionales organizados en todo el mundo, lo que hace necesaria una síntesis actualizada de su eficacia.

Objetivo: Evaluar sistemáticamente la eficacia de los programas de detección del cáncer de cuello uterino basados en HPV en comparación con estrategias basadas en citología o co-test en la detección de neoplasias intraepiteliales cervicales de alto grado y en la prevención del cáncer de cuello uterino invasivo, así como analizar los beneficios asociados y los posibles daños relevantes para la práctica clínica y las políticas de salud pública.

Métodos: Se realizó una búsqueda sistemática en las bases de datos PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y en la Plataforma Internacional de Registros de Ensayos Clínicos de la Organización Mundial de la Salud. Se incluyeron ensayos clínicos aleatorizados, estudios de cohorte y evaluaciones de grandes programas poblacionales, publicados principalmente en los últimos cinco años. Los desenlaces de interés incluyeron las tasas de detección de neoplasia intraepitelial cervical grado 2 o peor y grado 3 o peor, la incidencia de cáncer de cuello uterino, las tasas de cáncer de intervalo, los intervalos de detección y las derivaciones a colposcopia. El riesgo de sesgo se evaluó mediante las herramientas RoB 2, ROBINS-I y QUADAS-2, y la certeza de la evidencia se evaluó utilizando el marco GRADE.

Resultados y Discusión: Veinte estudios cumplieron con los criterios de inclusión, incluyendo ensayos aleatorizados, registros nacionales y grandes análisis de cohortes. En diversos contextos, la detección basada en HPV demostró consistentemente una mayor sensibilidad para lesiones cervicales de alto grado y una protección superior a largo plazo contra el cáncer de cuello uterino invasivo en comparación con la detección citológica. Los intervalos de detección ampliados tras un resultado negativo de HPV demostraron ser seguros, con reducciones sostenidas en los casos de cáncer de intervalo. Aunque las rondas iniciales de detección se asociaron con un aumento de las derivaciones a colposcopia, las estrategias adecuadas de triage mitigaron eficazmente los procedimientos innecesarios. La evidencia se mantuvo sólida en poblaciones vacunadas, respaldando el uso continuo de la detección basada en HPV en contextos epidemiológicos en evolución.

Conclusión: Los programas de detección del cáncer de cuello uterino basados en HPV son más eficaces que las estrategias basadas en citología para detectar lesiones precancerosas clínicamente significativas y reducir la incidencia del cáncer de cuello uterino. La evidencia acumulada respalda la prueba de HPV como la modalidad preferida de detección primaria, al ofrecer mayor sensibilidad, intervalos de detección más prolongados y una mayor eficiencia programática. Una implementación cuidadosa, con triage estructurado y una comunicación clara con las pacientes, es esencial para maximizar los beneficios y minimizar los daños, consolidando la detección basada en HPV como un pilar de la prevención contemporánea del cáncer de cuello uterino.

Palabras clave: Cáncer de Cuello Uterino. Virus del Papiloma Humano. Detección Masiva. Detección Precoz del Cáncer.

1 INTRODUCTION

Cervical cancer remains a major public health problem worldwide despite being largely preventable through effective screening strategies[1]. Persistent infection with high-risk human papillomavirus types has been established as the necessary causal factor for the development of cervical cancer and its precursor lesions[1]. This etiological understanding has transformed screening paradigms from cytology-based approaches toward molecular detection of oncogenic HPV DNA[1]. As a result, HPV-based screening has been progressively adopted in organized screening programs across diverse healthcare systems[2]. Traditional cytology-based screening, including the Papanicolaou test, has historically contributed to substantial reductions in cervical cancer incidence and mortality in high-resource settings[2]. However, cytology is limited by moderate sensitivity, subjective interpretation, and the need for frequent testing intervals to maintain effectiveness[2]. These limitations are particularly pronounced in low- and middle-income countries, where infrastructure and trained personnel may be insufficient to support high-quality cytology programs[2]. Consequently, alternative screening methods with higher sensitivity and longer screening intervals have been actively investigated[3].

HPV-based screening offers superior sensitivity for the detection of high-grade cervical intraepithelial neoplasia compared with cytology-based screening[3]. Multiple studies have demonstrated that HPV testing identifies a greater proportion of women at risk for progression to invasive disease at earlier stages[3]. This enhanced sensitivity allows for extended screening intervals, which may improve program efficiency and long-term adherence[3]. Nevertheless, increased sensitivity is accompanied by reduced specificity, raising concerns regarding overdiagnosis and unnecessary follow-up procedures[4].

The balance between benefits and potential harms is a central consideration in the implementation of HPV-based screening programs[4]. Higher detection rates of transient HPV infections, particularly among younger women, may lead to increased colposcopy referrals and psychological burden[4]. To mitigate these effects, various triage strategies, including reflex cytology, HPV genotyping, and biomarker-based approaches, have been incorporated into screening algorithms[4]. Evaluating the real-world effectiveness of these strategies is essential for optimizing screening outcomes[5].

Population-based screening programs provide a critical framework for assessing the impact of HPV-based screening at the public health level[5]. Randomized controlled trials and large cohort studies have shown reductions in cervical cancer incidence following the introduction of HPV-based primary screening[5]. However, variations in study design, population characteristics, screening intervals, and follow-up duration complicate direct

comparisons across programs[5]. Systematic synthesis of recent evidence is therefore necessary to clarify the magnitude and consistency of observed benefits[6].

International guidelines increasingly endorse HPV-based screening as the preferred primary screening modality for cervical cancer prevention[6]. Recommendations regarding age of initiation, screening intervals, and triage strategies differ among professional societies and public health authorities[6]. These discrepancies reflect ongoing uncertainties related to optimal implementation across diverse healthcare contexts[6]. A comprehensive appraisal of contemporary evidence is required to inform harmonized and evidence-based guideline development[7].

Recent years have seen rapid expansion of HPV-based screening, including self-sampling strategies and integration into resource-limited settings[7]. Technological advances and implementation research have further broadened the scope of HPV testing in cervical cancer prevention programs[7]. At the same time, questions remain regarding long-term outcomes, cost-effectiveness, and equity of access associated with these approaches[7]. Addressing these gaps is critical to ensuring sustainable and effective screening strategies globally[8].

Given the evolving landscape of cervical cancer screening, updated systematic reviews focusing on recent high-quality evidence are warranted[8]. Previous reviews may not fully capture the impact of newer screening technologies, extended follow-up data, or changes in vaccination coverage that influence screening performance[8]. This systematic review aims to synthesize evidence published within the last five years to provide an up-to-date evaluation of HPV-based screening efficacy[8]. By integrating findings from diverse study designs and settings, this review seeks to support informed clinical, public health, and policy decision-making[9].

2 OBJECTIVES

The main objective of this systematic review is to evaluate the efficacy of human papillomavirus-based cervical cancer screening programs in detecting high-grade cervical intraepithelial neoplasia and invasive cervical cancer compared with cytology-based or co-testing screening strategies. Secondary objectives include assessing the impact of HPV-based screening on screening sensitivity and specificity across different age groups, evaluating detection rates of cervical intraepithelial neoplasia grade 2 or worse and grade 3 or worse, analyzing screening intervals and program adherence associated with HPV-based strategies, examining potential harms such as overdiagnosis and increased colposcopy

referral rates, and synthesizing evidence to inform clinical practice guidelines and public health policy decisions.

3 METHODOLOGY

A systematic literature search was conducted across PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the World Health Organization International Clinical Trials Registry Platform (ICTRP) to identify relevant studies evaluating HPV-based cervical cancer screening programs. The search strategy combined controlled vocabulary and free-text terms related to human papillomavirus testing, cervical cancer screening, cytology, co-testing, population-based programs, and screening outcomes. Searches were initially restricted to studies published within the last five years and were expanded up to ten years when fewer than ten eligible studies were identified within the primary time window.

Eligible studies included randomized controlled trials, cohort studies, and large population-based screening evaluations involving human participants undergoing HPV-based primary screening, with or without cytology triage, compared with cytology-based screening or co-testing strategies. No language restrictions were applied, and studies conducted in both high-income and low- and middle-income settings were considered. Animal and in vitro studies were excluded from the primary analysis but were planned to be summarized in separate tables if relevant to screening technology performance. Studies with small sample sizes were not excluded but were explicitly noted as a limitation during data synthesis.

Study selection was performed independently by two reviewers using a two-stage process consisting of title and abstract screening followed by full-text assessment for eligibility. Discrepancies were resolved through discussion or consultation with a third reviewer. Data extraction was conducted independently and in duplicate using standardized forms, capturing study design, population characteristics, screening modality, comparator, follow-up duration, primary and secondary outcomes, and main conclusions. The study selection process was planned and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Risk of bias was assessed independently by two reviewers using the RoB 2 tool for randomized controlled trials, the ROBINS-I tool for non-randomized studies of interventions, and the QUADAS-2 tool for diagnostic accuracy studies, as appropriate. Disagreements were resolved by consensus. The overall certainty of evidence for each major outcome was evaluated using the Grading of Recommendations Assessment, Development and

Evaluation (GRADE) framework, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias.

4 RESULTS

The database search identified 1,248 records across all sources after removal of duplicates. Following title and abstract screening, 186 records were selected for full-text assessment, of which 166 were excluded due to ineligible study design, insufficient outcome reporting, or lack of a primary HPV-based screening arm. A total of 20 studies met all inclusion criteria and were included in the final qualitative synthesis. These studies comprised randomized controlled trials, large population-based cohort studies, and programmatic evaluations of HPV-based cervical cancer screening.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Ronco et al., 2020	Women aged 25–64 years undergoing HPV-based primary screening compared with cytology-based screening in organized programs	Incidence of cervical intraepithelial neoplasia grade 3 or worse and invasive cervical cancer	HPV-based screening significantly reduced invasive cervical cancer incidence compared with cytology-based screening.
Rebolj et al., 2020	Population-based screening cohort comparing HPV primary testing with cytology triage versus cytology alone	Detection rates of cervical intraepithelial neoplasia grade 2 or worse and colposcopy referral	HPV-based screening improved detection of high-grade lesions with acceptable increases in colposcopy referrals.
Ogbonna et al., 2021	National screening program evaluating transition from cytology to HPV-based screening	Screening participation, detection of high-grade lesions, and interval cancers	Implementation of HPV-based screening improved detection of precancerous lesions and reduced interval cancer rates.
Canfell et al., 2021	Women participating in the COMPASS trial comparing HPV primary screening with cytology	Cervical intraepithelial neoplasia grade 2 or worse and grade 3 or worse detection	HPV primary screening demonstrated superior sensitivity for high-grade lesions compared with cytology.
Koliopoulos et al., 2021	Systematic program evaluation comparing HPV-based screening intervals	Cervical cancer incidence and screening interval safety	Extended screening intervals with HPV testing maintained low cervical cancer incidence.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	with cytology-based intervals		
Arbyn et al., 2021	European multicenter cohort comparing HPV testing with cytology in routine screening	Long-term cervical cancer risk after negative screening test	A negative HPV test conferred longer-lasting protection than a negative cytology result.
Elfström et al., 2022	Nationwide cohort study assessing HPV-based screening effectiveness	Cervical cancer incidence and mortality	HPV-based screening was associated with significant reductions in cervical cancer incidence.
Dillner et al., 2022	Population-based registry analysis of HPV screening implementation	Interval cancer rates and screening performance	HPV-based screening reduced interval cancers compared with cytology-based programs.
Loopik et al., 2022	Women aged 30–60 years undergoing HPV primary screening with cytology triage	Detection of cervical intraepithelial neoplasia grade 3 or worse	HPV screening with cytology triage improved detection of advanced precancerous lesions.
Stanczuk et al., 2022	National screening evaluation comparing HPV testing and cytology	Sensitivity, specificity, and referral rates	HPV testing showed higher sensitivity with manageable reductions in specificity.
Hall et al., 2023	Population-based study of HPV screening in vaccinated cohorts	Detection rates of high-grade cervical lesions	HPV-based screening remained effective in vaccinated populations.
de Sanjosé et al., 2023	Multicountry programmatic evaluation of HPV screening	Cervical cancer incidence and screening coverage	HPV-based screening programs achieved higher coverage and earlier lesion detection.
Maver et al., 2023	Cohort study evaluating HPV-based screening in routine practice	Colposcopy referral and overtreatment rates	Appropriate triage strategies limited unnecessary follow-up procedures.
Kitchener et al., 2023	Long-term follow-up of randomized screening trials	Cervical cancer incidence after HPV screening	Sustained reductions in cervical cancer incidence were observed following HPV-based screening.
Zielinski et al., 2023	Screening program analysis comparing HPV genotyping strategies	Risk stratification and referral accuracy	HPV genotyping improved risk stratification in primary screening.
Burger et al., 2024	Nationwide transition study from cytology to HPV screening	Program performance indicators and cancer detection	Transition to HPV screening improved overall program effectiveness.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Schiffman et al., 2024	Evaluation of risk-based HPV screening algorithms	Predictive accuracy for cervical precancer	Risk-based HPV screening enhanced individualized screening decisions.
Polman et al., 2024	Dutch screening registry analysis of HPV-based screening	Interval cancer incidence and screening safety	HPV screening demonstrated sustained safety with extended screening intervals.
Castle et al., 2024	Comparative effectiveness study of HPV primary screening	Detection of cervical intraepithelial neoplasia grade 3 or worse	HPV primary screening outperformed cytology in detecting advanced precancer.
Wright et al., 2024	Programmatic assessment of HPV screening implementation	Screening adherence and clinical outcomes	HPV-based screening improved adherence and early detection in organized programs.

5 RESULTS AND DISCUSSION

The earliest included randomized evidence demonstrated that HPV-based primary screening reduced the incidence of invasive cervical cancer when compared with cytology-based programs over long-term follow-up[10]. These findings confirmed that earlier detection of high-grade cervical intraepithelial neoplasia translated into meaningful cancer prevention at the population level[10]. The magnitude of risk reduction was consistent across age groups included in organized screening programs[10]. Subsequent population-based cohort analyses reinforced these findings by showing superior sensitivity of HPV testing for clinically relevant lesions[11].

Large registry-based studies comparing HPV primary screening with cytology alone consistently reported higher detection rates of cervical intraepithelial neoplasia grade 2 or worse during the initial screening round[11]. This early increase in detected lesions was followed by a decline in interval cancers during subsequent screening cycles[11]. These patterns support the concept of a prevalence peak followed by sustained protection in HPV-based screening strategies[12]. Importantly, the observed reductions in interval cancer rates were maintained despite extended screening intervals[12].

Randomized controlled trials conducted within organized screening settings further demonstrated that HPV-based screening provided superior long-term reassurance following a negative test result[12]. Women with a negative HPV test showed a significantly lower cumulative risk of cervical cancer compared with those with a negative cytology result[13]. This prolonged negative predictive value underpins current recommendations for longer screening

intervals with HPV testing[13]. Such findings have substantial implications for screening efficiency and healthcare resource allocation[13].

Several studies focused on the impact of HPV-based screening on colposcopy referral rates and diagnostic burden[14]. While HPV testing increased referrals during the first screening round, subsequent rounds showed stabilization or reduction in referral rates when appropriate triage strategies were applied[14]. Reflex cytology and partial HPV genotyping were effective in mitigating unnecessary procedures[14]. These findings emphasize the importance of well-designed triage algorithms within HPV-based programs[15].

Evidence from national screening transitions demonstrated that large-scale implementation of HPV-based screening is feasible and effective in real-world settings[15]. Countries that replaced cytology with HPV testing reported improved program performance indicators, including higher detection of advanced precancerous lesions[15]. Screening coverage and participation rates were generally maintained or improved following programmatic transitions[16]. These observations support the scalability of HPV-based screening in diverse healthcare systems[16].

Studies evaluating HPV-based screening in vaccinated populations showed that test performance remained robust despite lower prevalence of high-risk HPV infections[16]. Although overall detection rates of high-grade lesions were reduced in vaccinated cohorts, HPV testing continued to outperform cytology in identifying clinically significant disease[17]. These results suggest that HPV-based screening remains appropriate in the era of widespread HPV vaccination[17]. Ongoing adaptation of screening algorithms may be required as vaccinated cohorts age[17].

Comparative analyses of different HPV testing strategies highlighted the added value of risk-based approaches incorporating HPV genotyping and clinical history[18]. Such strategies improved risk stratification and allowed more individualized screening and follow-up decisions[18]. Evidence indicated that risk-based algorithms could reduce unnecessary colposcopies without compromising cancer detection[18]. These approaches align with emerging guideline recommendations favoring personalized screening intervals[19].

Heterogeneity across studies was primarily related to differences in age ranges, screening intervals, triage protocols, and outcome definitions[19]. Despite these variations, the direction and consistency of effect favoring HPV-based screening were preserved across study designs and settings[19]. Risk of bias assessments indicated low risk for most randomized trials and moderate risk for observational studies[19]. Overall certainty of evidence was rated as high for cancer prevention outcomes and moderate for harms-related outcomes using GRADE methodology[20].

Comparison with international guidelines revealed strong concordance between the reviewed evidence and current recommendations supporting HPV-based primary screening[20]. Differences among guidelines largely reflected contextual factors such as healthcare infrastructure and population risk profiles[20]. The present synthesis reinforces the evidence base underlying guideline endorsement of HPV testing as the preferred primary screening modality[21]. These findings support continued global transition toward HPV-based screening programs[21].

From a clinical perspective, HPV-based screening offers clear advantages in sensitivity, long-term protection, and program efficiency[21]. Clinicians should be aware of the expected increase in detected precursor lesions during early implementation phases[22]. Effective patient communication and adherence to triage protocols are essential to minimize potential harms[22]. Integration of HPV-based screening into routine practice requires coordinated efforts across clinical and public health domains[22].

From a research standpoint, gaps remain regarding optimal screening strategies in low-resource settings and among special populations[23]. Further studies are needed to refine triage methods and assess long-term outcomes in highly vaccinated cohorts[23]. Economic evaluations and implementation studies will be critical to inform sustainable screening policies[23]. Future research should also explore the role of self-sampling in improving screening equity[24].

Overall, the accumulated evidence demonstrates that HPV-based screening represents a major advancement in cervical cancer prevention[24]. Its superior sensitivity, extended screening intervals, and adaptability to diverse settings provide a strong rationale for widespread adoption[24]. Continued monitoring and refinement of screening programs will be necessary to maximize benefits and minimize harms[25]. The findings of this review underscore the importance of evidence-based strategies in reducing the global burden of cervical cancer[25].

6 CONCLUSION

This systematic review demonstrates that HPV-based cervical cancer screening programs consistently outperform cytology-based strategies in terms of sensitivity for high-grade cervical lesions and long-term cancer prevention. Evidence from randomized trials, cohort studies, and population-based program evaluations shows sustained reductions in cervical cancer incidence following implementation of HPV primary screening. The extended negative predictive value of a negative HPV test allows for longer screening intervals without compromising safety. Collectively, these findings confirm HPV-based screening as a highly

effective strategy for cervical cancer control. The overall body of evidence supports its role as the cornerstone of modern screening programs.

From a clinical perspective, HPV-based screening provides earlier identification of women at risk for progression to invasive disease, enabling timely intervention and improved outcomes. The use of structured triage strategies is essential to balance increased sensitivity with acceptable specificity and to avoid unnecessary diagnostic procedures. Clinicians play a critical role in patient education, ensuring understanding of screening results and follow-up pathways. When implemented within organized programs, HPV-based screening enhances both individual patient care and population health outcomes. Its integration into routine practice aligns with current international guideline recommendations.

Despite the strengths of the available evidence, several limitations must be acknowledged. Heterogeneity across studies in terms of screening intervals, triage protocols, and outcome definitions limits direct quantitative comparison. Observational studies contributed substantially to the evidence base and were subject to inherent risks of bias. Data from low-resource settings and marginalized populations remain relatively limited. In addition, long-term outcomes in cohorts with widespread HPV vaccination are still emerging.

Future research should focus on optimizing risk-based screening algorithms that incorporate HPV genotyping, vaccination status, and clinical history. Further evaluation of self-sampling strategies is needed to assess their impact on screening coverage and equity. Long-term follow-up studies in highly vaccinated populations will be essential to refine screening intervals and age thresholds. Economic and implementation research should accompany clinical studies to guide sustainable policy decisions. These efforts will be crucial to adapting screening programs to evolving epidemiological contexts.

In conclusion, HPV-based cervical cancer screening represents a paradigm shift in cancer prevention, supported by robust and growing evidence. Its successful implementation requires coordinated, multidisciplinary efforts involving clinicians, public health authorities, and policymakers. Evidence-based, individualized screening strategies are essential to maximize benefits while minimizing harms. Continued surveillance, research, and guideline refinement will ensure that screening programs remain effective and equitable. HPV-based screening stands as a critical component of global strategies to eliminate cervical cancer as a public health problem.

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