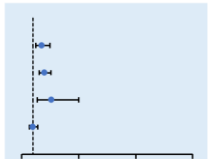
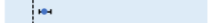
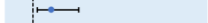
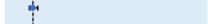
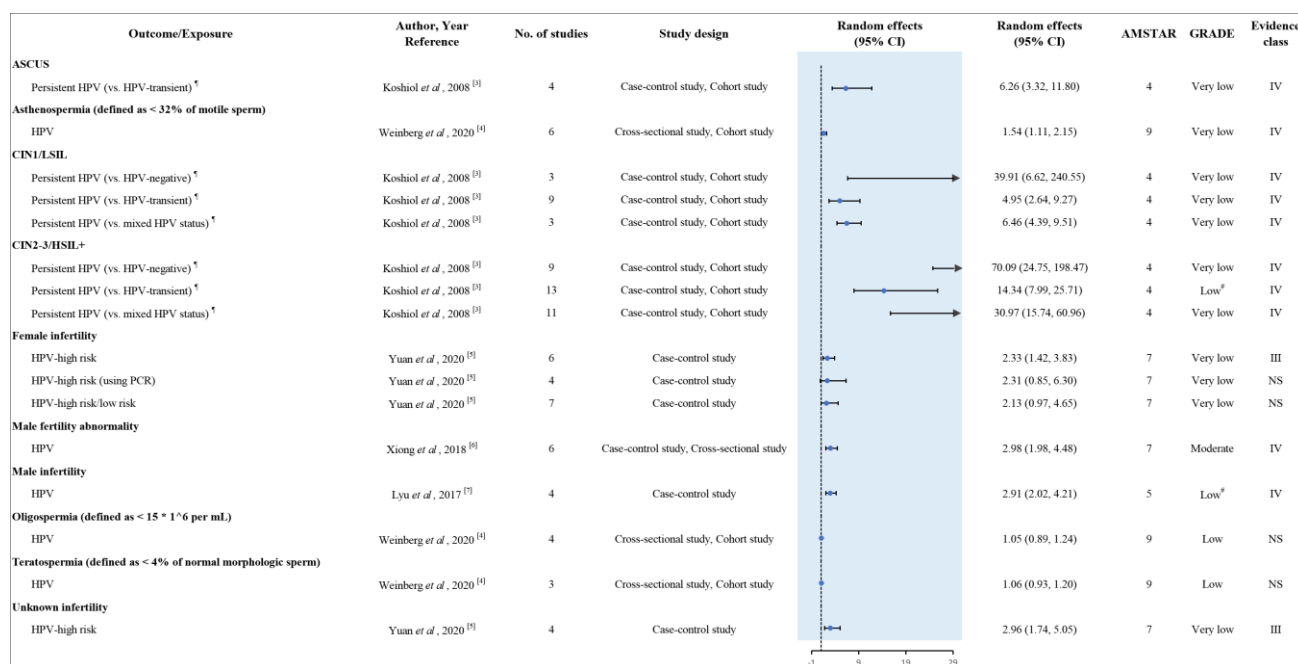


Outcome/Exposure	Author, Year Reference	No. of studies	Study design	Random effects (95% CI)	Random effects (95% CI)	AMSTAR	GRADE	Evidence class
HIV acquisition								
HPV	Looker <i>et al.</i> , 2018 ^[1]	7	Case-control study, Cohort study		1.75 (1.23, 2.49)	5	Very low	IV
HPV-high risk	Houlihan <i>et al.</i> , 2012 ^[2]	5	Case-control study, Cohort study		1.99 (1.54, 2.56)	7	Very low	IV
Nonpersistent HPV	Houlihan <i>et al.</i> , 2012 ^[2]	2	Case-control study, Cohort study		2.60 (1.35, 5.00)	7	Very low	IV
Persistent HPV	Houlihan <i>et al.</i> , 2012 ^[2]	2	Case-control study, Cohort study		0.97 (0.66, 1.41)	7	Very low	NS

Supplementary Figure 1. Summary random effects estimates with 95% confidence intervals from 4 meta-analyses of human papillomavirus and HPV acquisition. Evidence class of each meta-analysis was categorized into convincing, highly suggestive, suggestive, and weak, which was expressed as class I , II , III , and IV , respectively. AMSTAR, A Measurement Tool to Assess systematic Reviews; CI, confidence interval; GRADE, Grading of Recommendations; HIV, human immunodeficiency virus; HPV, human papillomavirus; NS, non-significant.

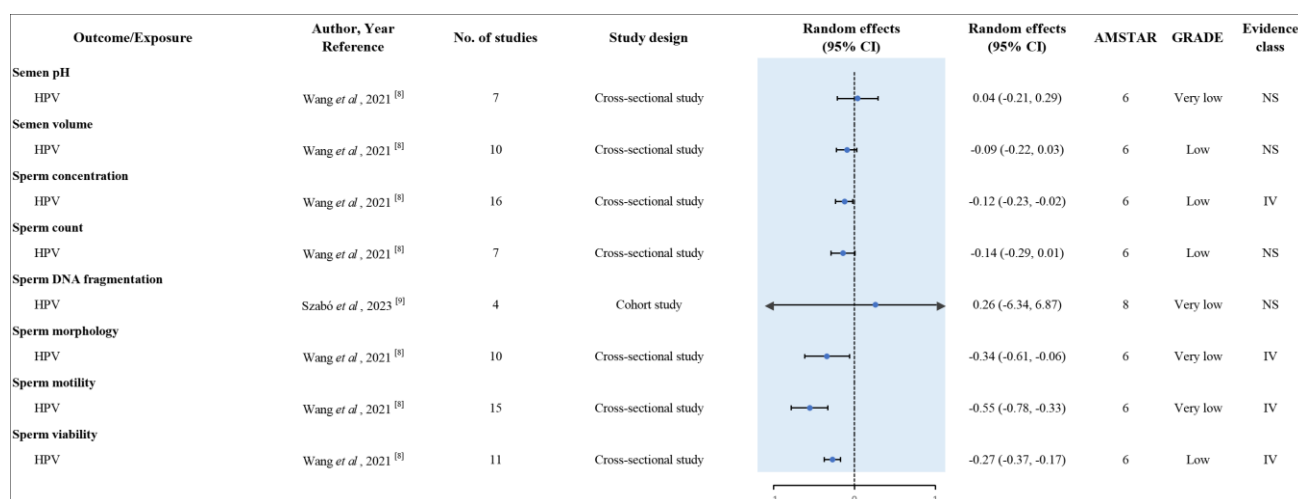


Supplementary Figure 2. Summary random effects estimates with 95% confidence intervals from 16 meta-analyses of human papillomavirus and genital system diseases. Evidence class of each meta-analysis was categorized into convincing, highly suggestive, suggestive, and weak, which was expressed as class I, II, III, and IV, respectively.

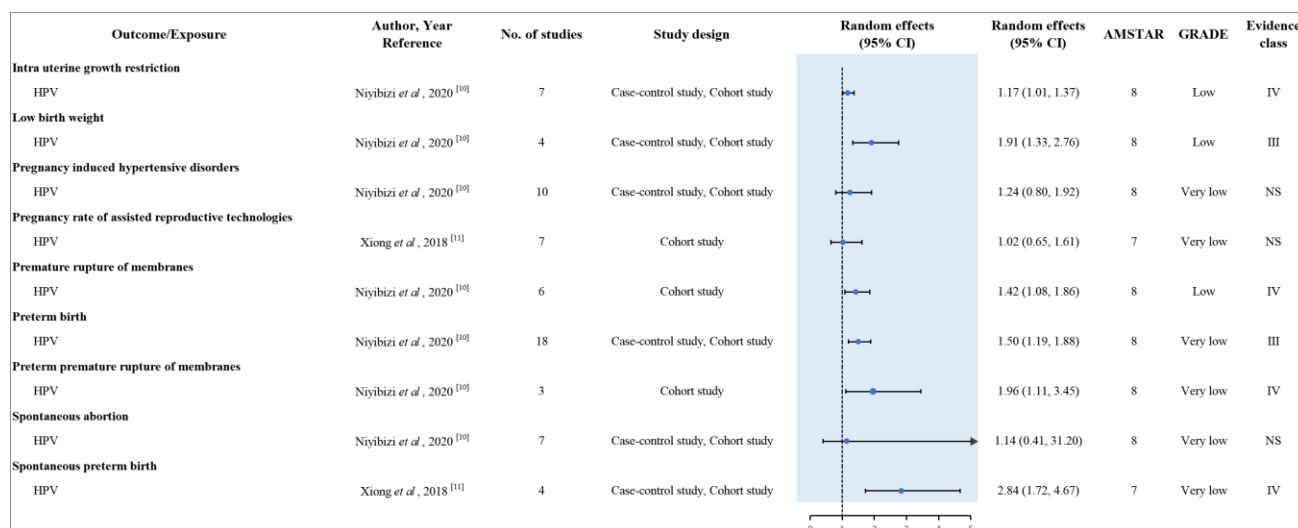
[‡] Other than these studies, the other studies are all HPV positive status compared with HPV negative status.

[#] Studies do not evaluate the risk of bias, so they cannot be downgraded or upgraded based on the factors above.

AMSTAR, A Measurement Tool to Assess systematic Reviews; ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; CIN, cervical intraepithelial neoplasia; CIN1, low-grade cervical intraepithelial neoplasia; CIN2-3, high-grade cervical intraepithelial neoplasia; GRADE, Grading of Recommendations; HPV, human papillomavirus; HSIL+, high-grade squamous intraepithelial lesions; LSIL, low-grade squamous intraepithelial lesions; NS, non-significant; PCR, polymerase chain reaction.



Supplementary Figure 3. Summary random effects estimates with 95% confidence intervals from 8 meta-analyses of human papillomavirus and sperm-related outcomes. Evidence class of each meta-analysis was categorized into convincing, highly suggestive, suggestive, and weak, which was expressed as class I, II, III, and IV, respectively. AMSTAR, A Measurement Tool to Assess systematic Reviews; DNA, deoxyribonucleic acid; GRADE, Grading of Recommendations; HPV, human papillomavirus; NS, non-significant; PH, potential of hydrogen.



Supplementary Figure 4. Summary random effects estimates with 95% confidence intervals from 8 meta-analyses of human papillomavirus and pregnancy outcomes. Evidence class of each meta-analysis was categorized into convincing, highly suggestive, suggestive, and weak, which was expressed as class I, II, III, and IV, respectively. AMSTAR, A Measurement Tool to Assess systematic Reviews; CI, confidence interval; GRADE, Grading of Recommendations; HPV, human papillomavirus; NS, non-significant.

References

1. Looker KJ, Rönn MM, Brock PM, *et al.* Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. *J Int AIDS Soc.* 2018 Jun;21(6):e25110. [DOI:10.1002/jia2.25110. PMID: 29873885; PMCID: PMC5989783]
2. Houlihan CF, Larke NL, Watson-Jones D, *et al.* Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. *AIDS.* 2012 Nov 13;26(17):2211-22. [DOI:10.1097/QAD.0b013e328358d908. PMID: 22874522; PMCID: PMC3831022]
3. Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. *Am J Epidemiol.* 2008 Jul 15;168(2):123-37. [DOI:10.1093/aje/kwn036. Epub 2008 May 15. PMID: 18483125; PMCID: PMC2878094]
4. Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. *Fertil Steril.* 2020 May;113(5):955-969.e4. [DOI:10.1016/j.fertnstert.2020.01.010. PMID: 32386620]
5. Yuan S, Qiu Y, Xu Y, Wang H. Human papillomavirus infection and female infertility: a systematic review and meta-analysis. *Reprod Biomed Online.* 2020 Feb;40(2):229-237. [DOI:10.1016/j.rbmo.2019.10.019. Epub 2019 Nov 16. PMID: 31987733]
6. Xiong YQ, Chen YX, Cheng MJ, He WQ, Chen Q. The risk of human papillomavirus infection for male fertility abnormality: a meta-analysis. *Asian J Androl.* 2018 Sep-Oct;20(5):493-497. [DOI:10.4103/aja.aja_77_17. PMID: 29623908; PMCID: PMC6116676]
7. Lyu Z, Feng X, Li N, *et al.* Human papillomavirus in semen and the risk for male infertility: a systematic review and meta-analysis. *BMC Infect Dis.* 2017 Nov 9;17(1):714. [DOI:10.1186/s12879-017-2812-z. PMID: 29121862; PMCID: PMC5679371]
8. Wang S, Liu L, Zhang A, Song Y, Kang J, Liu X. Association between human papillomavirus infection and sperm quality: A systematic review and a meta-analysis. *Andrologia.* 2021 Jun;53(5):e14034. [DOI:10.1111/and.14034. Epub 2021 Mar 5. PMID: 33666259]
9. Szabó A, Váncsa S, Hegyi P, *et al.* Lifestyle-, environmental-, and additional health factors associated with an increased sperm DNA fragmentation: a systematic review and meta-analysis. *Reprod Biol*

Endocrinol. 2023 Jan 18;21(1):5. [DOI:10.1186/s12958-023-01054-0. PMID: 36653793; PMCID: PMC9847125]

10. Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association Between Maternal Human Papillomavirus Infection and Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis. *J Infect Dis.* 2020 Jun 11;221(12):1925-1937. [DOI:10.1093/infdis/jiaa054. PMID: 32022858; PMCID: PMC7289546]

11. Xiong YQ, Mo Y, Luo QM, Huo ST, He WQ, Chen Q. The Risk of Human Papillomavirus Infection for Spontaneous Abortion, Spontaneous Preterm Birth, and Pregnancy Rate of Assisted Reproductive Technologies: A Systematic Review and Meta-Analysis. *Gynecol Obstet Invest.* 2018;83(5):417-427. [DOI:10.1159/000482008. Epub 2018 Apr 12. PMID: 29649818]

Supplementary Table 1: PRISMA checklist of items to include when reporting a systematic review or meta-analysis

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-4
METHODS			
Protocol registration	and 5	Indicate if a review protocol exists, if and where it can be accessed (<i>e.g.</i> , Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (<i>e.g.</i> , PICOS, length of follow-up) and report characteristics (<i>e.g.</i> , years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (<i>e.g.</i> , databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (<i>i.e.</i> , screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (<i>e.g.</i> , piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-5
Data items	11	List and define all variables for which data were sought (<i>e.g.</i> , PICOS, funding sources) and any assumptions and simplifications made.	4-5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6
Summary measures	13	State the principal summary measures (<i>e.g.</i> , risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (<i>e.g.</i> , I^2) for each meta-analysis.	5-6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (<i>e.g.</i> , publication bias, selective reporting within studies).	5-6
Additional analyses	16	Describe methods of additional analyses (<i>e.g.</i> , sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA

RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6, Figure1, Table S5
Study characteristics	18	For each study, present characteristics for which data were extracted (<i>e.g.</i> , study size, PICOS, follow-up period) and provide the citations.	4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	10、Figure2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7-10
Additional analysis	23	Give results of additional analyses, if done (<i>e.g.</i> , sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (<i>e.g.</i> , health care providers, users, and policy makers).	11-12
Limitations	25	Discuss limitations at study and outcome level (<i>e.g.</i> , risk of bias), and at review level (<i>e.g.</i> , incomplete retrieval of identified research, reporting bias).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (<i>e.g.</i> , supply of data); role of funders for the systematic review.	NA

NA, not available.

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7): e1000097. [DOI:10.1371/journal.pmed1000097].

Supplementary Table 2: MOOSE checklist for meta-analyses of observational studies

Item No.	Recommendation	Reported on Page No.
Reporting of background should include		
1	Problem definition	3-4
2	Hypothesis statement	3-4
3	Description of study outcome(s)	4
4	Type of exposure or intervention used	4
5	Type of study designs used	4

6	Study population	4
Reporting of search strategy should include		
7	Qualifications of searchers (<i>e.g.</i> , librarians and investigators)	NA
8	Search strategy, including time period included in the synthesis and key words	4、Table S3
9	Effort to include all available studies, including contact with authors	NA
10	Databases and registries searched	4
11	Search software used, name and version, including special features used <i>e.g.</i> , explosion)	NA
12	Use of hand searching (<i>e.g.</i> , reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	Figure 1、Table S5
14	Method of addressing articles published in languages other than English	4
15	Method of handling abstracts and unpublished studies	NA
16	Description of any contact with authors	NA
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	6-10
18	Rationale for the selection and coding of data (<i>e.g.</i> , sound clinical principles or convenience)	NA
19	Documentation of how data were classified and coded (<i>e.g.</i> , multiple raters, blinding and interrater reliability)	NA
20	Assessment of confounding (<i>e.g.</i> , comparability of cases and controls in studies where appropriate)	NA
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	6-10
22	Assessment of heterogeneity	10
23	Description of statistical methods (<i>e.g.</i> , 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	5-6
24	Provision of appropriate tables and graphics	Tables S1-S4
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	7-8
26	Table giving descriptive information for each study included	Table S6
27	Results of sensitivity testing (<i>e.g.</i> , subgroup analysis)	10
28	Indication of statistical uncertainty of findings	8-9
Reporting of discussion should include		
29	Quantitative assessment of bias (<i>e.g.</i> , publication bias)	NA
30	Justification for exclusion (<i>e.g.</i> , exclusion of non-English language citations)	Table S5
31	Assessment of quality of included studies	12-13
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	11-13
33	Generalization of the conclusions (<i>i.e.</i> , appropriate for the data presented and within the domain of the literature review)	11-13
34	Guidelines for future research	11-13
35	Disclosure of funding source	14

NA, not available.

From: Stroup DF, Berlin JA, Morton SC, *et al*, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. [DOI:10.1001/jama.283.15.2008]

Supplementary Table 3: Search strategy

Literature search strategy in PubMed
#1 (HPV [Title/Abstract] OR papillomavirus [Title/Abstract])
#2 (systematic review [Title/Abstract] OR meta analysis [Title/Abstract] OR systematic overview [Title/Abstract])
#3 #1 AND #2
Literature search strategy in Web of Science
#1 TS = (HPV OR papillomavirus)
#2 TS = (systematic review OR meta-analysis OR systematic overview)
#3 #1 AND #2
Literature search strategy in Embase
#1 ('HPV': ab,ti OR 'papillomavirus': ab,ti)
#2 ('systematic review': ab,ti OR 'meta analysis': ab,ti OR 'systematic overview': ab,ti)
#3 #1 AND #2
HPV, human papillomavirus; OR, odds ratio.

Supplementary Table 4: Criteria for categorizing the credibility of evidence in this umbrella review

Evidence classification	Criteria
Convincing (Class I)	$P < 10^{-6}$ under the random-effects models
	Number of cases > 1000
	Heterogeneity (I^2) < 50 %
	$P < 0.05$ of the largest study in the meta-analysis
	95 % prediction interval that excluded the null value
	No evidence of small-study effects ($P > 0.1$)
Highly suggestive (Class II)	No evidence of excess significance bias (O < E or $P > 0.1$)
	$P < 10^{-6}$ under the random-effects models
	Number of cases > 1000

	$P < 0.05$ of the largest study in the meta-analysis
Suggestive (Class III)	$P < 10^{-3}$ under the random-effects models
	Number of cases > 1000
Weak (Class IV)	$P < 0.05$ under the random-effects models
Not significant	$P > 0.05$ under the random-effects models

P , p -value.

Supplementary Table 5: The list of the excluded records during the process of full-text checking

Systematic review without meta-analysis ($n = 7$)	
1	Farsimadan, M. and M. Motamedifar, The effects of human immunodeficiency virus, human papillomavirus, herpes simplex virus-1 and -2, human herpesvirus-6 and -8, cytomegalovirus, and hepatitis B and C virus on female fertility and pregnancy. <i>British Journal of Biomedical Science</i> , 2021. 78(1): p. 1-11.
2	Garcia-Carrasco, M., <i>et al.</i> , Conceptual, statistical and clinical interpretation of results from a systematic review and meta-analysis of prevalence of cervical HPV infection in women with SLE Reply. <i>AUTOIMMUNITY REVIEWS</i> , 2019. 18(4): p. 435-436.
3	Gardella, B., <i>et al.</i> , Multiple human papillomavirus infection and ascus-Isil progression: A review. <i>Italian Journal of Gynaecology and Obstetrics</i> , 2021. 33(3): p. 145-154.
4	Popescu, S.D., <i>et al.</i> , Maternal HPV Infection and the Estimated Risks for Adverse Pregnancy Outcomes—A Systematic Review. <i>Diagnostics</i> , 2022. 12(6).
5	Raposo, A., <i>et al.</i> , Human papillomavirus infection and cervical lesions in rheumatic diseases: a systematic review. <i>Acta Reumatol Port</i> , 2016. 41(3): p. 184-190.
6	Souho, T., M. Benlemlih and B. Bennani, Human papillomavirus infection and fertility alteration: A systematic review. <i>PLoS ONE</i> , 2015. 10(5).
7	Lehtinen, M., <i>et al.</i> , Human papillomavirus infection, risk for subsequent development of cervical neoplasia and associated population attributable fraction. <i>JOURNAL OF CLINICAL VIROLOGY</i> , 2001. 22(1): p. 117-124.
Missing data ($n = 2$)	
1	Fuller, C., E. Hudgins and N. Finelt, Human-papillomavirus-related disease in pediatrics. <i>Current Opinion in Pediatrics</i> , 2018. 30(1): p. 169-174.
2	Klug, J., M. Hukelmann and M. Blettner, Systematic literature review on knowledge about infection with human papillomavirus (HPV). <i>EUROPEAN JOURNAL OF EPIDEMIOLOGY</i> , 2006. 21: p. 59-60.
Not systematic review or meta-analysie ($n = 4$)	
1	Colpani, V., <i>et al.</i> , Prevalence of papillomavirus in Brazil: A systematic review protocol. <i>BMJ Open</i> , 2016. 6(11).
2	Da Costa, J., <i>et al.</i> , Prevalence of epithelial lesions and penile human papillomavirus infection (HPV) in partners of women with cervical epithelial lesions. <i>Cytopathology</i> , 2014. 25: p. 58-59.
3	García-Carrasco, M., <i>et al.</i> , Corrigendum to 'Prevalence of cervical HPV infection in women with systemic lupus erythematosus: a systematic review and meta-analysis'. [AUTREV 18-2 (2019) 184-191] (S1568997218302878) (DOI:10.1016/j.autrev.2018.09.001). <i>Autoimmunity Reviews</i> , 2019. 18(4): p. 437.
4	Niyibizi, J., <i>et al.</i> , The association between adverse pregnancy outcomes and maternal human papillomavirus infection: A systematic review protocol. <i>Systematic Reviews</i> , 2017. 6(1).
Not interested exposure ($n = 15$)	
1	Beachler, D.C., <i>et al.</i> , Natural Acquired Immunity Against Subsequent Genital Human Papillomavirus Infection: A Systematic Review and Meta-analysis. <i>Journal of Infectious Diseases</i> , 2016. 213(9): p. 1444-1454.
2	Bravo CA, Walker MJ, Papadopoulos A, McWhirter JE. Social media use in HPV-, cervical cancer-, and cervical screening-related research: A scoping review. <i>Preventive Medicine</i> . 2024;179.
3	Carter KA, Fischer MD, Petrova MI, Balkus JE. Epidemiologic Evidence on the Role of Lactobacillus iners in Sexually Transmitted Infections and Bacterial Vaginosis: A Series of Systematic Reviews and Meta-Analyses. <i>Sex Transm Dis</i> . 2023;50(4):224-35.
4	Desmoulin A, Joly E, Tran P, Derancourt C, Bertolotti A. Methodological quality of systematic reviews of the local management of anogenital warts: a systematic review using AMSTAR II, ROBIS and PRISMA. <i>Sex Transm Infect</i> . 2023;99(5):345-7.
5	Fedele F, Bulfoni A, Parazzini F, Busnelli A. Neovagina creation methods in Müllerian anomalies and risk of malignancy: insights from a systematic review. <i>Arch Gynecol Obstet</i> . 2024;309(3):801-12.
6	Li Y, Hua C, Zhang M. Efficacy of non-invasive photodynamic therapy for female lower reproductive tract diseases associated with HPV infection: a comprehensive meta-analysis. <i>Lasers Med Sci</i> . 2023;38(1):42.

7 Liu A, Garcia-Torres LC, Johnson C, Haver MK, Gwede CK, Christy SM. Cancer screening educational interventions in rural and farmworker communities: a systematic literature review. *Ethn Health*. 2023;28(3):335-57.

8 Looker, K.J., *et al.*, What is the strength of evidence for HIV and HPV interactions? results from systematic reviews and meta-analyses of longitudinal studies. *Sexually Transmitted Infections*, 2017. 93: p. A41.

9 Zhao R, Sekar P, Bennis SL, Kulasingam S. A systematic review of the association between smoking exposure and HPV-related cervical cell abnormality among women living with HIV: Implications for prevention strategies. *Prev Med*. 2023;170:107494.

10 Zhou, P. and Y. Wang, Meta- analysis on relevant factors of cervical intraepithelial neoplasia residual or recurrence after cervical conization. *Chinese Journal of Practical Gynecology and Obstetrics*, 2014. 30(7): p. 546-552.

11 Zhuang Y, Yang H. The significance of nonsurgical therapies for cervical infection of high-risk human papilloma virus: A systematic review and meta-analysis. *J Obstet Gynaecol Res*. 2023;49(9):2213-31.

12 Dong M, Dong Y, Bai J, *et al.* Interactions between microbiota and cervical epithelial, immune, and mucus barrier. *Frontiers in Cellular and Infection Microbiology*. 2023;13.

13 Li Y, Hua C, Zhang M. Efficacy of non-invasive photodynamic therapy for female lower reproductive tract diseases associated with HPV infection: a comprehensive meta-analysis. *LASERS IN MEDICAL SCIENCE*. 2023;38(1).

14 Mawardi P, Kamilah L, Heryadi FF, Arrosyid A. The Effectiveness of Chemical Cautery and Electrosurgery on Anogenital Wart: Systematic Review. *Clinical, Cosmetic and Investigational Dermatology*. 2023;16:2773-80.

15 Naegele S, Ruiz-Torres DA, Zhao Y, Goss D, Faden DL. Comparing the Diagnostic Performance of qPCR, ddPCR, and NGS Liquid Biopsies for HPV-Associated Cancers. 2023.

Duplicate outcomes (n = 2)

1 Lissouba P, Van de Perre P, Auvert B. Association of genital human papillomavirus infection with HIV acquisition: a systematic review and meta-analysis. *Sex Transm Infect*. 2013 Aug;89(5):350-6.

2 Cao X, Wei R, Zhang X, Zhou J, Lou J, Cui Y. Impact of human papillomavirus infection in semen on sperm progressive motility in infertile men: a systematic review and meta-analysis. *Reprod Biol Endocrinol*. 2020 May 7;18(1):38.

Supplementary Table 6: GRADE classification of quality of evidence

Outcomes/Exposure	Author, Year, Reference	Downgrade factors					Upgrade factors			Quality
		Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	Magnitude of effect	Dose response	Plausible confounding	
Reproductive health outcomes										
HIV acquisition										
HPV	Looker <i>et al</i> , 2018 ^[10]	Unclear ¹	Not serious	Serious limitation ²	Not serious	Not serious ³	No	No	Would not reduce effect	Very low
HPV-high risk	Houlihan <i>et al</i> , 2012 ^[4]	Serious limitation ^a	Not serious	Not serious	Not serious	Serious limitation ^{3,4}	No	No	Would not reduce effect	Very low
Nonpersistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	Not serious	Not serious	Not serious	Serious limitation ⁵	Not serious ³	No	No	Would not reduce effect	Very low
Persistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	Not serious	Not serious	Not serious	Serious limitation ⁵	Not serious ³	No	No	Would not reduce effect	Very low
ASCUS										
Persistent HPV (vs. HPV-transient) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Not serious ³	Serious limitation ⁵	Not serious	No	No	Would not reduce effect	Very low

Asthenospermia (defined as < 32% of motile sperm)

HPV	Weinberg <i>et al</i> , 2020 ^[8]	Not serious	Not serious	Serious limitation ²	Not serious	Not serious ³	No	No	Would not reduce effect	Very low
-----	---	-------------	-------------	---------------------------------	-------------	--------------------------	----	----	-------------------------	----------

CIN1/LSIL

Persistent HPV (vs. HPV-negative) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Serious limitation ^{3 6}	Serious limitation ⁵	Not serious	No	No	Would not reduce effect	Very low
--	--	----------------------	-------------	-----------------------------------	---------------------------------	-------------	----	----	-------------------------	----------

Persistent HPV (vs. HPV-transient) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Serious limitation ^{2 3}	Not serious	Not serious	No	No	Would not reduce effect	Very low
---	--	----------------------	-------------	-----------------------------------	-------------	-------------	----	----	-------------------------	----------

Persistent HPV (vs. mixed HPV status) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Not serious ³	Serious limitation ⁵	Not serious	No	No	Would not reduce effect	Very low
--	--	----------------------	-------------	--------------------------	---------------------------------	-------------	----	----	-------------------------	----------

CIN2-3/HSIL+

Persistent HPV (vs. HPV-negative) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Serious limitation ^{2 3}	Not serious	Not serious	No	No	Would not reduce effect	Very low
--	--	----------------------	-------------	-----------------------------------	-------------	-------------	----	----	-------------------------	----------

Persistent HPV (vs. HPV-transient) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Not serious ³	Not serious	Not serious	No	No	Would not reduce effect	Low ⁷
---	--	----------------------	-------------	--------------------------	-------------	-------------	----	----	-------------------------	------------------

Persistent HPV (vs. mixed HPV status) ^l	Koshiol <i>et al</i> , 2008 ^[9]	Unclear ¹	Not serious	Serious limitation ^{3 6}	Not serious	Not serious	No	No	Would not reduce effect	Very low
--	--	----------------------	-------------	-----------------------------------	-------------	-------------	----	----	-------------------------	----------

Female infertility

HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	Not serious	Not serious	Serious limitation ⁶	Not serious	Not serious	No	No	Would not reduce effect	Very low
---------------	---	-------------	-------------	---------------------------------	-------------	-------------	----	----	-------------------------	----------

HPV-high risk (using PCR)	Yuan <i>et al</i> , 2020 ^[3]	Not serious	Not serious	Serious limitation ⁶	Not serious	Not serious	No	No	Would not reduce effect	Very low
---------------------------	---	-------------	-------------	---------------------------------	-------------	-------------	----	----	-------------------------	----------

HPV-high risk/low risk	Yuan <i>et al</i> , 2020 ^[3]	Not serious	Not serious	Serious limitation ⁶	Not serious	Not serious	No	No	Would not reduce effect	Very low
------------------------	---	-------------	-------------	---------------------------------	-------------	-------------	----	----	-------------------------	----------

Male fertility abnormality

HPV	Xiong <i>et al</i> , 2018 ^[5]	Not serious	Not serious	Not serious	Not serious	Not serious	Yes ⁸	No	Would not reduce effect	Moderate
-----	--	-------------	-------------	-------------	-------------	-------------	------------------	----	-------------------------	----------

Male infertility

[illegible]

[illegible]

HPV	Xiong <i>et al</i> , 2018 ^[6]	Not serious	Not serious	Not serious	Serious limitation ⁵	Not serious	No	No	Would not reduce effect	Very low
-----	---	-------------	-------------	-------------	------------------------------------	-------------	----	----	-------------------------------	----------

¹ Studies do not conduct methodological quality assessment;

² Downgraded by one level for inconsistency: substantial heterogeneity is seen between studies (I2 > 50%);

³ Studies do not carry out corresponding analyses or show corresponding results, so the results recalculated in this UR are used to assess the certainty of evidence;

⁴ Downgraded by one level for publication bias: asymmetry on funnel plot, the P of Egger's test or Begg's test < 0.05;

⁵ Downgraded by one level for imprecision: substantial imprecision is seen in studies (events < 300 or total population size < 400);

⁶ Downgraded by only one level for inconsistency: substantial heterogeneity is seen between studies (I2 > 75%), whereas heterogeneity was mainly explained;

⁷ Studies do not evaluate the risk of bias, so they cannot be downgraded or upgraded based on the factors above;

⁸ Upgraded by only one level for magnitude of effect: combined effect size > 2.

ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; CIN, cervical intraepithelial neoplasia; CIN1, low-grade cervical intraepithelial neoplasia; CIN2-3, high-grade cervical intraepithelial neoplasia; DNA, deoxyribonucleic acid; ELISA, enzyme linked immunosorbent assay; FFT, fresh frozen tissue; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSIL+, high-grade squamous intraepithelial lesions; LSIL, low-grade squamous intraepithelial lesions; PCR, polymerase chain reaction; PET, paraffin-embedded tissue; PH, potential of hydrogen.

References:

[1] Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association Between Maternal Human Papillomavirus Infection and Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis. J Infect Dis. 2020 Jun 11;221(12):1925-1937. [DOI:10.1093/infdis/jiaa054. PMID: 32022858; PMCID: PMC7289546]

[2] Lyu Z, Feng X, Li N, et al. Human papillomavirus in semen and the risk for male infertility: a systematic review and meta-analysis. BMC Infect Dis. 2017 Nov 9;17(1):714. [DOI:10.1186/s12879-017-2812-z. PMID: 29121862; PMCID: PMC5679371]

[3] Yuan S, Qiu Y, Xu Y, Wang H. Human papillomavirus infection and female infertility: a systematic review and meta-analysis. Reprod Biomed Online. 2020 Feb;40(2):229-237. [DOI:10.1016/j.rbmo.2019.10.019. Epub 2019 Nov 16. PMID: 31987733]

[4] Houlihan CF, Larke NL, Watson-Jones D, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS. 2012 Nov 13;26(17):2211-22. [DOI:10.1097/QAD.0b013e328358d908. PMID: 22874522; PMCID: PMC3831022]

[5] Xiong YQ, Chen YX, Cheng MJ, He WQ, Chen Q. The risk of human papillomavirus infection for male fertility abnormality: a meta-analysis. Asian J Androl. 2018 Sep-Oct;20(5):493-497. [DOI:10.4103/aja.aja_77_17. PMID: 29623908; PMCID: PMC6116676]

[6] Xiong YQ, Mo Y, Luo QM, Huo ST, He WQ, Chen Q. The Risk of Human Papillomavirus Infection for Spontaneous Abortion, Spontaneous Preterm Birth, and Pregnancy Rate of Assisted Reproductive Technologies: A Systematic Review and Meta-Analysis. Gynecol Obstet Invest. 2018;83(5):417-427. [DOI:10.1159/000482008. Epub 2018 Apr 12. PMID: 29649818]

[7] Wang S, Liu L, Zhang A, Song Y, Kang J, Liu X. Association between human papillomavirus infection and sperm quality: A systematic review and a meta-analysis. Andrologia. 2021 Jun;53(5):e14034. [DOI:10.1111/and.14034. Epub 2021 Mar 5. PMID: 33666259]

[8] Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. Fertil Steril. 2020 May;113(5):955-969.e4. [DOI:10.1016/j.fertnstert.2020.01.010. PMID: 32386620]

[9] Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. Am J Epidemiol. 2008 Jul 15;168(2):123-37. [DOI:10.1093/aje/kwn036. Epub 2008 May 15. PMID: 18483125; PMCID: PMC2878094]

[10] Looker KJ, Rönn MM, Brock PM, et al. Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. J Int AIDS Soc. 2018 Jun;21(6):e25110. [DOI:10.1002/jia2.25110. PMID: 29873885; PMCID: PMC5989783]

[11] Szabó A, Váncsa S, Hegyi P, et al. Lifestyle-, environmental-, and additional health factors associated with an increased sperm DNA fragmentation: a systematic review and meta-analysis. Reprod Biol Endocrinol. 2023 Jan 18;21(1):5. [DOI:10.1186/s12958-023-01054-0. PMID: 36653793; PMCID: PMC9847125]

Supplementary Table 7: Suggestive evidence (class III), weak evidence (class IV), and no evidence (non-significant association, *P* > 0.05) in 36 meta-analyses of the association between HPV and non-cancerous reproductive health outcomes

Outcomes	Exposure	Author, Year, Reference	Features used for grading the level of evidence				
			Random <i>P</i> -value	No. of cases/ participants	95% PI	<i>I</i> ²	Largest study (95% CI)
Genital system diseases							
Female infertility	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	8.29×10 ⁻⁴	2617/11,869	0.43, 12.78	92.20%	2.76 (2.00, 3.52)
Unknown infertility	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	6.66×10 ⁻⁵	2378/11,398	0.24, 36.16	93.90%	2.76 (2.00, 3.52)
Pregnancy outcomes							
Low birth weight	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	4.81×10 ⁻⁴	NA/296,524	0.71, 5.19	12.80%	2.56 (1.76, 3.36)
Preterm birth	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	4.60×10 ⁻⁴	NA/336,391	0.66, 3.42	68.50%	1.00 (0.33, 1.67)
Genital system diseases							
HIV acquisition	HPV	Looker <i>et al</i> , 2018 ^[10]	0.002	603/11,841	0.63, 4.89	62.70%	1.31 (0.63, 2.00)
HIV acquisition	HPV-high risk	Houlihan <i>et al</i> , 2012 ^[4]	1.30×10 ⁻⁷	358/7214	1.20, 3.29	8.50%	1.66 (1.00, 2.32)
HIV acquisition	Nonpersistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	4.24×10 ⁻³	NA/2495	0, 6015.57	78.00%	1.67 (1.00, 2.32)
ASCUS	Persistent HPV (vs. HPV-transient) ^a	Koshiol <i>et al</i> , 2008 ^[9]	1.37×10 ⁻⁸	72/1204	1.56, 25.15	0	4.70 (1.00, 8.40)
Asthenospermia (defined as < 32% of motile sperm)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	0.010	757/1554	0.61, 3.90	59.50%	1.17 (0.61, 1.73)
CIN1/LSIL	Persistent HPV (vs. HPV-negative) ^a	Koshiol <i>et al</i> , 2008 ^[9]	5.77×10 ⁻⁵	110/1700	0, 1.53×10 ¹¹	87.20%	117.70 (4.00, 231.40)
CIN1/LSIL	Persistent HPV (vs. HPV-transient) ^a	Koshiol <i>et al</i> , 2008 ^[9]	5.77×10 ⁻⁷	NA/2469	0.78, 31.50	64.60%	3.70 (2.00, 5.40)
CIN1/LSIL	Persistent HPV (vs. mixed HPV status) ^a	Koshiol <i>et al</i> , 2008 ^[9]	3.08×10 ⁻²¹	229/2239	0.53, 79.23	0	7.40 (4.00, 10.80)
CIN2-3/HSIL+	Persistent HPV (vs. HPV-negative) ^a	Koshiol <i>et al</i> , 2008 ^[9]	1.22×10 ⁻¹⁵	544/4822	2.98, 1648.74	68.70%	33.30 (1.00, 65.60)
CIN2-3/HSIL+	Persistent HPV (vs. HPV-transient) ^a	Koshiol <i>et al</i> , 2008 ^[9]	4.15×10 ⁻¹⁹	NA/3003	3.69, 55.70	30.30%	5.40 (3.00, 7.80)
CIN2-3/HSIL+	Persistent HPV (vs. mixed HPV status) ^a	Koshiol <i>et al</i> , 2008 ^[9]	2.83×10 ⁻²³	NA/11,607	3.58, 267.85	77.20%	94.60 (53.00, 136.20)
Male fertility abnormality	HPV	Xiong <i>et al</i> , 2018 ^[5]	1.52×10 ⁻⁷	NA/1742	1.55, 5.75	2.10%	2.94 (1.00, 4.88)
Male infertility	HPV	Lyu <i>et al</i> , 2017 ^[2]	1.24×10 ⁻⁸	853/1494	1.30, 6.53	0	2.94 (1.00, 4.88)
Sperm concentration	HPV	Wang <i>et al</i> , 2021 ^[7]	0.025	NA/3885	-0.39, 0.14	22.40%	-0.11 (-0.39, 0.17)
Sperm morphology	HPV	Wang <i>et al</i> , 2021 ^[7]	0.015	NA/1544	-1.26, 0.58	72.50%	-0.66 (-0.94, -0.38)
Sperm motility	HPV	Wang <i>et al</i> , 2021 ^[7]	1.72×10 ⁻⁶	NA/3842	-1.48, 0.37	80.60%	-0.65 (-0.93, -0.37)
Sperm viability	HPV	Wang <i>et al</i> , 2021 ^[7]	1.78×10 ⁻⁷	NA/2942	-0.38, -0.16	0	-0.22 (-0.50, 0.06)
Pregnancy outcomes							
Intra uterine growth restriction	HPV	Niyibizi <i>et al</i> , 2020[1]	0.037	7765/273,357	0.96, 1.43	0	1.20 (0.96, 1.43)
Premature rupture of membranes	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.013	NA/272,430	0.96, 2.09	0	1.08 (0.96, 1.20)
Preterm premature rupture of membranes	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.020	248/13,650	0.05, 76.18	0	2.07 (1.00, 3.14)
Spontaneous preterm birth	HPV	Xiong <i>et al</i> , 2018 ^[6]	4.25×10 ⁻⁵	NA/1501	0.61, 13.23	23.60%	3.69 (2.00, 5.38)

Genital system diseases								
HIV acquisition	Persistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	0.865	NA/2471	0.08, 11.24	0	0.82 (0.65, 0.99)	
Female infertility	HPV-high risk/low risk	Yuan <i>et al</i> , 2020 ^[3]	0.058	1974/3581	0.14, 32.22	92.20%	6.32 (5.00, 7.64)	
Female infertility (using PCR)	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	0.102	1017/2169	0.02, 249.69	91.40%	6.00 (4.77, 7.23)	
Oligospermia (defined as < 15 * 10 ⁶ per mL)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	0.570	481/1404	0.73, 1.50	0	1.05 (0.82, 1.28)	
Sperm DNA fragmentation	HPV	Szabó <i>et al</i> , 2023 ^[11]	0.938	NA/411	-27.06, 27.59	69.40%	-0.40 (-0.63, -0.17)	
Semen pH	HPV	Wang <i>et al</i> , 2021 ^[7]	0.757	NA/2778	-0.75, 0.82	73.70%	0.13 (-0.10, 0.36)	
Semen volume	HPV	Wang <i>et al</i> , 2021 ^[7]	0.145	NA/3174	-0.39, 0.21	29.20%	0.03 (-0.20, 0.26)	
Sperm count	HPV	Wang <i>et al</i> , 2021 ^[7]	0.062	NA/1239	-0.33, 0.04	0	-0.21 (-0.44, 0.02)	
Teratospermia (defined as < 4% of normal morphologic sperm)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	0.392	756/1339	0.47, 2.36	0	1.05 (0.82, 1.28)	
Pregnancy outcomes								
Pregnancy rate of assisted reproductive technologies	HPV	Xiong <i>et al</i> , 2018 ^[6]	0.932	NA/1404	0.26, 4.02	70.00%	0.69 (0.46, 0.92)	
Spontaneous abortion	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.804	262/1884	0.04, 31.20	80.40%	0.22 (0.00, 0.44)	

^aOther than these studies, the other studies are all HPV positive status compared with HPV negative status.
ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; CIN, cervical intraepithelial neoplasia; CIN1, low-grade cervical intraepithelial neoplasia; CIN2-3, high-grade cervical intraepithelial neoplasia; DNA, deoxyribonucleic acid; ESB, excess significance bias; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSIL+, high-grade squamous intraepithelial lesions; LSIL, low-grade squamous intraepithelial lesions; NA, not available; PCR, polymerase chain reaction; PH, potential of hydrogen; PI, prediction interval; SSE, small-study effect.

References:

[1] Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association Between Maternal Human Papillomavirus Infection and Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis. J Infect Dis. 2020 Jun 11;221(12):1925-1937. [DOI:10.1093/infdis/jiaa054. PMID: 32022858; PMCID: PMC7289546]

[2] Lyu Z, Feng X, Li N, et al. Human papillomavirus in semen and the risk for male infertility: a systematic review and meta-analysis. BMC Infect Dis. 2017 Nov 9;17(1):714. [DOI:10.1186/s12879-017-2812-z. PMID: 29121862; PMCID: PMC5679371]

[3] Yuan S, Qiu Y, Xu Y, Wang H. Human papillomavirus infection and female infertility: a systematic review and meta-analysis. Reprod Biomed Online. 2020 Feb;40(2):229-237. [DOI:10.1016/j.rbmo.2019.10.019. Epub 2019 Nov 16. PMID: 31987733]

[4] Houlihan CF, Larke NL, Watson-Jones D, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS. 2012 Nov 13;26(17):2211-22. [DOI:10.1097/QAD.0b013e328358d908. PMID: 22874522; PMCID: PMC3831022]

[5] Xiong YQ, Chen YX, Cheng MJ, He WQ, Chen Q. The risk of human papillomavirus infection for male fertility abnormality: a meta-analysis. Asian J Androl. 2018 Sep-Oct;20(5):493-497. [DOI:10.4103/aja.aja_77_17. PMID: 29623908; PMCID: PMC6116676]

[6] Xiong YQ, Mo Y, Luo QM, Huo ST, He WQ, Chen Q. The Risk of Human Papillomavirus Infection for Spontaneous Abortion, Spontaneous Preterm Birth, and Pregnancy Rate of Assisted Reproductive Technologies: A Systematic Review and Meta-Analysis. Gynecol Obstet Invest. 2018;83(5):417-427. [DOI:10.1159/000482008. Epub 2018 Apr 12. PMID: 29649818]

[7] Wang S, Liu L, Zhang A, Song Y, Kang J, Liu X. Association between human papillomavirus infection and sperm quality: A systematic review and a meta-analysis. Andrologia. 2021 Jun;53(5):e14034. [DOI:10.1111/and.14034. Epub 2021 Mar 5. PMID: 33666259]

[8] Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. Fertil Steril. 2020 May;113(5):955-969.e4. [DOI:10.1016/j.fertnstert.2020.01.010. PMID: 32386620]

[9] Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. Am J Epidemiol. 2008 Jul 15;168(2):123-37. [DOI:10.1093/aje/kwn036. Epub 2008 May 15. PMID: 18483125; PMCID: PMC2878094]

[10] Looker KJ, Rönn MM, Brock PM, et al. Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. J Int AIDS Soc. 2018 Jun;21(6):e25110. [DOI: 10.1002/jia2.25110. PMID: 29873885; PMCID: PMC5989783]

[11] Szabó A, Váncsa S, Hegyi P, et al. Lifestyle-, environmental-, and additional health factors associated with an increased sperm DNA fragmentation: a systematic review and meta-analysis. Reprod Biol Endocrinol. 2023 Jan 18;21(1):5. [DOI:10.1186/s12958-023-01054-0. PMID: 36653793; PMCID: PMC9847125]

Supplementary Table 8: Description of 36 associations investigating the associations between HPV and non-cancerous reproductive health outcomes

Outcomes	Exposure	Author, Year, Reference	Journal	No. of studies	No. of cases/ participants	Type of effect metric
Genital system diseases						
HIV acquisition	HPV	Looker <i>et al</i> , 2018 ^[10]	Journal of the International Aids Society	7	603/11,841	RR
HIV acquisition	HPV-high risk	Houlihan <i>et al</i> , 2012 ^[4]	Aids	5	358/7214	HR
HIV acquisition	Nonpersistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	Aids	2	NA/2495	HR
HIV acquisition	Persistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	Aids	2	NA/2471	HR
ASCUS	Persistent HPV (vs. HPV-transient) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	4	72/1204	RR
Asthenospermia (defined as < 32% of motile sperm)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	Fertility and Sterility	6	757/1554	RR
CIN1/LSIL	Persistent HPV (vs. HPV-negative) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	3	110/1700	RR
CIN1/LSIL	Persistent HPV (vs. HPV-transient) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	9	NA/2469	RR
CIN1/LSIL	Persistent HPV (vs. mixed HPV status) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	3	229/2239	RR
CIN2-3/HSIL+	Persistent HPV (vs. HPV-negative) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	9	544/4822	RR
CIN2-3/HSIL+	Persistent HPV (vs. HPV-transient) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	13	NA/3003	RR
CIN2-3/HSIL+	Persistent HPV (vs. mixed HPV status) ¹	Koshiol <i>et al</i> , 2008 ^[9]	American Journal of Epidemiology	11	NA/11,607	RR
Female infertility	HPV-high risk/low risk	Yuan <i>et al</i> , 2020 ^[3]	Reproductive BioMedicine Online	7	1974/3581	OR
Female infertility	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	Reproductive BioMedicine Online	6	2617/11,869	OR
Female infertility (using PCR)	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	Reproductive BioMedicine Online	4	1017/2169	OR
Male fertility abnormality	HPV	Xiong <i>et al</i> , 2018 ^[5]	Asian Journal of Andrology	6	NA/1742	OR
Male infertility	HPV	Lyu <i>et al</i> , 2017 ^[2]	BMC Infectious Diseases	4	853/1494	OR
Oligospermia (defined as < 15 * 1^6 per mL)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	Fertility and Sterility	4	481/1404	RR
Semen pH	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	7	NA/2778	SMD

Semen volume	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	10	NA/3174	SMD
Sperm concentration	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	16	NA/3885	SMD
Sperm count	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	7	NA/1239	SMD
Sperm DNA fragmentation	HPV	Szabó <i>et al</i> , 2023 ^[11]	Reproductive Biology and Endocrinology	4	NA/411	MD
Sperm morphology	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	10	NA/1544	SMD
Sperm motility	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	15	NA/3842	SMD
Sperm viability	HPV	Wang <i>et al</i> , 2021 ^[7]	Andrologia	11	NA/2942	SMD
Teratospermia (defined as < 4% of normal morphologic sperm)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	Fertility and Sterility	3	756/1339	RR
Unknown infertility	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	Reproductive BioMedicine Online	4	2378/11,398	OR
Pregancy outcomes						
Intra uterine growth restriction	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	The Journal of Infectious Diseases	7	7765/273,357	OR
Low birth weight	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	The Journal of Infectious Diseases	4	NA/296,524	OR
Pregnancy rate of assisted reproductive technologies	HPV	Xiong <i>et al</i> , 2018 ^[6]	Gynecologic and Obstetric Investigation	7	NA/1404	RR
Premature rupture of membranes	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	The Journal of Infectious Diseases	6	NA/272,430	OR
Preterm birth	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	The Journal of Infectious Diseases	18	NA/336,391	OR
Preterm premature rupture of membranes	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	The Journal of Infectious Diseases	3	248/13,650	OR
Spontaneous abortion	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	The Journal of Infectious Diseases	7	262/1884	OR
Spontaneous preterm birth	HPV	Xiong <i>et al</i> , 2018 ^[6]	Gynecologic and Obstetric Investigation	4	NA/1501	OR

¹Other than these studies, the other studies are all HPV positive status compared with HPV negative status.

ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; CIN, cervical intraepithelial neoplasia; CIN1, low-grade cervical intraepithelial neoplasia; CIN2-3, high-grade cervical intraepithelial neoplasia; DNA, deoxyribonucleic acid; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSIL+, high-grade squamous intraepithelial lesions; LSIL, low-grade squamous intraepithelial lesions; NA, not available; PCR, polymerase chain reaction; PH, potential of hydrogen.

References:

[1] Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association Between Maternal Human Papillomavirus Infection and Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis. J Infect Dis. 2020 Jun 11;221(12):1925-1937. [DOI:10.1093/infdis/jiaa054. PMID: 32022858; PMCID: PMC7289546]

[2] Lyu Z, Feng X, Li N, et al. Human papillomavirus in semen and the risk for male infertility: a systematic review and meta-analysis. BMC Infect Dis. 2017 Nov 9;17(1):714. [DOI:10.1186/s12879-017-2812-z. PMID: 29121862; PMCID: PMC5679371]

[3] Yuan S, Qiu Y, Xu Y, Wang H. Human papillomavirus infection and female infertility: a systematic review and meta-analysis. Reprod Biomed Online. 2020 Feb;40(2):229-237. [DOI:10.1016/j.rbmo.2019.10.019. Epub 2019 Nov 16. PMID: 31987733]

[4] Houlihan CF, Larke NL, Watson-Jones D, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS. 2012 Nov 13;26(17):2211-22. [DOI:10.1097/QAD.0b013e328358d908. PMID: 22874522; PMCID: PMC3831022]

[5] Xiong YQ, Chen YX, Cheng MJ, He WQ, Chen Q. The risk of human papillomavirus infection for male fertility abnormality: a meta-analysis. Asian J Androl. 2018 Sep-Oct;20(5):493-497. [DOI:10.4103/aja.aja_77_17. PMID: 29623908; PMCID: PMC6116676]

[6] Xiong YQ, Mo Y, Luo QM, Huo ST, He WQ, Chen Q. The Risk of Human Papillomavirus Infection for Spontaneous Abortion, Spontaneous Preterm Birth, and Pregnancy Rate of Assisted Reproductive Technologies: A Systematic Review and Meta-Analysis. *Gynecol Obstet Invest*. 2018;83(5):417-427. [DOI:10.1159/000482008. Epub 2018 Apr 12. PMID: 29649818]

[7] Wang S, Liu L, Zhang A, Song Y, Kang J, Liu X. Association between human papillomavirus infection and sperm quality: A systematic review and a meta-analysis. *Andrologia*. 2021 Jun;53(5):e14034. [DOI:10.1111/and.14034. Epub 2021 Mar 5. PMID: 33666259]

[8] Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. *Fertil Steril*. 2020 May;113(5):955-969.e4. [DOI:10.1016/j.fertnstert.2020.01.010. PMID: 32386620]

[9] Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. *Am J Epidemiol*. 2008 Jul 15;168(2):123-37. [DOI:10.1093/aje/kwn036. Epub 2008 May 15. PMID: 18483125; PMCID: PMC2878094]

[10] Looker KJ, Rönn MM, Brock PM, et al. Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. *J Int AIDS Soc*. 2018 Jun;21(6):e25110. [DOI: 10.1002/jia2.25110. PMID: 29873885; PMCID: PMC5989783]

[11] Szabó A, Váncsa S, Hegyi P, et al. Lifestyle-, environmental-, and additional health factors associated with an increased sperm DNA fragmentation: a systematic review and meta-analysis. *Reprod Biol Endocrinol*. 2023 Jan 18;21(1):5. [DOI:10.1186/s12958-023-01054-0. PMID: 36653793; PMCID: PMC9847125]

Supplementary Table 9: The results of the Egger’s regression asymmetry test and the excess statistical significance test for suggestive evidence (class III), weak evidence (class IV), and no evidence (non-significant association, P > 0.05)

Outcomes	Exposure	Author, Year, Reference	Egger's <i>P</i> -value ^a	Excess significance	
				O/E ^b	<i>P</i> -value ^c
Suggestive evidence (class III)					
Genital system diseases					
Female infertility	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	0.558	4/3.0425	0.688
Unknown infertility	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	0.980	4/2.0125	0.125
Pregnancy outcomes					
Low birth weight	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.151	2/0.9231	0.230
Preterm birth	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.025	8/7.7141	1.000
Weak evidence (class IV)					
Genital system diseases					
HIV acquisition	HPV	Looker <i>et al</i> , 2018 ^[10]	0.310	2/2.1867	0.879
HIV acquisition	HPV-high risk	Houlihan <i>et al</i> , 2012 ^[4]	0.006	5/0.9952	0
HIV acquisition	Nonpersistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	0.092	3/1.1553	NA
ASCUS	Persistent HPV (vs. HPV-transient) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.835	2/0.6091	0.113
Asthenospermia (defined as < 32% of motile sperm)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	0.178	3/1.6936	0.360
CIN1/LSIL	Persistent HPV (vs. HPV-negative) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.001	2/0.1113	0.004

CIN1/LSIL	Persistent HPV (vs. HPV-transient) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.382	6/3.0556	0.070
CIN1/LSIL	Persistent HPV (vs. mixed HPV status) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.058	3/0.3504	0.002
CIN2-3/HSIL+	Persistent HPV (vs. HPV-negative) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.374	8/2.6047	0
CIN2-3/HSIL+	Persistent HPV (vs. HPV-transient) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.002	10/3.5294	0
CIN2-3/HSIL+	Persistent HPV (vs. mixed HPV status) ^d	Koshiol <i>et al</i> , 2008 ^[9]	0.988	11/4.8934	0
Male fertility abnormality	HPV	Xiong <i>et al</i> , 2018 ^[5]	0.970	2/0.8726	0.213
Male infertility	HPV	Lyu <i>et al</i> , 2017 ^[2]	0.807	2/0.3871	0.049
Sperm concentration	HPV	Wang <i>et al</i> , 2021 ^[7]	0.614	1/3.1020	0.184
Sperm morphology	HPV	Wang <i>et al</i> , 2021 ^[7]	0.078	3/5.0109	0.203
Sperm motility	HPV	Wang <i>et al</i> , 2021 ^[7]	0.665	14/5.4926	0
Sperm viability	HPV	Wang <i>et al</i> , 2021 ^[7]	0.055	3/1.9966	0.433
Pregnancy outcomes					
Intra uterine growth restriction	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.336	1/0.5406	0.430
Premature rupture of membranes	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.445	2/1.1540	0.326
Preterm premature rupture of membranes	HPV	Niyibizi <i>et al</i> , 2020 ^[1]	0.786	2/0.3857	0.045
Spontaneous preterm birth	HPV	Xiong <i>et al</i> , 2018 ^[6]	0.662	3/0.8526	0.033
No evidence (non-significant association, $P > 0.05$)					
Genital system diseases					
HIV acquisition	Persistent HPV	Houlihan <i>et al</i> , 2012 ^[4]	0.079	0/0.3243	1.000
Female infertility	HPV-high risk/low risk	Yuan <i>et al</i> , 2020 ^[3]	0.165	3/4.2987	0.441
Female infertility (using PCR)	HPV-high risk	Yuan <i>et al</i> , 2020 ^[3]	0.151	2/2.2434	1.000
Oligospermia (defined as $< 15 \times 10^6$ per mL)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	0.392	0/0.2634	1.000
Sperm DNA fragmentation	HPV	Szabó <i>et al</i> , 2023 ^[11]	0.227	1/1.2056	1.000
Semen pH	HPV	Wang <i>et al</i> , 2021 ^[7]	0.233	1/3.0087	0.125
Semen volume	HPV	Wang <i>et al</i> , 2021 ^[7]	0.156	2/3.0257	0.480
Sperm count	HPV	Wang <i>et al</i> , 2021 ^[7]	0.458	1/1.0915	0.924
Teratospermia (defined as $< 4\%$ of normal morphologic sperm)	HPV	Weinberg <i>et al</i> , 2020 ^[8]	0.415	0/0.1640	1.000
Pregnancy outcomes					

[7] Wang S, Liu L, Zhang A, Song Y, Kang J, Liu X. Association between human papillomavirus infection and sperm quality: A systematic review and a meta-analysis. *Andrologia*. 2021 Jun;53(5):e14034. [DOI:10.1111/and.14034. Epub 2021 Mar 5. PMID: 33666259]

[8] Weinberg M, Sar-Shalom Nahshon C, Feferkorn I, Bornstein J. Evaluation of human papilloma virus in semen as a risk factor for low sperm quality and poor in vitro fertilization outcomes: a systematic review and meta-analysis. *Fertil Steril*. 2020 May;113(5):955-969.e4. [DOI:10.1016/j.fertnstert.2020.01.010. PMID: 32386620]

[9] Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. *Am J Epidemiol*. 2008 Jul 15;168(2):123-37. [DOI:10.1093/aje/kwn036. Epub 2008 May 15. PMID: 18483125; PMCID: PMC2878094]

[10] Looker KJ, Rönn MM, Brock PM, et al. Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. *J Int AIDS Soc*. 2018 Jun;21(6):e25110. [DOI:10.1002/jia2.25110. PMID: 29873885; PMCID: PMC5989783]

[11] Szabó A, Váncsa S, Hegyi P, et al. Lifestyle-, environmental-, and additional health factors associated with an increased sperm DNA fragmentation: a systematic review and meta-analysis. *Reprod Biol Endocrinol*. 2023 Jan 18;21(1):5. [DOI:10.1186/s12958-023-01054-0. PMID: 36653793; PMCID: PMC9847125]

Supplementary Table 11: Sensitivity analysis results of excluded meta-analyses due to overlap

Outcomes/Exposure	Author, Year, Reference	Comparison	Effect size	Random effect size (95% CI)	Primary
					No. of studies
HIV acquisition					
HPV	Looker <i>et al</i> , 2018 ^[3]	Highest <i>vs.</i> Lowest	RR	1.75 (1.23, 2.49)	7
HPV	Looker <i>et al</i> , 2018 ^[3]	Highest <i>vs.</i> Lowest	RR	1.75 (1.23, 2.49)	7
HPV-high risk	Houlihan <i>et al</i> , 2012 ^[2]	Highest <i>vs.</i> Lowest	HR	1.99 (1.54, 2.56)	5
Preterm birth					
HPV	Niyibizi <i>et al</i> , 2020 ^[1]	Highest <i>vs.</i> Lowest	OR	1.50 (1.19, 1.88)	18
Sperm progressive motility					
HPV	Wang <i>et al</i> , 2021 ^[4]	Highest <i>vs.</i> Lowest	SMD	-0.55 (-0.78, -0.33)	15
Spontaneous abortion					
HPV	Niyibizi <i>et al</i> , 2020 ^[1]	Highest <i>vs.</i> Lowest	OR	1.14 (0.41, 31.20)	7
HPV	Niyibizi <i>et al</i> , 2020 ^[1]	Highest <i>vs.</i> Lowest	OR	1.14 (0.41, 31.20)	7

^a Assessed by the established GRADE criteria utilized in previous umbrella reviews.

^b Studies do not evaluate the risk of bias, so they cannot be downgraded or upgraded based on the factors above.

CI, confidence interval; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HIV, human immunodeficiency virus; HPV, human papillomavirus; HR, hazard ratio; OR, odd ratio; RR, relative risk; SMD, standardized mean difference.

References:

[1] Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association Between Maternal Human Papillomavirus Infection and Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis. *J Infect Dis*. 2020 Jun 11;221(12):1925-1937. [DOI:10.1093/infdis/jiaa054. PMID: 32022858; PMCID: PMC7289546]

[2] Houlihan CF, Larke NL, Watson-Jones D, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS. 2012 Nov 13;26(17):2211-22. [DOI:10.1097/QAD.0b013e328358d908. PMID: 22874522; PMCID: PMC3831022]

[3] Looker KJ, Rönn MM, Brock PM, et al. Evidence of synergistic relationships between HIV and Human Papillomavirus (HPV): systematic reviews and meta-analyses of longitudinal studies of HPV acquisition and clearance by HIV status, and of HIV acquisition by HPV status. J Int AIDS Soc. 2018 Jun;21(6):e25110. [DOI:10.1002/jia2.25110. PMID: 29873885; PMCID: PMC5989783]

[4] Wang S, Liu L, Zhang A, Song Y, Kang J, Liu X. Association between human papillomavirus infection and sperm quality: A systematic review and a meta-analysis. Andrologia. 2021 Jun;53(5):e14034. [DOI:10.1111/and.14034. Epub 2021 Mar 5. PMID: 33666259]

Supplementary Table 12: Sensitivity analysis results of omission of small-sized studies (*i.e.*, < 25th percentile) from those meta-analyses with evidence of small-study effects

Outcomes/Exposure	Author, Year, Reference	Comparison	Effect size	Primary analysis			Sensitivity analysis: Excluding studies with small sample size (< 25 th percentile)		
				No.of studies	Random effect size (95% CI)	GRADE ^a	No. of studies	Random effect size (95% CI)	GRADE ^a
CIN2-3/HSIL+									
Persistent HPV (<i>vs.</i> HPV-transient) ^b	Koshiol <i>et al</i> , 2008 ^[1]	Highest <i>vs.</i> Lowest	RR	13	14.34 (7.99, 25.71)	Very low	10	17.12 (8.24, 35.58)	Very low
Preterm birth									
HPV	Niyibizi <i>et al</i> , 2020 ^[2]	Highest <i>vs.</i> Lowest	OR	18	1.50 (1.19, 1.88)	Very low	13	1.42 (1.12, 1.80)	Very low
HIV acquisition									
Nonpersistent HPV	Houlihan <i>et al</i> , 2012 ^[3]	Highest <i>vs.</i> Lowest	HR	2	2.60 (1.35, 5.00)	Very low	NA-remaining studies are not enough to conduct meta-analysis		Very low

^a Assessed by the established GRADE criteria utilized in previous umbrella reviews.

^b Other than these studies, the other studies are all HPV positive status compared with HPV negative status.

CI, confidence interval; CIN2-3, high-grade cervical intraepithelial neoplasia; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; HIV, human immunodeficiency virus; HPV, human papillomavirus; HR, hazard Ratio; HSIL+, high-grade squamous intraepithelial lesions; NA, not available; OR, odd ratio; RR, relative risk.

References:

[1] Koshiol J, Lindsay L, Pimenta JM, Poole C, Jenkins D, Smith JS. Persistent human papillomavirus infection and cervical neoplasia: a systematic review and meta-analysis. Am J Epidemiol. 2008 Jul 15;168(2):123-37. [DOI:10.1093/aje/kwn036IF: 5.0 Q1. Epub 2008 May 15. PMID: 18483125; PMCID: PMC2878094]

[2] Niyibizi J, Zanré N, Mayrand MH, Trottier H. Association Between Maternal Human Papillomavirus Infection and Adverse Pregnancy Outcomes: Systematic Review and Meta-Analysis. J Infect Dis. 2020 Jun 11;221(12):1925-1937. [DOI:10.1093/infdis/jiaa054. PMID: 32022858; PMCID: PMC7289546]

[3] Houlihan CF, Larke NL, Watson-Jones D, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS. 2012 Nov 13;26(17):2211-22. [DOI:10.1097/QAD.0b013e328358d908. PMID: 22874522; PMCID: PMC3831022]

Supplementary Table 13: The summary results of meta-analyses excluded due to lack of data for quantitative synthesis

Author, Year, Reference	No. of included Studies	Exposure	Outcomes	Results
-------------------------	-------------------------	----------	----------	---------

Popescu <i>et al</i> , 2022 ^[1]	21	HPV	Adverse pregnancy outcomes	Increased risk	HPV is associated with higher risks of adverse pregnancy c
Farsimadan <i>et al</i> , 2021 ^[2]	16	HPV	Female fertility and pregnancy	Increased risk	HPV is associated with higher risks of female infertility and
Souho <i>et al</i> , 2015 ^[3]	21	HPV	Reproductive health	Increased risk	HPV is associated with higher risks of reproductive health
Gardella <i>et al</i> , 2021 ^[4]	15	HPV	Severe cervical lesions	Increased risk	HPV is associated with higher risks of severe cervical lesior

ASCUS, Atypical squamous cells of undetermined significance; HPV, human papillomavirus; LSIL, Low-grade squamous intraepithelial lesion.

References:

[1] Popescu, S.D., et al., Maternal HPV Infection and the Estimated Risks for Adverse Pregnancy Outcomes—A Systematic Review. *Diagnostics*, 2022. 12(6).

[2] Farsimadan, M. and M. Motamedifar, The effects of human immunodeficiency virus, human papillomavirus, herpes simplex virus-1 and -2, human herpesvirus-6 and -8, cytomegalovirus, and hepatitis B and C virus on female fertility and pregnancy. *British Journal of Biomedical Science*, 2021. 78(1): p. 1-11.

[3] Souho, T., M. Benlemlih and B. Bennani, Human papillomavirus infection and fertility alteration: A systematic review. *PLoS ONE*, 2015. 10(5).

[4] Gardella, B., et al., Multiple human papillomavirus infection and ascus-lsil progression: A review. *Italian Journal of Gynaecology and Obstetrics*, 2021. 33(3): p. 145-154.