## Supplement

**Table 1S.** PRISMA-S Checklist

| Section/topic | # | Checklist item | Location(s) Reported |
|---|---|---|---|
| **INFORMATION SOURCES AND METHODS** | | | |
| Database name | 1 | Name each individual database searched, stating the platform for each. | See "Material and methods" section; MEDLINE (PubMed, STNext platforms), EMBASE, IPA, DDFU, PQSCITECH (STNext) and COCHRANE, MedRxiv (free online archive) databases were searched. |
| Multi-database searching | 2 | If databases were searched simultaneously on a single platform, state the name of the platform, listing all of the databases searched. | STNext: MEDLINE, EMBASE, IPA, DDFU, PQSCITECH; PubMed: MEDLINE; COCHRANE; free online archive of complete manuscript preprints deposited in server: MedRxiv |
| Study registries | 3 | List any study registries searched. | Not applicable |
| Online resources and browsing | 4 | Describe any online or print source purposefully searched or browsed (e.g., tables of contents, print conference proceedings, web sites), and how this was done. | To identify unpublished studies, we searched Embase for conference proceedings. |
| Citation searching | 5 | Indicate whether cited references or citing references were examined, and describe any methods used for locating cited/citing references (e.g., browsing reference lists, using a citation index, setting up email alerts for references citing included studies). | Recursive search of references in published review or meta-analysis articles were manually screened to identify additional studies. |
| Contacts | 6 | Indicate whether additional studies or data were sought by contacting authors, experts, manufacturers, or other. | Not done |
| Other methods | 7 | Describe any additional information sources or search methods used. | Not done |
| **SEARCH STRATEGIES** | | | |
| Full search strategies | 8 | Include the search strategies for each database and information source, copied and pasted exactly as run. | See "Material and methods" section; eTable 4 – search strategy. |
| Limits and restrictions | 9 | Specify that no limits were used, or describe any limits or restrictions applied to a search (e.g., date or time period, language, study design) and provide justification for their use. | We imposed no language or other restrictions on any of the searches. The inclusion criteria are defined in the "Material and Methods" section. |
| Search filters | 10 | Indicate whether published search filters were used (as originally designed or modified), and if so, cite the filter(s) used. | For our MEDLINE search, we created RSS feeds in PubMed with the keywords "immunization" and "vaccine". |
| Prior work | 11 | Indicate when search strategies from other literature reviews were adapted or reused for a substantive part or all of the search, citing the previous review(s). | Not applicable |

| Section/topic | # | Checklist item | Location(s) Reported |
|---|---|---|---|
| Updates | 12 | Report the methods used to update the search(es) (e.g., rerunning searches, email alerts). | PubMed RSS feeds were set up to provide daily updates of new literature. |
| Dates of searches | 13 | For each search strategy, provide the date when the last search occurred. | A comprehensive literature search was initially run on 7 October and then rerun on 18 January and 25 May 2023. |
| **PEER REVIEW** | | | |
| Peer review | 14 | Describe any search peer review process. | The strategies were peer reviewed by a senior information specialist prior to execution. |
| **MANAGING RECORDS** | | | |
| Total Records | 15 | Document the total number of records identified from each database and other information sources. | "Results" section. A total of 14 322 publications were identified and retrieved from three databases. Flowchart – Figure 1. |
| Deduplication | 16 | Describe the processes and any software used to deduplicate records from multiple database searches and other information sources. | Duplicates were removed by an information specialist (MF) using internal strategy of platform and then manually. Duplicates were manually revised after merging with literature obtained from MedRxiv. |

Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, Koffel JB; PRISMA-S Group. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev. 2021 Jan 26;10(1):39. doi: 10.1186/s13643-020-01542-z. PMID: 33499930; PMCID: PMC7839230.

**Table 2S. PRISMA Checklist**

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review. | Title |
| **ABSTRACT** | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | Abstract |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | Introduction |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | Methods |
| **METHODS** | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | Methods |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Methods, Supplement |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | Methods, Supplement |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Methods, Supplement |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Methods, Supplement, Contributors |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Methods, Supplement |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Methods, Supplement |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Methods, Supplement |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | Methods |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Methods |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | Methods |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | Methods |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | Methods |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | Methods |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | Methods, Supplement |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | Methods, Supplement |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | Methods, Supplement |
| **RESULTS** | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | Flowchart |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | Not applicable |
| Study characteristics | 17 | Cite each included study and present its characteristics. | Supplement |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | Supplement |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Figures |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | Results, Supplement |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the | Results, Supplement |

| Section and Topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | | direction of the effect. | |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | Not applicable |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | Replaced by prediction intervals |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | Results, Supplement |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | Results |
| **DISCUSSION** | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | Discussion |
| | 23b | Discuss any limitations of the evidence included in the review. | Discussion |
| | 23c | Discuss any limitations of the review processes used. | Discussion |
| | 23d | Discuss implications of the results for practice, policy, and future research. | Discussion, Conclusion |
| **OTHER INFORMATION** | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | PROSPERO |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | Authors |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | None |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | Cooperatio 31 fund; Charles University, Czech Republic |
| Competing interests | 26 | Declare any competing interests of review authors. | Declaration |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Authors |

**Table 3S.** MOOSE Checklist

| Criteria | Brief description |
|---|---|
| **Introduction** | |
| Problem definition | HPV vaccine effectiveness in women after conization |
| Hypothesis statement | Null hypothesis: vaccine effectiveness >50% |
| A statement of objectives that includes the study population, condition of interest, exposure or intervention, and the outcome(s) considered | Study outcome: vaccine effectiveness<br>Study exposure: vaccination<br>Study population: female population in risk of high-grade cervical intraepithelial neoplasia |
| **Sources** | |
| Qualifications of literature searchers (e.g., librarians and investigators) | The credential of the only literature researcher (MF) is available in the author team. |
| Search strategy including the time period required for the synthesis and keywords | The search strategy is detailed in Supplement, eTable 4. |
| Effort to include all available studies, including contact with authors | Recursive search of references in published review or meta-analysis articles |
| Databases and registries searched | MEDLINE (PubMed, STNext platforms), EMBASE, IPA, DDFU, PQSCITECH (STNext platform); COCHRANE; free online archive of complete manuscript preprints deposited in server: MedRxiv |
| Search software used, name and version, including special features used (e.g., explosion) | No special search software was used. |
| Use of hand searching (e.g., reference lists of eligible articles) | References of all retrieved articles and recent reviews were searched. |
| List of citations located and those excluded, including justification | Details of the literature search process are outlined in a flowchart (Figure 1) |
| Method of addressing articles published in languages other than English | No language restrictions. |
| Method of handling abstracts and unpublished studies | The search process was not restricted to peer-reviewed studies. |
| Description of any contact with authors | Not done. |
| **Study selection** | |
| Types of study designs considered | Observational studies: case-control, cohort studies or cross-over studies and clinical trials including post-hoc analysis of clinical trials |
| Relevance or appropriateness of studies gathered for assessing the hypothesis to be tested | See study selection (Material and methods) |
| Rationale for the selection and coding of data (e.g., sound clinical principles or convenience) | Study characteristics were extracted independently by two investigators (MP and RM). Effect sizes (incl. 95% CI) of vaccinated versus unvaccinated women were assessed separately whenever possible. In cases where a study reported more than one record of effect size (vaccine effectiveness), each size was related to a particular group according to the investigated factor. |
| Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability) | Data were independently extracted and analyzed by two investigators (MP and RM) with the final decision reached by consensus. Extracted data were placed into a unique database for subsequent arrangement and clustered. |

| Criteria | Brief description |
|---|---|
| Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate) | The adjusted or matched-groups outcomes were prioritized. Moreover, risk of bias was assessed in all studies with NOS stars. |
| Assessment of study quality, including blinding of quality assessors: stratification or regression on possible predictors of study results | The quality of each study was assessed by four assessors (RM, IKL, DL and SN) using the Newcastle-Ottawa Quality Assessment Scale (NOS). NOS-based assessment was different for cohort and case-control studies. |
| Assessment of heterogeneity | The Q-statistic and I-squared statistics were used to assess the heterogeneity of studies. |
| Statistical methods (e.g., complete description of fixed- or random-effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated | Description of the methods of meta-analyses/meta-regression, subgroup analyses, and assessment of publication bias are detailed in the "Statistical methods" and "Results" sections. |
| **Results** | |
| A graph summarizing individual study estimates and the overall estimate | A summary chart of pooled results and those stratified in groups is incorporated in the main body of text (Figures 2, Table 2). |
| A table giving descriptive information for each study included | Table 1 |
| Results of sensitivity testing (e.g., subgroup analysis) | See "Results" section and Table 2, including eTables 6 and 7. |
| Indication of statistical uncertainty of findings | 95% confidence intervals are provided with all summary effect estimates including prediction interval. |
| **Discussion** | |
| Strengths and weaknesses | The strength of evidence; assessment of RoB; additional analyzes of effect of small and unpublished studies were performed. Publication bias was tested using outcomes of both models of random and fixed effects. |
| Potential biases in the review process (e.g., publication bias) | See "Statistical Methods", "Results" and "Discussion" sections. |
| Justification for exclusion (e.g., exclusion of non-English-language citations) | See "Material and methods" section (inclusion criteria) |
| Assessment of quality of included studies | See "Results" section (Quality of evidence) |
| Consideration of alternative explanations for observed results | The outcome of pre-conization vaccination must be interpreted with caution given the limited number of studies. |
| Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review) | The study outcome can be generally accepted because criteria supporting the strength of evidence were met. |
| Guidelines for future research | We underlined that our findings cannot be regarded as conclusive for pre-conization immunization. |
| Disclosure of funding source | This research was funded by the Cooperatio 31 fund, Health Sciences, Charles University, Prague, Czech Republic. |

**Table 4S.** Search strategy

| **Search query: MEDLINE, EMBASE, PQSCITECH, IPA, DDFU (STNext platform)** |
|---|
| L1 QUE ?VACCIN? OR ?IMMUNIS? OR ?IMMUNIZ? |
| L2 QUE GARDASIL OR CERVARIX OR CECOLIN |
| L3 QUE "VACCINATION"/CT OR "VACCINE"/CT OR "VACCINES"/CT OR "VIRAL VACCINES"/CT OR |
| "IMMUNIZATION"/CT OR "IMMUNIZATION PROGRAMS"/CT OR "IMMUNIZATION, SECONDARY"/CT |
| L4 QUE "CANCER VACCINES"/CT OR "MASS VACCINATION"/CT |
| L5 QUE "PAPILLOMAVIRUS VACCINES"/CT OR "HUMAN PAPILLOMAVIRUS RECOMBINANT VACCINE |
| QUADRIVALENT, TYPES 6, 11, 16, 18"/CT |
| L6 QUE "HUMAN PAPILLOMAVIRUS 6"/CT OR "HUMAN PAPILLOMAVIRUS 11"/CT OR "HUMAN PAPILLOMAVIRUS 16"/CT OR "HUMAN PAPILLOMAVIRUS 18"/CT OR "HUMAN PAPILLOMAVIRUS 31"/CT L7 QUE "ALPHAPAPILLOMAVIRUS"/CT OR "PAPILLOMAVIRIDAE"/CT OR "PAPILLOMAVIRUS INFECTIONS"/CT |
| L8 QUE HPV OR HUMAN(W)PAPILLOMA(W)VIR? OR HUMAN(W)PAPILLOMAVIR? OR HUMANPAPILLOMAVIR? OR ALPHAPAPILLOMAVIR? OR PAPILLOMA(W)VIR? OR PAPILLOMAVIR? |
| L9 QUE "COMPARATIVE EFFECTIVENESS RESEARCH"/CT OR "VACCINE EFFICACY"/CT |
| L10 QUE EFFECTIV? OR REAL(W)WORLD |
| L11 QUE (EFFECT? OR IMPACT OR REDUCTION OR DURABL? OR DURABIL? OR DURATION OR REAL)(8A)(L1 OR L2) |
| L12 QUE EFFECTIV?/TI OR (REAL/TI(W)WORLD/TI) OR DURABL?/TI OR DURABIL?/TI OR DURATION/TI OR INCIDENCE/TI(W)RATE/TI(W)RATIO/TI OR IRR/TI |
| L13 QUEL9ORL11ORL12 |
| L14 QUE (HPV/BI OR HUMAN/BI(W)PAPILLOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILLOMA/BI(W)VIR?/BI OR PAPILLOMAVIR?/BI)(8A)((EFFECT?/BI OR IMPACT/BI OR REDUCTION/BI OR DURABL?/BI OR DURABIL?/BI OR DURATION/BI OR REAL/BI)(8A)((?VACCIN?/BI OR ?IMMUNIS?/BI OR ?IMMUNIZ?/BI) OR (GARDASIL/BI OR CERVARIX/BI OR CECOLIN/BI))) |
| L15 QUE (L5 OR (GARDASIL/TI OR CERVARIX/TI OR CECOLIN/TI) OR ((L3 OR L4 OR (?VACCIN?/TI OR ?IMMUNIS?/TI OR ?IMMUNIZ?/TI)) AND (L6 OR L7 OR (HPV/TI OR HUMAN/TI(W)PAPILLOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILLOMA/TI(W)VIR?/TI OR PAPILLOMAVIR?/TI)))) AND L13 |

**FILE 'EMBASE' ENTERED**

L16 QUE "VACCINE"/CT OR "VACCINATION"/CT OR "IMMUNIZATION"/CT OR "MASS IMMUNIZATION"/CT OR "RNA IMMUNIZATION"/CT

L17 QUE "HUMAN PAPILLOMAVIRUS VACCINATION"/CT OR "HUMAN PAPILLOMAVIRUS VACCINE L1, TYPE 6,11,16,18"/CT OR "HUMAN PAPILLOMAVIRUS VACCINE, L1 TYPE 16, 18"/CT

L18 QUE "HUMAN PAPILLOMA VIRUS VACCINE"/CT OR "HPV VACCINATION"/CT

L19 QUE "HUMAN PAPILLOMAVIRUS TYPE 11"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 16"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 18"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 31"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 33"/CT

L20 QUE "HUMAN PAPILLOMAVIRUS TYPE 35"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 36"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 37"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 38"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 39"/CT

L21 QUE "HUMAN PAPILLOMAVIRUS TYPE 84"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 40"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 41"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 42"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 43"/CT

L22 QUE "HUMAN PAPILLOMAVIRUS TYPE 44"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 45"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 85"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 50"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 500"/CT

L23 QUE "HUMAN PAPILLOMAVIRUS TYPE 50S"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 51"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 52"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 53"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 54"/CT

L24 QUE "HUMAN PAPILLOMAVIRUS TYPE 55"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 56"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 58"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 59"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 6"/CT

L25 QUE "HUMAN PAPILLOMAVIRUS TYPE 61"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 62"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 63"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 64"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 65"/CT

L26 QUE "HUMAN PAPILLOMAVIRUS TYPE 66"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 67"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 68"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 70"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 71"/CT

L27 QUE "HUMAN PAPILLOMAVIRUS TYPE 72"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 73"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 74"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 75"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 76"/CT

L28 QUE "HUMAN PAPILLOMAVIRUS TYPE 77"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 8"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 81"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 82"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 83"/CT

L29 QUE "HUMAN PAPILLOMAVIRUS TYPE 4"/CT OR "HUMAN PAPILLOMAVIRUS TYPE 5"/CT OR "PAPILLOMA VIRUS"/CT OR PAPILLOMAVIRIDAE/CT OR "PAPILLOMAVIRUS INFECTION"/CT OR "PAPILLOMAVIRUS INFECTIONS"/CT

L30 QUE L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29

L31 QUE "CLINICAL EFFECTIVENESS"/CT OR "COMPARATIVE EFFECTIVENESS"/CT OR "DRUG EFFECT"/CT OR "PROGRAM EFFECTIVENESS"/CT

L32 QUE "VACCINE EFFECTIVENESS"/ST OR EFFECTIVENESS/ST OR "REAL-WORLD"/ST OR POST VACCINE SURVEILLANCE/ST

L33 QUEL31ORL32ORL11ORL12

L34 QUE (HPV/BI OR HUMAN/BI(W)PAPILLOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILLOMA/BI(W)VIR?/BI OR PAPILLOMAVIR?/BI)(8A)((EFFECT?/BI OR IMPACT/BI OR REDUCTION/BI OR DURABL?/BI OR DURABIL?/BI OR DURATION/BI OR REAL/BI)(8A)((?VACCIN?/BI OR ?IMMUNIS?/BI OR ?IMMUNIZ?/BI) OR (GARDASIL/BI OR CERVARIX/BI OR CECOLIN/BI)))

L35 QUE (L17 OR L18 OR (GARDASIL/TI OR CERVARIX/TI OR CECOLIN/TI) OR ((L16 OR (?VACCIN?/TI OR ?IMMUNIS?/TI OR ?IMMUNIZ?/TI)) AND (L30 OR (HPV/TI OR HUMAN/TI(W)PAPILLOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILLOMA/TI(W)VIR?/TI OR PAPILLOMAVIR?/TI)))) AND L33

**FILE 'PQSCITECH' ENTERED**

L36 QUE VACCINES/CT OR VACCINATION/CT OR VACCINES/CT OR "VIRAL VACCINES"/CT OR IMMUNIZATION/CT

L37 QUE "CLINICAL EFFECTIVENESS"/CT OR "VACCINE EFFICACY"/CT OR EFFECTIVENESS/CT OR "EFFECTIVENESS STUDIES"/CT

L38 QUE "HUMAN PAPILLOMA VIRUSES"/CT OR "HUMAN PAPILLOMAVIRUS"/CT OR "HUMAN PAPILLOMAVIRUS 16"/CT OR "HUMAN PAPILLOMAVIRUSES"/CT OR "PAPILLOMA"/CT OR "PAPILLOMA VIRUSES"/CT OR "PAPILLOMAVIRUS INFECTIONS"/CT

L39 QUE "PAPILLOMAVIRUS VACCINES"/CT

L40 QUE L37 OR L11 OR L12

L41 QUE (HPV/BI OR HUMAN/BI(W)PAPILLOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILLOMA/BI(W)VIR?/BI OR PAPILLOMAVIR?/BI)(8A)((EFFECT?/BI OR IMPACT/BI OR REDUCTION/BI OR DURABL?/BI OR DURABIL?/BI OR DURATION/BI OR REAL/BI)(8A)((?VACCIN?/BI OR ?IMMUNIS?/BI OR ?IMMUNIZ?/BI) OR (GARDASIL/BI OR CERVARIX/BI OR CECOLIN/BI)))

L42 QUE (L39 OR (GARDASIL/TI OR CERVARIX/TI OR CECOLIN/TI) OR ((L36 OR (?VACCIN?/TI OR ?IMMUNIS?/TI OR ?IMMUNIZ?/TI)) AND (L38 OR (HPV/TI OR HUMAN/TI(W)PAPILLOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILLOMA/TI(W)VIR?/TI OR PAPILLOMAVIR?/TI)))) AND L40

**FILE 'IPA' ENTERED**

L43 QUE VACCIN? OR IMMUNIS? OR IMMUNIZ?

L44 QUE "VACCINES"/CT OR "VACCINES, IMMUNIZATION"/CT OR "VACCINES, NEOPLASMS"/CT OR "VACCINES, VIRUS DISEASES"/CT OR "IMMUNIZATION"/CT OR "IMMUNIZATION, DISEASES"/CT OR "IMMUNIZATION, VACCINES"/CT

L45 QUE "VACCINES, PAPILLOMAVIRUS"/CT OR "VACCINES, PAPILLOMAVIRUS VACCINES"/CT OR "VACCINES, PAPILLOMAVIRUSES"/CT OR "PAPILLOMAVIRUS VACCINES"/CT OR "PAPILLOMAVIRUSES, VACCINES"/CT

L46 QUE "IMMUNIZATION, PAPILLOMAVIRUS VACCINES"/CT OR "IMMUNIZATION, PAPOVAVIRIDAE INFECTIONS"/CT OR "PAPILLOMAVIRUSES, PAPILLOMAVIRUS VACCINES"/CT OR "PAPILLOMAVIRUSES, PROPHYLAXIS"/CT

L47 QUE "PAPILLOMA"/CT OR "PAPILLOMAVIRUSES"/CT

L48 QUE (EFFECT? OR IMPACT OR REDUCTION OR DURABL? OR DURABIL? OR DURATION OR REAL)(8A)(L43 OR L2)

L49 QUE L48 OR L12

L50 QUE (HPV/BI OR HUMAN/BI(W)PAPILLOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILLOMA/BI(W)VIR?/BI OR PAPILLOMAVIR?/BI)(8A)((EFFECT?/BI OR IMPACT/BI OR REDUCTION/BI OR DURABL?/BI OR DURABIL?/BI OR DURATION/BI OR REAL/BI)(8A)((VACCIN?/BI OR IMMUNIS?/BI OR IMMUNIZ?/BI) OR (GARDASIL/BI OR CERVARIX/BI OR CECOLIN/BI)))

L51 QUE (L45 OR L46 OR (GARDASIL/TI OR CERVARIX/TI OR CECOLIN/TI) OR ((L44 OR (VACCIN?/TI OR IMMUNIS?/TI OR IMMUNIZ?/TI)) AND (L47 OR (HPV/TI OR HUMAN/TI(W)PAPILLOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILLOMA/TI(W)VIR?/TI OR PAPILLOMAVIR?/TI)))) AND L49

L52 QUE L11 OR L12

L53 QUE (HPV/BI OR HUMAN/BI(W)PAPILLOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILLOMA/BI(W)VIR?/BI OR PAPILLOMAVIR?/BI)(8A)((EFFECT?/BI OR IMPACT/BI OR REDUCTION/BI OR DURABL?/BI OR DURABIL?/BI OR DURATION/BI OR REAL/BI)(8A)((?VACCIN?/BI OR ?IMMUNIS?/BI OR ?IMMUNIZ?/BI) OR (GARDASIL/BI OR CERVARIX/BI OR CECOLIN/BI)))

L54 QUE ((GARDASIL/TI OR CERVARIX/TI OR CECOLIN/TI) OR ((?VACCIN?/TI OR ?IMMUNIS?/TI OR ?IMMUNIZ?/TI) AND (HPV/TI OR HUMAN/TI(W)PAPILLOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILLOMA/TI(W)VIR?/TI OR PAPILLOMAVIR?/TI))) AND L52

**FILE 'DDFU' ENTERED**

L55 QUE VACCINES/CT OR VACCINATION/CT OR VACCINES/CT OR "VIRAL VACCINES"/CT OR IMMUNIZATION/CT OR "THERAPEUTIC-VACCINES"/CT OR VACCINE/CT

L56 QUE PAPILLOMA/CT OR "PAPILLOMA-VIRUS"/CT

L57 QUE "PAPILLOMA-VACCINE"/CT OR GARDASIL/CT

L58 QUE L11 OR L12

L59 QUE (HPV/BI OR HUMAN/BI(W)PAPILLOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILLOMA/BI(W)VIR?/BI OR PAPILLOMAVIR?/BI)(8A)((EFFECT?/BI OR IMPACT/BI OR REDUCTION/BI OR DURABL?/BI OR DURABIL?/BI OR DURATION/BI OR REAL/BI)(8A)((?VACCIN?/BI OR ?IMMUNIS?/BI OR ?IMMUNIZ?/BI) OR (GARDASIL/BI OR CERVARIX/BI OR CECOLIN/BI)))

L60 QUE (L57 OR (GARDASIL/TI OR CERVARIX/TI OR CECOLIN/TI) OR ((L36 OR (?VACCIN?/TI OR ?IMMUNIS?/TI OR ?IMMUNIZ?/TI)) AND (L56 OR (HPV/TI OR HUMAN/TI(W)PAPILLOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILLOMA/TI(W)VIR?/TI OR PAPILLOMAVIR?/TI)))) AND L58

**Search query: MEDLINE (platform PubMed)**

("Papillomavirus Vaccines"[Mesh] OR "Human Papillomavirus Recombinant Vaccine Quadrivalent, Types 6, 11, 16, 18"[Mesh] OR "human papillomavirus vaccine, L1 type 16, 18" [Supplementary Concept] OR "human papillomavirus vaccine, L1 type 16, 18" [Supplementary Concept] OR Cervarix[Title] OR Gardasil[Title] OR "human papillomavirus vaccine"[Title] OR "HPV vaccine"[Title] OR ((HPV[Title] OR "human papilloma virus"[Title] OR "human papillomavirus"[Title] OR alphapapillomavirus[Title] OR papillomavirus[Title] OR "Human papillomavirus 6"[Mesh] OR "Human papillomavirus 11"[Mesh] OR "Human papillomavirus 18"[Mesh] OR "Human papillomavirus 31"[Mesh] OR "Human papillomavirus 16"[Mesh] OR "Alphapapillomavirus"[Mesh] OR "Papillomaviridae"[Mesh]) AND (vaccine[Title] OR vaccination[Title] OR immunisation[Title] OR immunization[Title] OR "Cancer Vaccines"[Mesh]))) AND ("2022/09/30"[Date - Publication] : "2022/11/15"[Date - Publication]) AND Humans[Mesh] AND ("Vaccine Efficacy"[Mesh] OR effectiveness[Title/Abstract] OR efficacy[Title/Abstract] OR impact[Title/Abstract] OR reduction[Title/Abstract] OR durability[Title/Abstract] OR duration[Title/Abstract] OR "protective effect"[Title/Abstract] OR "real-world"[Title/Abstract] OR "real world"[Title/Abstract])

**Search query: Cochrane**

"#1 425 MeSH descriptor: [Papillomavirus Vaccines] explode all trees

#2 21 MeSH descriptor: [Vaccine Efficacy] explode all trees

#3 825062 (effectiveness OR efficacy OR impact OR reduction OR durability OR duration OR ""protective effect"" OR ""real-world"" OR ""real world""):ti,ab,kw"

"#4" 444 "MeSH descriptor: [Papillomaviridae] this term only"

"#5" 298 "MeSH descriptor: [Alphapapillomavirus] explode all trees"

"#6" 3996 "(HPV OR ""human papilloma virus"" OR ""human papillomavirus"" OR alphapapillomavirus OR"

"papillomavirus):ti,ab,kw"

"#7" 953 "(Cervarix OR Gardasil OR ""human papillomavirus vaccine"" OR ""HPV vaccine""):ti,ab,kw"

| | | |
|---|---|---|
| "#8" | 346 | "MeSH descriptor: [Cancer Vaccines] explode all trees" |
| "#9" | 14255 | "MeSH descriptor: [Vaccines] explode all trees" |
| "#10" | 2915 | "MeSH descriptor: [Vaccination] explode all trees" |
| "#11" | 722 | "(#4 OR #5 OR #6) AND (#8 OR #9 OR #10)" |
| "#12" | 1213 | "#1 OR #7 OR #11" |
| "#13" | 641 | "#12 AND (#2 OR #3)" |

**Search query: MedRxiv**

(papilloma* OR humanpapillomavir* OR alphapapillomavir*) and (vaccin* OR immunis* OR immuniz*) AND effectiveness

**Table 5S. Data extraction and quality assessment**

| **A** | **Data extraction** |
|---|---|
| 1 | Study design (cohort study, case-control study, cross-sectional studies, randomized clinical trial) |
| 2 | Study period (start and end dates of study) |
| 3 | Study characteristics (title, 1st author name and year of publication, including country of study population) |
| 4 | Specification of the population |
| 5 | Total number of women, number of vaccinated women |
| 6 | Age of the study population characterized by any of the following parameters: mean age including standard deviation; or median age including interquartile range; minimum and, if applicable, maximum age |
| 7 | Type of conization and reason for conization (proportion of high-grade cervical intraepithelial neoplasia – high-grade CIN) |
| 8 | The follow-up period after conization characterized by any of the following parameters: mean period including standard deviation; or median period including interquartile range; range of period (minimum – maximum) |
| 9 | HPV genotypes |
| 10 | Analysis including the method used and adjustment or matching |
| 11 | Effect size including confidence interval, or eligible data for calculation of odds ratio |
| 12 | Intervention (commercial vaccine, number received doses, vaccination timing, i.e., fully immunized before conization, start of vaccination before or after conization or start of vaccination exclusively after conization) |
| 13 | Outcome (effect size related to high-grade CIN recurrence) |
| | Note: The data were extracted by two reviewers. |

| **B** | **Assessment of risk of bias (RoB) according to the Newcastle-Ottawa Quality Assessment Scale, NOS stars** |
|---|---|
| 1 | Randomized clinical trials and cross-sectional studies were evaluated according to the NOS questionnaire developed for cohort studies (This procedure maintained proxy consistency for the final evaluation of all studies). |
| 2 | Comparability: the most important factors were sex and age (note: only women); there could be at least one additional factor. |
| 3 | Long-term follow-up was defined as one lasting at least 12 months |
| 4 | Adequacy of follow-up of cohorts: subjects lost to follow-up unlikely to introduce bias – small number lost (<20%) |
| 5 | Non-Response rate: the same rate for both groups was if the number of cases was not different from that of controls by more than 20%. |
| | Note: As the assessment of RoB was performed independently by a total of 4 assessors, a standard operating procedure had been developed. Each study was evaluated by 2 assessors. If consensus had not been achieved, the discrepancy was resolved through discussions among all assessors. |

| **C** | **Assessment of evidence quality** |
|---|---|
| 1 | A sufficient number was ≥10 VE records [1]. |
| 2 | No serious limitation was assumed in studies if the NOS domain of selection was ≥3 stars and that of the outcome was ≥2 stars [2]. |
| 3 | No serious indirectness was assumed if the NOS domain of comparability was 2 stars [2]. |
| 4 | No serious inconsistency was assumed if the pooled inconsistency index ($I^2$) was |

<50%; undetected inconsistency was at $I^2 = 0\%$ [3,4].

5 NOS domain of imprecision was assumed if the standard error of pooled vaccine effectiveness was <10%.

6 No serious publication bias of studies was documented if difference between effectiveness obtained from both models, i.e., fixed-effect and random-effects models, was <10% [5].

7 Effect of small studies was used as only supportive information with no inclusion in the overall assessment of quality. Also, detection of missing studies was only informative and it exhibited a possible impact on the original result after accounting imputed studies.

Note: These criteria were adopted to assess the strength of evidence according to GRADE.

**References**

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3 Xie S, Xu H, Shan X, Liu B, Wang K, Cai Z. Clinicopathological and Prognostic Significance of Survivin Expression in Patients with Oral Squamous Cell Carcinoma: Evidence from a Meta-Analysis. *PLOS ONE* 2015; 10: e0116517.

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**Table 6S. Review of included studies (extended summary)**

| Author, Year | Country | Type of study | Study period | Total/ Vaccinated women | Age (in years)[1] | Reason for conization (CIN2+ proportion, %) | Treatment | Vaccination | | | Follow-up (in months)[2] | Adjustment | ES | NOS stars/RoB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Vaccine (proportion, %) | 3 doses | Timing | | | | |
| Grzes[23], 2011 | Poland | C | Before 2011 | 75/25 | n.r. | 81 % | LEEP, CKC | HPV4 | 100 % | After conization | 24-24 | None | OR | 6 moderate |
| Joura[24], 2012 | Global | pha-RCT | 2001–2005 | 1 066/474 | 20±2 | 100 % | LEEP (85%), conization (13%), cryotherapy (1%) | HPV4 | ∽100 % | Previous vaccination - mean of 28 and 30 months before conization | 2-48 | Matched | IRR | 9 low |
| Kang[25], 2013 | Korea | C | 2007–2010 | 737/360 | 37±6 | 100 % | LEEP | HPV4 | 100 % | 1 week after conization | 6-48 | Adjusted | HR | 9 low |
| Hildesheim[26], 2016 | Costa Rica | pha-RCT | 2004–2010 | 737/362* | 18–25 | 100 % | LEEP | HPV2 | 80 % | Previous vaccination - median of 28 months before conization | 15-40 | None | IRR | 9 low |
| Garland[27], 2016 | Global | pha-RCT | 2004–2009 | 454/190 | 21±4 | 100 % | LEEP, Conization | HPV2 | n.r. | Previous vaccination - mean of 19 and 27 months before conization | 2-48 | Matched | IRR | 7 moderate |
| Ortega-Quiñonero[28], 2018 | Spain | C | 2011–2015 | 242/103 | 37±15 | 100 % | LEEP | HPV2 (68%); HPV4 (33%) | 100 % | 1 month before (45%) and 1 month after (55%) conization | 24-24 | Adjusted | OR | 7 moderate |
| Pieralli[29], 2018 | Italy | RCT | 2013–2017 | 178/89 | 32± n.r. | 100 % | Conization | HPV4 | 100 % | 3 months after conization | 36-36 | None | OR | 8 low |
| Ghelardi[30], 2018 | Italy | CC | 2013–2017 | 344/172 | 18-45 | 100 % | LEEP | HPV4 | 100 % | 1 month after conization | 6-48 | None | RR | 8 low |
| Sand[31], 2019 | Denmark | C | 2006–2016 | 17 128/2 074 | 32± n.r. | 100 % | Conization | HPV4 | 100 % | 3 months before (19%) and ≤12 months after conization (81%) | 12-12 | Adjusted | HR | 6 moderate |
| Vinnytska[3 | Ukraine | C | 2010- | 113/76 | n.r. | 100 % | LEEP | HPV2 (n.r.), | 100 % | 2 months before conization | 36-36 | None | OR | 6 |

| Author, Year | Country | Type of study | Study period | Total/ Vaccinated women | Age (in years)[1] | Reason for conization (CIN2+ proportion, %) | Treatment | Vaccination | | | Follow-up (in months)[2] | Adjustment | ES | NOS stars/RoB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Vaccine (proportion, %) | 3 doses | Timing | | | | |
| 2], 2019 | | | 2018 | | | | | HPV4 (n.r.) | | (2nd dose at conization) | | | | moderate |
| Bogani[33], 2020 | Italy | C | 2010-2019 | 300/100 | 33± n.r. | 100 % | LEEP | HPV4 (93%) | 68 % | <3 months after conization (82%); 3–6 months after conization (4%) | 60-60 | Matched | OR | 9 low |
| Del Pino[34], 2020 | Spain | C | 2013–2018 | 265/153 | 40±10 | 90.6% | LEEP | HPV2 (20%), HPV4 (5%), HPV9 (64%) | 100 % | 0–12 months after conization | 8-77 | Adjusted | OR | 8 low |
| Karimi-Zarchi[35], 2020 | Iran | RCT | 2011–2015 | 162/93 | 33±5 | 100 % | LEEP[4] | HPV4 | 75 % | At the time of conization | 24-24 | None | OR | 9 low |
| Petrillo[36], 2020 | Italy | C | 2012–2018 | 285/182 | 39±15 | 97.5% | LEEP | HPV4 (98%) | 100 % | 1 month after conization | 24-60 | None | OR | 8 low |
| Zhao[37], 2020 | China | pha-RCT | 2008–2016 | 625/330* | 18-25 | 18.7% (HSIL) | LEEP, CKC | HPV2 | 100 % | Previous vaccination - median of 17 months before conization | 32-64 | Matched | IRR | 9 low |
| Gómez de la Rosa[38], 2021 | Spain | C | 2012–2015 | 331/160 | 38±8 | 100 % | LEEP | HPV2 (n.r.), HPV4 (n.r.) | n.r. | <6 months after conization | 48-48 | Adjusted | HR | 9 low |
| Casajuana-Pérez[39], 2022 | Spain | C | 2009–2019 | 563/277 | 37±8 | 93.6% | LEEP | HPV2 (n.r.), HPV4 (n.r.) HPV9 (n.r.) | 92 % | >1 month before (21%), <1 month before (4%), <1 month after (5%), 1–6 months after (51%), >6 months (19%) after conization | 15-51 | None | HR | 9 low |
| Henere[40], 2022 | Spain | C | 2016–2019 | 398/306 | 40±10 | 100% (HSIL) | LEEP | HPV9 | 92 % | 4 months before (37%); mean 5 months after | 9-31 | None | OR | 8 low |

| Author, Year | Country | Type of study | Study period | Total/ Vaccinated women | Age (in years)[1] | Reason for conization (CIN2+ proportion, %) | Treatment | Vaccination | | | Follow-up (in months)[2] | Adjustment | ES | NOS stars/RoB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Vaccine (proportion, %) | 3 doses | Timing | | | | |
| | | | | | | | | | | (63%) conization | | | | |
| Shiravani[41], 2022 | Iran | CC | 2018–2020 | 300/150 | 33±5 | 54.7% | LEEP[4] | HPV4 | n.r. | After conization | 24-24 | None | OR | 6 moderate |
| Chen[42], 2023 | China | C | 2017-2020 | 421/148 | 20-45 | 100 % | LEEP | HPV4 | 100 % | <3 months after conization | 24-48 | None | OR | 9 low |

[1]) mean±standard deviation or median±interquartile range or min-max range; [2]) minimum – maximum, 1st – 3rd quartile, or sum of mean and ±standard deviation of follow-up; [3]) person-days; [4]) algorithm of American Society for Colposcopy and Cervical Pathology; n.r. – not reported; C – cohort study, C-C – case-control study; RCT – randomized clinical trial; pha-RCT – post-hoc analysis of randomized clinical trial; CIN2+ – high-grade cervical intraepithelial neoplasia; HSIL – high-grade intraepithelial lesions; LEEP – loop electrosurgical excision procedure; CKC – cold knife cone; HPV2/HPV4/HPV9 – bivalent/quadrivalent/nonavalent human papillomavirus vaccine; ES – effect size; NOS – Newcastle-Ottawa Quality Assessment Scale; RoB – risk of bias; OR – odds ratio; IRR– incidence rate ratio; HR – hazard ratio; RR – risk ratio

**Table 7S. Results of additional analyses supporting the strength of evidence**

| Effectiveness | Strata | N° of estimates | Pooled VE (95% CI) | $I^2$ (%) | SE (%) | Publication bias (%) | Small study effect | N°of imputed studie | Imputed VE (95% CI) | Prediction interval |
|---|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | 21 | 69.5% (54.7 – 79.5) | 62.8 | 6.1 | 19.4 | no | 5 | 63.4% (46.6 – 74.9) | -22.8 – 92.4 |
| **Stratified by** | **Timing of immunization** | | | | | | | | | |

| Effectiveness | Strata | N° of estimates | Pooled VE (95% CI) | $I^2$ (%) | SE (%) | Publication bias (%) | Small study effect | N°of imputed studie | Imputed VE (95% CI) | Prediction interval |
|---|---|---|---|---|---|---|---|---|---|---|
| | **Post-excision** | 12 | 78.1% (68.7 – 84.7) | 0.0 | 4.0 | 0.0 | yes | 5 | 75.0% (64.7 – 82.2) | **67.1 – 85.4** |
| | **Pre- or Pre/Post-excision** | 5 | 47.8% (14.0 – 68.3) | 54.5 | 13.3 | 18.5 | no | 2 | 35.8% (3.3 – 57.3) | -136.1 – 88.5 |
| | **Previously immunized** | 4 | 49.8% (-45.5 – 82.7) | 42.3 | 27.3 | -7.1 | no | 0 | 49.8% (-45.5 – 82.7) | -2225.9 – 98.9 |
| | **HPV vaccine** | | | | | | | | | |
| | **HPV2** | 4 | 48.4% (-55.0 – 82.8) | 40.7 | 29.0 | -5.1 | no | 0 | 48.4% (-55.0 – 82.8) | -2476.8 – 99.0 |
| | **HPV4+** | 14 | 75.9% (58.3 – 86.1) | 72.3 | 6.7 | 26.1 | no | 6 | 67.7% (48.1 – 79.9) | -44.1 – 96.0 |
| | **Unspecific** | 3 | 59.8% (32.1 – 76.3) | 0.0 | 10.8 | 0.0 | no | 0 | 59.8% (32.1 – 76.3) | -1112.1 – 98.7 |
| | **Follow-up duration** | | | | | | | | | |
| | **≤2 years** | 5 | 72.3% (17.5 – 90.7) | 79.4 | 15.4 | 36.3 | no. | 2 | 56.7% (-20.9 – 84.5) | -910.7 – 99.2 |
| | **3-4 years** | 10 | 68.4% (53.9 – 78.3) | 0.0 | 6.1 | 0.0 | no | 2 | 66.2% (50.5 – 76.9) | **50.8 – 79.7** |
| | **≥5 years** | 6 | 70.1% (53.7 – 80.6) | 0.0 | 6.7 | 0.0 | yes | 1 | 69.3% (52.7 – 80.0) | **44.4 – 83.9** |
| | **Study type** | | | | | | | | | |
| | **Case-control** | 2 | 91.2% (46.9 – 98.6) | 58.3 | 8.1 | 2.4 | no | 1 | 81.2% (-17.2 – 97.0) | -1000 – 100 |
| | **Cohort** | 12 | 65.4% (45.4 – 78.1) | 61.6 | 8.1 | 22.4 | no | 4 | 58.9% (38.3 – 72.6) | -33.1 – 91.0 |
| | **Clinical trial** | 7 | 68.0% (41.8 – 82.4) | 24.6 | 9.8 | -1.2 | no | 1 | 67.4% (41.8 – 81.7) | -14.0 – 91.0 |
| | **Risk of Bias** | | | | | | | | | |
| | **Low** | 15 | 70.3% (60.6 – 77.7) | 0.0 | 4.3 | 0.0 | yes | 2 | 69.2% (59.2 – 76.8) | **59.4 – 78.3** |
| | **Moderate** | 6 | 69.0% (20.2 – 87.9) | 70.9 | 14.9 | 35.4 | no | 3 | 39.2% (-53.0 – 75.9) | -400.6 – 98.1 |
| | | | | | | | | | | |
| **Specific*** | | 9 | 76.3% (64.9 – 84.0) | 0.0 | 0.0 | 0.0 | no | 3 | 74.4% (62.5 – 82.5) | **62.0 – 85.2** |

HPV2/HPV4+ – bivalent/quadrivalent or nonavalent human papillomavirus vaccine; $I^2$ – index of inconsistency; SE – standard deviation; VE – vaccine effectiveness; 95% CI – 95% confidence interval; *) post-excision immunization mostly with HPV4+ vaccine followed up at least 3 years in studies with low risk of bias

Note: Publication bias was assessed with the difference between VE of random- and fixed-effect models.

**Table 8S. Pooled and adjusted vaccine effectiveness (VE), including regression coefficients for timing of immunization, used HPV vaccine, proxy time of follow-up, type of study and study risk of bias**

| Predictor | Strata | N° of estimates | pooled VE (95% CI) | adjusted VE (95% CI) | regression coefficient (95% CI) | adjusted VE (95% CI) | regression coefficient (95% CI) | adjusted VE (95% CI) | regression coefficient (95% CI) | adjusted VE (95% CI) | regression coefficient (95% CI) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Timing of immunization** | **Post-excision** | 12 | 78.1 (68.7–84.7) | 77.7 (65.8–85.5) | ref | 80.0 (65.5–88.3) | ref | 76.1 (59.5–85.9) | ref | 79.0 (68.4–86.0) | ref |
| | **Pre- or Pre/Post-excision** | 5 | 47.8 (14.0–68.3) | 41.2 (-24.6–72.3) | 1.02 (0.40–1.64) | 50.0 (-15.8–78.4) | 0.91 (0.27–1.55) | 43.4 (-32.2–75.8) | 0.86 (0.20–1.53) | 44.0 (-31.1–76.1) | 0.98 (0.23–1.73) |
| | **Previously immunized** | 4 | 49.8 (-45.5–82.7) | 52.9 (-34.3–83.4) | 0.80 (-0.16–1.76) | 54.9 (-30.7–84.4) | 0.81 (-0.11–1.73) | 50.6 (-64.4–85.2) | 0.73 (-0.35–1.81) | 55.0 (-16.8–82.7) | 0.76 (-0.10–1.62) |
| **HPV vaccine** | **HPV2** | 4 | 48.4 (-55.0–82.8) | 80.8 (43.6–93.4) | -0.10 (-1.09–0.89) | | | | | | |
| | **HPV4+** | 14 | 75.9 (58.3–86.1) | 77.7 (65.8–85.5) | ref | | | | | | |
| | **unspecific** | 3 | 59.8 (32.1–76.3) | 81.3 (55.7–92.1) | -0.12 (-0.87–0.63) | | | | | | |
| **Follow-up duration** | **≤2 years** | 5 | 72.3 (17.5–90.7) | | | 75.9 (39.3–90.4) | 0.18 (-0.56–0.93) | | | | |
| | **3-4 years** | 10 | 68.4 (53.9–78.3) | | | 80.0 (65.5–88.3) | ref | | | | |
| | **≥5 years** | 6 | 70.1 (53.7–80.6) | | | 79.3 (49.4–91.5) | 0.03 (-0.67–0.74) | | | | |
| **Study type** | **Cohort** | 12 | 65.4 (45.4–78.1) | | | | | 76.1 (59.5–85.9) | ref | | |
| | **Case-control** | 2 | 91.2 (46.9–98.6) | | | | | 89.3 (58.1–97.3) | -0.80 (-2.05–0.46) | | |
| | **Clinical trial** | 7 | 68.0 (41.8–82.4) | | | | | 78.2 (36.4–92.5) | -0.09 (-1.02–0.84) | | |
| **Risk of Bias** | **Low** | 15 | 70.3 (60.6–77.7) | | | | | | | 79.0 (68.4–86.0) | ref |
| | **Moderate** | 6 | 69.0 (20.2–87.9) | | | | | | | 78.6 (49.8–90.9) | 0.02 (-0.73–0.77) |

HPV2/HPV4+ – bivalent/quadrivalent or nonavalent human papillomavirus vaccine; VE – vaccine effectiveness; 95% CI – 95% confidence interval; ref – reference

Note: Adjusted VE was obtained from coefficients of bivariate regression model including always timing of immunization as an independent variable. The exponential-transformation of regression constant was applied to reference strata of appropriate variable while other strata were obtained from the exponential-transformed sum of the coefficient and the constant of regression model.
The confidence interval was calculated in a similar way; from standard error of sum that was obtained from standard errors of constant and coefficient as square root of the sum of their squares. Both limits of confidence interval were calculated according to the metric closest to normality followed by exponential transformation. Final result was expressed as (1- [exponential-transformed result])*100%.

**Table 9S. Sensitivity analysis in women with only CIN2+ before conization**

| Effectiveness | Strata | N° of estimates | Pooled VE (95% CI) | $I^2$ (%) | SE (%) | Publication bias (%) | Small study effect | N°of imputed studie | Imputed VE (95% CI) | Prediction interval |
|---|---|---|---|---|---|---|---|---|---|---|
| **Overall** | | 15 | 67.5% (49.0 – 79.2) | 63.4 | 7.4 | 21.7 | no | 4 | 62.2% (42.7 – 75.0) | -36.0 – 92.2 |
| **Stratified by** | **Timing of immunization** | | | | | | | | | |
| | **Post-excision** | 8 | 75.9% (63.5 – 84.1) | 0.0 | 5.1 | 0.0 | no | 3 | 73.6% (60.7 – 82.3) | **59.6 – 85.6** |
| | **Pre- or Pre/Post-excision** | 4 | 45.2% (1.0 – 69.6) | 51.1 | 16.5 | 20.0 | no | 2 | 20.7% (-39.6 – 55.0) | -419.2 – 94.2 |
| | **Previously immunized** | 3 | 59.7% (-28.3 – 87.4) | 46.7 | 23.8 | -1.9 | no | 0 | 59.7% (-28.3 – 87.4) | -199900.0 – 100.0 |