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Review Article

Role of prior and peri-excisional Human Papillomavirus Vaccination, including the 9-Valent vaccine, on subsequent lower genital tract dysplasia following cervical excisional surgery: A Systematic review.

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Abstract
Background
Cervical excisional procedures, such as the loop electrosurgical excision procedure and conization, are standard treatments for high-grade cervical intraepithelial neoplasia. Despite effective lesion removal, recurrence or persistence of lower genital tract dysplasia remains a clinically relevant concern. Prophylactic human papillomavirus vaccination, particularly the 9-valent vaccine, has been proposed as a secondary preventive strategy to reduce post-treatment disease recurrence.
Objective: To systematically evaluate the effect of human papillomavirus vaccination administered prior to or around the time of cervical excisional surgery, with emphasis on the 9-valent vaccine, on subsequent lower genital tract dysplasia.
Methods
This systematic review followed PRISMA 2020 guidelines. A comprehensive search was conducted across PubMed/MEDLINE, Embase, Scopus, Web of Science, and Google Scholar. Comparative studies evaluating vaccinated versus unvaccinated women undergoing cervical excisional treatment and reporting post-treatment dysplasia outcomes were included. Owing to heterogeneity in vaccine type, vaccination timing, and outcome definitions, a qualitative narrative synthesis was performed.
Results
Seven studies met the inclusion criteria, including post-hoc analyses of randomized trials and observational cohort studies. One study specifically evaluated prior 9-valent human papillomavirus vaccination, while the remaining studies assessed quadrivalent or mixed vaccine schedules administered before or after excisional treatment. Across all studies, vaccinated women consistently demonstrated lower rates of recurrent cervical intraepithelial neoplasia grade 2 or higher, high-grade squamous intraepithelial lesions, or lower genital tract dysplasia compared with unvaccinated controls.
Conclusion
Current evidence indicates that human papillomavirus vaccination administered prior to or around cervical excisional surgery is associated with a reduced risk of subsequent lower genital tract dysplasia. While most data support peri- or post-excisional vaccination, emerging evidence suggests additional benefit with prior 9-valent vaccination.
Future research
Prospective randomized trials and large population-based cohort studies are needed to clarify optimal vaccination timing, compare vaccine valencies, and standardize post-treatment outcome assessment.

Keywords: *Human papillomavirus; 9-valent HPV vaccine; Cervical excision; Loop electrosurgical excision procedure; Cervical intraepithelial neoplasia; Lower genital tract dysplasia; Secondary prevention*
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Introduction

Persistent infection with high-risk human papillomavirus (HPV) types represents the principal etiological factor in the development of cervical intraepithelial neoplasia (CIN) and cervical cancer[1,2]. Despite advances in screening and preventive strategies, HPV-associated cervical disease continues to pose a substantial global public health burden, particularly in low- and middle-income countries where access to organized screening and vaccination programs remains limited[3,4]. High-grade CIN (CIN2-3) is widely recognized as a true premalignant condition with a significant risk of progression to invasive carcinoma if left untreated [5,6].

Cervical excisional procedures, including loop electrosurgical excision procedure (LEEP) and cold-knife conization, constitute the standard of care for the management of high-grade CIN [7,8]. These interventions aim to achieve complete removal of dysplastic epithelium while preserving cervical structure and reproductive function. Although excisional treatment is highly effective in achieving initial disease clearance, post-treatment recurrence or persistence of dysplasia remains a clinically relevant challenge [9,10,11]. Reported recurrence rates range from approximately 5% to 15%, necessitating prolonged surveillance and, in some cases, repeat surgical interventions, which may adversely impact fertility, obstetric outcomes, and overall quality of life [12,13].

Recurrence following excisional treatment is increasingly recognized as a multifactorial process. Persistent infection with high-risk HPV types remains the most important determinant, while additional contributing factors include positive surgical margins, host immune status, smoking, and reinfection with oncogenic HPV genotypes [14,15,16]. Importantly, while excisional treatment removes the morphological manifestation of disease, it does not eliminate susceptibility to HPV infection or reinfection [17]. Consequently, strategies aimed at reducing post-treatment HPV persistence and preventing reinfection have emerged as an important focus in cervical disease prevention [18,19].

Prophylactic HPV vaccines were originally developed for primary prevention and have demonstrated high efficacy in preventing HPV infection and HPV-associated premalignant lesions in HPV-naïve populations [20,21]. Over time, widespread vaccination programs have resulted in substantial reductions in HPV prevalence and cervical disease incidence. The introduction of the 9-valent HPV vaccine, which protects against additional oncogenic HPV types beyond those covered by earlier vaccines, has further expanded preventive coverage and enhanced population-level protection [22,23].

In recent years, increasing attention has been directed toward the potential role of HPV vaccination as a secondary preventive strategy in women undergoing excisional treatment for high-grade CIN. Proposed mechanisms include prevention of new HPV infections, reduction of reinfection from sexual partners, limitation of viral reactivation, and enhancement of immune-mediated viral clearance in the post-treatment cervical microenvironment. Although HPV vaccines are not therapeutic, vaccination may favorably modify the biological milieu following excisional treatment, thereby lowering the likelihood of disease recurrence [24,25].

Despite accumulating evidence supporting a protective role of HPV vaccination in the post-treatment setting, the available literature remains heterogeneous. Studies vary considerably with respect to vaccine type, timing of vaccination relative to excisional surgery, study design, and outcome definitions. Moreover, although the 9-valent HPV vaccine offers broader oncogenic coverage, data specifically evaluating prior or peri-excisional administration of the 9-valent vaccine remain limited. This evidence gap complicates the development of clear clinical recommendations regarding optimal vaccination timing and vaccine selection for women undergoing cervical excisional procedures.

Therefore, the present systematic review was undertaken to synthesize and critically evaluate the available evidence on the effect of HPV vaccination administered before or around the time of cervical excisional surgery on subsequent lower genital tract dysplasia, with particular emphasis on the role of the 9-valent HPV vaccine. By consolidating existing data, this review aims to clarify current evidence, identify gaps in knowledge, and inform future research directions and clinical practice.

Materials and methods

Study design and reporting guidelines

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020[26] statement to ensure methodological rigor, transparency, and reproducibility.

Review question

The review addressed the following question:
Does HPV vaccination administered prior to or around the time of cervical excisional surgery reduce the risk of subsequent lower genital tract dysplasia?

Search strategy

A comprehensive electronic literature search was performed across the following databases:

- PubMed/MEDLINE

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- Embase
- Scopus
- Web of Science
- Google Scholar

The search covered studies published from database inception to January 2026. The search strategy employed combinations of Medical Subject Headings (MeSH) terms and free-text keywords, including:
"HPV vaccination", "9-valent HPV vaccine", "conization", "LEEP", "cervical excision", "CIN recurrence", "HSIL", and "lower genital tract dysplasia". In addition, the reference lists of all included studies were manually screened to identify any additional relevant articles not captured through the electronic search.

Eligibility criteria

Inclusion criteria

- Studies were eligible for inclusion if they met the following criteria:
- Included women undergoing cervical excisional surgery (LEEP or conization)
- Employed a comparative design evaluating vaccinated versus unvaccinated cohorts
- Reported HPV vaccination administered prior to or around the time of excisional treatment
- Assessed outcomes related to recurrent CIN, HSIL, or lower genital tract dysplasia
- Used randomized or observational study designs

Exclusion criteria

- Studies were excluded if they:
- Reported only immunogenicity or virological outcomes without dysplasia-related endpoints
- Lacked post-treatment follow-up
- Were case reports, editorials, commentaries, or narrative reviews

Study selection

Two reviewers independently screened titles and abstracts for eligibility. Full-text articles were subsequently assessed for inclusion based on the predefined criteria. Any discrepancies between reviewers were resolved through discussion and consensus.

Data extraction

Data were independently extracted from each included study using a standardized data extraction form. Extracted variables included:

- Author and year of publication
- Country and study design
- Vaccine type and timing of administration
- Type of excisional procedure
- Duration of follow-up
- Outcome measures

Data synthesis

Given the heterogeneity among studies in terms of vaccine type, timing of vaccination, outcome definitions, and follow-up duration, a quantitative meta-analysis was not performed. Instead, results were synthesized using a qualitative narrative approach.

Results

Study selection

The initial electronic search across PubMed/MEDLINE, Embase, Scopus, Web of Science, and Google Scholar yielded 312 records. After removal of 86 duplicate studies, 226 records remained for title and abstract screening, of which 198 were excluded due to irrelevance to the review question, lack of cervical excisional treatment, or non-comparative study design. The full texts of 28 potentially eligible articles were assessed in detail, resulting in the exclusion of 21 studies for reasons including reporting only HPV immunogenicity or viral clearance without dysplasia outcomes, absence of post-treatment follow-up, or inappropriate study design. Ultimately, seven studies met all predefined inclusion criteria and were included in the final qualitative synthesis. (Figure 1)

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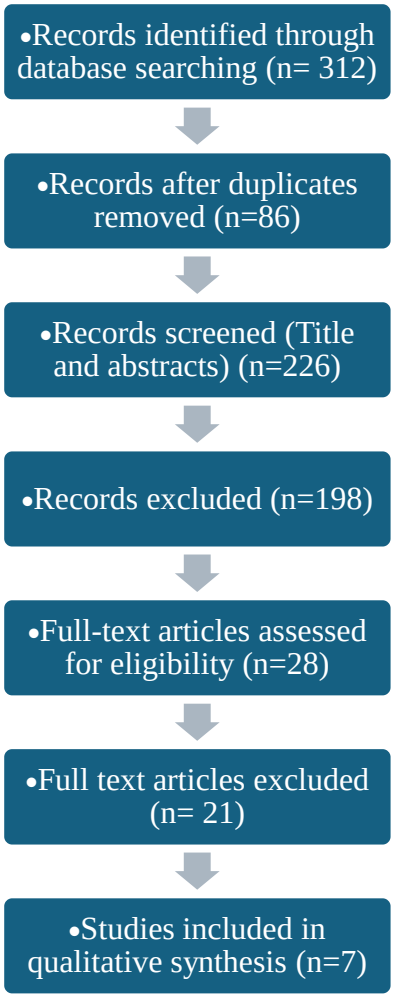

Figure 1: PRISMA Flowchart

Characteristics of included studies

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Table 1. Characteristics of studies included in the systematic review

Author (Year)	Country	Study Design	Sample Size (Vaccinated / Unvaccinated)	Vaccine Type	Timing of Vaccination	Excisional Procedure	Follow-up Duration	Outcome Assessed	Key Findings
Joura et al. (2026) [27]	Multinational	Post-hoc analysis of randomized controlled trials	1,350 / 5,619	9-valent HPV vaccine	Prior to excision (0.1–4.4 years before surgery)	LEEP / Conization	Up to 6 years	Cervical, vaginal, and vulvar SIL	Significantly reduced risk of subsequent lower genital tract dysplasia in women vaccinated prior to excisional surgery
Petráš et al. (2025) [28]	Czech Republic	Retrospective cohort study	707 / 1,133	Prophylactic HPV (mixed, incl. 9vHPV)	Pre- and post-excision	Conization	Median 48 months	CIN2+ recurrence	HPV vaccination is associated with significantly lower recurrence risk, independent of margin status
Chen et al. (2023) [29]	China	Prospective cohort study	148 / 273	Quadrivalent HPV vaccine	After LEEP	LEEP	24 months	CIN2+ recurrence	HPV vaccination significantly reduced CIN2+ recurrence and persistent HPV infection
Gómez de la Rosa et al. (2021)[30]	Spain	Longitudinal observational study	160 / 171	Quadrivalent HPV vaccine	Post-conization	Conization	4 years	HSIL recurrence	Vaccinated women had a 73.5% relative risk reduction in recurrence compared with unvaccinated controls.
Piñó et al. (2020)[31]	Spain	Observational real-world study	191 / 197	Quadrivalent HPV vaccine	Adjuvant to excision	Conization	24 months	Persistent /recurrent HSIL	Lower persistence and recurrence of HSIL observed in vaccinated women
Ghelardi et al. (2018)[32]	Italy	Multicenter cohort study (SPERANZA project)	165 / 201	Quadrivalent HPV vaccine	Post-treatment	LEEP / Conization	30 months	CIN2+ recurrence	HPV vaccination after treatment significantly reduced the recurrence of high-grade cervical lesions
Kang et al. (2013)[33]	South Korea	Retrospective cohort study	360 / 317	Quadrivalent HPV vaccine	Post-LEEP	LEEP	Mean 24 months	CIN2–3 recurrence	Recurrence rates were significantly lower in vaccinated patients compared with unvaccinated patients.

Risk of bias in studies

Overall, the included studies demonstrated moderate methodological quality. Observational cohort studies were subject to potential selection bias and residual confounding, particularly related to vaccination uptake and baseline HPV status. Post-hoc analyses of randomized trials were limited by non-randomized exposure to vaccination in the excision subgroup. Most studies adequately reported follow-up duration and outcome definitions, although blinding and adjustment for behavioral confounders were inconsistently described.

Results of individual studies

Across all included studies, vaccinated cohorts consistently showed lower rates of recurrent CIN2+, HSIL, or lower genital tract dysplasia compared with unvaccinated controls. Effect estimates reported in individual studies demonstrated relative risk reductions

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ranging from approximately 40% to over 70%, with confidence intervals indicating statistical significance in most analyses. Summary statistics and effect estimates for each study are presented in Table 1.

Results of syntheses

The narrative synthesis demonstrated consistent directionality of effect favoring HPV vaccination across diverse study designs and populations. Studies evaluating vaccination administered prior to excisional surgery showed the largest reductions in subsequent dysplasia, while peri- and post-excisional vaccination was associated with moderate but clinically meaningful benefit. Risk of bias among contributing studies was moderate, primarily due to observational designs.

Reporting biases

Assessment of reporting bias did not reveal systematic non-reporting of outcomes across included studies. Most studies reported prespecified dysplasia-related endpoints. However, variability in outcome definitions and follow-up intervals limited cross-study comparability.

Certainty of evidence

The certainty of evidence was judged to be moderate for recurrence of CIN2+ and HSIL, supported by consistency across multiple cohorts and meta-analyses. Certainty was lower for outcomes specific to prior 9-valent HPV vaccination due to limited direct evidence.

Discussion

The present systematic review demonstrated that human papillomavirus (HPV) vaccination administered prior to or around the time of cervical excisional surgery was associated with a reduced risk of subsequent lower genital tract dysplasia. Across all seven included studies, vaccinated women consistently exhibited lower rates of recurrent CIN2+, high-grade squamous intraepithelial lesions (HSIL), or related dysplastic lesions compared with unvaccinated controls, despite heterogeneity in study design, population characteristics, vaccination timing, and surgical modality. The uniform direction of effect observed across diverse clinical settings suggested that HPV vaccination may have provided an additional protective benefit beyond surgical excision alone, particularly in women who remained susceptible to persistent or recurrent HPV infection.

Among the included studies, the most direct evidence supporting a true pre-treatment vaccination effect was reported by Joura et al. (2026) [27], who demonstrated a statistically significant reduction in subsequent cervical, vaginal, and vulvar dysplasia among women vaccinated with the 9-valent HPV vaccine before undergoing excisional treatment. This study was distinct in evaluating vaccination administered well before surgery, thereby strengthening the temporal association and reducing the likelihood of reverse causality. In contrast, the remaining included studies primarily assessed peri- or post-excisional vaccination, most commonly using quadrivalent vaccine schedules. Nevertheless, these studies consistently reported reduced recurrence or persistence of high-grade lesions, as observed in cohorts reported by Ghelardi et al. (2018) [32], Kang et al. (2013) [33], Chen et al. (2023)[29], Piñó et al. (2020)[31], Casajuana-Pérez et al. (2022)[34], and Petráš et al. (2025)[28]. Collectively, these findings suggested that vaccination administered around the time of excision, including after treatment, may have conferred a measurable reduction in subsequent dysplastic outcomes.

The findings of the present review were strongly supported by multiple high-quality meta-analyses and systematic reviews. Jentschke et al. (2020)[35] demonstrated a significant reduction in recurrent cervical dysplasia following conization among vaccinated women, while Bartels et al. (2020)[36] reported comparable reductions across pooled observational cohorts. Di Donato et al. (2021)[37] further reinforced this association by showing that adjuvant HPV vaccination significantly reduced the risk of recurrent CIN after surgical treatment. Consistent conclusions were reported by Eriksen et al. (2022) [38], who demonstrated that HPV vaccination administered in relation to excisional treatment was associated with a lower recurrence risk across different populations. Similarly, the systematic review by Lichter et al. (2020)[39] supported the protective role of adjuvant vaccination, particularly in previously unvaccinated women, aligning closely with the observational evidence included in the present synthesis.

Population-based and registry-derived studies provided additional real-world validation of these findings. The Danish cohort study by Sand et al. (2020)[40] reported a significantly lower risk of CIN2+ recurrence after conization among vaccinated women, supporting the effectiveness of vaccination at the population level. Likewise, the VENUS study by Casajuana-Pérez et al. (2022)[34] demonstrated reduced recurrence of HSIL/CIN2–3 following vaccination in women treated by conization. More recent real-world cohorts, including those reported by Dvořák et al. (2024)[41] and Sørbye et al. (2026)[42], further demonstrated reduced recurrence or favorable HPV-related outcomes following vaccination, particularly in clinical settings where 9-valent vaccines were increasingly utilized. These observations complemented the findings reported by Joura et al.

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(2026)[27] and suggested that broader genotype coverage may have enhanced post-treatment protection.

The timing of vaccination emerged as a critical modifier of effect across the available literature. The meta-analysis and meta-regression conducted by Petráš et al. (2023)[28] demonstrated that earlier vaccination relative to surgical excision was associated with greater reductions in recurrence risk, providing a plausible explanation for the stronger protective effect observed in women vaccinated prior to surgery. This temporal relationship also explained the variability in effect sizes across studies in which vaccination was administered at different intervals before or after treatment. Studies evaluating delayed vaccination generally reported smaller, yet still favorable, effects, indicating that peri-excisional immunization may have conferred partial protection even after surgical clearance of dysplastic tissue.

Biological plausibility for the observed association was supported by mechanistic and translational studies. Although prophylactic HPV vaccines were not therapeutic, they were shown to prevent new HPV infections, reduce reinfection with oncogenic types, and induce immune responses that exceeded those generated by natural infection. Reuschenbach et al. (2023)[43] emphasized that vaccine-induced immunity may have reduced viral persistence in the post-excisional cervix, thereby lowering the probability of recurrent dysplasia. Foundational work on HPV natural history by Schiffman et al. (2016)[44] further supported this rationale by highlighting that excisional treatment removes dysplastic tissue but does not eliminate susceptibility to future HPV infection. Additionally, virological studies by Rykkelid et al. (2024)[45] and Palumbo et al. (2025)[46] demonstrated improved HPV viral clearance or favorable viral status following vaccination, indirectly supporting the reduced histologic recurrence observed in clinical outcome studies.

Evidence from primary vaccine efficacy trials also provided important contextual support. Landmark trials such as the PATRICIA study (Paavonen et al., 2009)[47], the FUTURE II trial (2007)[48], and the randomized trial by Zhu et al. (2019)[49] demonstrated strong prophylactic efficacy of HPV vaccines against persistent infection and high-grade precancerous lesions in HPV-naïve populations. Although these trials did not specifically evaluate post-excisional recurrence, their findings reinforced the preventive capacity of HPV vaccination and supported the biological rationale that reduced incident infections may contribute to lower post-treatment disease risk. Furthermore, population-level analyses such as the meta-analysis by Drolet et al. (2019)[50] documented substantial reductions in HPV-related outcomes following widespread vaccination programs, suggesting that both individual and herd immunity effects may have influenced recurrence risk in vaccinated cohorts.

Despite the overall consistency of findings, several limitations across the evidence base required careful consideration. Most included studies were observational in nature and were therefore susceptible to residual confounding and selection bias. Vaccine type, vaccination timing, outcome definitions, and follow-up duration varied considerably, limiting direct comparability and precluding quantitative meta-analysis in the present review. Moreover, not all syntheses reported uniformly positive findings; the meta-analysis by Cao et al. (2024)[51] highlighted variability in effect estimates depending on study design and endpoints, underscoring the need for cautious interpretation. Importantly, evidence specific to prior 9-valent HPV vaccination remained limited, with only one included study [Joura et al. (2026)][27] directly addressing this exposure, indicating a critical gap in the literature.

Nevertheless, the consistency of reduced recurrence observed across multiple independent cohorts, meta-analyses, and population-based studies supported the potential role of HPV vaccination as an adjunctive preventive strategy in women undergoing cervical excisional treatment. This interpretation was reflected in contemporary clinical guidance, including the ASCCP Committee Opinion (2023)[52] and the ACOG Practice Advisory (2023)[53], both of which acknowledged accumulating evidence supporting adjuvant HPV vaccination in appropriately selected patients while emphasizing individualized clinical decision-making.

In summary, the present systematic review suggested that HPV vaccination administered prior to or around cervical excisional surgery was associated with a reduced risk of subsequent lower genital tract dysplasia. While peri-excisional vaccination demonstrated consistent benefit across multiple studies, emerging evidence indicated that prior 9-valent HPV vaccination may have conferred additional protection. Future well-designed prospective studies focusing on vaccine valency, optimal timing, and standardized outcome definitions are warranted to refine clinical recommendations and establish definitive guidelines.

Limitations of the evidence

Most included studies were observational, introducing susceptibility to confounding and selection bias. Variability in vaccine type, timing of administration, outcome definitions, and follow-up duration limited quantitative synthesis. Evidence specific to prior 9-valent HPV vaccination remains sparse.

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Limitations of the review process

This review did not include unpublished data or trial registry searches, raising the possibility of publication bias. Meta-analysis was not performed due to heterogeneity, which may limit the precision of pooled effect estimates.

Implications for Practice and Policy

The findings support consideration of HPV vaccination as an adjunctive strategy in women undergoing cervical excisional treatment. Integration of vaccination into post-treatment care pathways may reduce recurrence risk and long-term surveillance burden, particularly in settings with high HPV prevalence.

Conclusion

This systematic review demonstrated that human papillomavirus (HPV) vaccination administered prior to or around the time of cervical excisional surgery was associated with a reduced risk of subsequent lower genital tract dysplasia, with vaccinated women consistently exhibiting lower rates of recurrent CIN2+, high-grade squamous intraepithelial lesions (HSIL), or related dysplastic lesions compared with unvaccinated controls across diverse study designs and populations. While the majority of available evidence supported peri- or post-excisional vaccination with quadrivalent HPV vaccines, emerging data indicated that prior vaccination with the 9-valent HPV vaccine may have conferred additional protection due to broader oncogenic HPV type coverage; however, evidence specific to this exposure remained limited. Heterogeneity in vaccination timing, vaccine type, outcome definitions, and follow-up duration precluded quantitative synthesis and highlighted important gaps in the existing literature. Overall, these findings supported the potential role of HPV vaccination as an adjunctive secondary preventive strategy in women undergoing cervical excisional treatment and underscored the need for well-designed prospective studies to clarify optimal vaccination timing, vaccine valency, and standardized clinical outcomes in order to inform definitive clinical guidelines.

Acknowledgement

The authors acknowledge the contributions of the investigators of the original studies included in this review.

List of abbreviations

CIN – Cervical intraepithelial neoplasia
HSIL – High-grade squamous intraepithelial lesion
HPV – Human papillomavirus
LEEP – Loop electrosurgical excision procedure

Author contributions

SP conceived the study. KS conducted the literature search, data extraction, and manuscript drafting. Both authors reviewed and approved the final manuscript.

Author biography

Dr. Suvarna Palanivelu is an Associate Professor of Obstetrics and Gynecology at Meenakshi Medical College Hospital and Research Institute, Tamil Nadu, India.

Dr. Karthik Shunmugavelu is an Assistant Professor in the Department of Dentistry with academic and clinical interests in oral pathology, translational research, and evidence synthesis.

Registration and protocol

This systematic review was not registered in a public database. A formal review protocol was not prepared prior to study initiation.

Support

No external funding or non-financial support was received for this study.

Competing interests

The authors declare no competing interests.

Availability of data, code, and materials

All data extracted and analyzed in this review are derived from published studies and are available within the article. No analytic code was generated.

References

1. Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. Am J Epidemiol. 2008 Jul 15;168(2):123-37.

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https://doi.org/10.1093/aje/kwn036 PMid:18483125 PMCid:PMC2878094

2. Liu Y, Ai H. Comprehensive insights into human papillomavirus and cervical cancer: Pathophysiology, screening, and vaccination strategies. Biochim Biophys Acta Rev Cancer. 2024 Nov;1879(6):189192. https://doi.org/10.1016/j.bbcan.2024.189192 PMid:39349261
3. Allanson ER, Schmeler KM. Cervical Cancer Prevention in Low- and Middle-Income Countries. Clin Obstet Gynecol. 2021 Sep 1;64(3):501-518.https://doi.org/10.1097/GRF.0000000000000629 PMid:34120126 PMCid: PMC8324570
4. Huang Y, Lin W, Chen X, Zheng X, Yi H, Zhang L. Analyzing and forecasting global cervical cancer burden based on WHO's elimination strategy: insights and projections from a 1990-2021 global burden of disease (GBD) study covering 204 countries and territories. J Adv Res. 2025 Sep 25:S2090-1232(25)00742-8. doi: 10.1016/j.jare.2025.09.038. Epub ahead of print. PMID: 41015178.
5. Ehlers U, Hoischen L, Stalp JL, Hachenberg J, Ramachandran D, Brüning B, Jentschke M, Hillemanns P, Denecke A. The treatment of cervical intraepithelial neoplasia grade 2 (HSIL): between active surveillance and surgery-a 10-year monocentric data analysis. Arch Gynecol Obstet. 2025 Oct;312(4):1125-1132. https://doi.org/10.1007/s00404-025-08097-1 PMid:40627062 PMCid:PMC12414026
6. Mello V, Sundstrom RK. Cervical Intraepithelial Neoplasia. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544371/
7. Khan MJ, Smith-McCune KK. Treatment of cervical precancers: back to basics. Obstet Gynecol. 2014 Jun;123(6):1339-1343. https://doi.org/10.1097/AOG.0000000000000287 PMid:24807323 PMCid:PMC4077778
8. Khunnarong J, Bunyasontikul N, Tangjitgamol S. Treatment Outcomes of Patients With Cervical Intraepithelial Neoplasia or Invasive Carcinoma Who Underwent Loop Electrosurgical Excision Procedure. World J Oncol. 2021 Aug;12(4):111-118. https://doi.org/10.14740/wjon1391 PMid:34349855 PMCid:PMC8297047
9. Wang XI, Huang F, Zhang S. Loop Electrosurgical Excision Procedure vs. Cold Knife Cone in Treatment of Cervical Intraepithelial Neoplasia: Review of 447 Cases. Ann Clin Lab Sci. 2017 Nov;47(6):663-667. PMID: 29263039.
10. Alsomali, Rawdah & wahishi, Amna & Alfaraj, Nahlah & Almutairi, Nadiyah & Almalki, Fatimah. (2025). Perioperative Nursing Care and Clinical Outcomes in Cold Knife Conization of the Cervix: Pre-Procedure Assessment, Intraoperative Support, and Postoperative Surveillance. Saudi Journal of Medicine and Public Health. 2. 2841-2852. 10.64483/202522480. https://doi.org/10.64483/202522480
11. Connor, J., Hartenbach, E., Glob. libr. women's med., (ISSN: 1756-2228) 2008; DOI 10.3843/GLOWM.10228
12. Kocken M, Helmerhorst TJ, Berkhof J, Louwers JA, Nobbenhuis MA, Bais AG, Hogewoning CJ, Zaal A, Verheijen RH, Snijders PJ, Meijer CJ. Risk of recurrent high-grade cervical intraepithelial neoplasia after successful treatment: a long-term multi-cohort study. Lancet Oncol. 2011 May;12(5):441-50. https://doi.org/10.1016/S1470-2045(11)70078-X PMid:21530398
13. Lili E, Chatzistamatiou K, Kalpaktsidou-Vakiani A, Moysiadis T, Agorastos T. Low recurrence rate of high-grade cervical intraepithelial neoplasia after successful excision and routine colposcopy during follow-up. Medicine (Baltimore). 2018 Jan;97(4):e9719. https://doi.org/10.1097/MD.0000000000009719 PMid:29369205 PMCid:PMC5794389
14. Mitta K, Tsertanidou A, Tsakiridis I, Zoubanioti E, Dagklis T, Mamopoulos A, Athanasiadis A, Kalogiannidis I. Risk factors related to recurrence after surgical excision procedure for cervical dysplasia. Hippokratia. 2023 Oct-Dec;27(4):132-140. PMID: 39372323; PMCID: PMC11451503.
15. Frega A, Sopracordevole F, Scirpa P, Biamonti A, Lorenzon L, Scarani S, De Sanctis L, Pacchiarotti A, Moscarini M, French D. The re-infection rate of high-risk HPV and the recurrence rate of vulvar intraepithelial neoplasia (VIN) usual type after surgical treatment. Med Sci Monit. 2011 Sep;17(9):CR532-5. https://doi.org/10.12659/MSM.881941 PMid:21873951 PMCid:PMC3560503

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https://doi.org/10.51168/sjhrafrica.v5i12.2397
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16. Na J, Li Y, Lu Q, Wang Y, Han S, Wang J. Investigating the impact of persistent HPV infection on recurrence of lesions post-surgery for early-stage cervical cancer and related influencing factors. Front Oncol. 2025 Feb 4;15:1506521. https://doi.org/10.3389/fonc.2025.1506521 PMid:39968075 PMCid:PMC11832401
17. Khairkhah N, Bolhassani A, Najafipour R. Current and future direction in treatment of HPV-related cervical disease. J Mol Med (Berl). 2022 Jun;100(6):829-845. https://doi.org/10.1007/s00109-022-02199-y PMid:35478255 PMCid:PMC9045016
18. Huber J, Mueller A, Sailer M, Regidor PA. Human papillomavirus persistence or clearance after infection in reproductive age. What is the status? Review of the literature and new data of a vaginal gel containing silicate dioxide, citric acid, and selenite. Women's Health (Lond). 2021 Jan-Dec;17:17455065211020702. https://doi.org/10.1177/17455065211020702 PMid:34096424 PMCid:PMC8785287
19. Huiling Ni, Canhua Huang, Zhi Ran, Shan Li, Chunmei Kuang, Yu Zhang, Kai Yuan, Targeting HPV for the prevention, diagnosis, and treatment of cervical cancer, Journal of Molecular Cell Biology, Volume 16, Issue 10, October 2024, mjae046, https://doi.org/10.1093/jmcb/mjae046 PMid:39402008 PMCid: PMC12080229
20. Mo Y, Ma J, Zhang H, Shen J, Chen J, Hong J, Xu Y, Qian C. Prophylactic and Therapeutic HPV Vaccines: Current Scenario and Perspectives. Front Cell Infect Microbiol. 2022 Jul 4;12:909223. https://doi.org/10.3389/fcimb.2022.909223 PMid:35860379 PMCid:PMC9289603
21. Poljak M. Prophylactic human papillomavirus vaccination and primary prevention of cervical cancer: issues and challenges. Clin Microbiol Infect. 2012 Oct;18 Suppl 5:64-9. https://doi.org/10.1111/j.1469-0691.2012.03946.x PMid:22862799
22. Luckett R, Feldman S. Impact of 2-, 4- and 9-valent HPV vaccines on morbidity and mortality from cervical cancer. Hum Vaccin Immunother. 2016 Jun 2;12(6):1332-42. https://doi.org/10.1080/21645515.2015.1108500 PMid:26588179 PMCid:PMC4964711
23. Bhalerao V, Gotarkar S, Muneshwar K. The Impact of HPV Vaccination on Cervical Cancer in adolescent females: A narrative review. J Family Med Prim Care. 2024 Nov;13(11):4775-4782. https://doi.org/10.4103/jfmpc.jfmpc_235_24 PMid:39722908 PMCid:PMC11668371
24. Md.Rezaul Islam, Abdur Rauf, Most.Nazmin Aktar, Md Naeem Hossain Fakir, Sadiya Islam Trisha, Asraful Islam Asif, Md.Harun Or Rashid, Md.Ibrahim Khalil Al-Imran, Gazi Kaifeara Thufa, Farhana Prodhan Emu, Hassan A. Hemeg, Hanan A. Ogaly, Rekha Thiruvengadam, Seung-Hyun Kim, Muthu Thiruvengadam, Recent advances in human papillomavirus vaccines and therapeutic strategies: Combating cervical and non-cervical cancers, Genes & Diseases, 2025, 101880, ISSN 2352-3042, https://doi.org/10.1016/j.gendis.2025.101880.
25. Trottier H, Ferreira S, Thomann P, Costa MC, Sobrinho JS, Prado JC, Rohan TE, Villa LL, Franco EL. Human papillomavirus infection and reinfection in adult women: the role of sexual activity and natural immunity. Cancer Res. 2010 Nov 1;70(21):8569-77. https://doi.org/10.1158/0008-5472.CAN-10-0621 PMid:20978200 PMCid:PMC4068337
26. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. https://doi.org/10.1136/bmj.n71 PMid:33782057 PMCid: PMC8005924
27. Joura E, Kjaer SK, Bautista O, Luxembourg A, Saah A, Giuliano A. Effect of Prior 9-Valent Human Papillomavirus Vaccination on Subsequent Lower Genital Tract Dysplasia After Cervical Excisional Surgery. Obstet Gynecol. 2026 Jan 1;147(1):73-82. https://doi.org/10.1097/AOG.0000000000006113 PMid:41166720 PMCid:PMC12704676
28. Petráš M, Lomozová D, Dvořák V, Dvořák V Jr, Malinová J, Trnková M, Fišer I, Dlouhý P, Rosina J, Lesná IK. Early and long-term effects of prophylactic and post-excision human papillomavirus vaccination on recurrent high-grade cervical intraepithelial neoplasia relative to margin status: a retrospective cohort study in the Czech Republic. Lancet Reg Health Eur. 2025 Jun 3;55:101337.

Student's Journal of Health Research Africa
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Vol.5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.2397
Review Article

https://doi.org/10.1016/j.lanepe.2025.101337 PMid:40525201 PMCid:PMC12167485

29. Chen M, Li C, Cui Q, Zhou C, Chen P, Yao S. The efficacy of human papillomavirus prophylactic vaccination after conization in preventing cervical intraepithelial neoplasia recurrence: A prospective observational study in China. Eur J Obstet Gynecol Reprod Biol. 2023 Jul;286:10-15. https://doi.org/10.1016/j.ejogrb.2023.04.014 PMid:37159990
30. Gómez de la Rosa AG, Quesada López-Fe A, Vilar Chesa M, Ferrer Machín A, Gimeno Gil A, Molina Bethancourt A, García Bello MÁ, Pérez-Méndez LI. Efficacy of Human Papillomavirus Vaccination 4 Years After Conization for High-Grade Cervical Neoplasia. J Low Genit Tract Dis. 2021 Oct 1;25(4):287-290. https://doi.org/10.1097/LGT.0000000000000625 PMid:34456270
31. Del Pino M, Martí C, Torras I, Henere C, Munmany M, Marimon L, Saco A, Torné A, Ordi J. HPV Vaccination as Adjuvant to Conization in Women with Cervical Intraepithelial Neoplasia: A Study under Real-Life Conditions. Vaccines (Basel). 2020 May 23;8(2):245. https://doi.org/10.3390/vaccines8020245 PMid:32456136 PMCid:PMC7349984
32. Ghelardi A, Parazzini F, Martella F, Pieralli A, Bay P, Tonetti A, Svelato A, Bertacca G, Lombardi S, Joura EA. SPERANZA project: HPV vaccination after treatment for CIN2. Gynecol Oncol. 2018 Nov;151(2):229-234. https://doi.org/10.1016/j.ygyno.2018.08.033 PMid:30197061
33. Kang WD, Choi HS, Kim SM. Is vaccination with the quadrivalent HPV vaccine after a loop electrosurgical excision procedure effective in preventing recurrence in patients with high-grade cervical intraepithelial neoplasia (CIN2-3)? Gynecol Oncol. 2013 Aug;130(2):264-8. https://doi.org/10.1016/j.ygyno.2013.04.050 PMid:23623831
34. Casajuana-Pérez A, Ramírez-Mena M, Ruipérez-Pacheco E, Gil-Prados I, García-Santos J, Bellón-Del Amo M, Hernández-Aguado JJ, de la Fuente-Valero J, Zapardiel I, Coronado-Martín PJ. Effectiveness of Prophylactic Human Papillomavirus Vaccine in the Prevention of Recurrence in Women Conized for HSIL/CIN 2-3: The VENUS Study. Vaccines (Basel). 2022 Feb 14;10(2):288.https://doi.org/10.3390/vaccines10020288 PMid:35214747 PMCid:PMC8879017
35. Jentschke M, Kampers J, Becker J, Sibbertsen P, Hillemanns P. Prophylactic HPV vaccination after conization: A systematic review and meta-analysis. Vaccine. 2020 Sep 22;38(41):6402-6409. https://doi.org/10.1016/j.vaccine.2020.07.055 PMid:32762871
36. Bartels HC, Postle J, Rogers AC, Brennan D. Prophylactic human papillomavirus vaccination to prevent recurrence of cervical intraepithelial neoplasia: a meta-analysis. Int J Gynecol Cancer. 2020 Jun;30(6):777-782. doi: 10.1136/ijgc-2020-001197. Epub 2020 Apr 9. Erratum in: Int J Gynecol Cancer. 2020 Jul;30(7):1085-1086. https://doi.org/10.1136/ijgc-2020-001197corr1 PMid:32487687
37. Di Donato V, Caruso G, Petrillo M, Kontopantelis E, Palaia I, Perniola G, Plotti F, Angioli R, Muzii L, Benedetti Panici P, Bogani G. Adjuvant HPV Vaccination to Prevent Recurrent Cervical Dysplasia after Surgical Treatment: A Meta-Analysis. Vaccines (Basel). 2021 Apr 21;9(5):410. https://doi.org/10.3390/vaccines9050410 PMid:33919003 PMCid:PMC8143003
38. Eriksen DO, Jensen PT, Schroll JB, Hammer A. Human papillomavirus vaccination in women undergoing excisional treatment for cervical intraepithelial neoplasia and subsequent risk of recurrence: A systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2022 Jun;101(6):597-607. https://doi.org/10.1111/aogs.14359 PMid:35470865 PMCid:PMC9564558
39. Lichter K, Krause D, Xu J, Tsai SHL, Hage C, Weston E, Eke A, Levinson K. Adjuvant Human Papillomavirus Vaccine to Reduce Recurrent Cervical Dysplasia in Unvaccinated Women: A Systematic Review and Meta-analysis. Obstet Gynecol. 2020 May;135(5):1070-1083. doi: 10.1097/AOG.0000000000003833. Erratum in: Obstet Gynecol. 2020 Jun;135(6):1489. doi: 10.1097/AOG.0000000000003937. PMID: 32282601.
40. Sand FL, Kjaer SK, Frederiksen K, Dehlendorff C. Risk of cervical intraepithelial neoplasia grade 2 or worse after conization in relation to HPV vaccination status. Int J Cancer. 2020 Aug 1;147(3):641-647. https://doi.org/10.1002/ijc.32752 PMid:31648368

Student's Journal of Health Research Africa
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Vol.5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.2397
Review Article

41. Dvořák V, Petráš M, Dvořák V, Lomozová D, Dlouhý P, Králová Lesná I, Pilka R. Reduced risk of CIN2+ recurrence in women immunized with a 9-valent HPV vaccine post-excision: Retrospective cohort study. Hum Vaccin Immunother. 2024 Dec 31;20(1):2343552. https://doi.org/10.1080/21645515.2024.2343552 PMid:38723789 PMCid:PMC11086040
42. Sørbye, S. W., Antonsen, M., & Richardsen, E. (2026). HPV Vaccination and HPV Outcomes After LEEP: A Retrospective Population-Based Cohort Study from Northern Norway, 2022-2024. Vaccines, 14(1), 44. https://doi.org/10.3390/vaccines14010044 PMid:41600960 PMCid:PMC12846414
43. Reuschenbach M, Doorbar J, Del Pino M, Joura EA, Walker C, Drury R, Rauscher A, Saah AJ. Prophylactic HPV vaccines in patients with HPV-associated diseases and cancer. Vaccine. 2023 Oct 6;41(42):6194-6205. https://doi.org/10.1016/j.vaccine.2023.08.047 PMid:37704498
44. Schiffman M, Doorbar J, Wentzensen N, de Sanjosé S, Fakhry C, Monk BJ, Stanley MA, Franceschi S. Carcinogenic human papillomavirus infection. Nat Rev Dis Primers. 2016 Dec 1;2:16086.https://doi.org/10.1038/nrdp.2016.86 PMid:27905473
45. Rykkelid M, Wennberg HM, Richardsen E, Sørbye SW. Post-Conization HPV Vaccination and Its Impact on Viral Status: A Retrospective Cohort Study in Troms and Finnmark, 2022. Pathogens. 2024 May 2;13(5):381. https://doi.org/10.3390/pathogens13050381 PMid:38787233 PMCid:PMC11124440
46. Palumbo M, Lavitola G, Di Filippo C, Foreste V, Granata M, Imperatore O, Ascione M, Della Corte L, Bifulco G. Impact of Human papillomavirus 9-valent vaccine on viral clearance after surgical treatment: A single-center retrospective observational study. Eur J Obstet Gynecol Reprod Biol. 2025 Jun;310:113994. doi: 10.1016/j.ejogrb.2025.113994. Epub 2025 Apr 20. PMID: 40267822.
47. Paavonen J, Naud P, Salmerón J, Wheeler CM, Chow SN, Apter D, Kitchener H, Castellsague X, Teixeira JC, Skinner SR, Hedrick J, Jaisamrarn U, Limson G, Garland S, Szarewski A, Romanowski B, Aoki FY, Schwarz TF, Poppe WA, Bosch FX, Jenkins D, Hardt K, Zahaf T, Descamps D, Struyf F, Lehtinen M, Dubin G; HPV PATRICIA Study Group. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. Lancet. 2009 Jul 25;374(9686):301-14. doi: 10.1016/S0140-6736(09)61248-4. Epub 2009 Jul 6. Erratum in: The Lancet. 2010 Sep 25;376(9746):1054. PMID: 19586656.
48. FUTURE II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. N Engl J Med. 2007 May 10;356(19):1915-27. https://doi.org/10.1056/NEJMoa061741 PMid:17494925
49. Zhu FC, Hu SY, Hong Y, Hu YM, Zhang X, Zhang YJ, Pan QJ, Zhang WH, Zhao FH, Zhang CF, Yang X, Yu JX, Zhu J, Zhu Y, Chen F, Zhang Q, Wang H, Wang C, Bi J, Xue S, Shen L, Zhang YS, He Y, Tang H, Karkada N, Suryakiran P, Bi D, Struyf F. Efficacy, immunogenicity and safety of the AS04-HPV-16/18 vaccine in Chinese women aged 18-25 years: End-of-study results from a phase II/III, randomised, controlled trial. Cancer Med. 2019 Oct;8(14):6195-6211.https://doi.org/10.1002/cam4.2399 PMid:31305011 PMCid:PMC6797633
50. Drolet M, Bénard É, Pérez N, Brisson M; HPV Vaccination Impact Study Group. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. Lancet. 2019 Aug 10;394(10197):497-509. doi: 10.1016/S0140-6736(19)30298-3. Epub 2019 Jun 26. PMID: 31255301; PMCID: PMC7316527.
51. Cao Q, Hou Y, Wang C, Yin J. Effect of human papillomavirus (HPV) vaccination on HPV infection and recurrence of HPV related disease after local surgical treatment: A systematic review and meta-analysis. PLoS One. 2024 Dec 31;19(12):e0312128. https://doi.org/10.1371/journal.pone.0312128 PMid:39739895 PMCid:PMC11687797
52. Sharpless, Kathryn E. MD, PhD1; Marcus, Jenna Z. MD2; Kuroki, Lindsay M. MD, MSCI3; Wiser, Amy L. MD4; Flowers, Lisa MD, MPH5. ASCCP Committee Opinion: Adjuvant Human Papillomavirus Vaccine for Patients Undergoing Treatment for Cervical Intraepithelial Neoplasia. Journal of Lower Genital Tract Disease 27(1):p 93-96, January 2023.

Student's Journal of Health Research Africa
e-ISSN: 2709-9997, p-ISSN: 3006-1059
Vol.5 No. 12 (2024): December 2024 Issue
https://doi.org/10.51168/sjhrafrica.v5i12.2397
Review Article

https://doi.org/10.1097/LGT.0000000000000703 PMid:36538783 PMCid:PMC9770105

53. American College of Obstetricians and Gynecologists (ACOG). Adjuvant HPV vaccination for patients undergoing treatment for CIN2+. Practice Advisory. 2023.

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