

## Supplement

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

Section/topic	#	Checklist item	Location(s) Reported
<b>INFORMATION SOURCES AND METHODS</b>			
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	To identify unpublished studies, we searched Embase for conference proceedings.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
<b>SEARCH STRATEGIES</b>			
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

<b>Section/topic</b>	<b>#</b>	<b>Checklist item</b>	<b>Location(s) Reported</b>
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.
<b>PEER REVIEW</b>			
Peer review	14	Describe any search peer review process.	The strategies were peer reviewed by a senior information specialist prior to execution.
<b>MANAGING RECORDS</b>			
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
<b>TITLE</b>			
Title	1	Identify the report as a systematic review.	Title
<b>ABSTRACT</b>			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
<b>INTRODUCTION</b>			
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
<b>METHODS</b>			
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
<b>RESULTS</b>			
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
<b>DISCUSSION</b>			
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
<b>OTHER INFORMATION</b>			
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

<b>Criteria</b>	<b>Brief description</b>
<b>Introduction</b>	
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 Study exposure: vaccination Study population: female population in risk of high-grade cervical intraepithelial neoplasia
<b>Sources</b>	
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.
<b>Study selection</b>	
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.

<b>Criteria</b>	<b>Brief description</b>
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.
<b>Results</b>	
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.
<b>Discussion</b>	
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

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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 QUE L31 OR L32 OR L11 OR L12

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, PAPILOMAVIRUS"/CT OR "VACCINES, PAPILOMAVIRUS VACCINES"/CT OR "VACCINES, PAPILOMAVIRUSES"/CT OR "PAPILOMAVIRUS VACCINES"/CT OR "PAPILOMAVIRUSES, VACCINES"/CT

L46 QUE "IMMUNIZATION, PAPILOMAVIRUS VACCINES"/CT OR "IMMUNIZATION, PAPOVAVIRIDAE INFECTIONS"/CT OR "PAPILOMAVIRUSES, PAPILOMAVIRUS VACCINES"/CT OR "PAPILOMAVIRUSES, PROPHYLAXIS"/CT

L47 QUE "PAPILLOMA"/CT OR "PAPILOMAVIRUSES"/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 PAPILOMA/BI(W)VIR?/BI OR PAPILOMAVIR?/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 PAPILOMA/TI(W)VIR?/TI OR PAPILOMAVIR?/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 PAPILOMA/BI(W)VIR?/BI OR PAPILOMAVIR?/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 PAPILOMA/TI(W)VIR?/TI OR PAPILOMAVIR?/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 PAPILOMA/CT OR "PAPILOMA-VIRUS"/CT

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

L58 QUE L11 OR L12

L59 QUE (HPV/BI OR HUMAN/BI(W)PAPILOMA/BI(W)VIR?/BI OR HUMAN/BI(W)PAPILLOMAVIR?/BI OR HUMANPAPILLOMAVIR?/BI OR ALPHAPAPILLOMAVIR?/BI OR PAPILOMA/BI(W)VIR?/BI OR PAPILOMAVIR?/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)PAPILOMA/TI(W)VIR?/TI OR HUMAN/TI(W)PAPILLOMAVIR?/TI OR HUMANPAPILLOMAVIR?/TI OR ALPHAPAPILLOMAVIR?/TI OR PAPILOMA/TI(W)VIR?/TI OR PAPILOMAVIR?/TI)))) AND L58

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**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])

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**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"

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"#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)"

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**Search query: MedRxiv**

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

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

<b>A</b>	<b>Data extraction</b>
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>B</b>	<b>Assessment of risk of bias (RoB) according to the Newcastle-Ottawa Quality Assessment Scale, NOS stars</b>
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.	
<b>C</b>	<b>Assessment of evidence quality</b>
1	A sufficient number was $\geq 10$ VE records [1].
2	No serious limitation was assumed in studies if the NOS domain of selection was $\geq 3$ stars and that of the outcome was $\geq 2$ 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.

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

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### References

- 1 Higgins JPT, Cochrane Collaboration, editors. Cochrane handbook for systematic reviews of interventions, Second edition. Hoboken, NJ: Wiley-Blackwell, 2020.
- 2 McPheeters ML, Kripalani S, Peterson NB, Idowu RT, Jerome RN, Potter SA, Andrews JC. Quality Improvement Interventions To Address Health Disparities. Closing the Quality Gap: Revisiting the State of the Science. Evidence Report No. 208. (Prepared by the Vanderbilt University Evidence-based Practice Center under Contract No. 290-2007-10065.) AHRQ Publication No. 12-E009-EF. Rockville, MD: Agency for Healthcare Research and Quality. August 2012. [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).
- 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) <sup>1</sup>	Reason for conization (CIN2+ proportion, %)	Treatment	Vaccination			Follow-up (in months) <sup>2</sup>	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-Quiñero[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
Vinnyska[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) <sup>1</sup>	Reason for conization (CIN2+ proportion, %)	Treatment	Vaccination			Follow-up (in months) <sup>2</sup>	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 <sup>4</sup>	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) <sup>1</sup>	Reason for conization (CIN2+ proportion, %)	Treatment	Vaccination			Follow-up (in months) <sup>2</sup>	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 <sup>4</sup>	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

<sup>1</sup>) mean±standard deviation or median±interquartile range or min-max range; <sup>2</sup>) minimum – maximum, 1<sup>st</sup> – 3<sup>rd</sup> quartile, or sum of mean and ±standard deviation of follow-up; <sup>3</sup>) person-days; <sup>4</sup>) 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 <sup>2</sup> (%)	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 <sup>2</sup> (%)	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)	<b>67.1 – 85.4</b>
	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)	<b>50.8 – 79.7</b>
	≥5 years	6	70.1% (53.7 – 80.6)	0.0	6.7	0.0	yes	1	69.3% (52.7 – 80.0)	<b>44.4 – 83.9</b>
	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)	<b>59.4 – 78.3</b>
	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)	<b>62.0 – 85.2</b>

HPV2/HPV4+ – bivalent/quadrivalent or nonavalent human papillomavirus vaccine; I<sup>2</sup> – 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 <sup>2</sup> (%)	SE (%)	Publication bias (%)	Small study effect	N° of imputed studie	Imputed VE (95% CI)	Prediction interval
<b>Overall</b>		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
<b>Stratified by</b>	<b>Timing of immunization</b>									
	<b>Post-excision</b>	8	75.9% (63.5 – 84.1)	0.0	5.1	0.0	no	3	73.6% (60.7 – 82.3)	<b>59.6 – 85.6</b>
	<b>Pre- or Pre/Post-excision</b>	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
	<b>Previously immunized</b>	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