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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary appendix

Table S1. LIST OF AUTHORS, AFFILIATIONS, CONTRIBUTIONS, AND DECLARATION OF INTERESTS

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Contributors

MC-B conceived the study and participated in the design of the meta-analysis. All other authors (HA, VB, PB, JMLB, DC, MC, EPFC, SC, TD, SLD, CD, BD, CKF, EWF, JWG, SMG, NG, BTH, CH, EH, TMI, AMJ, JAK, KK, SKK, EVK, BL, DAM, LM, DM, CM, LN, MN, GO, JO, KGP,MJPH, MAS, MSt, ASS, PSo, PSp, CT,CMW, PJW, BNY) provided data, after having done supplementary analyses for the purposes of this meta-analysis. All authors interpreted the results and critically revised the manuscript for scientific content. All authors approved the final version of the article.

Declaration of interests

HA reports grants and non-financial support from CSL Biotherapies and grants from Australian Department of Health. VB reports grants, personal fees and non-financial support from MSD, GSK, Sanofi, and Seqirus. JMLB reports unrestricted investigator-initiated grants from MSD (papillomatosis typing study) and Seqirus (cervical cancer typing study), she has never received any personal financial benefits. DC reports grants from Australian Department of Health and Seqirus (CSL Limited), and grants from Australian Research Council, New South Wales Ministry of Health, Australian Department of Health, and National Health and Medical Research Council.

EPFC reports grants from Merck Sharp & Dohme, Seqirus, and other financial relationships with the National Health and Medical Research Council. SC reports grants and non-financial support from MSD, and non-financial support from Sanofi and Pfizer. BD reports grants from Australian Department of Health and Seqirus, and personal fees from Merck. CKF owns shares in CSL biotherapies. SMG reports grants from Commonwealth Department of Health Australia, CSL, GSK, Merck and personal fees from Merck (outside the submitted work and conducted in personal time). She is also a member of the Merck global advisory board for HPV vaccines.

BTH reports that his affiliated institution has received grants from MSD Norway. CH reports other funding outside of the submitted work through arm's length research agreements with the Australian Government Department of Health, AstraZeneca (Australia), Novartis Pharmaceuticals Australia, Seqirus (Australia), and with Sanofi-Aventis Australia. AMJ reports grants from MRC, Wellcome Trust, EPSRC, NIHR, and received personal fees from Wellcome Trust. SKK reports personal fees from Sanofi Pasteur MSD and Merck, and grants from Merck. EVK reports grants from Manitoba Health. BL reports grants from Australian NHMRC and other financial relationships from BioCSL. DAM reports grants from Australian Department of Health, National Health and Medical Research Council, and Seqirus, and honoraria (donated to her institute) from MSD. CM reports lecture fees and support for conference participation from Sanofi Pasteur MSD Denmark. LN reports grants from US Centers for Disease Control and Prevention, and personal fees from Merck. MN reports grants, through affiliating institute, from MSD Norway. JO reports grants from Seqirus. KGP reports financial relationships with Merck and personal fees from GSK. MSt reports grants from the Ministère de la Santé et des Services sociaux du Québec, grants and personal fees from Merck, Valeant, and Paladin. CT reports grants from the Medical Research Council and Wellcome Trust. CMW reports cooperative agreements, through University of New Mexico, from the National Institutes of Health related to HPV vaccine impact. MCB, PB, MC, TD, SLD, CD, EWF, JWG, NG, EH, TMI, JAK, KK, LM, DM, GO,MJPH, MAS, ASS, PSo, PSp, PJW, and BNY declare no competing interests.

Table S2. PRISMA CHECKLIST

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.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4, 5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No protocol
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5, 6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix Table S2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6, Table 1
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.	6, Appendix Tables S5-S7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Appendix, Tables S5-S7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
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.	7, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7, Table 1
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).	Appendix, Tables S5-S7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Appendix Figures S1-S3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figures 2-6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, Appendix, Tables S5-S7
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Appendix Tables S9-S11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8,9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	7,11, Appendix Tables S5-S7

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

Table S3. Full electronic search strategy for Pubmed/Medline

("papillomavirus vaccines"[mesh] OR "HPV vaccine"[tiab] OR "HPV vaccination"[tiab] OR "papillomavirus vaccine"[tiab] OR "papillomavirus vaccination"[tiab])
AND
("program evaluation"[mesh] OR "immunization programs"[mesh] OR "program evaluation"[tiab] OR "population surveillance"[mesh] OR "population surveillance"[tiab] OR "sentinel surveillance"[mesh] OR "sentinel surveillance"[tiab] OR "incidence"[mesh] OR "incidence"[tiab] OR "prevalence"[mesh] OR "prevalence"[tiab] OR "rate"[tiab])
AND
("papillomavirus infections"[mesh] OR "papillomavirus infections"[tiab] OR "HPV"[tiab] OR "uterine cervical neoplasms"[mesh] OR "uterine cervical neoplasms"[tiab] OR "cervical intraepithelial neoplasia"[mesh] OR "cervical intraepithelial neoplasia"[tiab] OR "HPV related diseases"[tiab] OR "condylomata acuminata"[mesh] OR "condylomata acuminata"[tiab] OR "genital warts"[tiab])
NOT
("models, theoretical"[mesh] OR "HIV infections"[mesh] OR "cost-benefit analysis"[mesh] OR "health education"[mesh])

Table S4. Methodological quality and risk of bias in studies examining changes in HPV infection between the pre- and post-vaccination periods.

Authors	**Chow 2015a/2017**	**Cummings 2012**	**Dillner 2018**	**Dunne 2015**	**Grün 2016**	**Kahn 2012/2016**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Australia**	**USA**	**Denmark, Norway, Sweden**	**USA**	**Sweden**	**USA**
Funding	Australian National Health and Medical Research Council	National Institutes of Health	Merck & Co.	Centers for Disease Control and Prevention	Swedish Research Council; Swedish Cancer Foundation; Stockholm Cancer Society; other foundations	National Institutes of Health
Risk of selection bias						
Subjects included in the study	Clinic-based: Women and men aged ≤ 25 yrs attending the Melbourne Sexual Health Center diagnosed with chlamydia	Clinic-based: Women attending 1 of 3 urban primary care clinics in Indianapolis	Clinic-based: Women attending routine cervical screening in Denmark, Norway, Sweden	Clinic-based: Women undergoing cervical screening at Kaiser Permanente Northwest	Clinic-based: Women aged 15-23 yrs advised on birth control and STD at a youth clinic in Stockholm	Clinic-based: Women attending 3 primary care clinics in Cincinnati who had had sexual contact
Potential for selection bias: Changes in the study population characteristics between pre- and post-vaccination periods	Medium/High Possible changes in the clientele of the sexual health services between pre- and post-vaccination periods	Low Unlikely changes in the clientele of primary care clinics between pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between pre- and post-vaccination periods	Medium/High Possible changes in the clientele of the clinic between pre- and post-vaccination periods	Low Unlikely changes in the clientele of primary care clinics between pre- and post-vaccination periods
Risk of information bias						
HPV testing	Pap Type assay including PCR amplification and genotyping of 16 HPV types	PCR Roche Linear Array test which detects 37 HPV types	Luminex system (Bio-Rad) with type-specific probes for 35 HPV types	PCR Roche Linear Array test which detects 37 HPV types	Luminex-based genotyping assay which detects 27 HPV types	PCR Roche Linear Array test which detects 36 HPV types
Performance of the HPV test	Unreported	Unreported	Unreported	Unreported	Unreported	Unreported
Outcome used in original publication	HPV prevalence (crude) and HPV prevalence ratio (crude and adjusted)	Odds ratios of HPV prevalence (crude)	HPV prevalence difference (crude)	HPV prevalence ratio (crude and adjusted)	HPV prevalence (crude)	HPV prevalence difference (adjusted)
Potential for information bias: Errors in the identification of HPV+ during the pre and post-vaccination period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period
Risk of confounding						
Potential confounders considered	Analysis stratified by age and country of birth. Other analyses adjusted for number of sex partners, condom use and anatomical sampling site.	Analysis matched on age at enrollment, clinic site and reported sexual activity (yes, never) at time of enrollment	No adjustment in the analysis of change of HPV prevalence over time	No adjustment in the analysis of changes of HPV prevalence over time. Other analysis adjusted for age at screening, age at 1st dose, race, poverty, HIC, C. trachomatis, pregnancy	No adjustment in the analysis of changes of HPV prevalence over time	Analysis adjusted for demographics (race, health insurance plan…), gynecologic history, sex activity using propensity scores

Potential for confounding: Changes in HPV infection between the pre and post-vaccination periods could be diluted/exacerbated by other variables	Medium Several risk factors considered. However, residual confounding by other factors associated with HPV vaccination and infection may be present	Medium Few risk factors considered and residual confounding by other factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)	Medium/High Confounding by factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)	Medium/high Confounding by factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)	Medium/High Confounding by factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)	Low/Medium Several risk factors were considered. However, residual confounding by other factors associated with HPV vaccination and infection may be present
External validity						
External validity: Results can be generalized to the population at the country/region level	Medium Young men/women attending to urban primary care clinics may not represent the general population (e.g., different vaccination coverage)	Medium Young women attending to urban primary care clinics may not represent the general population (e.g., different vaccination coverage)	Medium Women participating in cervical cancer screening may not be representative of the general population (e.g., different vaccination coverage)	Medium Women participating in cervical cancer screening may not be representative of the general population (e.g., different vaccination coverage)	Medium Young women attending the clinic may not represent the general population (e.g., different vaccination coverage)	Low/Medium Women attending the 3 primary care clinics may not be representative of the general population (e.g., different vaccination coverage). Minorities and women from low socio-economic status are overrepresented

Table S4: continued

Authors	**Kavanagh 2014/ Cameron 2016/ Kavanagh 2017**	**Machalek 2018**	**Markowitz 2013/2016/ Oliver 2017**	**Mesher 2013/2016/2018**	**Purriños-Hermida 2018**	**Söderlun-Strand 2014**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Scotland**	**Australia**	**USA**	**England**	**Spain**	**Sweden**
Funding	Scottish government	Australian Government Department of Health HPV Surveillance Fund	Centers for Disease Control and Prevention	Public Health England	Direccion xeral de Saude Publica	Public Health Agency of Sweden
Risk of selection bias						
Subjects included in the study	Clinic-based: Women aged 20-24 yrs attending cervical screening across Scotland	Clinic-based: Women recruited from participating family planning clinics for Pap screening in Victoria and New South Wales	Population-based: Participants in NHANES, designed to be nationally representative of the general population	Clinic-based: Women undergoing chlamydia screening at community sexual health services, general practice and youth clinics in 7 regions	Clinic-based: Post-vaccination: Women attending 7 health areas of the Galician public health; pre-vaccination: women attending 1/7 health areas	Clinic-based: Women undergoing chlamydia screening in the Skane region in Southern Sweden
Potential for selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between pre- and post-vaccination periods	Low Unlikely changes in the clientele of family planning clinics between pre- and post-vaccination periods	Low Unlikely changes in the NHANES participants between pre- and post-vaccination periods	Medium Documented changes in the clientele receiving chlamydia testing between pre- and post-vaccination periods	High Potential differences between women attending 1 health service (pre-vaccination) compared to the 7 health services (post-vaccination). However, in the pre-vaccination period, there was no difference in sexual activity between women who participated in the study and a random sample of women from the 7 health services	Medium Possible changes in participants to chlamydia screening between pre- and post-vaccination periods
Risk of information bias						
HPV testing	Multimetrix HPV Assay which detects 18 high-risk types	2005-2007: HPV+ Amplicor HPV test kit (Roche Molecular system-13 types), and PGMY09-PGMY11 PCR-ELISA Roche Linear Array genotyping test (37 types); 2015: HPV+ Cobas HPV test (Roche Diagnosis) and Roche Linear Array genotyping test (37 types)	PCR Roche Linear Array test which detects 37 different HPV types	2008: Hybrid Capture 2 and Roche Linear Array 2010-2013: HPV+ In-house multiplex PCR and Luminex-based genotyping test (20 HPV types)	HPV+ Cobas 4800 HPV test with Linear Array HPV genotyping (Roche Diagnostic) (12 types)	HPV + In-house multiplex PCR with genotyping by MALDI-TOF mass spectrometry (16 types)
Performance of the HPV test	Unreported	Unreported	Unreported	Unreported	Unreported	Unreported
Outcome used in original publication	HPV prevalence over time (crude)	HPV prevalence ratio (crude and adjusted)	HPV prevalence ratio (crude and adjusted)	Odds ratios of HPV prevalence (adjusted)	HPV prevalence ratio (crude and adjusted)	HPV prevalence (crude)

Authors	**Kavanagh 2014/ Cameron 2016/ Kavanagh 2017**	**Machalek 2018**	**Markowitz 2013/2016/ Oliver 2017**	**Mesher 2013/2016/2018**	**Purriños-Hermida 2018**	**Söderlun-Strand 2014**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Scotland**	**Australia**	**USA**	**England**	**Spain**	**Sweden**
Potential for information bias: Errors in the identification of HPV+ during the pre and post-vaccination period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period. High concordance has been reported between AMP and Cobas	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period;	High Potential for masking by HPV-16/18, particularly in the pre-vaccine period; different assays used in the pre- and post-vaccination periods, which may have contributed to higher prevalence of non-vaccine types in the post-vaccination period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period
Risk of confounding						
Potential confounders considered	No adjustment in the analysis of changes of HPV prevalence over time	Analysis stratified by age and adjusted for smoking. Confounding for a range of socio-demographic and behavioral characteristics was verified and there was no difference between the groups	Analyses adjusted for one or more of the following: race/ethnicity, number of lifetime sex partners, number of past year sex partners, poverty. All analyses weighted to present the general population	Analysis adjusted for sexual history, age, venue type, ethnicity and chlamydia positivity	Analysis stratified by age and adjusted for age at first intercourse, number of sexual partners (lifetime, past year)	Analysis stratified by age
Potential for confounding: Changes in HPV infection between the pre and post-vaccination periods could be diluted/exacerbated by other variables	Medium/High Confounding by factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)	Medium Few sexual behavior factors considered and residual confounding by other factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)	Low/Medium Few factors considered, but weighted analysis to represent the general population	Medium Several risk factors were considered. However, residual confounding by other factors associated with HPV vaccination and infection can be present (e.g., changes in sexual activity)	Low/Medium Several risk factors were considered. Changes in sexual activity between pre- and post-vaccination periods were documented and adjusted for. However, residual confounding can be present	Medium/High Confounding by other factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)
External validity						
External validity: Results can be generalized to the population at the country/region level	Medium Women participating in screening may not represent the general population (e.g., different vaccination coverage)	Medium Young women attending family planning clinics may not represent the general population (e.g., different vaccination coverage)	Medium/High The survey was designed to be representative of the general population but non-participants could still be different than participants with respect to variables not considered in the sampling design	Medium Chlamydia screening recommended for all sexually-active young women and uptake was 40% in 2011. However, women undergoing chlamydia screening may not be representative of the general population (e.g., different vaccination coverage)	Medium Women attending primary care center, gynecology department or family counseling center may not represent the general population	Medium Women participating in chlamydia screening program may not be representative of the general population (e.g., different vaccination coverage)

Table S4: continued

Authors	**Sonnenberg 2013**	**Tabrizi 2012/2014**
Study design	**Time-trend analysis**	**Time-trend analysis**
Country	**Britain**	**Australia**
Funding	UK Medical Research Council, Wellcome Trust, Economic and Social Research Council and the Department of Health	Australian National Health and Medical Research Council, and Anti- Cancer Council for Victoria
Risk of selection bias		
Subjects included in the study	Population-based: Participants in NATSAL, designed to be nationally representative of the British population	Clinic-based: Women recruited from participating family planning clinics for Pap screening in Sydney, Melbourne, and Perth
Potential for selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Low/Medium Potential changes in the NATSAL participants between pre- and post-vaccination periods (> 10 yrs). Surveys weighted to Census data from the time.	Low Unlikely changes in the clientele of family planning clinics between pre- and post-vaccination periods
Risk of information bias		
HPV testing	In-house Luminex-based genotyping assay (20 HPV types) in urine samples	HPV+ Amplicor HPV test kit (Roche Molecular system-13 types), and PGMY09-PGMY11 PCR-ELISA Roche Linear Array genotyping test (37 types)
Performance of the HPV test	Unreported	Unreported
Outcome used in original publication	Odds ratios of HPV prevalence (adjusted)	Odds ratios of HPV prevalence (adjusted)
Potential for information bias: Errors in the identification of HPV+ during the pre and post-vaccination period	High Potential for masking by HPV-16/18, particularly in the pre-vaccine period; Urine is a suboptimum specimen for the detection of HPV; Differences in methods of sample collection, preparation and storage between the pre- and post-vaccination periods	Medium Potential for masking by HPV-16/18, particularly in the pre-vaccine period

Authors	**Sonnenberg 2013**	**Tabrizi 2012/2014**
Study design	**Time-trend analysis**	**Time-trend analysis**
Country	**Britain**	**Australia**
Risk of confounding		
Potential confounders considered	No adjustment in the comparison of HPV prevalence between the pre- and post-vaccination periods, but all analysis weighted to represent the British population	Analysis adjusted for age, contraceptive use, region, socioeconomic group and smoking status (these variables differed significantly between the 3 groups of women)
Potential for confounding: Changes in HPV infection between the pre and post-vaccination periods could be diluted/exacerbated by other variables	Medium/High No adjusted analysis of changes in HPV prevalence over time and likely changes over a 10-year period in factors associated with HPV vaccination and infection (e.g., changes in sexual activity documented when comparing NATSAL2-3 [1])	Medium Few sexual behavior factors considered and residual confounding by other factors associated with HPV vaccination and infection is possible (e.g., changes in sexual activity)
External validity		
External validity: Results can be generalized to the population at the country/region level	Medium/High The survey was designed to be representative of the general population. However, participants and those providing urine samples might not be fully representative of the general population, despite adjustment for known biases and use of additional weights for urine selection and urine non-response	Medium Young women attending family planning clinics may not represent the general population (e.g., different vaccination coverage)

NATSAL: National Survey of Sexual Attitudes and Lifestyles; PCR: polymerase chain reaction; STD: Sexually transmitted diseases

References:

1. Mercer CH, Tanton C, Prah P, Erens B, Sonnenberg P, Clifton S, Macdowall W, Lewis R, Field N, Datta J, Copas AJ, Phelps A, Wellings K, Johnson AM. Changes in sexual attitudes and lifestyles in Britain through the life course and over time: findings from the National Surveys of Sexual Attitudes and Lifestyles (Natsal). *Lancet* 2013; **382**:1781-94

Table S5. Methodological quality and risk of bias in studies examining changes in anogenital warts (AGW) diagnosis between the pre- and post-vaccination periods.

Authors	**Ali 2013/Chow 2015b,Ali 2017, Callander 2016**	**Baandrup 2013/Bollerup 2016**	**Bauer 2012**	**Cocchio 2017**	**Dominiak-Felden 2015**	**Flagg 2013/Flagg 2018**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Australia**	**Denmark**	**USA**	**Italy**	**Belgium**	**USA**
Funding	CSL Biotherapies	Aragon Foundation, Aase and Ejnar Danielsen Foundation, Mermaid II Project	Centers for Disease Control and Prevention, California Department of Public Health	University grant	Sanofi Pasteur MSD	Centers for Disease Control and Prevention
Risk of selection bias						
Subjects included in the study	Clinic-based: New clients of 40 sexual health services across Australia (Australian born)	Population-based: Denmark population from Statistics Denmark	Health provider/ insurance-based: Clients of the California Family Planning access care & treatment (FPACT) program	Population-based: All residents of the Veneto region (Italy) between 2004-2015	Health provider/ insurance-based: Clients of the National Union of Independent Sick Funds (MLOZ)	Health provider/insurance-based : Enrollees in approximately 100 private health insurance plans across US
Potential for of selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Medium/High Possible changes in the clientele of the sexual health services in the pre- and post-vaccination periods (increasing annual number of clients and % of clients with chlamydia after 2006)	Low Entire population of Denmark	Low Unlikely change in the FPACT (family planning program for low-income individuals) clientele between pre- and post-vaccination periods	Low Entire population of Veneto	Low Unlikely change in clients of MLOZ between pre and post-vaccination periods.	Low Unlikely change in enrollees of insurance plans between pre- and post-vaccination periods. No decrease in Pap or pelvic exam (opportunities to diagnose AGW) over time
Risk of information bias						
Data source	Medical records	National patient register (hospital or outpatient clinics) and the National Prescription Registry	FPACT database (clinical encounter claims data)	Hospital discharge records and Veneto Regional Authority's statistical office	MLOZ database	Truven Health Analytics MarketScan Commercial Claims and Encounters Database
AGW case definition	Clinical diagnosis	ICD-10 code A63.0 and/or prescription of Podophyllotoxin	ICD-9 codes 078.10, 078.11 OR prescription of Imiquimod or Podophyllotoxin	ICD9-CM code 078.11 AND one the following ICD9-CM surgical codes (70,71, 58.3, 64, 49)	First prescription of imiquimod with a level of reimbursement specific for AGW	1) ICD-9 codes 078.11 OR 2) ICD-9 code 078.1, 078.10, 078.19 and therapeutic procedure or diagnosis of benign anogenital neoplasm OR 3) ≥ 1 prescription for AGW treatment and therapeutic procedure or diagnosis of benign anogenital neoplasm
Outcome used	Annual proportion of new clients diagnosed with AGW	Annual incidence rate of diagnosed AGW in the population	Annual proportion of FPACT clients diagnosed with AGW	Annual hospitalization rate for AGW in the population	Annual incidence rate of diagnosed AGW among MLOZ clients	Annual proportion of insured individuals with diagnosed AGW

Authors	**Ali 2013/Chow 2015b,Ali 2017, Callander 2016**	**Baandrup 2013/Bollerup 2016**	**Bauer 2012**	**Cocchio 2017**	**Dominiak-Felden 2015**	**Flagg 2013/Flagg 2018**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Australia**	**Denmark**	**USA**	**Italy**	**Belgium**	**USA**
Numerator	Number of newly diagnosed AGW cases per year	Number of newly diagnosed AGW cases each year (washout of 12 months)	Number of newly diagnosed cases after 2007 per year	Number of hospitalization for AGW each year	Number of newly diagnosed AGW case per year	Number of patients with AGW diagnosis each year
Denominator	Annual number of new patients	Annual population estimates	Annual number of clients registered in the FPACT	Annual population estimates	Annual number of MLOZ clients	Annual number of clients in health insurance plans
Potential for information bias: Errors in the identification of diagnosed AGW cases during the pre and post-vaccination period	Low AGW are directly diagnosed by physicians	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified and AGW treated by GP not included, unlikely to change over time unless awareness is associated with likelihood of including code	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including AGW reimbursement code or there is a change in using imiquod for treatment	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code
Risk of confounding						
Potential confounders considered	Analysis stratified by age, gender, sexual orientation and residential status	Analysis stratified by age and gender	Analysis stratified by age and gender	Analysis stratified by age, gender	Analysis stratified by age, gender	Analysis stratified by age, gender, region, and insurance plan type
Potential for confounding: Changes in diagnosed AGW between pre and post-vaccination periods could be diluted/exacerbated by other variables	High Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour); data suggest increasing % of clients with chlamydia >2007	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)	Medium Other factors could potentially cause changes in hospital admission for AGW over time (e.g., health seeking behaviour, medical practice, increasing treatment of AGW outside the hospital)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour)
External validity						
External validity: Results can be generalized to the population at the country/region level	Medium Clients of 40 sexual health clinics possibly representative of sexual health clinic clients in Australia, but may not represent the general population (e.g., different vaccination coverage)	Medium/High Entire population. Contains all cases of AGW admitted to hospital, in outpatient clinics or treated by GP	Medium FPACT is a program for low-income individuals and 87% of participants are females. Results could be different for medium/high-income individuals (e.g., different vaccination coverage)	Medium Entire population, contains all cases of AGW admitted to hospital. Results can be extrapolated to AGW cases admitted to hospitals (small subset of all AGW) but may not be representative of all AGW cases	Medium/High MLOZ is one of the three biggest sick funds in Belgium. It represents about 18% of the Belgian population with more than 2 million affiliates.	Medium/High The Truven Health Analytics contains data from 100 health insurance plan throughout the USA (n=13 million in 2010). Results could be different for uninsured individuals

Table S5: continued

Authors	**Guerra 2016**	**Harrison 2014**	**Howell-Jones 2013/Canvin 2017**	**Kliewer 2012/Thompson 2016**	**Leval 2012/Herweijer 2018**	**Liu 2014**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Canada**	**Australia**	**England**	**Canada**	**Sweden**	**Australia**
Funding	Public Health Ontario	Australian Government, Institute of Health and Welfare, National Prescribing Service, Other companies*	Public Health England	Manitoba Health	National Research School in Health Care Sciences, Strategic Research Program (Karolinska Institutet), Erasmus Program, Swedish Foundation for Strategic Research	Australian National Health and Medical Research Council (NHMRC) and the Victorian Cytology Service
Risk of selection bias						
Subjects included in the study	Population-based: All Ontario residents aged 15-26 years old	Clinic-based: Patients attending general practitioners	Population-based : Patients diagnosed at Genitourinary medicines (GUM) and England population from national statistics	Population-based: Manitoba population from the population registry	Population-based: Sweden population from Statistics Sweden	Population-based: Women aged 18–39 years participating in an Australian-wide survey on reproductive health
Potential for of selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Low Entire population of Ontario	Low Unlikely change in the general practitioners clientele between the pre- and post-vaccination periods	Low/Medium Possible changes in GUM clientele in pre- and post-vaccination periods and documented changes in service provision of GUM	Low Entire population of Manitoba	Low Entire population of Sweden	Medium Possible changes in women participating in the pre- and post-vaccination periods
Risk of information bias						
Data source	Ontario Health Insurance Program (OHIP) administrative database (outpatient visits) and Registered Persons Database	Data from the Bettering Evaluation and Care of Health (BEACH) program (records details from 100 consecutive encounters from 1000 randomly selected GPs annually)	Genitourinary Medicine Clinic Activity Dataset (GUMCAD) (diagnoses at GUM clinics nationally)	Manitoba medical claims, hospital discharges, and Manitoba population registry	National patient register, Prescribed drug register	Data from two population-based telephone surveys conducted 10 years apart in 2001 and 2011
Anogenital wart case definition	Combination of diagnosis and procedure codes: 099 only if billed with Z117; or, 079 only if billed with Z117; or, 629 only if billed with Z117; or, Z549; or, Z758; or, Z733, Z736, or Z769 only in females; or, Z767 or Z701 only in males	ICPC 2 codes Y76 for males and X91 for females	Clinical diagnosis	Treatments (1 of 14 tariff codes for AGW treatments) OR hospitalization for AGW with ICD-9 code 078.11 OR (078.1, 078.10, 078.19 and related procedure) OR (ICD-10 A630 OR B07 and related procedure)	ICD-10 code A63 OR prescription of Imiquimod or Podophyllotoxin	Self-reported diagnosis of AGW (ever)
Outcome used	Annual incidence rate of diagnosed AGW in the population	Annual management rate of AGW per 1000 encounters	Annual incidence rate of GUM-diagnosed AGW in the population	Annual incidence rate of diagnosed AGW in the population	Annual incidence rate of diagnosed AGW in the population	Proportion of women reporting ever having a diagnosis of AGW (weighted to represent the Australian population)

Authors	**Guerra 2016**	**Harrison 2014**	**Howell-Jones 2013/Canvin 2017**	**Kliewer 2012/Thompson 2016**	**Leval 2012/Herweijer 2018**	**Liu 2014**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Canada**	**Australia**	**England**	**Canada**	**Sweden**	**Australia**
Numerator	Number of newly diagnosed AGW cases per year (washout period of 12 months)	Number of AGW management per year	Number of first diagnosed AGW cases since 2006, each year	Number of newly diagnosed AGW case each year (washout period of 12 months)	Number of newly diagnosed AGW cases each year, (washout period of 6 months)	Number of self-reported AGW cases in the pre (2001) and post (2011) vaccination periods
Denominator	Annual population estimates	Annual number of encounters	Annual population estimates	Annual population estimates	Annual population estimates	Total number of women completing the survey in pre and post vaccination surveys
Potential for information bias: Errors in the identification of diagnosed AGW cases during the pre and post-vaccination period	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified and AGW treated by GP not included, unlikely to change over time unless awareness is associated with likelihood of including code	Low AGW are directly diagnosed by physicians	Low AGW are directly diagnosed by physicians in GUM clinics	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code	High AGW cases are self-reported ever
Risk of confounding						
Potential confounders considered	Analysis stratified by age, gender and adjusted for Pap test for females	Analysis stratified by age and gender	Analysis of changes over time stratified by age and gender,	Analysis stratified by age and gender	Analysis stratified by age and gender	Analysis stratified by age,
Potential for confounding: Changes in diagnosed AGW between pre and post-vaccination periods could be diluted/exacerbated by other variables	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity); data suggest increasing sexual activity over time in Sweden	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)
External validity						
External validity: Results can be generalized to the population at the country/region level	High Entire population	Medium/High The Bettering Evaluation and Care of Health (BEACH) program contains data on all Australian general practice activity	Medium/High About 95% of AGW diagnoses are made in GUM clinics (~85% sample of national data used)	High Entire population	High Entire population	Medium Survey designed to be representative of the general population. However, participants might not be fully representative of the general population, despite adjustments

Table S5: continued 2

Authors	**Mikolajczyk 2013/Thöne 2017**	**Oliphant 2011/ 2017**	**Smith 2015/2016**	**Sonnenberg 2017**	**Steben 2018**	**Woestenberg 2017**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Germany**	**New Zealand**	**Australia**	**Britain**	**Canada**	**Netherlands**
Funding	Sanofi-Pasteur MSD	No funding required	Australian Government Department of Health, NSW Ministry of Health, Children's Hospital at Westmead, National Health and Medical Research Council Australia	UK Medical Research Council, Wellcome Trust, Economic and Social Research Council and the Department of Health	Ministère de la santé et des services sociaux du Québec	Ministry of Health, Welfare and Sport
Risk of selection bias						
Subjects included in the study	Health provider/insurance-based : Enrollees in 1 large health insurance company across Germany	Clinic-based: New clients of 4 sexual health service in Auckland	Population-based: All resident of Australia between 1999–2011	Population-based: Participants in NATSAL, designed to be nationally representative of the British population	Health provider/insurance-based : Individuals from the province of Quebec with public drug coverage (41% of the Quebec population)	Clinic-based: Clients aged 16-24 years attending STI clinics located throughout the Netherlands (data from PASSYON study)
Potential for of selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Low Unlikely change in enrollees of insurance plans between the pre- and post-vaccination periods	Medium/High Possible changes in the clientele of the sexual health service as reflected by an increasing annual number of clients in the post-vaccination period	Low Entire population of Australia	Low/Medium Potential changes in the NATSAL participants between pre- and post-vaccination periods (> 10 yrs). Surveys weighted to Census data from the time.	Low Analysis restricted to individuals continuously covered by the public drug insurance throughout the study	High Documented changes in the clientele of the sexual health services in pre- and post-vaccination periods (STI clinics are recently prioritizing high-risk people and AGW cases are not considered high-risk)
Risk of information bias						
Data source	German Pharmaco-epidemiological research database	Medical records (available in the sexual health clinic database)	National Hospital Morbidity Database (NHMD) and the Australian Bureau of Statistics	Self-reported	Provincial physician service claims and public drug insurance plan databases	Data from the PASSYON (Papillomavirus Surveillance among STI clinic Youngsters in the Netherlands) study
Anogenital wart case definition	ICD-10 code A63.0	Clinical diagnosis	Hospital admissions including the ICD-10-AM code A63.0	Ever having a diagnosis of AGW (self-reported)	ICD-9 code 078.1OR medical procedure specific to condyloma (05314, 06169) OR dispensation of podofilox/podophyllotoxin, imiquimod, or fluorouracil	Clinical diagnosis
Outcome used	Annual incidence rate of diagnosed AGW among insured individuals	Annual proportion of new clients diagnosed with AGW	Annual incidence rate of hospitalization for AGW in the population	Proportion of the population with 1+ lifetime partner who reported ever having a diagnosis of AGW pre- and post-vaccination	Annual incidence of rate of diagnosed AGW among individual covered by the public drug insurance plan	Proportion of STI clients diagnosed with AGW

Authors	**Mikolajczyk 2013/Thöne 2017**	**Oliphant 2011/ 2017**	**Smith 2015/2016**	**Sonnenberg 2017**	**Steben 2018**	**Woestenberg 2017**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Germany**	**New Zealand**	**Australia**	**Britain**	**Canada**	**Netherlands**
Numerator	Number of newly diagnosed case each year, (washout period of 12 months)	Number of newly diagnosed AGW cases between Jan 2007 – June 2013	Number of hospitalization involving AGW per year	Number of participants who reported ever having a diagnosis of AGW	Number of newly diagnosed case each year (washout period of 12 months)	Number of diagnosed AGW cases in the pre (2009) and post (2011, 2013, 2015) vaccination periods
Denominator	Total number of clients of 1 large insurance company each year	Total number of new patients per year	Annual population estimates	Number of NATSAL participants, weighted to be nationally representative of the British population	Annual number of individuals covered by the public drug insurance plan	Total number of people participating in PASSYON
Potential for information bias: Errors in the identification of diagnosed AGW cases during the pre and post-vaccination period	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code	Low AGW are directly diagnosed by physicians	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified and AGW treated by GP not included, unlikely to change over time unless awareness is associated with likelihood of including code	High Recall bias of ever having a diagnosis of AGW. Increased awareness of the population about AGW since the introduction of HPV vaccination could influence answers in the post-vaccination period	Medium Sensitivity/specificity of algorithm to correctly identify diagnosed AGW not specified, unlikely to change over time unless awareness is associated with likelihood of including code	Low AGW are directly diagnosed by physicians in the clinics
Risk of confounding						
Potential confounders considered	Analysis stratified by age and gender	Analysis stratified by age and gender	Analysis stratified by age and gender. Sensitivity analysis excluded admissions related to cervical screening follow-up	Analysis stratified by age and gender. All analysis weighted to represent the British population	Analysis stratified by age and gender	Analysis stratified by age and gender, adjusted for ethnicity, education level and number of sex partners in the past 6 months
Potential for confounding: Changes in diagnosed AGW between pre and post-vaccination periods could be diluted/exacerbated by other variables	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour)	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)	Medium Other factors could potentially cause changes in hospital admissions involving AGW over time (e.g., health seeking behaviour, medical practice, increasing treatment of AGW outside hospital)	Medium/High Other factors could potentially cause changes in AGW frequency over a 10-year period (e.g., changes in sexual activity documented when comparing NATSAL2-3 [1])	Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity)	Low/Medium Other factors could potentially cause changes in AGW frequency over time (e.g., changes in sexual activity, health seeking behaviour)
External validity						
External validity: Results can be generalized to the population at the country/region level	Medium/High The insurance plan includes > 6million individuals, 8% of the German population. Results could be different in uninsured individuals	Medium Clients of 1 sexual health clinic may not represent the general population (e.g., different vaccination coverage)	Medium Entire population, contains all cases of AGW admitted to hospital. Results can be extrapolated to AGW cases admitted to hospitals (small subset of AGW) but may not be representative of all AGW	Medium/High The survey was designed to be representative of the general population. However, participants might not be fully representative of the general population, despite adjustment for known biases	Medium The public drug insurance plan covers 41% of the Quebec population. Results could be different among individuals with private drug insurance	Medium Clients of sexual health clinics may possibly not represent the general population (e.g., different vaccination coverage

AGW: Anogenital warts; ICD: International Classification of Diseases

* AstraZeneca, Janssen-Cilag, Merck, Sharpe and Dohme, Pfizer, Abbott, Sanofi-Aventis, Wyeth, Novartis, GSK, Roche Products, BioCSL, Bayer

Table S6. Methodological quality and risk of bias in studies examining changes in high-grade lesions between the pre- and post-vaccination periods.

Authors	**Baldur-Felskov 2014/2015**	**Benard 2017**	**Brotherton 2011/AIHW 2016/ 2018**	**Flagg 2016**	**Gargano 2018**	**Niccolai 2013/2017**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Denmark**	**United States**	**Australia**	**USA**	**USA**	**USA**
Funding	Mermaid project (MERMAID II)	National Institute of Allergy and Infectious Diseases	Australian Institute of Health and Welfare	Centers for Disease Control and Prevention	Centers for Disease Control and Prevention	Centers for Disease Control and Prevention
Risk of selection bias						
Subjects included in analysis	Population-based: Girls/Women included in the Nationwide Danish Pathology Data Bank	Population-based: Girls/Women included in the New Mexico HPV Pap Registry	Population-based: Girls/Women participating in the National Cervical Screening Program of Australia	Health-provider/insurance-based : Girls/Women enrolled in 100 to 170 private health insurance plans across USA (MarketScan Commercial Claims and Encounters Database) and screened for cervical cancer in each given year	Population-based: Girls/Women with a confirmed high-grade lesion in HPV-IMPACT, a laboratory-based surveillance system (catchment areas from California, Connecticut, New York, Oregon, and Tennessee). Number of screened women in each area obtained from different sources (individual or aggregate data)	Population-based: Girls/Women with a confirmed high grade lesion in the Connecticut surveillance system. Numbers of screened women in Connecticut estimated from the Behavioral Risk Factor Surveillance System-BRFSS (self-reported data)
Potential for selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods. Potential changes in the characteristics of enrollees over time.	Medium/High Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods Identification of women screened not directly available for all areas	Medium/High Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods. Identification of women screened not directly available (estimated from self-reported data in the BRFSS)
Risk of information bias						
Diagnosis of cervical lesions	The Bank contains information on all specimens from all Danish pathology departments, including cervical cytology and cervical biopsies and cones	The registry receives data from all cytological and HPVtesting and histopathologic findings ascertained as part of clinical cervical screening taken in New Mexico	The registry receives data from almost all cytology and cervical histopathology taken in Australia	Marketscan receives diagnosis codes for all medical experience of enrollees, including ICD-9_CM diagnosis codes for histologically detected CIN2 and CIN3	The HPV-IMPACT surveillance system receives data from all histologically confirmed CIN2+ identified in local and commercial laboratories serving each catchment area	The Connecticut statewide surveillance system receives data from all 34 pathology laboratories in Connecticut
Outcome used	Annual incidence of high grade lesions among screened Girls/Women .	Annual incidence of high grade lesions among screened Girls/Women	Annual incidence of high grade lesions among screened Girls/Women	Annual prevalence of high grade lesions among screened Girls/Women	Annual incidence of high grade lesions among an estimated number of screened Girls/Women	Published rates included all women; these were recalculated for the meta-analysis: annual incidence of high grade lesions among an estimated number of screened Girls/Women (BRFSS)

Authors	**Baldur-Felskov 2014/2015**	**Benard 2017**	**Brotherton 2011/AIHW 2016/ 2018**	**Flagg 2016**	**Gargano 2018**	**Niccolai 2013/2017**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Denmark**	**United States**	**Australia**	**USA**	**USA**	**USA**
Potential for information bias: Errors in the identification of pre-cancerous cervical lesions during the pre and post-vaccination period	Medium/High Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program. Better reporting of cervical lesions (mandatory reporting of results >2005). Change to LBC (better sensitivity vs conventional cytology (Appendix Table S2)	Medium/High Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program. Increased use of HPV-testing could lead to higher CIN2+ detection (Appendix Table S2)	Medium Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program	Medium/High Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program. Increased use of HPV-testing could lead to higher CIN2+ detection (Appendix Table S2)	Medium/High Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program. Increased use of HPV-testing could lead to higher CIN2+ detection. Recommended decreased referral for young women could lead to lower CIN2+ detection under age 25 (Appendix Table S2)	Medium/High Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program. Increased use of HPV-testing) could lead to higher CIN2+ detection (Appendix Table S2)
Risk of confounding						
Potential confounders considered	Analysis stratified by age	Analysis stratified by age	Analysis stratified by age	Analysis stratified by age	Analysis stratified by age	Analysis stratified by age
Potential for confounding: Changes in precancerous between pre and post-vaccination periods could be diluted/exacerbated by other variables	Medium Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening and management guidelines, sexual activity)	High Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening and management guidelines, participation, sexual activity). Less frequent screening and older age at screening start documented in the USA (Appendix Table S2)	Medium Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening and management guidelines, sexual activity)	High Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening and management guidelines, participation, sexual activity). Less frequent screening and older age at screening start documented in the USA (Appendix Table S2)	High Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening and management guidelines, participation, sexual activity). Less frequent screening and older age at screening start documented in the USA(Appendix Table S2)	High Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening and management guidelines, participation, sexual activity). Less frequent screening and older age at screening start documented in the USA (Appendix Table S2)
External validity						
Results can be generalized to the population at the country/region level	High Women participating in screening may not be representative of the general population (e.g., different vaccination coverage). However, the vaccination coverage is high in Denmark and the vaccination coverage of women screened most likely represent the general population coverage	Medium Women participating in screening may not be representative of the general population (e.g., different vaccination coverage), particularly in the USA where the vaccination coverage is medium and variable. Women from New Mexico may not be representative of all USA women	High Women participating in screening may not be representative of the general population (e.g., different vaccination coverage as shown in a study from Victoria which found that vaccinated women were less likely to be screened[1]). However, vaccination coverage is high in Australia and vaccination coverage of women screened most likely represent the general population coverage	Medium Women participating in screening may not be representative of the general population (e.g., different vaccination coverage), particularly in the USA where the vaccination coverage is medium and variable. In addition, results could be different for uninsured individuals	Medium Women participating in screening may not be representative of the general population (e.g., different vaccination coverage), particularly in the USA where the vaccination coverage is medium and variable. Women from areas included in HPV-IMPACT may not be representative of all USA women	Medium Women participating in screening may not be representative of the general population (e.g., different vaccination coverage), particularly in the USA where the vaccination coverage is medium and variable. Women from Connecticut may not be representative of all USA women

Table S6: Continued

Authors	**Nygård 2017 (via Liaw 2014)***	**Ogilvie 2015**	**Pollock 2014**
Study design	**Time-trend analysis**	**Time-trend analysis**	**Time-trend analysis**
Country	**Norway**	**Canada**	**Scotland**
Funding	Governments and non-profit cancer societies.	BC Centre for Disease Control Foundation for Public and Population Health	Scottish Government and the CSO grant
Risk of selection bias			
Subjects included in analysis	Clinic-based: All women participating in the Norwegian Cervical Cancer Screening Program	Clinic-based: Girls/Women participating in the BC Cancer Agency‘s population-based cervical cancer program	Clinic-based : Women participating in the Scottish Cervical Screening Program
Potential for selection bias: Changes in the study population characteristics between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods	Medium Possible changes in participants to cervical cancer screening between the pre- and post-vaccination periods
Risk of information bias			
Diagnosis of cervical lesions	The Program registry of contains all cervical cancer screening results and diagnosis	The Program registry contains all Pap tests, cervical biopsies and disease outcomes in BC, Canada	The Program registry contains all Pap tests, cervical biopsies and disease outcomes
Outcome used	Annual incidence of high grade lesions among screened Girls/Women	Annual incidence of high grade lesions among screened Girls/Women	Annual incidence of high grade lesions among screened Girls/Women
Potential for information bias: Errors in the identification of pre-cancerous cervical lesions during the pre and post-vaccination period	Medium/High Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program. Gradual implementation of LBC (better sensitivity vs conventional cytology(Appendix Table S2)	Medium Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program	Medium Performance of screening test may change after vaccination, but unlikely to change during the first years of the vaccination program

Risk of confounding			
Potential confounders considered	Analysis stratified by age	Analysis stratified by age	Analysis stratified by age
Potential for confounding: Changes in precancerous between pre and post-vaccination periods could be diluted/exacerbated by other variables	High Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening guidelines, sexual activity). Older age at screening start documented in Norway (Appendix Table S2)	High Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening guidelines, sexual activity). Older age at screening start documented in British Columbia (Appendix Table S2)	Medium Other factors could potentially cause changes in the incidence of precancerous cervical lesions (e.g., changes in screening guidelines and/or participation, sexual activity)
External validity			
Results can be generalized to the population at the country/region level	Medium/High Women participating in screening may not be representative of the general population (e.g., different vaccination coverage), particularly in Norway where the vaccination coverage is relatively low among women eligible for screening	Medium/High Women participating in screening may not be representative of the general population (e.g., different vaccination coverage)	High Women participating in screening may not be representative of the general population (e.g., different vaccination coverage). However, vaccination coverage among screened women is available in this study and is similar to age-specific vaccination coverage of the general population

ICD: International Classification of Diseases**;** CIN: Cervical intraepithelial neoplasia AIHW: Australian Institute of Health and Welfare; BRFSS: Behavioral Risk Factor Surveillance System; LBC: Liquid-based cytology

* CIN2+ data from Norway were identified in the article by Liaw et al 2014 and were provided by Mari Nygård (personal communication)

REFERENCE

1. Budd Ac, Brotherton JM, Gertig DM, Chau T, Drennan KT, Saville M. Cervical screening rates for women vaccinated against human papillomavirus. *Med J Aus* 2014; 201(5):279-82.

Table S7. Description of HPV vaccination programs and population-level vaccination coverage (1 / 2/ 3 doses) for each study country/region until 2015-2016 (date of the most recent data available in this systematic review).

Country	Vaccine	Financing	Availability of vaccine/ Program start	Program description*	Vaccination coverage ≥1 dose / 2 doses / 3 doses (year)
Australia	Quadrivalent	Public	April 2007	School-based program: • Girls 12-13 yrs • Boys 12-13 yrs since 02/2013 School-based catch-up: • Girls 14-17 yrs (2007-2009) • Boys 14-15 yrs (2013-2014)	School-based program: • Girls turning 15 yrs in 2015: 86%/84%/78% (2015) • Boys turning 15 yrs in 2015: 78%/75%/67% (2015) School-based catch-up: • Girls 14-15 yrs: 84%/80%/74% (2009) • Girls 16-17 yrs: 84%/80%/72% (2009) • Boys 14-15 yrs: 76%/72%/65% (2014)
			July 2007	GP/Community catch-up: • Women 18-26 yrs (2007-2009)	GP/Community catch-up: • Women 18-19 yrs: -/-/78% (2009) • Women 20-26 yrs: -/-/56% (2009)‡
Belgium	Quadrivalent and Bivalent	Partially subsidized	November 2007	Opportunistic vaccination: • Girls 12-15 yrs	Opportunistic vaccination: • Girls 12-14 yrs: -/-/43% (2008-2009)
			December 2008	Opportunistic vaccination: • Girls 12-18 yrs	• Girls 17 yrs: 75%/-/66% (2008-2009)
	Quadrivalent	Public	September 2010 (Flemish community)	School-based program: • Girls 12-13 yrs	School-based program: • Girls, by 14 yrs: 90%/-/87% (2012)
	Bivalent		September 2011 (French community)	School-based program: • Girls 13-14 yrs	School-based program: • Girls 13-14 yrs: -/-/29% (2013)
Canada (Quebec)	Quadrivalent	Public	2008	School-based program • Girls 9 yrs (2 doses) School-based catch-up: • Girls 14 yrs (3 doses, 2008-2013)	School-based program • Girls 9 yrs -/78%/- (2012-2013) School-based catch-up: • Girls 14 yrs: -/-/78% (2012-2013)
Canada (Ontario)	Quadrivalent	Public	2007/2008	School-based program: • Girls Grade 8 (≈ 13-14 yrs)	School-based program: • Girls 13-14 yrs: -/-/80% (2013)
Canada (Manitoba)	Quadrivalent	Private	August 2006 (vaccine available privately)	Private vaccination: • Girls/women 9-26 yrs	Private vaccination: • Girls/women 9-26 yrs: -/-/3% (2009)
		Public	September 2008	School-based program: • Girls Grade 6 (≈ 11-12 yrs)	School-based program: • Girls 11-12 yrs: -/-/70% (2011)

Canada (British Columbia)	Quadrivalent	Public	September 2008	School-based program: • Girls Grade 6 (≈ 11-12 yrs) School-based catch-up: • Girls Grade 9 (14-15 yrs) (2008-2011)	School-based program: • Girls Grade 6: -/65%/- (2015) School-based catch-up: • Girls Grade 9: -/-/62% (2011)
			September 2015	Program for high-risk males up to 26 yrs	NA
Denmark	Quadrivalent	Private	October 2006	Private vaccination: • Girls and boys ≥ 9 yrs	Private vaccination: • Girls 20-27 yrs: 46%/35%/2% (2012)
		Public	January 2009	GP Childhood vaccination program: • Girls 12 yrs	GP Childhood vaccination program: • Girls 12 yrs:-/-/≈ 90% (2012)
			October 2008	GP Catch-up girls: • Girls 13-15 yrs (2008-2010)	Catch-up: • Girls 13-15 yrs: 87-90%/83-86%/74-82% (2012)
			August 2012	GP Catch-up women: • Women 20-27 yrs (2012-2013)	GP Catch-up women: • Women 20-27 yrs: -/-/75% (2013)
Germany	Quadrivalent and Bivalent (Quadrivalent: 90% of doses)	Public	March 2007	GP/community program • Girls 12-17 yrs	GP/community program Girls 12-18: 6-48%/-/ - (2012)
Italy (Veneto)	Quadrivalent	Public	2008	Public health department program • Girls 12 yrs	Public health department program • Girls 12 yrs: 67-76%/-/ 56-72% (2017)
Netherlands	Bivalent	Public	2010	Public health department program: • Girls 12 yrs	Public Health department Program: • Girls 13 yrs: -/-/61% (2016)
			2009	Public health department catch-up: • Girls 12-16 yrs (2009)	Public health department Catch-up: • Girls 12-16 yrs: -/-/52%
New Zealand	Quadrivalent	Public	September 2008	School-based/GP/community program: • Girls 11-12 yrs (since 2009) School-based/GP/community catch-up: • Females 18-19 yrs (since 2008) • Females 13-17 yrs (2009-2016)	School-based/GP/community program: • Girls 11-12 yrs: -/-/66% (2013) School-based/GP/community catch-up: • Girls 13-20 yrs (2008-2010): -/-/50% (2012)
Norway	Quadrivalent	Private	2007	NA	NA
		Public	August 2009	School-based program: • Girls 12 yrs	School-based program: • Girls 12 yrs: 70-83%/-/68-76% (2013)
Spain (Galicia)	Bivalent	Public	End 2008	Primary care providers vaccination: • Girls 14 yrs	Primary care providers vaccination: • Girls 14 yrs: -/-/72% (2013)

Sweden	Quadrivalent	Partially subsidized	October 2006 (Opportunistic vaccination)	Opportunistic vaccination: • Girls 13-20 yrs	Opportunistic vaccination: • Girls 13-20 yrs: -/-/25-30% (2006-2011)
		Public	2012	School-based program: • Girls 10-12 yrs; School-based catch-up: • Girls 13-18 yrs	School-based program: • Girls 10-12yrs: 80%/75%/- (2016) School-based catch-up: • Girls 13-18 yrs: -/-/60% (2013)
UK - England	Bivalent, switch to Quadrivalent from September 2012	Public	September 2008	School-based program: • Girls 12-13 yrs School-based/GP catch-up: • Girls 14-17 yrs	School-based program: • Girls 12-13 yrs: 91%/90%/88% (2013/14) Catch-up: • Girls 14-17 yrs: -/-/56% (range from 39 to 76%) (2011)
UK- Scotland	Bivalent, switch to Quadrivalent in September 2012	Public	September 2008	School-based program: • Girls 12-13 yrs School-based/GP catch-up: • Girls 14-17 yrs (2008-2011)	School-based program: • Girls 12-13 yrs: -/-/90% (2011) • Girls12-13 yrs: 91%/ -/- (2014/15) Catch-up (in and out of school): • Girls 13-17 yrs: -/-/88% (33% among school leavers) (2011)
USA	Quadrivalent and Bivalent (mostly Quadrivalent)	Mix of public and private	June 2006	Primary care providers vaccination: • Girls/women 11-12 yrs routine and 13-26 yrs, if not previously vaccinated • Boys/men 11-12 yrs routine and 13-21 yrs if not previously vaccinated since 2011 • MSM 22-26 yrs or immunocompromised	Routine and catch-up vaccination: • Girls 13-17 yrs: 60%/50%/40% (2014) • Boys 13-17 yrs: 42%/31%/22% (2014) • Women 19-26 yrs: 42% at least one dose, ever (2015) • Men 19-26 yrs:10% at least one dose, ever (2015)

* The main delivery method is stated where different methods were allowed
‡ Possible underreporting of HPV vaccination coverage for women 20-26 years old as reported in Brotherton et al. Vaccine 2014

REFERENCES

Australia

1. Ali H, Donovan B, Wand H, et al. Genital warts in young Australians five years into national human papillomavirus vaccination program: national surveillance data. *BMJ* 2013; **346**: f2032.
2. Australian Government Department of Health. Information about the national Human papillomavirus (HPV) Vaccination Program funded under the Immunise Australia Program. http://www.health.gov.au/internet/immunise/publishing.nsf/content/immunise-hpv/. (accessed April 14, 2014).
3. Brotherton JM, Liu B, Donovan B, Kaldor JM, Saville M. Human papillomavirus (HPV) vaccination coverage in young Australian women is higher than previously estimated: independent estimates from a nationally representative mobile phone survey. *Vaccine* 2014; **32**(5): 592-7.
4. National HPV Vaccination Program Register. Coverage Data. HPV vaccination coverage by dose number (Australia) for adolescents by age group. http://www.hpvregister.org.au/research/coverage-data. (accessed May 10, 2017).

Belgium

1. Arbyn M, Broeck DV, Benoy I, et al. Surveillance of effects of HPV vaccination in Belgium. *Cancer Epidemiol*. 2016; **41:152**-8.
2. Arbyn M, de Sanjose S, Saraiya M, et al. EUROGIN 2011 roadmap on prevention and treatment of HPV-related disease. *Int J Cancer*. 2012; **131**(9):1969-82.

3. Merckx M, Broeck DV, Benoy I, Depuydt C, Weyers S, Arbyn M. Early effects of human papillomavirus vaccination in Belgium. *Eur J Cancer Prev*. 2015; **24**(4):340-2.
4. Lefevere E, Theeten H, Hens N, De Smet F, Top G, Van Damme P. From non-school-based, co-payment to school-based, free Human Papillomavirus vaccination in Flanders (Belgium): a retrospective cohort study describing vaccination coverage, age-specific coverage and socio-economic inequalities. *Vaccine*. 2015; **33**(39):5188-95.

Canada

1. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Immunization coverage report for school pupils: 2012–13 school year. Toronto, ON: Queen's Printer for Ontario; 2014.
2. Personal communication CancerCare Manitoba. Number of girls who received at least one dose of the HPV vaccine in the publicly funded program 2008-2011.
3. Kliewer E, Mahmud S, Demers A, Lambert P, Musto G. Human papillomavirus vaccination and anogenital warts in Manitoba. Winnipeg: CancerCare Manitoba, 20pp, 2012.
4. Kliewer E, Demers A, Lambert P. Uptake of the human papillomavirus vaccine in Manitoba August 2006-December 2009. Winnipeg: CancerCare Manitoba, 43pp, 2012.
5. Thompson LH, Nugent Z, Blanchard JF, Ens C, Yu BN. Increasing incidence of anogenital warts with an urban-rural divide among males in Manitoba, Canada, 1990-2011. *BMC Public Health*. 2016; **16**:219.
6. Drolet M, Deeks SL, Kliewer E, Musto G, Lambert P, Brisson M. Can high overall human papillomavirus vaccination coverage hide sociodemographic inequalities? An ecological analysis in Canada. *Vaccine.* 2016; **34**(16):1874-80.
7. BC Centre for Disease Control. Immunization Uptake in Grade 6 Students 2002-2015. http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/Immunization/Coverage/Grade6_Coverage_Results.pdf . (accessed July 20, 2016).
8. BC Centre for Disease Control. Immunization Uptake in Grade 9 Students 2002-2015. http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/Immunization/Coverage/Grade9_Coverage_Results.pdf . (accessed July 20, 2016).
9. Ogilvie GS, Naus M, Money DM, et al. Reduction in cervical intraepithelial neoplasia in young women in British Columbia after introduction of the HPV vaccine: An ecological analysis. *Int J Cancer*. 2015; **137**(8):1931-7.
10. BC Centre for Disease Control. Human Papillomavirus (HPV) Vaccine. http://www.bccdc.ca/health-info/immunization-vaccines/vaccines-in-bc/human-papillomavirus-(hpv)-vaccine (accessed July 2016).
11. Flash Vigie. Bulletin Québécois de vigie, de surveillance et d'intervention en protection de la santé publique. Vol 8 (7) : Septembre 2013. http://publications.msss.gouv.qc.ca/msss/fichiers/flashvigie/06-271-02W-vol8_no7.pdf

Denmark

1. Widgren K, Simonsen J, Valentier-Branth P, Molbak K. Uptake of the human papillomavirus-vaccination within the free-of-charge childhood vaccination program in Denmark. *Vaccine* 2011; **29**: 9663-7.
2. Baandrup L, Blomberg M, Dehlendorff C, Sand C, Andersen KK, Kjaer SK. Significant decrease in the incidence of genital warts in young Danish women after implementation of a national human papillomavirus vaccination program. *Sex Transm Dis* 2013; **40**(2): 130-5.
3. Blomberg M, Dehlendorff C, Munk C, Kjaer SK. Strongly decreased risk of genital warts after vaccination against human papillomavirus: nationwide follow-up of vaccinated and unvaccinated girls in Denmark. *Clin Infect Dis* 2013; **57**(7): 929-34.
4. Statens Serum Institut. HPV vaccination-Coverage 2012. http://www.ssi.dk/English/News/EPI-NEWS/2013/No%2020%20-%202013.aspx. (accessed May11, 2017).
5. Statens Serum Institut. Uptake in the temporary HPV vaccination program for females born in 1985-1992. http://www.ssi.dk/English/News/EPI-NEWS/2014/No%2047%20-%202014.aspx. (accessed July 9, 2016).

Germany

1. Mikolajczyk RT, Kraut AA, Horn J, Schulze-Rath R, Garbe E. Changes in incidence of anogenital warts diagnoses after the introduction of human papillomavirus vaccination in Germany-an ecologic study. *Sex Transm Dis* 2013; **40**(1): 28-31.

Italy (Veneto)
1. Cocchio S, Baldovin T, Bertoncello C, et al. Decline in hospitalization for genital warts in the Veneto region after an HPV vaccination program: an observational study. BMC Infect Dis 2017; **17**:249.
2. Ministry of Health (Italy). HPV Italian coverage at 31/12/2015. http://www.salute.gov.it/imgs/C_17_tavole_27_allegati_iitemAllegati_0_fileAllegati_itemFile_0_file.pdf. (accessed May 5, 2017).

Netherland
1. Woestenberg PJ, King AJ, van der Sande MAB, et al., No evidence for cross-protection of the HPV-16/18 vaccine against HPV-6/11 positivity in female STI clinic visitors. *J Infect* 2017; **74**: 393-400.
2. The National Immunisation Programme in the Netherlands Developments in 2013. RIVM Report 150202002/2013. https://www.rivm.nl/bibliotheek/rapporten/150202002.pdf (accessed December 10, 2017).
3. The National Immunisation Programme in the Netherlands Surveillance and developments in 2016-2017 RIVM Report 2017-0143. https://www.rivm.nl/bibliotheek/rapporten/2017-0143.pdf. (accessed December 7, 2017).
4. The National Immunisation Programme in the Netherlands Developments in 2011. RIVM report 210021015/2011. https://www.rivm.nl/bibliotheek/rapporten/210021015.pdf. (accessed May 30, 2018).

New Zealand
1. Ministry of Health. History of the HPV immunisation programme. http://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/hpv-immunisation-programme/history-hpv-immunisation-programme. (accessed May 30, 2018).
2. Oliphant J, Perkins N. Impact of the human papillomavirus (HPV) vaccine on genital wart diagnoses at Auckland Sexual Health Services. *N Z Med J.* 2011; **124**(1339): 51-8.
3. HPV immunisation Coverage December 2016.http://www.health.govt.nz/system/files/documents/pages/hpv_-selected_cohorts_-all_dhbs_-31_dec_2016_final_for_web.pdf (accessed December 10, 2017)

Norway
1. Hansen BT, Campbell S, Burger E, Nygard M. Correlates of HPV vaccine uptake in school-based routine vaccination of preadolescent girls in Norway: A register-based study of 90,000 girls and their parents. *Prev Med*. 2015;**77**:4-10.
2. Norwegian Institute of Public Health. Barnevaksinasjonsprogrammet i Norge. Rapport for 2013. https://www.fhi.no/globalassets/dokumenterfiler/rapporter/vaksine/barnevaksinasjonsprogrammet-i-norge-rapport-2013. (accessed May 15, 2018)
3. Feiring B, Laake I, Molden T, et al. Do parental education and income matter? A nationwide register-based study on HPV vaccine uptake in the school-based immunisation programme in Norway. *BMJ Open*. 2015;**5**(5):e006422.

Spain (Galicia)
1. Purriños-Hermida MJ, Santiago-Pérez MI, Treviño M, et al. Direct, indirect and total effectiveness of bivalent HPV vaccine in women in Galicia, Spain
2. Personal communication MJ Purriños-Hermida, Vaccination coverage in Galicia, 2014-2017

Sweden
1. Leval A, Herweijer E, Arnheim-Dahlstrom L, et al. Incidence of genital warts in Sweden before and after quadrivalent human papillomavirus vaccine availability. *J Infect Dis* 2012; **206**(6): 860-6.
2. Andelen flickor med minst en respektive två registrerade doser HPV-vaccin. https://www.folkhalsomyndigheten.se/globalassets/statistik-uppfoljning/vaccinationsstatistik/hpv/hpv-statistik-2016-till-webbsida.pdf. (accessed December13, 2017)
3. Herweijer E, Ploner A, Sparen P. Substantially reduced incidence of genital warts in women and men six years after HPV vaccine availability in Sweden. Vaccine 2018; 36(15): 1917-20.

UK (England)
1. Mesher D, Soldan K, Howell-Jones R, et al. Reduction in HPV 16/18 prevalence in sexually active young women following the introduction of HPV immunisation in England. *Vaccine* 2013; **32**(1): 26-32.
2. Department of Health. Annual HPV vaccine coverage in England201/2011. http://media.dh.gov.uk/network/211/files/2012/03/120319_HPV_UptakeReport2010-11-revised_acc.pdf. (accessed April 5, 2014).

3. Human Papillomavirus (HPV) vaccination coverage in adolescent females in England: 2014/15. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/487514/HPV_2014_15_ReportFinal181215_v1.1.pdf. (accessed December 11, 2017).

UK (Scotland)

1. Kavanagh K, Pollock KG, Potts A, et al. Introduction and sustained high coverage of the HPV bivalent vaccine leads to a reduction in prevalence of HPV 16/18 and closely related HPV types. *Br J Cancer* 2014; **110**(11): 2804-11.
2. Information Services Division. HPV immunisation uptake rates by mid-August 2012, for girls in the catch-up cohort. https://isdscotland.scot.nhs.uk/Health-Topics/Child-Health/Publications/2012-09-25/HPV_Catch-up_Programme.xls. (accessed June 6, 2014).

USA

1. Williams WW, Lu P, O'Halloran A, et al. Surveillance of Vaccination Coverage Among Adult Populations — United States, 2014. *MMWR Surveill Summ* 2016; **65**(No. SS-1):1-36
2. Reagan-Steiner S, Yankey D, Jeyarajah J, et al. National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13-17 Years--United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;**6 4**(29):784-92.
3. Centers for Disease Control and Prevention. 2014 Adolescent Human Papillomavirus (HPV) Vaccination Coverage Report. https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/hpv/dashboard/2014.html. (accessed December 3, 2017).
4. Centers for Disease Control and Prevention. Vaccination Coverage Among Adults in the United States, National Health Interview Survey, 2015. https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/coverage-estimates/2015.html. (accessed December 5, 2017).

Table S8. Summary of changes in cervical cancer screening recommendations and participation since the introduction of HPV vaccination programs.

	Recommendation during years included in this review				Documented changes over the years included in the review			
Countries	**Age at start of screening**	**Screening intervals**	**HPV testing**	**Other**	**Age at start of screening**	**Screening intervals**	**HPV testing**	**Other**
Australia	18-20 yrs or 2 yrs after sex initiation	2 yrs	No	Primary HPV testing will began in 12/2017	No significant change	No significant change	No significant change	Change to follow-up of abnormalities (repeat Pap for LSIL rather than colposcopy), colposcopy for persistent ASC-US rather than annual testing. Decline in participation of women <45 and lower participation in vaccinated young women
Canada (BC)	Since 2011: 21 yrs or 3 yrs after sex initiation	1-2 yrs	No	New guidelines in 2016 (start age = 25 yrs; interval = 3 yrs)	Steady decline in screening of girls 15-17 yrs	No significant change	No significant change	
Denmark	23 yrs	3 yrs (women 23-49 yrs); 5 yrs (women 50-64 yrs)	Since 2005: triage of ASCUS, LSIL, unsatisfactory		No significant change	No significant change	Introduction of HPV testing 1 yrs before the start of HPV vaccination	Better registration over time of CIN; Since 2000, gradual implementation of LBC and better sensitivity of LBC vs conventional cytology
Norway	25 yrs	3 yrs	Since 2005: triage of ASCUS, LSIL, unsatisfactory		Steady decline in screening of women < 25yrs	No significant change	Introduction of HPV testing 2 yrs before the start of HPV vaccination	Since 2006, gradual implementation of LBC
UK-Scotland	20 yrs	3 yrs	No	New guidelines in 2016 (start age =25; screening interval = 3 yrs (25-49 yrs), 5 yrs (50-64 yrs))	No significant change	No significant change	No significant change	
USA	Since 2009: 21 yrs	Since 2009: 2 yrs (women 21-29 yrs); 3 yrs (women ≥30 yrs after 3 negative tests); Since 2012: 3 yrs for cytology alone (women 30-65 yrs), 5 yrs for co-testing (women 30-65 yrs)	Since 2004: recommendations for co-testing (women ≥30 yrs) and triage of ASCUS for all women. Since 2012: co-testing (women 30-65 yrs)	Since 2012: change in recommendation for management of women 21-24 yrs with abnormal cytology limiting referrals for colposcopy; Changes in diagnostic terminology for high-grade lesions: may have an impact on case classification by grade	Steady decline in screening of women < 21yrs	Increased, especially for women screened by co-testing. Increase from a median of 1.5 yrs (2007) to 3yrs (2014) (unpublished data from New Mexico)	Since 2007, 82% of ASCUS triaged with HPV-testing. Important increase in co-testing (women 30-65 yrs). Regional differences in the timing of HPV testing uptake	HPV testing of abnormal cytology led to higher CIN2+ and CIN3+ detection rates

ASCUS: Atypical squamous cells of undetermined significance; CIN: Cervical intraepithelial neoplasia; LSIL: low-grade squamous intraepithelial lesions; LBC: Liquid-based cytology

REFERENCES

Australia

1) Brotherton JM, Fridman M, May CL, Chappell G, Saville AM, Gertig DM. Early effect of the HPV vaccination programme on cervical abnormalities in Victoria, Australia: an ecological study. *Lancet* 2011; **377**:2085-92.
2) National cervical screening program. http://www.cancerscreening.gov.au/. (accessed November 11, 2017).

Canada, British Columbia

1) BC Cancer Agency Cervical Cancer Screening Program Annual Report, 2012. Vancouver, BC, 2012. http://www.bccancer.bc.ca/screening/Documents/CCSP_Report-AnnualReport2012.pdf. (accessed December 5, 2017).
2) BC Cancer Agency Cervical Cancer Screening Policy Change. http://www.bccancer.bc.ca/screening/Documents/CCSP_GuidelinesManual-CervicalCancerScreeningProtocols.pdf (accessed November 5, 2017).
3) Ogilvie GS , Naus M, Money DM, et al. Reduction in cervical intraepithelial neoplasia in young women in British Columbia after introduction of the HPV vaccine: An ecological analysis, *Int J Cancer* 2015: **137**; 1931-37.

Denmark

1) Baldur-Felskov B, Dehlendorff C, Junge J, Munk C, Kjaer SK. Incidence of cervical lesions in Danish women before and after implementation of a national HPV vaccination
Program, *Cancer Causes Control*, 2014: **25**: 915-22.
2) National Board of Health, Cervical cancer screening 2007. https://www.sst.dk/~/media/4028E09321C1403480B3E86020F58A18.ashx. (accessed November 3, 2017).

Norway

1) Kreft registeret. Institutt for populasjons-basert kreftforskning. https://www.kreftregisteret.no/globalassets/publikasjoner-og-rapporter/livmorhalskreft/arsrapport/aarsrapport-livmorhalsprogrammet-2015.pdf . (accessed November 3, 2017).
2) Nygård M, Røysland K, Campbell S, Dillner J. Comparative effectiveness study on human papillomavirus detection methods used in the cervical cancer screening programme. *BMJ Open* 2014: **4**(1); e003460.

UK- Scotland

1) National Services Scotland, Cervical cancer screening. http://www.isdscotland.org/Health-topics/Cancer/Cervical-screening/. (accessed November 5, 2017).

USA

1) American College of Obstetricians and Gynecologists, ACOG Practice Bulletin Number 109: Cervical cytology screening. *Obstet Gynecol*. 2009; **114**(6):1409-20
2) American College of Obstetricians and Gynecologists, ACOG Practice Bulletin Number 131: Screening for cervical cancer. *Obstet Gynecol*. 2012; **120**(5):1222-38
3) Benard VB, Castle PE, Jenison SA, et al., Population-based incidence rates of cervical intraepithelial neoplasia in the human papillomavirus vaccine era. *JAMA Oncol* 2017; **3**(6):833-37
4) Centers for Disease Control and Prevention (CDC). Cervical cancer screening among women aged 18-30 years – United States, 2000-2010. *MMWR Morb Mortal Wkly Rep* 2013; **61**(51-52): 1038-42.
5) Cuzick J, Myers O, Hunt WC, et al. Human papillomavirus testing 2007–2012: Co-testing and triage utilization and impact on subsequent clinical management. *Int J Cancer* 2015; **136**: 2854-63
6) Cuzick J, Myers O, Lee JH, et al. Outcomes in women with cytology showing atypical squamous cells of undetermined significance with vs without human papillomavirus testing. *JAMA Oncol*; **3**(10): 1327-34
7) Fowler CI, Saraiya M, Moskosky SB, Miller JW, Gable J, Mautone-Smith N. Trends in Cervical Cancer Screening in Title X-Funded Health Centers – United States, 2005-2015. *MMWR Morb Mortal Wkly Rep* 2017; **66**(37):981-5.

8) Huh WK, Ault KA, Chelmow D, et al. Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. *J Low Genit Tract Dis*. 2015; **19**(2): 91-6.
9) Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. *CA Cancer J Clin*. 2012; **62**(3):147–72.
10) Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis*. 2013. **17**(5 Suppl 1): S1-s27.
11) Silver MI, Rositch AF, Phelan-Emrick DF, Gravitt PE. Uptake of HPV testing and extended cervical cancer screening intervals following cytology alone and Pap/HPV cotesting in women aged 30-65 years. *Cancer Causes Control*. 2018 ;**29**(1):43-50.
12) U.S. Preventive Services Task Force. Screening for cervical cancer: U.S. Preventive Services Task Force recommendation statement. AHRQ publication no. 11–05156-EF-2. March 2012.
13) Wright TC Jr, Cox JT, Massad LS, Twiggs LB, Wilkinson EJ; ASCCP-Sponsored Consensus Conference. 2001 consensus guidelines for the management of women with cervical cytological abnormalities. *JAMA*. 2002. **28**7(16), 2120-9.
14) Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D; 2006 ASCCP-Sponsored Consensus Conference. 2006 consensus guidelines for the management of women with abnormal cervical screening tests. *J Low Genit Tract Dis*, 2006. **11**(4), 201-22.

Table S9. Pre- and post-vaccination years considered in the meta-analysis (normal font: years included in our previous review; bold font: years from updates/new studies identified in the current review).

Study	Country	Study population	HPV vaccination introduction female-only/ gender-neutral	Pre-vaccination years considered in meta-analysis	Post-vaccination years								
					1	2	3	4	5	6	7	8	9
HPV infection													
Chow 2015/Chow 2017	Australia	Females/males	2007/2013	2005-2007	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**		
Cummings 2012	USA	Females	2006/2011	1995-2005				2010					
Dillner 2018	Denmark Sweden	Females Females	2009 2012†	2006-2008 2006-2008	**2012**	**2013**	**2012**	**2013**					
Dunne 2015	USA	Females	2006/2011	2007						**2012**	**2013**		
Grün 2016	Sweden	Females/males*	2012†	2008-2011		**2013**	**2014**	**2015**					
Kavanagh 2014/Cameron 2016/Kavanagh 2017	Scotland	Females	2008	2009-2010			2011	2012	**2013**	**2014**	**2015**		
Kahn 2012/Kahn 2016	USA	Females	2006/2011	2006-2007			2009	2010			**2013**	**2014**	
Machalek 2018	Australia	Females	2007/2013	2005-2007								**2015**	
Markowitz 2013/Markowitz 2016/Oliver 2017	USA	Females	2006/2011	2003-2006	2007	2008	2009	2010	**2011**	**2012**	**2013**	**2014**	
Mesher 2013/Mesher 2016/ Mesher 2018	England	Females	2008	2008		2010	2011	2012	**2013**	**2014**	**2015**	**2016**	
Purriños-Hermida 2018	Spain (Galicia)	Females	End 2008	2008-2010					**2014**	**2015**	**2016**	**2017**	
Söderlund-Strand 2014	Sweden	Females	2012†	2008	**2012**	**2013**							
Sonnenberg 2013	U.K.	Females/males	2008	1999-2001		2010	2011	2012					
Tabrizi 2012/Tabrizi 2014	Australia	Females	2007/2013	2005-2007			2010	2011	2012				
AGW consultations													
Ali 2013/Callander 2016	Australia	Females/males	2007/2013	2005-2007	2008	2009	2010	2011	2012	**2013**	**2014**	**2015**	
Baandrup 2013/Bollerup 2016	Denmark	Females/males	2009	2007-2009	2010	2011	**2012**	**2013**					
Bauer 2012	USA	Females/males	2006/2011	2007		2008	2009	2010					
Cocchio 2017	Italy	Females/males	2008	2006-2008	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**		
Dominiak-Felden 2015	Belgium	Females/males	2007 §	2006-2007	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**			
Flagg 2013/Flagg 2018	USA	Females/males	2006/2011	2004-2006	2007	2008	2009	2010	**2011**	**2012**	**2013**	**2014**	
Guerra 2016	Canada (Ontario)	Females/males	2007	2005-2007	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**			

Study	Country	Study population	HPV vaccination introduction female-only/ gender-neutral	Pre-vaccination years considered in meta-analysis	Post-vaccination years								
					1	2	3	4	5	6	7	8	9
Harrison 2014[€]	Australia	Females/males	2007/2013	2005-2007	**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	
Howell-Jones 2013/Canvin 2017	England	Females/males	2008	2006-2008	2009	2010	2011	**2012**	**2013**	**2014**	**2015**		
Kliewer 2012/Thompson 2016	Canada (Manitoba)	Females/males	2008/2016	2006-2008	2009	**2010**	**2011**						
Leval 2012/Herweijer 2018	Sweden	Females/males	2006	2006 [‡]	2007	2008	2009	2010	**2011**	**2012**			
Liu 2014	Australia	Females	2007/2013	2001				**2011**					
Mikolajczyk 2013/Thöne 2017	Germany	Females/males	2007	2005-2007	2008	**2009**	**2010**						
Oliphant 2011/ Oliphant 2017	New Zealand	Females/males	2008	2007-2008	2009	2010	**2011**	**2012**	**2013**				
Smith 2015	Australia	Females/males	2007/2013	2005-2007	**2008**	**2009**	**2010**	**2011**					
Sonnenberg 2017	U.K.	Females/males	2008	1999-2001		**2010**	**2011**	**2012**					
Steben 2018	Canada (Quebec)	Females/males	2008/2016	2004-2007	**2009**	**2010**	**2011**	**2012**					
Woestenberg 2017	Netherlands	Females/males	2009	2009		**2011**		**2013**					
CIN2+													
Baldur-Felskov 2014	Denmark	Females	2009	2007-2009	**2010**	**2011**	**2012**	**2013**					
Benard 2017	USA (New Mexico)	Females	2006/2011	2007		**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	
Brotherton 2011/AIHW 2016/AIHW2018	Australia	Females	2007/2013	2005-2007	2008	2009	2010	2011	**2012**	**2013**	**2014**	**2015**	**2016**
Flagg 2016	USA	Females	2006/2011	2007		**2008**	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	
Gargano 2018 [£]	USA (California, Connecticut, New York, Oregon, Tennessee)	Females	2006/2011	2008			**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**
Niccolai 2013/2017[¥£]	USA (Connecticut)	Females	2006/2011	2008				2010		**2012**		**2014**	
Nygård 2017 (via Liaw 2014)	Norway	Females	2009	2007-2009	**2010**	**2011**	**2012**	**2013**	**2014**				
Ogilvie 2015	Canada (British Columbia)	Females	2008	2005-2008	**2009**	**2010**	**2011**	**2012**					
Pollock 2014	Scotland	Females	2008	2008	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**			

* Cervical and oral HPV prevalence was available for women but only data about Cervical HPV prevalence are presented over time; only oral HPV prevalence was available for men.

† The vaccine is available since 2006 in Sweden and was reimbursed from 2007. However, the organized, publicly funded program was launched in 2012. Söderlund-Strand et al. considered 2008 as a pre-vaccination year and 2012, 2013 as post-vaccination years; vaccination coverage increased substantially in 2012. We considered 2012 as the first year post-vaccination for the 3 studies about HPV infections in Sweden.

§ The vaccine is available and reimbursed since 2007 in Belgium. However, the school-based program began in 2010 in the Flemish region and in 2011 in the French region. Dominiak-Felden considered 2006-2007 as pre-vaccination years.

€ Published data were available until 2012, but the author provided data up to 2015.

‡ The vaccine is available since 2006 in Sweden and was reimbursed from 2007. However, the organized, publicly funded program was launched in 2012. The authors of this study considered 2006 as the beginning of HPV vaccination.

£ 2008 was considered as a pre-vaccination year in these studies since 1) data were not available prior to 2008 and 2) the vaccination coverage was still very low in 2008.

¥ Number of CIN2+ were available for each year from 2008 to 2015, however estimates of the number of screened women were only available for 2008, 2010, 2012, and 2014. For this reason analyses were restricted to years with available estimates of number of women screened.

Table S10. Characteristics of the studies included in the systematic review and meta-analysis

Author (Country)	Vaccine	Data source*	Study population	Population used in meta-analysis	Data collection dates†	Sample size used in meta-analysis ‡	Case definition	Effect measure in publication	Effect measure recalculated ß
HPV infection									
Chow 2015a Chow 2017 (Australia) [12, 13]	Quadrivalent	Clinic-based: STI clinics	Females and males 15-25 yrs attending the Melbourne Sexual Health Centre diagnosed with chlamydia	Females and males 15-24 yrs[Ω]	Prevaccine:2005-2007 Postvaccine:2008-2014	Females N prevaccine:128 N postvaccine:260 Males N prevaccine:115 N postvaccine:411	HPV+ PapType HR HPV genotyping kit (Genera Biosystem) Females: cervical & vaginal swabs Males: urine and urethal swabs	Crude HPV prevalence over time	RR of HPV prevalence (crude)
Cummings 2012 (U.S.)[14]	Quadrivalent	Clinic-based: Primary care clinics	Females 14-17 yrs attending 1 of 3 urban primary care clinics in Indianapolis	Females 14-17 yrs	Prevaccine:1999-2005 Postvaccine:2010	N prevaccine:150 N postvaccine:75	HPV+ Roche Linear Array (Roche, 37 types)	OR of HPV prevalence (crude)	RR of HPV prevalence (crude)
Dillner 2018 [11]	Quadrivalent	Clinic-based: Nationwide cervical screening program of Denmark, Sweden, Norway	Females 18-50 attending routine cervical cancer	Females 18-29 yrs from Denmark and Sweden[**]	Prevaccine: 2006-2008 Postvaccine: 2012-2013	Denmark/ Sweden N prevaccine: 1,188/1,112 N postvaccine: 1,163/1,164	HPV+ Luminex system (Bio-Rad, 35 types)	Difference of HPV prevalence (crude)	RR of HPV prevalence (crude)
Dunne 2015 (USA)[15]	Quadrivalent	Clinic-based: Kaiser Permanente NorthWest	Females 20-29 yrs attending routine cervical cancer screening (cytology)	Females 20-29 yrs	Prevaccine:2007 Postvaccine:2012-2013	N prevaccine:4,138 N postvaccine:4,171	HPV+ Roche Linear Array & HPV-52 quantitative PCR	RR of HPV prevalence (crude)	RR of HPV prevalence (crude)
Grün 2016 (Sweden)[16]	Quadrivalent	Clinic-based: Youth clinic in Stockholm	Females and males (oral infections for males) 15-23 yrs attending a Stockholm youth clinic	Females 15-23 yrs[Ω]	Prevaccine: 2008-2011 Postvaccine: 2013-2015	N prevaccine: 544 [γ] N postvaccine: 332	HPV+ Luminex-based genotyping assay (27 types)	Crude HPV prevalence over time	RR of HPV prevalence (crude)
Kahn 2012/ Kahn 2016 (USA)[20, 21]	Quadrivalent	Clinic-based: Hospital and health department	Females 13-26 yrs attending 1 hospital-based teen clinic and 2 health department sites in Cincinnati	Females 13-26 yrs, Had had sexual contact	Prevaccine:2006-2007 Postvaccine1:2009-2010 Postvaccine2:2013-2014	N prevaccine:355 N postvaccine1:408 N postvaccine2:400	HPV+ Roche Linear Array (Roche, 37 types)	HPV prevalence difference (adjusted)	RR of HPV prevalence (adjusted)
Kavanagh 2014/ Cameron 2016/Kavanagh 2017(Scotland)[17-19]	Bivalent	Clinic-based: Scottish Cervical screening Call & Recall System	Females 20-21 yrs participating in cervical cancer screening in Scotland	Females 20-21 yrs	Prevaccine:2009-2010 Postvaccine1:2011-2012 Postvaccine2:2013-2015	N prevaccine:2,705 N postvaccine1:1,994 N postvaccine2:3,702	HPV+ Multimetrix HPV assay (18 types)	Crude HPV prevalence over time	RR of HPV prevalence (crude)
Machalek 2018 [Ŧ] (Australia) [22]	Quadrivalent	Clinic-based: Family planning clinics	Females 18-35 yrs attending family planning clinics in Victoria and New South Wales	Females 25-29 yrs	Prevaccine:2005-2007 Postvaccine:2015	N prevaccine:102 N postvaccine:114	2005-2007: HPV+ Amplicor HPV test kit (Roche Molecular system-13 types), and PGMY09-PGMY11 PCR-ELISA Roche Linear Array genotyping test (37 types); 2015: HPV+ Cobas HPV test (Roche Diagnosis) and Roche Linear Array	RR of HPV prevalence (adjusted)	RR of HPV prevalence (adjusted)

Author (Country)	Vaccine	Data source*	Study population	Population used in meta-analysis	Data collection dates†	Sample size used in meta-analysis ‡	Case definition	Effect measure in publication	Effect measure recalculated ß
							genotyping test (37 types)		
Markowitz 2013/ Markowitz 2016/ Oliver 2017 (USA)[23-25]	Quadrivalent	Population-based: NHANES participants	Nationally representative sample of USA females aged 14-59 yrs	Females 14-29 yrs	Prevaccine:2003-2006 Postvaccine1:2007-2010 Postvaccine2:2011-2014	N prevaccine:2,198 N postvaccine1:1,599 N postvaccine2:1,634	HPV+ Roche Linear Array (Roche, 37 types)	RR of HPV prevalence (adjusted)	RR of HPV prevalence (adjusted)
Mesher 2013/ Mesher 2016/ Mesher 2018 (England)[26-28]	Bivalent	Clinic-based: Community sexual health clinics, GP	Females 16-24 yrs undergoing chlamydia screening in community sexual health / GP /Youth clinics in 7 regions around England	Females 16-24 yrs	Prevaccine:2008 Postvaccine1:2010-2012 Postvaccine2:2013-2016	N prevaccine:2,354 N postvaccine1:7,924 N postvaccine2:7,535	2008: Hybrid Capture 2 and Roche Linear Array ≥2010: HPV+ In-house multiplex PCR and Luminex-based genotyping (20 types)[I]	OR of HPV prevalence (adjusted)	RR of HPV prevalence (adjusted)
Purriños-Hermida 2018 (Spain) [29]	Bivalent	Clinic-based: Primary care center, gynecology department, family counseling center	Females 18-26 yrs attending health areas of the Galician Public Health Services	Females 18-26 yrs	Prevaccine:2008-2010 Postvaccine:2014-2017	N prevaccine:523 N postvaccine:745	HPV+ Cobas 4800 HPV test with Linear Array HPV genotyping (Roche Diagnostic) (12 types)	RR of HPV prevalence (crude and adjusted)	RR of HPV prevalence (adjusted)
Söderlund-Strand 2014 (Sweden)[30]	Quadrivalent	Clinic-based: Chlamydia screening	Females all ages attending to Chlamydia screening	Females 15-29 yrs	Prevaccine:2008 Postvaccine:2012-2013	N prevaccine:15,767 N postvaccine:5216	HPV + In-house multiplex PCR with genotyping by MALDI-TOF mass spectrometry (16 types)	Crude HPV prevalence over time	RR of HPV prevalence (crude)
Sonnenberg 2013 (England, Scotland, Wales) [31]	Bivalent	Population-based: Natsal participants	Nationally representative sample of males and females aged 16-44 yrs Natsal-2, 16-74 yrs Natsal-3 in Britain	Females and males 18-29 yrs	Prevaccine:1999-2001 Postvaccine:2010-2012	Females N prevaccine:684 N postvaccine:1,426 Males N prevaccine:462 N postvaccine:1061	HPV+ In-house Luminex-based genotyping assay (18 types)[I] in urine samples	OR of HPV prevalence (age-adjusted)	RR of HPV prevalence (age-adjusted)
Tabrizi 2012/2014 (Australia)[32, 33]	Quadrivalent	Clinic-based: Family planning clinics	Females 18-24 yrs attending 1 of 6 family planning clinics in Sydney, Melbourne, Perth	Females 18-24 yrs	Prevaccine:2005-2007 Postvaccine1:2010-2011 Postvaccine2: 2012	N prevaccine:202 N postvaccine1:404 N postvaccine2:654	HPV+ Amplicor HPV test kit (Roche Molecular system-13 types), and PGMY09-PGMY11 PCR-ELISA Roche Linear Array genotyping test (37 types)	RR of HPV prevalence (adjusted)	RR of HPV prevalence (adjusted)
Anogenital warts									
Ali 2013/ Chow 2015b, Ali 2017, Callander 2016 (Australia) [34-37]	Quadrivalent	Clinic-based: STI clinics	New clients of 40 sexual health centers across Australia aged ≥ 12 yrs (Australian born)	Australian born females and heterosexual males 15-39 yrs	2004-2015 Prevaccine: 2005-2007 Postvaccine:2008-2015	P-yr prevaccine: 51,010 P-yr postvaccine: 134,614	Clinical diagnosis	Annual proportion of new clients with AGW	RR of AGW proportion (crude)

Author (Country)	Vaccine	Data source*	Study population	Population used in meta-analysis	Data collection dates†	Sample size used in meta-analysis ‡	Case definition	Effect measure in publication	Effect measure recalculated ß
Baandrup 2013/ Bollerup 2016 (Denmark)[38, 39]	Quadrivalent	Population-based: Statistics Denmark, National Patient Registry	Entire population of Denmark ≥ 12 yrs	Females and males 15-39 yrs	2006-2013 Prevaccine: 2007-2009 Postvaccine:2010-2013	P-yr prevaccine: 5,144,888 P-yr postvaccine: 6,945,980	ICD-10 code A63.0 OR prescription of Podophyllotoxin	Annual incidence rate of diagnosed AGW in the population	RR of AGW incidence (crude)
Bauer 2012 (USA)[40]	Quadrivalent	Health provider /insurance-based: Clinical encounters claims data of a health program	Clients of the California Family Planning access care & treatment (PACT) program aged ≥ 10 yrs (87% females)	Females and males 15-39 yrs Program serves low-income individuals	2007-2010 Prevaccine: 2007 Postvaccine:2008-2010	P-yr prevaccine: 1,750,980 P-yr postvaccine: 5,555,420	ICD-9 codes 078.10, 078.11 OR prescription of Imiquimod or Podophyllotoxin	Annual proportion of PACT clients diagnosed with AGW	RR of AGW proportion (crude)
Cocchio 2017 (Italy)[41]	Quadrivalent	Population-based: Hospital records of all Veneto residents (public & private)	Entire population from Veneto, Italy	Females and males 15-39 yrs	2004-2015 Prevaccine:2006-2008 Postvaccine:2009-2015	P-yr prevaccine: 4,567,864 P-yr postvaccine: 9,913,192	ICD-9 code 078.11 and 1 ICD-9 surgical code (70-71, 58, 64, 58.3, 49)	Annual rate of hospitalization for AGW in the population	RR of AGW hospitalization (crude)
Dominiak-Felden 2015 (Belgium)[42]	Quadrivalent	Health provider /insurance-based: Medical claims, National Union of Independent Sick Funds (MLOZ)	Enrollees in MLOZ, one of the 3 biggest sick fund in Belgium (18% of the Belgium population; 2 million individuals)	Females and males 15-39 yrs	2006-2013 Prevaccine:2006-2007 Postvaccine:2008-2013	P-yr prevaccine: 960,777 P-yr postvaccine: 3,858,172	First prescription of Imiquimod with a level of reimbursement specific for AGW onset	RR of AGW incidence (crude)	RR of AGW incidence (crude)
Flagg 2013/Flagg 2018 (USA)[43, 44]	Quadrivalent	Health provider /insurance-based: Truven Health Analytics Market Scan Commercial Claims and Encounters Database	Enrollees in approximately 100 health private insurance plans across the U.S. aged 10-39 yrs	Females and males 15-39 yrs, Insured employees, early retirees and their dependents	2003-2014 Prevaccine: 2004-2006 Postvaccine:2007-2014	P-yr prevaccine: 11,864,207 P-yr postvaccine: 85,817,435	1) ICD-9 codes 078.11 OR 2 ICD-9 code 078.1, 078.10, c 078.19 and therapeutic procedure diagnosis of benign AG neoplasm OR 3) ≥1 prescription for AGW treatment and therapeutic procedure r diagnosis of benign AG neoplasm	Annual proportion of insured individuals with diagnosed AGW	RR of AGW proportion (crude)
Guerra 2016 (Canada-Ontario)[45]	Quadrivalent	Population-based: Health care encounter database (covers all Ontario residents)	All Ontario residents aged ≥ 15 yrs with a valid health card number	Females and males 15-26 yrs	2004-2013 Prevaccine:2005-2007 Postvaccine:2008-2013	P-yr prevaccine: 6,242,786 P-yr postvaccine: 13,069,534	First physician office visit (12-month wash-out period) with one of 10 possible combination codes: 099 + Z117, 079 + Z117, 629 + Z117, Z549, Z758, Females: Z733, Z736, or Z769; males Z767, Z701	Annual incidence rate of diagnosed AGW in the population	RR of AGW incidence (crude)
Harrison 2014 Ψ (Australia)[46]	Quadrivalent	Clinic-based (BEACH program: randomly selected GP-encounters in Australia)	Patients of 1,000 randomly selected GP across Australia (each year)	Females and males 15-39 yrs	2002-2015 Prevaccine:2005-2007 Postvaccine:2008-2015	P-yr prevaccine: 77,258 P-yr postvaccine: 190,268	ICPC 2 code Y76 (males), X91 (females)	Annual proportion of patients with AGW management	RR of AGW management proportion (crude)

Author (Country)	Vaccine	Data source*	Study population	Population used in meta-analysis	Data collection dates†	Sample size used in meta-analysis ‡	Case definition	Effect measure in publication	Effect measure recalculated ß
Howell-Jones 2013/ Canvin 2017 (England) [47, 48]	Bivalent Quadrivalent for some girls 15-16 yrs in 2014-2015 α	Population-based: Office for National Statistics, Genitourinary medicine (GUM) clinics	Entire population of England aged 15-24 yrs;	Females and males 15-24 yrs	2002-2015 Prevaccine: 2006-2008 Postvaccine:2009-2015	P-yr prevaccine: 20,370,695 P-yr postvaccine: 48,041,371	Clinical diagnosis	Annual incidence rate of diagnosed AGW in the population	RR of AGW incidence (crude)
Kliewer 2012/ Thompson 2016 (Canada-Manitoba)[49, 50]	Quadrivalent	Population-based: Medical claims and hospital discharge database of all Manitoba residents	Entire population of Manitoba	Females and males 15-39 yrs	2006-2011 Prevaccine: 2006-2008 Postvaccine:2009-2011	P-yr prevaccine: 1,194,786 P-yr postvaccine: 1,245,073	Treatments (1 of 14 tariff codes) OR (hospitalization for AGW + ICD-9 code 078.11) OR (078.1, 078.10, 078.19 and related procedure) OR ICD-10 A630 OR (B07 and related procedure)	Annual incidence rate of diagnosed AGW in the population	RR of AGW incidence (crude)
Leval 2012/ Herweijer 2018 (Sweden)[51, 52]	Quadrivalent	Population-based: Statistics Sweden, National Patient Register, Prescribed Drug Register	Entire population of Sweden aged ≥ 10 yrs	Females and males 15-39 yrs	2006-2012 Prevaccine: 2006 Postvaccine:2007-2012	P-yr prevaccine: 2,930,263 P-yr postvaccine: 18,089,134	ICD-10 code A63.0 OR prescription of Imiquimod or Podophyllotoxin	Annual incidence rate of diagnosed AGW in the population	RR of AGW incidence (crude)
Liu 2014 (Australia)[53]	Quadrivalent	Population-based: Australia-wide survey	All Australian women aged 18-39 yrs	Females 18-39 yrs	2001 and 2011 Prevaccine:2001 Postvaccine:2011	P-yr prevaccine: 4,874 P-yr postvaccine: 2,394	Self-reported AGW diagnosis (ever had AGW)	Proportion of women reporting AGW among all respondents	RR of AGW proportion (crude)
Mikolajczyk 2013/ Thönes 2017 (Germany)[54, 55]	Quadrivalent	Health provider /insurance-based: German Pharmaco-epidemiological Research Database	Enrollees in 1 large health insurance company across Germany aged 10-79 yrs	Females and males 15-39 yrs	2005-2010 Prevaccine: 2005-2007 Postvaccine:2008-2010	P-yr prevaccine: 4,974,000 P-yr postvaccine: 5,372,000	ICD-10 code A63.0	Annual incidence rate of diagnosed AGW among insured individuals	RR of AGW incidence (crude)
Oliphant 2011/2017 (New Zealand)[56, 57]	Quadrivalent	Clinic-based: STI clinic	New clients of 4 sexual health service in Auckland aged ≥ 10 yrs	Females and males 15-39 yrs	2007-2013 Prevaccine:2007-2008 Postvaccine:2009-2013	P-yr prevaccine: 9,559 P-yr postvaccine: 26,258	Clinical diagnosis	Annual proportion of new clients diagnosed with AGW	RR of AGW proportion (crude)
Smith 2015/2016 (Australia)[58, 59]	Quadrivalent	Population-based: National Hospital Morbidity Database, Australian Bureau of Statistics	Entire population of Australia aged 12-69 yrs	Females and males 12-69 yrs¥	2005-2011 Prevaccine:2005-2007 Postvaccine:2008-2011	P-yr prevaccine: 45,887,699 P-yr postvaccine: 65,192,250	Hospitalization including ICD-10 code A63.0 as main or contributory diagnosis	Annual rate of hospitalization with AGW diagnosis in the population	RR of AGW hospitalization (crude)
Sonnenberg 2017 [60]	Bivalent	Population-based: Natsal participants	Nationally representative sample of males and females aged 16-44 yrs Natsal-2, 16-74 yrs Natsal-3 in Britain	Females and males 16-39 yrs	Prevaccine:1999-2001 Postvaccine:2010-2012	N prevaccine:8,294 N postvaccine:5,849	Ever having a diagnosis of AGW (self-reported)	Proportion of the population who reported ever having a diagnosis of AGW	RR of AGW proportion (crude)

Author (Country)	Vaccine	Data source*	Study population	Population used in meta-analysis	Data collection dates†	Sample size used in meta-analysis ‡	Case definition	Effect measure in publication	Effect measure recalculated ß
Steben 2018 [61]	Quadrivalent	Health provider /insurance-based : Quebec physician claim and public drug insurance databases	Individuals covered by the Quebec public drug insurance	Females and males 15- ≥30 yrs	2004-2012 Prevaccine:2004-2007 Postvaccine:2009-2012	P-yr prevaccine: 13,159,362 P-yr postvaccine: 13,241,313	ICD-9 code 078.1OR medical procedure specific to condyloma (05314, 06169) OR dispensation of podofilox, imiquimod, or fluorouracil	Annual incidence rate of diagnosed AGW among insured individuals	RR of AGW incidence (crude)
Woestenberg 2017 (Netherlands)[62]	Bivalent	Clinic-based PASSYON study in STI clinics	Patients of STI clinics aged 16-24 yrs old across the Netherlands	Females and males 16-24 yrs	2009, 2011, 2013 Prevaccine: 2009 Postvaccine: 2011, 2013	P-yr prevaccine: 1,662 P-yr postvaccine: 3,859	Clinical diagnosis	Proportion of STI patients diagnosed with AGW	RR of AGW proportion (adjusted)
Cervical intraepithelial neoplasia grade 2+									
Baldur-Felskov 2014/2015 (Denmark) [63, 64]	Quadrivalent	Population-based: Nationwide Danish Pathology Data Bank	Females aged ≥ 12 yrs living in Denmark and screened for cervical cancer	Screened females 15-39 yrs	2007-2013 Prevaccine:2007-2009 Postvaccine:2010-2013	P-yr prevaccine: 1,810,881 P-yr postvaccine: 1,840,066	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)
Benard 2017 (USA)[65]	Quadrivalent	Population-based: New Mexico HPV pap registry	Females aged 15-29 yrs living in New Mexico and screened for cervical cancer	Screened females 15-29 yrs	2007-2014 Prevaccine:2007 Postvaccine:2008-2014	P-yr prevaccine: 74,115 P-yr postvaccine: 386,146	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)
Brotherton 2011/ AIHW 2016/2018 (Australia) §[66-68]	Quadrivalent	Population-based: Cervical cancer screening program registry	Females aged <69 yrs living in Australia and screened for cervical cancer	Screened females 15-39 yrs	2005-2016 Prevaccine:2005-2007 Postvaccine:2008-2016	P-yr prevaccine: 3,213,016 P-yr postvaccine: 9,200,381	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)
Flagg 2016 (USA)[69]	Quadrivalent	Health provider /insurance-based: Truven Health Analytics Market Scan Commercial Claims and Encounters Database	Females aged 15-39 yrs, enrolled in 100-170 employers and health private insurance plans across USA and screened for cervical cancer	Screened females 15-39 yrs	2007-2014 Prevaccine:2007 Postvaccine:2008-2014	P-yr prevaccine: 1,542,598 P-yr postvaccine: 15,643,924	Histopathologically confirmed CIN2+ (ICD-9 code 622.12, 233.1)	Annual prevalence of CIN2+ among screened females	RR of CIN2+ proportion (crude)
Gargano 2018 (USA- California, Connecticut, New York, Oregon, Tennessee) [70]	Quadrivalent	Population-based: HPV-IMPACT surveillance system. Number of screened women estimated from different sources	Females aged 18-39 yrs with a high-grade lesion in HPV-IMPACT (a laboratory-based surveillance system including areas from California, Connecticut, New York, Oregon, and Tennessee)	Screened females 18-39 yrs£	2008-2015 Prevaccine:2008 Postvaccine:2009-2015	P-yr prevaccine: 268,186 P-yr postvaccine: 1,470,273	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)

Author (Country)	Vaccine	Data source*	Study population	Population used in meta-analysis	Data collection dates†	Sample size used in meta-analysis ‡	Case definition	Effect measure in publication	Effect measure recalculated ß
Niccolai 2013/2017 (USA- Connecticut)€ [71, 72]	Quadrivalent	Population-based: Connecticut surveillance system (all 34 pathology laboratories). Number of screened women estimated from BRFSS	Females aged 21-39 yrs living in Connecticut with a high-grade lesion in the surveillance system	Screened females 20-39 yrs£, ø	2008-2014 Prevaccine:2008 Postvaccine:2009-2014	P-yr prevaccine: 211,134 P-yr postvaccine: 643,071	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among general population	RR of CIN2+ incidence among screened women∂ (crude)
Nygård 2017 (via Liaw 2014) (Norway) [73 Φ]	Quadrivalent	Population-based: Norwegian cervical cancer screening program registry	All females living in Norway and screened for cervical cancer	Screened females 15-39 yrs	2007-2014 Prevaccine:2007-2009 Postvaccine:2010-2014	P-yr prevaccine: 1,262,014 P-yr postvaccine: 1,948,739	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)
Ogilvie 2015 (Canada-British Columbia) [74]	Quadrivalent	Population-based: BC Cervical cancer screening program registry	Females aged 15-22 yrs living in British-Columbia (Canada) and screened for cervical cancer	Screened females 15-17 yrs ¶	2006-2012 Prevaccine:2006-2008 Postvaccine:2009-2012	P-yr prevaccine: 27,523 P-yr postvaccine: 27,054	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)
Pollock 2014 (Scotland) [75]	Bivalent	Population-based: Scottish Cervical cancer screening program registry	Females aged 20-21 yrs living in Scotland and screened for cervical cancer	Screened females 20-21 yrs	2008-2014 Prevaccine:2008 Postvaccine:2008-2014	P-yr prevaccine: 20,891 P-yr postvaccine: 111,230	Histopathologically confirmed CIN2+	Annual incidence of CIN2+ among screened females	RR of CIN2+ incidence (crude)

AGW: Anogenital warts; AIHW: Australian Institute of Health and Welfare; BRFSS: Behavioral Risk Factor Surveillance System; NHANES: National Health and Nutrition Examination Survey; NATSAL: National Survey of Sexual Attitudes and Lifestyles; OR: Odds ratio; RR: Relative risk (Post-vaccination prevalence or incidence / Pre-vaccination prevalence or incidence); STI: Sexually transmitted infection: GP: General practitioner

* Data sources are considered as: 1) Population-based when the study population includes the total population of a given country/region or a registry, 2) Health provider/insurance-based when the study population is constituted of a subgroup of the total population enrolled in a specific insurance plan, 3) Clinic-based when the study population is constituted of individuals who received health services (e.g., medical consultation).

† For studies on HPV infection, the pre- and post-vaccination periods were already determined in most original publications (except for Kavanagh et al.). For studies on AGW and cervical lesions studies, the pre- and post-vaccination periods were determined for the purposes of this systematic review as described in the Appendix-Table S8.

‡ The sample size is restricted to the age groups used in the review. For studies on HPV infection, the pre and post-vaccination sample sizes were already determined in original studies. For studies on AGW and cervical lesions, the pre-vaccination sample size corresponds to the cumulative number of person-years up to three years pre-vaccination. The post-vaccination sample size corresponds to the cumulative number of person-years from 1 to 8 years after the introduction of vaccination, depending on data available in each study.

ß For HPV infection, the investigators recalculated the RR (adjusted or crude) of prevalence using the original data from their specific studies. For AGW and precancerous lesions, we estimated pre-vaccination frequency by aggregating the data for up to three years prior to vaccination, and calculated RR by dividing each post-vaccination year by the pre-vaccination estimate.

** The study by Dillner et al. included data from Denmark, Sweden and Norway among women aged ≥ 18 years in 2012-2013. However , since the vaccination program of 12 year-old girls began in 2009 in Norway, women included in the study (≥ 18 years old) were too old to be covered by the vaccination program (vaccination coverage < 2%). For this reason, we did not include data from Norway in the meta-analysis.

Ω Since only oral infections were available for males, we did not include data for males from this study in our meta-analysis.

γ The pre-vaccine sample excludes 65 women who were vaccinated (10.6% of the sample). The prevalence of all HPV types, HPV 16/18, and other common HPV types did not statistically differ between the vaccinated and unvaccinated women of the pre-vaccination sample (unpublished data).

Ŧ The study by Machalek includes a subset of women included in the studies by Tabrizi and a group of women aged 25-35 years (not previously included in Tabrizi). To avoid double counting the same women, we only kept the results from the older group of women not previously included in Tabrizi.

ǁ 13 HR-HPV types were presented in the original publications whereas the 18 HR-HPV types available were used for the purposes of this meta-analysis

Ψ Published data were available until 2012, but the author provided data up to 2015.

α In 2014: 14% and 72% of 15 yr old girls received the quadrivalent and bivalent vaccine, respectively. In 2015, 57% and 29% of 15 yr old girls received the quadrivalent and bivalent vaccine, respectively; 14% and 57% of 16 yr old girls received the quadrivalent and bivalent vaccine, respectively.

¥ Permission could not be obtained from the data custodian to release data in the age strata requested for this meta-analysis, therefore results for age groups 15-19, 20-24, 25-29 and 30-39 years in this meta-analysis used published data from the age groups 12-17, 18-26, 27-30 and 31-69 years, respectively, as reported in Smith 2015. [58]

§ Data from Brotherton et al. 2011 [66] are restricted to the Victorian registry data. Supplementary data from the Australian Institute of Health and Welfare 2016 report were provided by Dr. Brotherton. Since the report covers all regions of Australia, it was used as our main data source for the review.

£ The number of screened women is not directly available in these studies. Different data sources (individual or aggregate-level) have been used to estimate the denominator (i.e., the number of screened women of the different catchment areas).

€ One county from Connecticut (New Haven) is included in the HPV-IMPACT surveillance system. To avoid double counting women from this county in estimates from HPV-IMPACT (Gargano 2018) and Connecticut (Niccolai 2017), we decided with the authors, to excluded New Haven from the Connecticut data to keep them in HPV-IMPACT.

ø The study population in the original publication was restricted to women aged 21-39 years, but data for women aged 20 years were provided for this meta-analysis

∂ For the purposes of this meta-analysis, the rates were recalculated using estimates of number of screened women from the Behavioral Risk Factor Surveillance System (BRFSS).

Φ CIN2+ data from Norway were identified in the article by Liaw et al [73] and were provided by Mari Nygård (personal communication)

¶ Data directly available in the article to estimate RR of CIN2+ incidence among screened females available only for females ages 15-17 years old.

Table S11. Subgroup analyses of the changes in prevalence of HPV infection between the pre- and post-vaccination periods (1-4 yrs and 5-8 yrs) among girls/women.

---------	15-19 years		20-24 years		25-29 years	
	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs
Study characteristics	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****
HPV16/18						
Vaccine						
Quadrivalent (n=11)	0·23 [0·13;0·41]	0·21 [0·13;0·36]	0·55 [0·42;0·73]	0·27 [0·17;0·42]	0·87 [0·68;1·12]	0·68 [0·43;1·06]
Bivalent (n=3)	0·42 [0·36;0·49] *p=0·05*	0·14 [0·11;0·18] *p=0·16*	0·80 [0·60;1·06] *p=0·06*	0·46 [0·23;0·94] *p=0·21*	0·81 [0·48;1·38] *p=0·80*	0·31 [0·08;1·22] *p=0·29*
Study and age-specific coverage [¥]						
Low (<50%) (n=1 / n=6 / n=7)	0·50 [0·34;0·74]	0·28 [0·14;0·56]	0·80 [0·66;0·97]	0·42 [0·28;0·64]	0·87 [0·68;1·12]	0·67 [0·53;0·83]
High (≥50%) (n=10/ n= 6 / n=1)	0·28 [0·19;0·41] *p=0·04*	0·15 [0·11;0·21] *p=0·12*	0·43 [0·28;0·65] *p=0·01*	0·27 [0·24;0·31] *p=0·05*	NA	0·08 [0·01;0·62] *p=0·04*
Effect measure						
Adjusted (n=6)	0·33 [0·21;0·52]	0·17 [0·11;0·26]	0·68 [0·43;1·08]	0·35 [0·19;0·62]	0·89 [0·30;2·62]	0·54 [0·23;1·25]
Unadjusted (n=8)	0·18 [0·06;0·58] *p=0·34*	0·17 [0·02;1·27] *p=1.00*	0·60 [0·51;0·71] *p=0·61*	0·31 [0·22;0·46] *p=0·78*	0·80 [0·67;0·95] *p=0·85*	0·63 [0·49;0·81] *p=0·73*
Data source [§]						
Population-based (n=2)	0·47 [0·34;0·67]	0·28 [0·14;0·56]	0·98 [0·72;1·33]	0·38 [0·22;0·65]	1·04 [0·67;1·62]	0·83 [0·50;1·38]
Health provider/insurance-based (n=0)	NA	NA	NA	NA	NA	NA
Clinic-based (n=12)	0·26 [0·17;0·40] *p=0·04*	0·15 [0·11;0·21] *p=0·12*	0·59 [0·49;0·71] *p=0·006*	0·33 [0·22;0·50] *p=0·67*	0·80 [0·65;0·98] *p=0·28*	0·51 [0·25;1·05] *p=0·28*
HPV types 31/33/45						
Vaccine						
Quadrivalent (n=11)	0·93 [0·79;1·08]	0·50 [0·30;0·82]	1·03 [0·86;1·24]	0·74 [0·58;0·94]	0·98 [0·75;1·28]	0·92 [0·70;1·21]
Bivalent (n=3)	0·81 [0·65;1·01] *p=0·34*	0·29 [0·06;1·30] *p=0·50*	0·91 [0·64;1·29] *p=0·52*	0·68 [0·29;1·59] *p=0·87*	1·61 [0·68;3·83] *p=0·28*	1·14 [0·37;3·49] *p=0·71*
Study and age-specific coverage [¥]						
Low (<50%) (n=1 / n=6 / n=7)	NA	0·71 [0·29;1·75]	1·07 [0·89;1·28]	0·92 [0·68;1·24]	0·98 [0·75;1·28]	0·93 [0·71;1·23]
High (≥50%) (n=10/ n= 6 / n=1)	0·89 [0·78;1·01]	0·44 [0·30;0·64] *p=0·34*	0·88 [0·68;1·14] *p=0·23*	0·59 [0·34;1·03] *p=0·17*	NA	0·91 [0·30;2·75] *p=0·97*
Effect measure						
Adjusted (n=6)	0·81 [0·66;0·99]	0·45 [0·33;0·61]	1·11 [0·86;1·44]	0·91 [0·69;1·19]	0·65 [0·15;2·70]	1·15 [0·68;1·93]
Unadjusted (n=8)	0·91 [0·72;1·15] *p=0·44*	0·89 [0·30;2·66] *p=0·24*	0·93 [0·76;1·13] *p=0·28*	0·60 [0·33;1·07] *p=0·20*	1·01 [0·89;1·15] *p=0·54*	0·86 [0·63;1·18] *p=0·36*

	15-19 years		20-24 years		25-29 years	
	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs
Study characteristics	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****	**RR [95% CI]** ***p-value****
Data source [§]						
Population-based (n=2)	NA	0·71 [0·29;1·75]	0·92 [0·63;1·35]	0·60 [0·26;1·39]	1·22 [0·77;1·93]	1·25 [0·60;2·59]
Health provider/insurance-based (n=0)	NA	NA	NA	NA	NA	NA
Clinic-based (n=12)	0·89 [0·78;1·00]	0·44 [0·30;0·64] *p=0·34*	1·00 [0·84;1·20] *p=0·71*	0·73 [0·46;1·15] *p=0·69*	0·95 [0·69;1·32] *p=0·40*	0·89 [0·66;1·18] *p=0·39*
High-risk HPV types (except 16/18)						
Vaccine						
Quadrivalent (n=11)	1·08 [0·96;1·22]	0·95 [0·76;1·18]	1·07 [0·98;1·16]	1·07 [0·92;1·24]	1·00 [0·89;1·11]	1·10 [0·69;1·77]
Bivalent (n=3)	1·38 [1·11;1·70] *p=0·06*	1·55 [1·41;1·71] *p=0·0001*	1·23 [0·92;1·65] *p=0·36*	1·37 [0·81;2·32] *p=0·37*	1·13 [0·76;1·67] *p=0·55*	1·46 [0·85;2·51] *p=0·45*
Study and age-specific coverage [¥]						
Low (<50%) (n=1 / n=6 / n=7)	0·79 [0·60;1·04]	0·83 [0·63;1·09]	1·22 [1·03;1·45]	1·26 [0·92;1·73]	1·00 [0·89;1·11]	1·33 [0·93;1·91]
High (≥50%) (n=10/ n= 6 / n=1)	1·19 [1·05;1·35] *p=0·007*	1·20 [0·86;1·67] *p=0·09*	1·01 [0·91;1·12] *p=0·06*	1·03 [0·84;1·28] *p=0·31*	NA	0·67 [0·39;1·16] *p=0·04*
Effect measure						
Adjusted (n=6)	1·04 [0·79;1·37]	1·06 [0·75;1·50]	1·22 [1·00;1·49]	1·21 [0·85;1·73]	1·09 [0·86;1·39]	1·00 [0·75;1·34]
Unadjusted (n=8)	1·14 [1·07;1·23] *p=0·50*	1·55 [0·97;2·49] *p=0·20*	1·05 [0·99;1·11] *p=0·15*	1·08 [0·87;1·34] *p=0·58*	0·99 [0·88;1·11] *p=0·47*	1·73 [1·54;1·95] *p=0·0005*
Data source [§]						
Population-based (n=2)	0·84 [0·66;1·08]	0·83 [0·63;1·09]	1·14 [0·93;1·39]	1·04 [0·78;1·39]	1·14 [0·89;1·46]	0·98 [0·72;1·34]
Health provider/insurance-based (n=0)	NA	NA	NA	NA	NA	NA
Clinic-based (n=12)	1·20 [1·05;1·36] *p=0·01*	1·20 [0·86;1·67] *p=0·09*	1·11 [0·98;1·25] *p=0·83*	1·18 [0·92;1·52] *p=0·52*	0·98 [0·86;1·11] *p=0·27*	1·23 [0·78;1·94] *p=0·42*

RR = Relative Risk: HPV prevalence in the post-vaccination periods (1-4 yrs or 5-8 yrs) compared to the pre-vaccination period.
CI = Confidence Interval.
* p-values indicate the statistical significance of comparisons between subgroups of studies.
[¥] The vaccination coverage for at least one dose of studies of HPV infection is available directly for study participants. The age-specific vaccination coverage varies greatly between the different age groups. For this reason, we indicate the number of studies in each vaccination coverage category for girls aged 13-19 years old / women 20-24 years old / women 25-29 years old.
[§] Studies using health provider/insurance based data and studies using clinic-based data were compared to studies using population-based data.

Table S12. Subgroup analyses of the changes in anogenital warts (AGW) diagnosis between the pre- and post-vaccination periods (1-4 yrs and 5-8 yrs) among girls/women and boys/men.

A) Girls/women

Study characteristics	15-19 years		20-24 years		25-29 years		30-39 years	
	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs
	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**
Vaccine								
Quadrivalent (n=15)	0·60 [0·47;0·76]	0·33 [0·24;0·46]	0·76 [0·67;0·86]	0·46 [0·36;0·60]	0·89 [0·80;0·98]	NA	1·02 [0·93;1·13]	NA
Bivalent (n=3)	0·91 [0·89;0·92] *p=0·001*	0·70 [0·69;0·71] *P<0·0001*	0·90 [0·55;1·45] *p=0·50*	0·89 [0·88;0·90] *P<0·0001*	0·80 [0·50;1·28] *p=0·67*		1·07 [0·80;1·43] *p=0·77*	
Quadrivalent vaccine only (n=15)								
Overall proportion vaccinated [¥]								
Low (single cohort and/or low vaccination coverage (<50%)) (n=8)	0·85 [0·75;0·96]	0·56 [0·42;0·75]	0·92 [0·85;0·99]	0·68 [0·59;0·78]	0·99 [0·88;1·12]	0·91 [0·73;1·12]	1·07 [0·94;1·21]	1·01 [0·73;1·39]
Medium/High (multiple cohorts and high vaccination coverage (≥50%)) (n=7)	0·36 [0·27;0·48] *p<0·00001*	0·12 [0·06;0·24] *p=0·0001*	0·59 [0·49;0·72] *p<0·00001*	0·23 [0·11;0·48] *p=0·005*	0·76 [0·66;0·87] *p=0·003*	0·39 [0·23;0·65] *p=0·003*	0·94 [0·89;1·00] *p=0·07*	0·74 [0·65;0·84] *p=0·08*
Data source [§]								
Population-based (n=7)	0·68 [0·41;1·15]	0·66 [0·46;0·94]	0·78 [0·64;0·95]	0·74 [0·61;0·90]	0·89 [0·83;0·95]	0·82 [0·73;0·91]	0·96 [0·88;1·05]	0·82 [0·49;1·38]
Health provider/insurance-based (n=5)	0·68 [0·57;0·80] *p=0·97*	0·46 [0·33;0·63] *p=0·13*	0·89 [0·78;1·01] *p=0·27*	0·55 [0·29;1·04] *P=0·39*	1·04 [0·89;1·22] *p=0·08*	1·09 [0·88;1·37] *p=0·02*	1·11 [0·94;1·30] *p=0·14*	1·24 [0·79;1·93] *p=0·24*
Clinic-based (n=3)	0·35 [0·20;0·63] *p=0·09*	0·12 [0·06;0·24] *p<0·00001*	0·52 [0·39;0·69] *p=0·02*	0·23 [0·11;0·48] *p=0·003*	0·66 [0·50;0·88] *p=0·05*	0·39 [0·23;0·65] *p=0·005*	0·96 [0·81;1·14] *p=0·97*	0·74 [0·65;0·84] *p=0·70*

B) Boys/men

Study characteristics	15-19 years		20-24 years		25-29 years		30-39 years	
	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs	1-4 yrs	5-8 yrs
	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**
Vaccine								
Quadrivalent (n=14)	0·80 [0·62;1·04]	0·52 [0·37;0·75]	0·93 [0·82;1·06]	0·67 [0·47;0·97]	1·04 [0·93;1·17]	NA	1·08 [0·99;1·19]	NA
Bivalent (n=3)	0·99 [0·97;1·08] *p=0·10*	0·83 [0·81;0·86] *p=0·01*	0·96 [0·71;1·29] *p=0·86*	0·99 [0·97;1·00] *p=0·04*	1·15 [0·69;1·91] *p=0·73*		0·96 [0·71;1·29] *p=0·45*	
Quadrivalent vaccine (n=14)								
Overall proportion vaccinated [¥]								
Low (single cohort and /or low vaccination coverage (<50%)) (n=8)	1·03 [0·90;1·18]	0·99 [0·80;1·22]	1·05 [0·90;1·23]	0·95 [0·72;1·25]	1·14 [0·98;1·34]	1·18 [0·83;1·68]	1·18 [1·06;1·32]	1·36 [1·04;1·77]
Medium/High (multiple cohorts and high vaccination coverage (≥50%)) (n=6)	0·56 [0·42;0·73] *p<0·00001*	0·14 [0·10;0·18] *p<0·00001*	0·80 [0·71;0·89] *p=0·005*	0·37 [0·23;0·61] *p=0·001*	0·91 [0·83;1·01] *p=0·02*	0·59 [0·41;0·85] *p=0·008*	0·98 [0·91;1·05] *p=0·005*	0·68 [0·62;0·73] *p<0·00001*
Data source [§]								
Population-based (n=6)	0·92 [0·57;1·47]	0·95 [0·90;1·01]	0·94 [0·83;1·06]	0·94 [0·80;1·11]	1·03 [0·98;1·09]	1·02 [0·90;1·16]	1·07 [1·00;1·14]	1·23 [1·17;1·29]
Health provider/insurance-based (n=5)	0·92 [0·72;1·18] *p=0·99*	0·82[0·28;2·33] *p=0·78*	1·05 [0·82;1·36] *p=0·43*	0·91 [0·36;2·31] *p=0·95*	1·14 [0·90;1·44] *p=0·42*	1·30 [0·68;2·48] *p=0·48*	1·16 [0·98;1·39] *p=0·37*	1·46 [0·95;2·21] *p=0·44*
Clinic-based (n=3)	0·44 [0·37;0·51] *p=0·004*	0·14 [0·10;0·18] *p<0·00001*	0·71 [0·61;0·84] *p=0·008*	0·37 [0·23;0·61] *p=0·0005*	0·86 [0·75;0·98] *p=0·01*	0·59 [0·41;0·85] *p=0·006*	0·94 [0·87;1·01] *p=0·007*	0·68 [0·62;0·73] *p<0·00001*

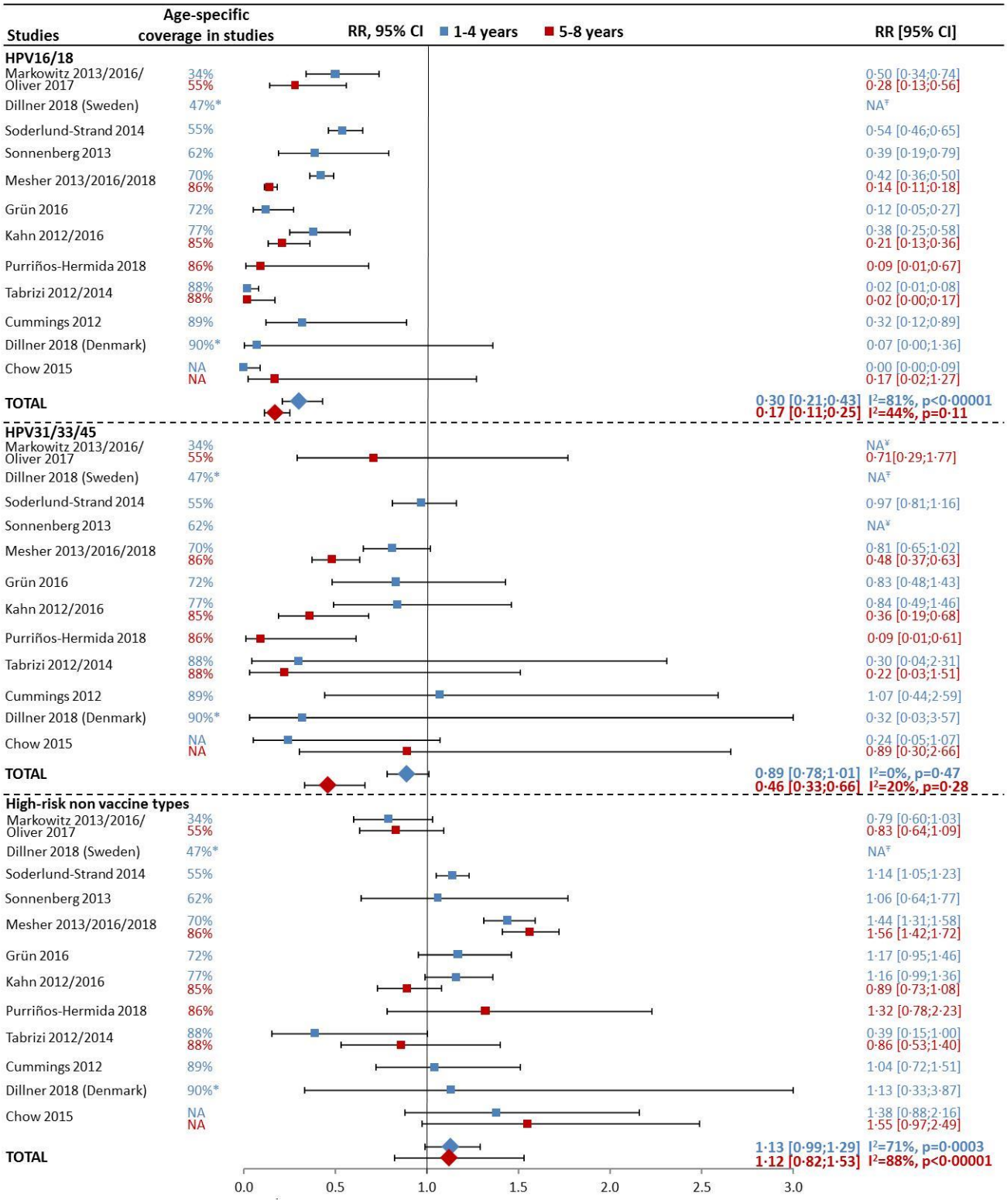
RR = Relative Risk: incidence/prevalence of AGW in the post-vaccination periods (1-4 yrs or 5-8 yrs) compared to the pre-vaccination period.
CI = Confidence Interval.
* p-values indicate the statistical significance of comparisons between subgroups of studies.
[¥] For studies on AGW, the vaccination coverage is not available specifically for study participants. We classified studies into 2 groups according to 1) whether the country/setting vaccinate a single routine cohort of girls or multiple cohorts of girls and 2) the vaccination coverage in routine age groups is < or ≥50%.
[§] Studies using health provider/insurance based data and studies using clinic-based data were compared to studies using population-based data.

Table S13. Subgroup analyses of the changes in CIN2+ between the pre- and post-vaccination periods (1-4 yrs and 5-8 years) among girls/women.

Study characteristics	15-19 years		20-24 years		25-29 years		30-39 years	
	1-4 yrs	5-9 yrs	1-4 yrs	5-9 yrs	1-4 yrs	5-9 yrs	1-4 yrs	5-9 yrs
	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value*	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**	RR [95% CI] *p-value**
Vaccine								
Quadrivalent (n=8)	0·73 [0·67;0·79]	0·49 [0·42;0·58]	0·98 [0·85;1·13]	0·78 [0·64;0·95]	1·12 [1·05;1·20]	1·19 [1·06;1·32]	1·07 [1·00;1·14]	1·23 [1·13;1·34]
Bivalent (n=1)	NA	NA	0·66 [0·57;0·77] *p=0· 0002*	0·29 [0·23;0·36] *p<0·00001*	NA	NA	NA	NA
Overall proportion vaccinated ¥								
Low (single cohort and/or low vaccination coverage (<50%)) (n=1)	0·86 [0·61;1·22]	1·73 [1·02;2·93]	1·41 [1·28;1·54]	2·08 [1·83;2·36]	1·23 [1·17;1·30]	1·55 [1·44;1·66]	1·05 [1·01;1·10]	1·23 [1·16;1·30]
Medium/High (multiple cohorts and high vaccination coverage (≥50%)) (n=8)	0·72 [0·66;0·78] *p=0·31*	0·43 [0·40;0·46] *p<0·00001*	0·88 [0·77;1·02] *P<0·00001*	0·59 [0·50;0·68] *p<0·00001*	1·11 [1·03;1·19] *p=0·02*	1·12 [1·03;1·21] *p<0·00001*	1·07 [0·99;1·15] *p=0·73*	1·24 [1·12;1·37] *p=0·90*
HPV testing utilisation (any time during study period)								
Yes (n=6)	0·75 [0·64;0·88]	0·59 [0·43;0·83]	0·97 [0·77;1·21]	0·80 [0·55;1·17]	1·12 [1·02;1·24]	1·21 [0·99;1·47]	1·04 [1·01;1·07]	1·22 [1·11;1·34]
No (n=3)	0·71 [0·67;0·75] *p=0·45*	0·41 [0·38;0·44] *p=0·03*	0·84 [0·53;1·31] *p=0·57*	0·46 [0·19;1·09] *p=0·25*	1·13 [1·11;1·15] *p=0·91*	1·10 [1·08;1·12] *p=0·36*	1·17 [1·14;1·19] *p<0·00001*	1·30 [1·28;1·32] *p=0·18*
Introduction of HPV testing in the post-vaccination period								
Yes (n=4)	0·66 [0·63;0·69]	0·44 [0·42;0·47]	0·81 [0·66;1·00]	0·63 [0·47;0·84]	1·08 [0·95;1·22]	1·13 [0·97;1·32]	1·04 [0·97;1·12]	1·21 [1·05;1·40]
No (n=5)	0·81 [0·67;1·00] *p=0·04*	0·82 [0·20;3·36] *p=0·39*	1·08 [0·88;1·32] *p=0·06*	0·76 [0·33;1·74] *p=0·68*	1·18 [1·12;1·24] *p=0·21*	1·30 [0·93;1·82] *p=0·45*	1·08 [1·00;1·18] *p=0·47*	1·27 [1·20;1·34] *p=0·54*
Older age at start of screening in the post-vaccination period								
Yes (n=6)	0·67 [0·64;0·70]	0·59 [0·43;0·83]	0·91 [0·72;1·14]	0·80 [0·55;1·17]	NA	NA	NA	NA
No (n=3)	0·85 [0·57;1·26] *p=0·24*	0·41 [0·39;0·44] *p=0·03*	0·99 [0·78;1·24] *p=0·62*	0·46 [0·19;1·09] *p=0·25*				
Longer screening intervals in the post-vaccination period								
Yes (n=4)	0·66 [0·63;0·69]	0·44 [0·42;0·47]	0·81 [0·66;1·00]	0·63 [0·47;0·84]	1·08 [0·95;1·22]	1·13 [0·97;1·32]	1·04 [0·97;1·12]	1·21 [1·05;1·40]
No (n=5)	0·82 [0·67;1·00] *p=0·04*	0·82 [0·20;3·36] *p=0·39*	1·08 [0·88;1·32] *p=0·06*	0·76 [0·33;1·75] *p=0·69*	1·18 [1·12;1·24] *p=0·21*	1·30 [0·93;1·82] *p=0·45*	1·09 [1·00;1·18] *p=0·47*	1·27 [1·20;1·34] *p=0·54*

RR = Relative Risk: incidence of CIN2+ in the post-vaccination periods (1-4 yrs or 5-8 yrs) compared to the pre-vaccination period.
CI = Confidence Interval.
* p-values indicate the statistical significance of comparisons between subgroups of studies.
¥ For studies on CIN2+, the vaccination coverage is not available specifically for study participants. We classified studies into 2 groups according to 1) whether the country/setting vaccinate a single routine cohort of girls or multiple cohorts of girls and 2) the vaccination coverage in routine age groups is < or ≥50%.

Figure S1. Changes in the prevalence of HPV infections between the pre- and post-vaccination periods, stratified by years of follow-up, and ranked by age-specific vaccination coverage for at least one dose.
A) Girls aged 13-19 years old

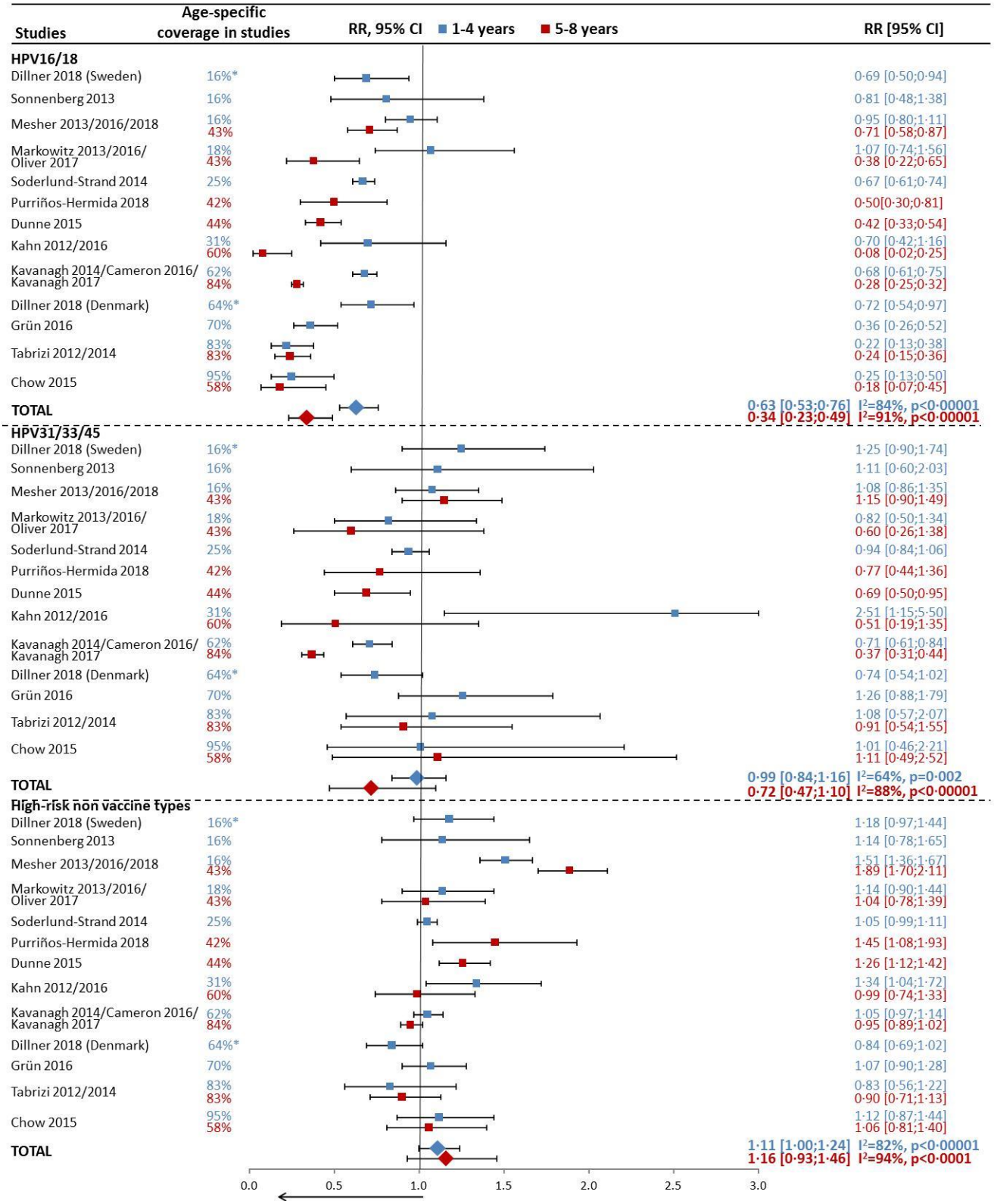


* Vaccination status of women included in the study was not available. We present the age-specific coverage at the country level.

‡ Data from Sweden not included since there was only 1 woman in the youngest age group.

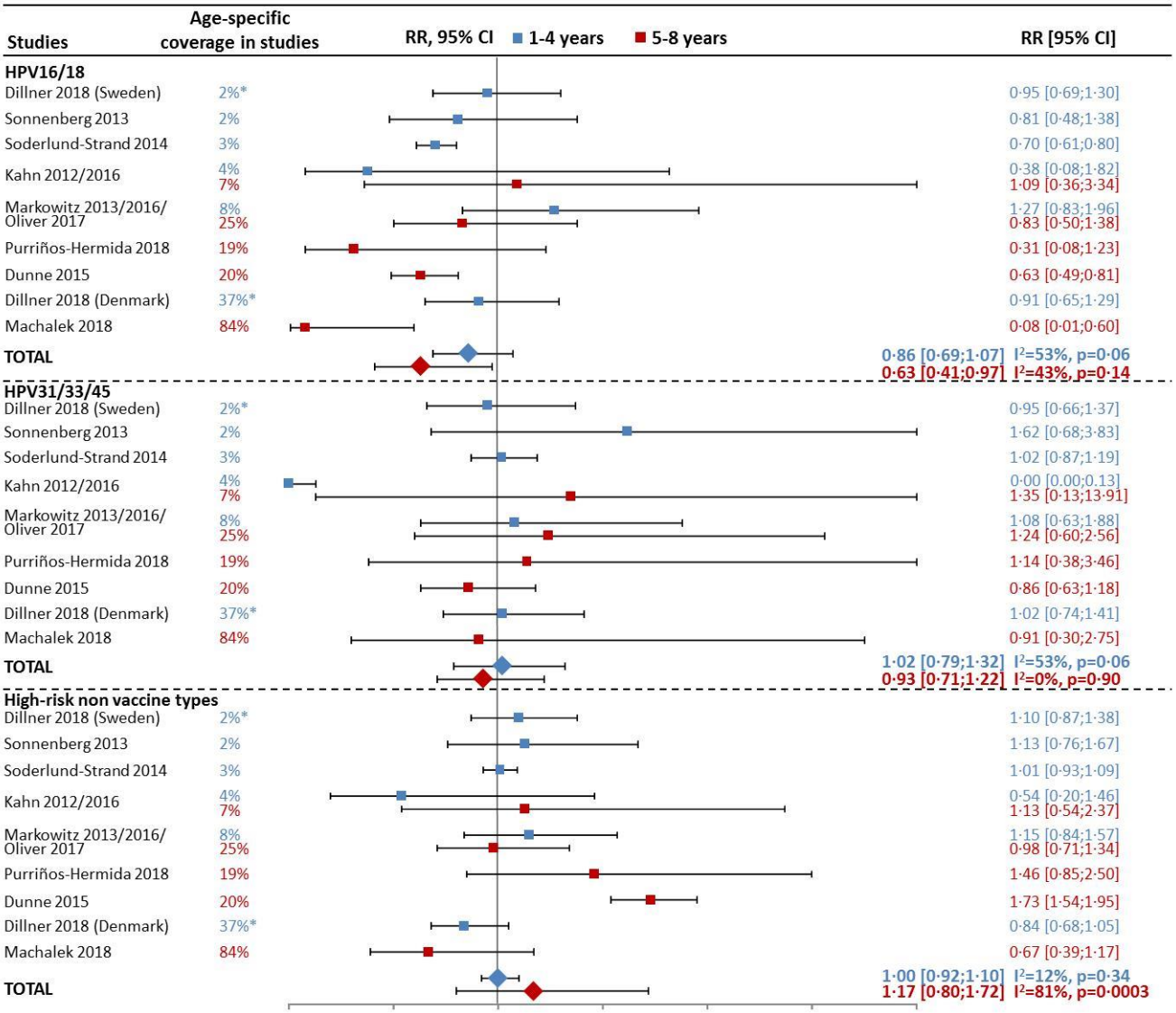
¥ Data not provided/included because they were judged potentially unreliable according to NHANES Survey analytic guidelines (prevalence estimates had a relative standard error of >30% and the sample size was below that recommended for analyses of complex survey data, by design effect and specified proportion).

B) Women aged 20-24 years old



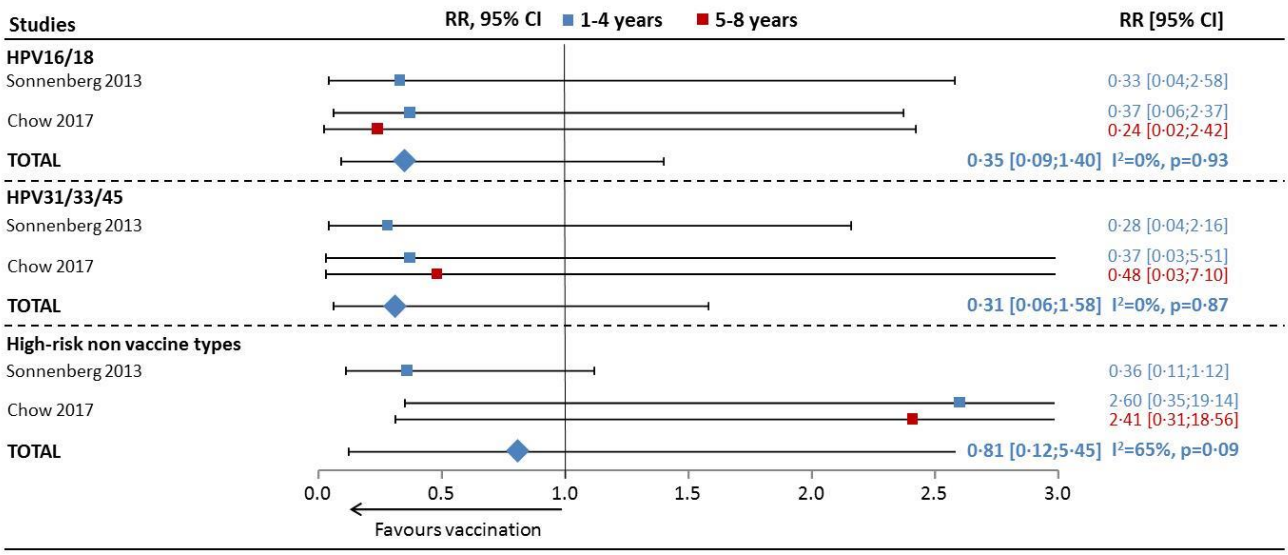
* Vaccination status of women included in the study was not available. We present the age-specific coverage at the country level.

C) Women aged 25-29 years old



* Vaccination status of women included in the study was not available. We present the age-specific coverage at the country level.

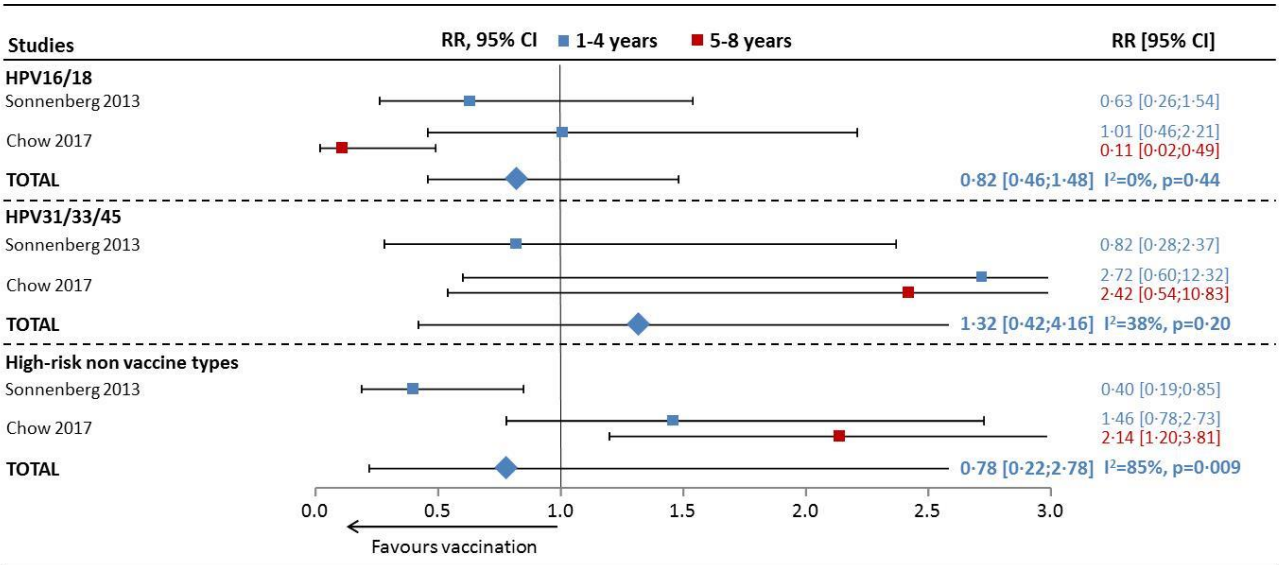
D) Boys aged 16-19 years old*‡



*****For both studies, HPV prevalence for males was estimated from urine samples, which have a lower sensitivity for detection of HPV and could lead to an underestimation of RR.

‡ Data for Sonnenberg were available for boys aged 18-19 years old.

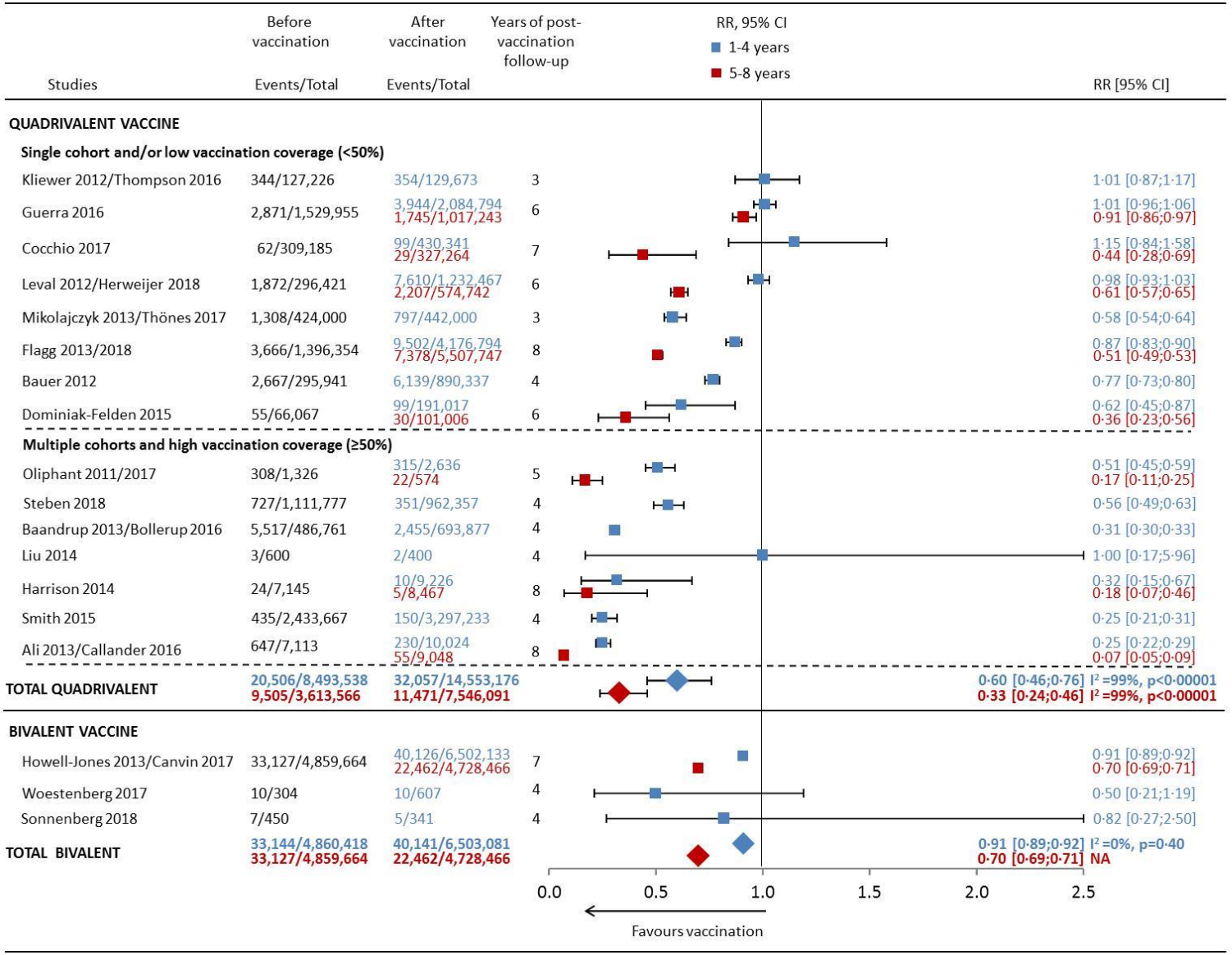
E) Men aged 20-24 years old*



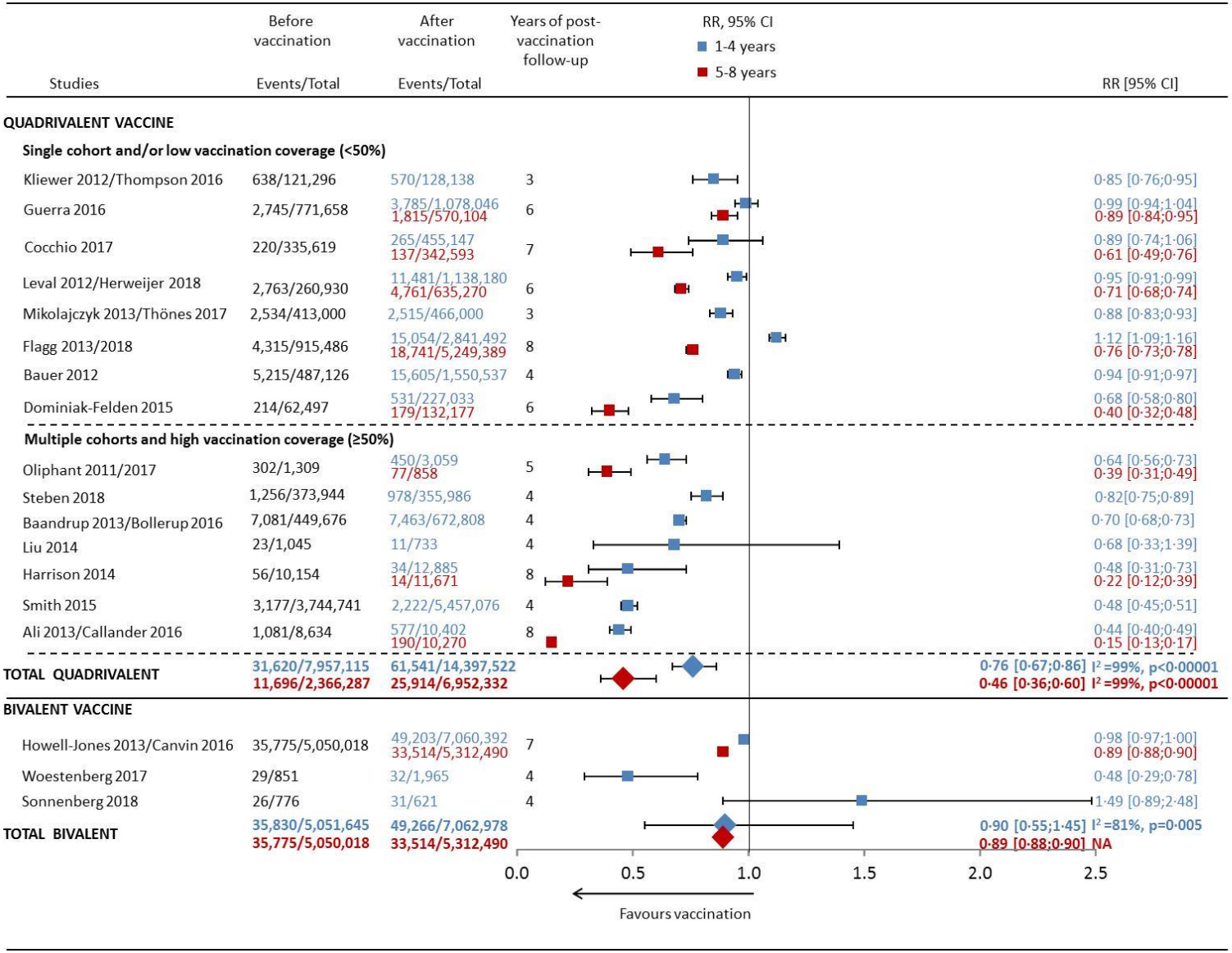
*****For both studies, HPV prevalence for males was estimated from urine samples, which have a lower sensitivity for detection of HPV and could lead to an underestimation of RR.

Figure S2. Changes in anogenital warts diagnoses between the pre- and post-vaccination periods, ranked by the number of cohorts vaccinated (single vs multiple-age cohorts) vaccination coverage.

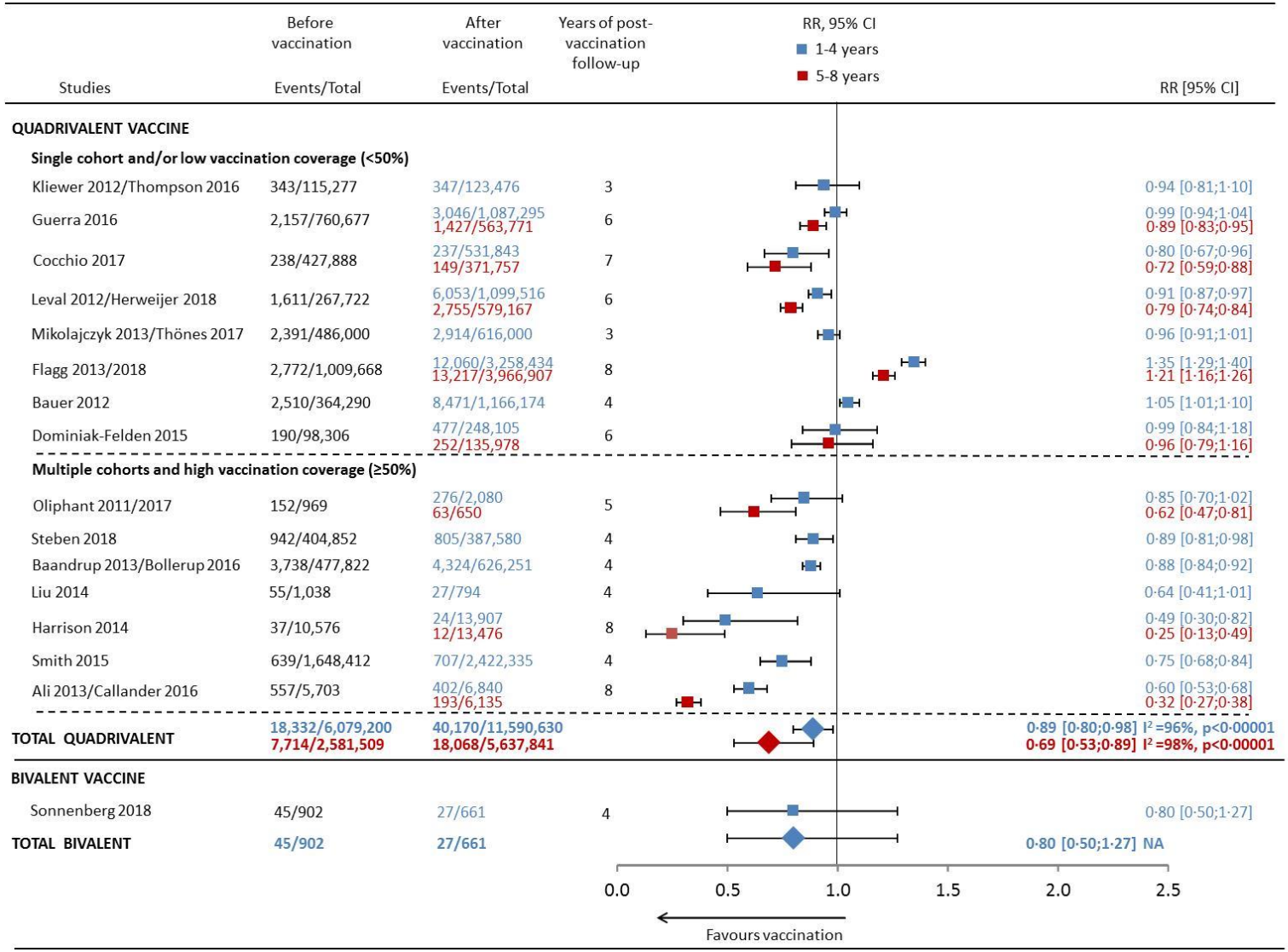
A) Girls aged 15-19 years old



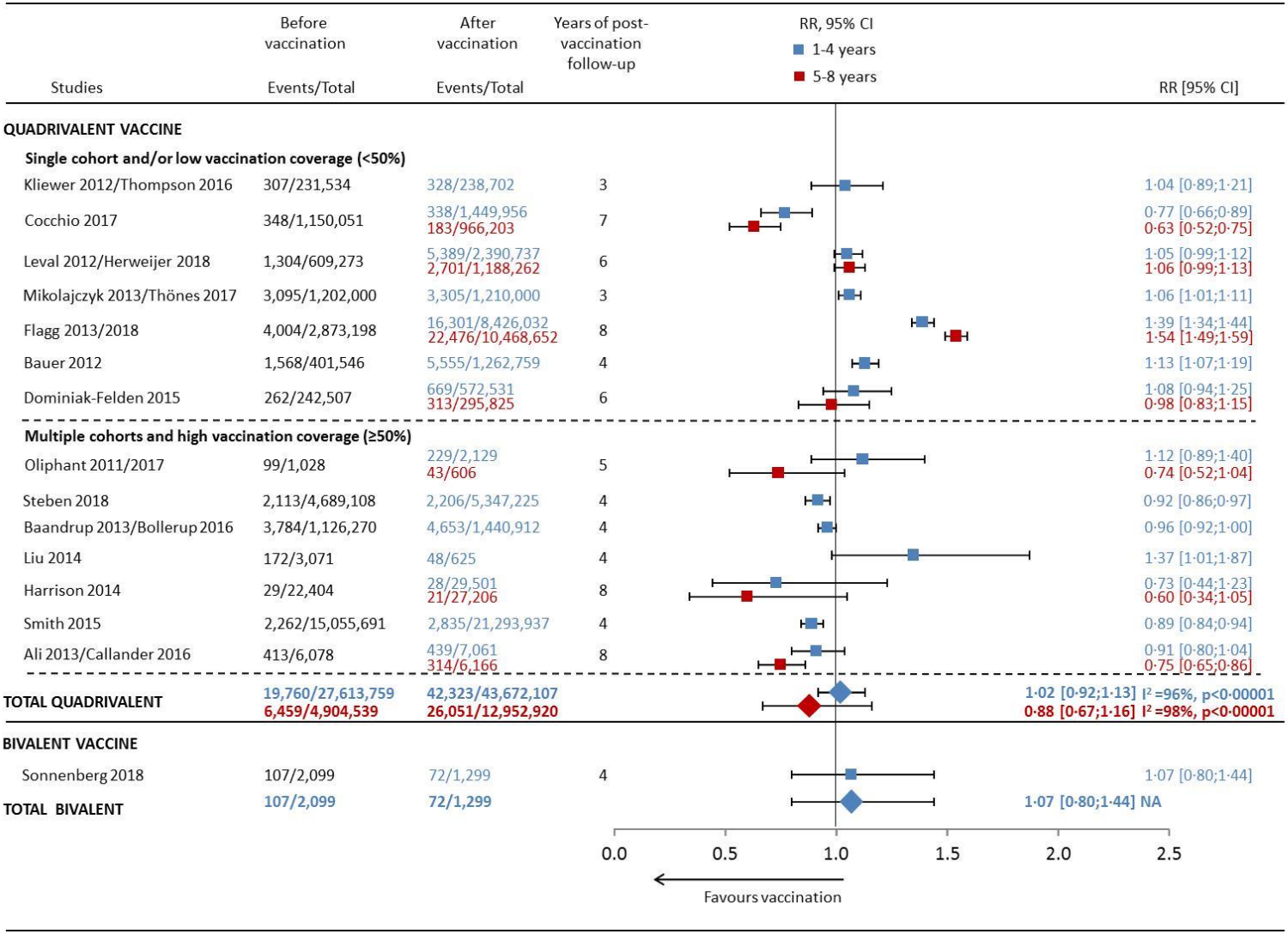
B) Women aged 20-24 years old



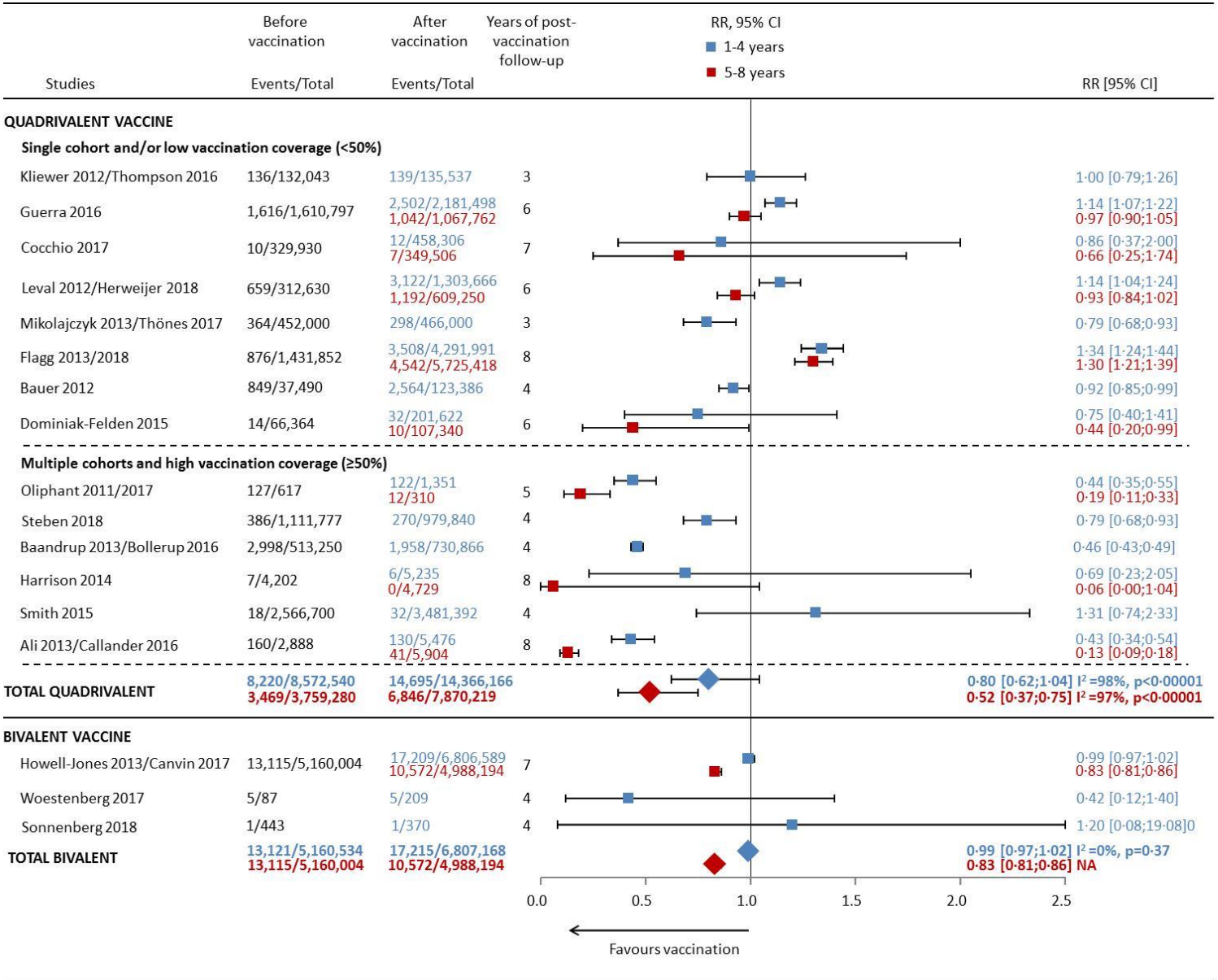
C) Women aged 25-29 years old



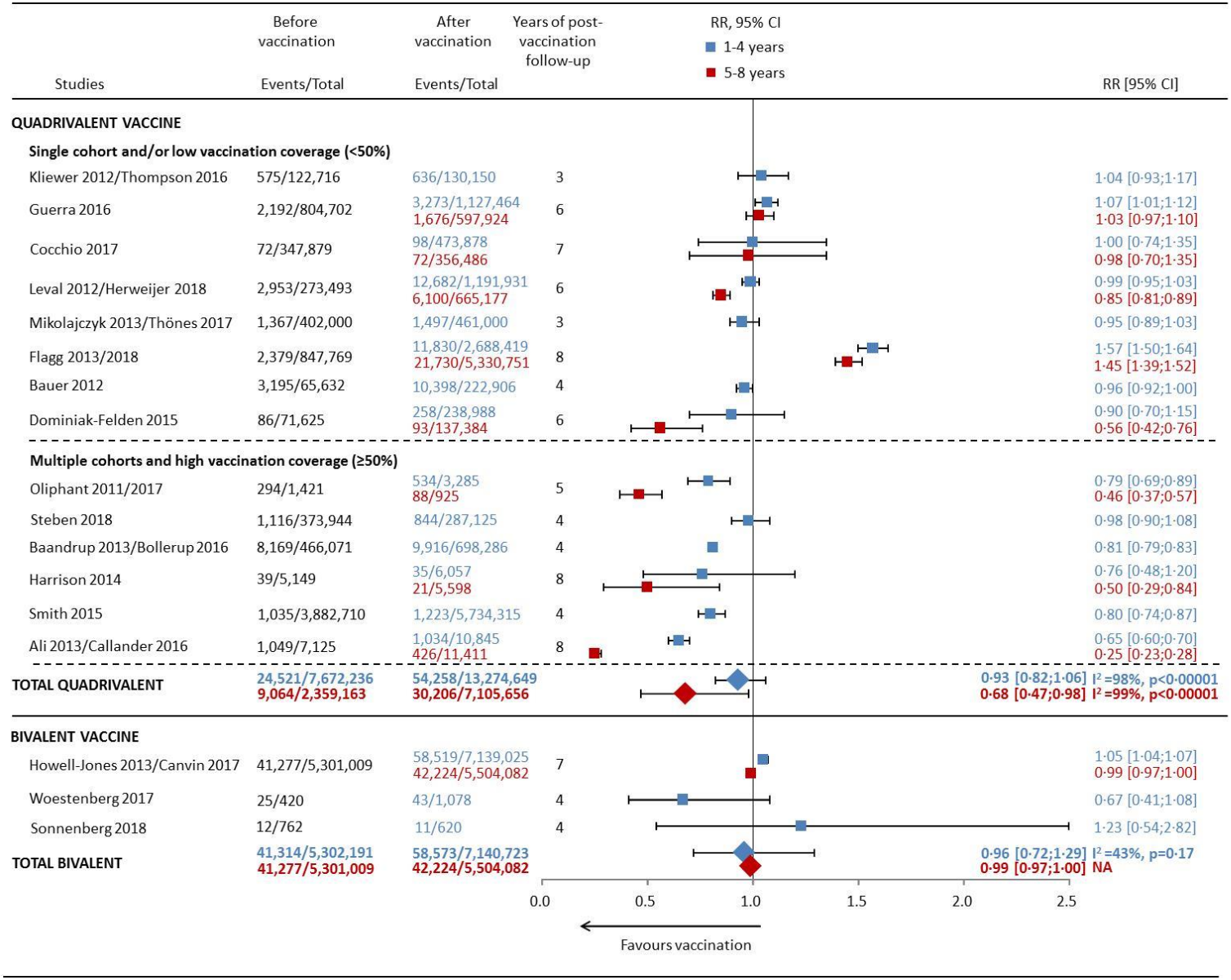
D) Women aged 30-39 years old



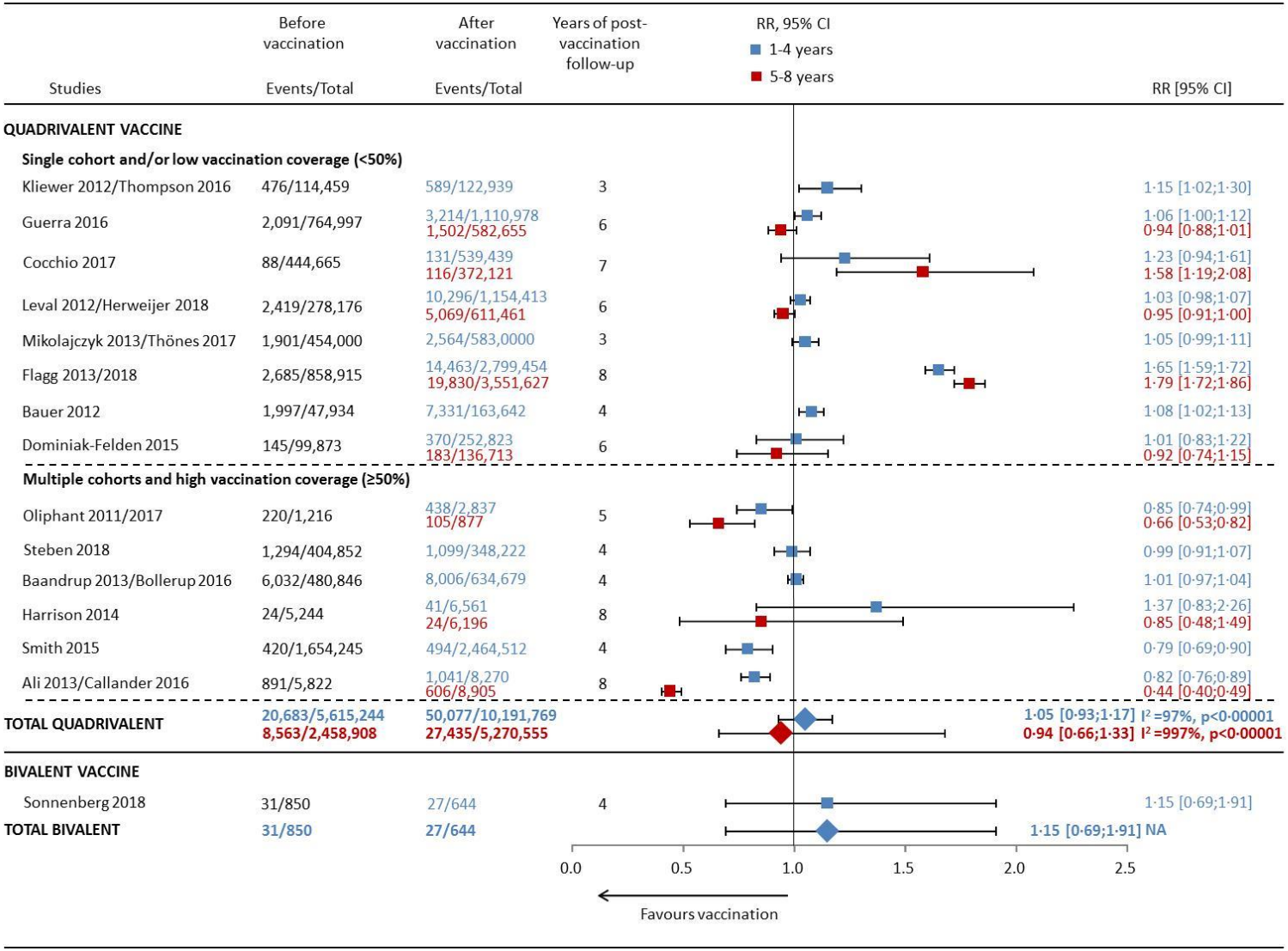
E) Boys aged 15-19 years old



F) Men aged 20-24 years old



G) Men aged 25-29 years old



H) Men aged 30-39 years old

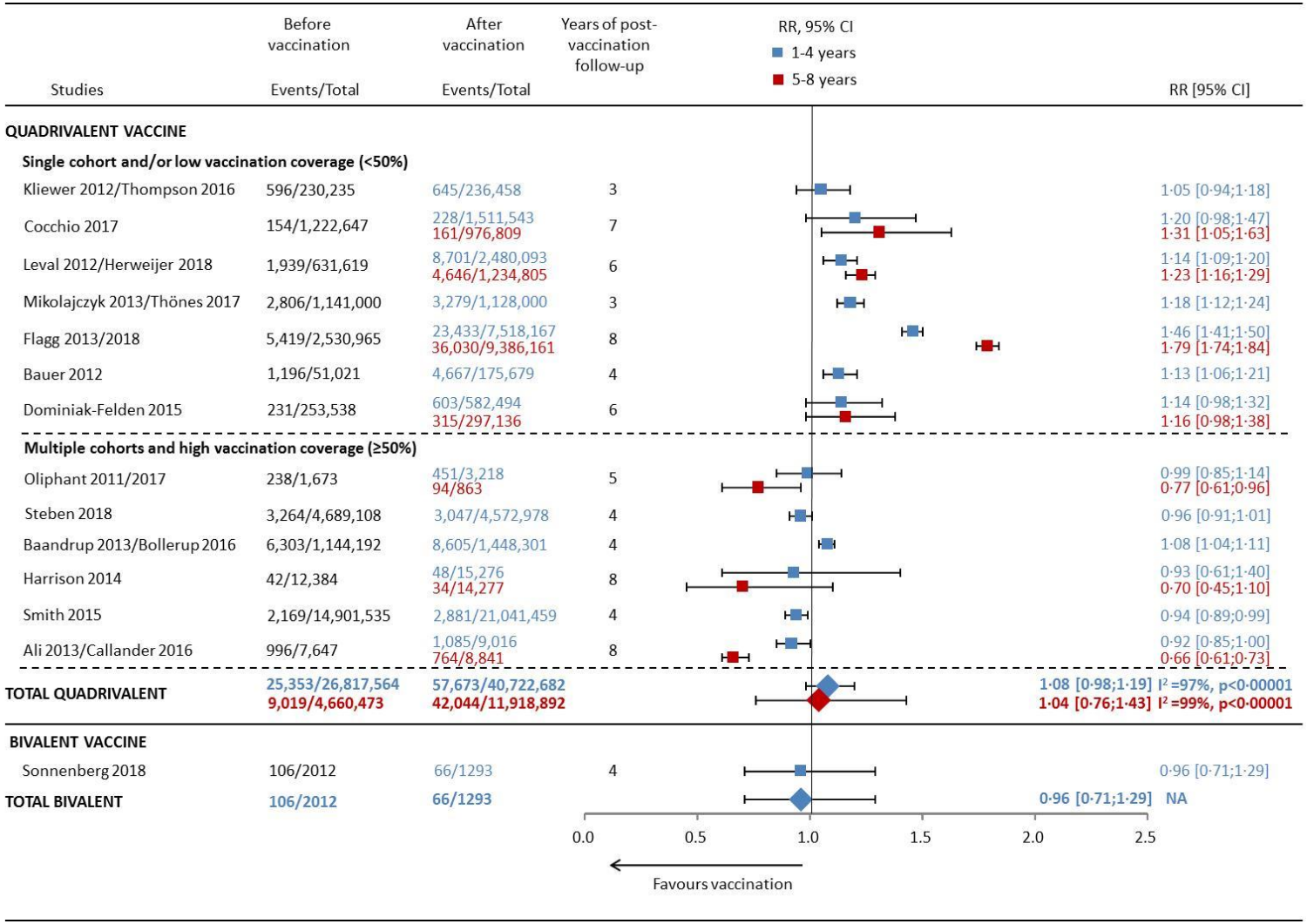
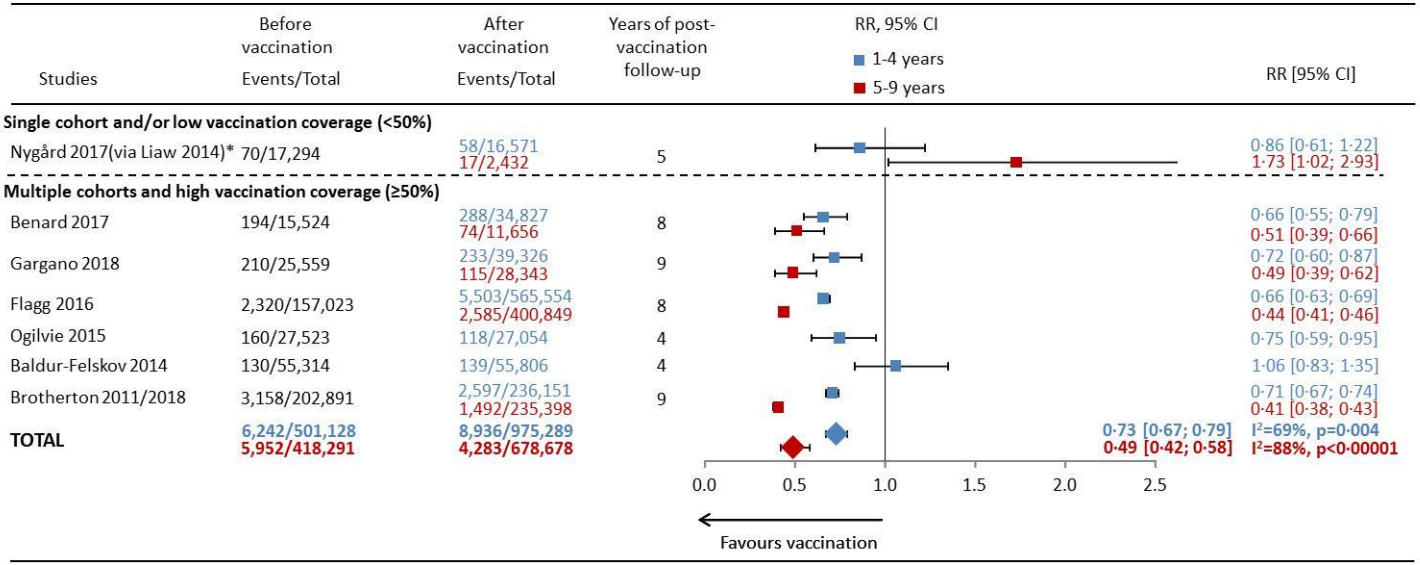
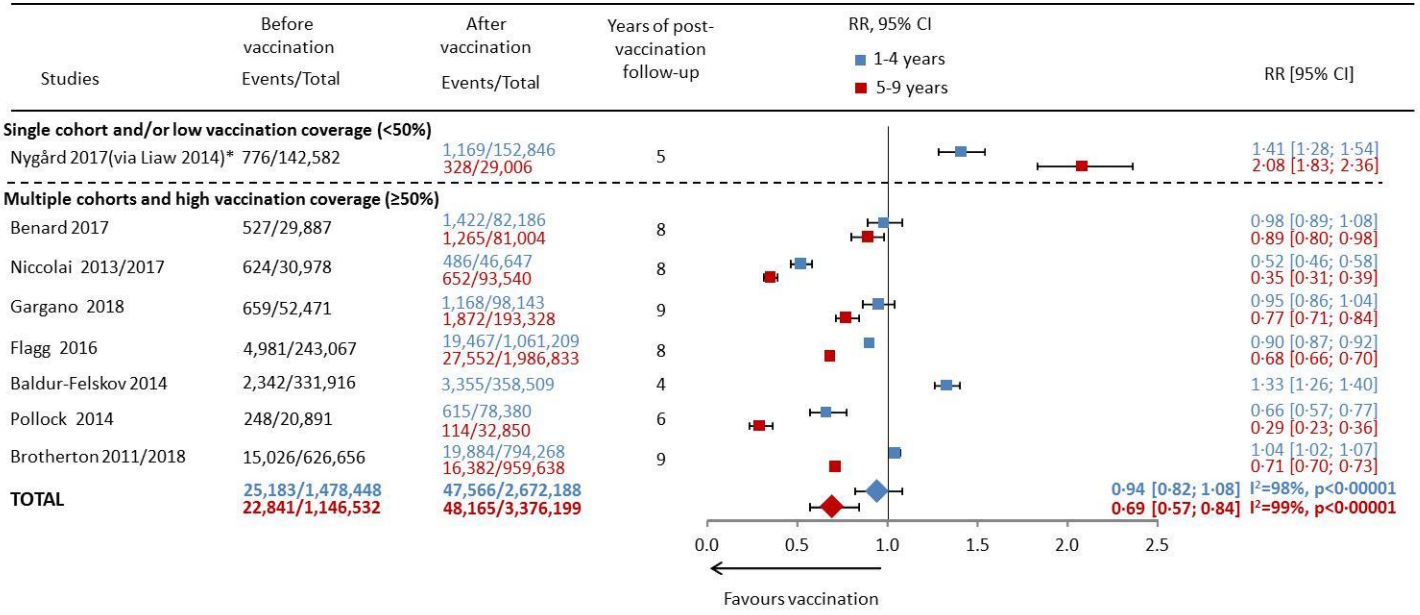


Figure S3. Changes in CIN2+ between the pre- and post-vaccination periods, ranked by the number of cohorts vaccinated (single vs multiple-age cohorts) and female vaccination coverage.

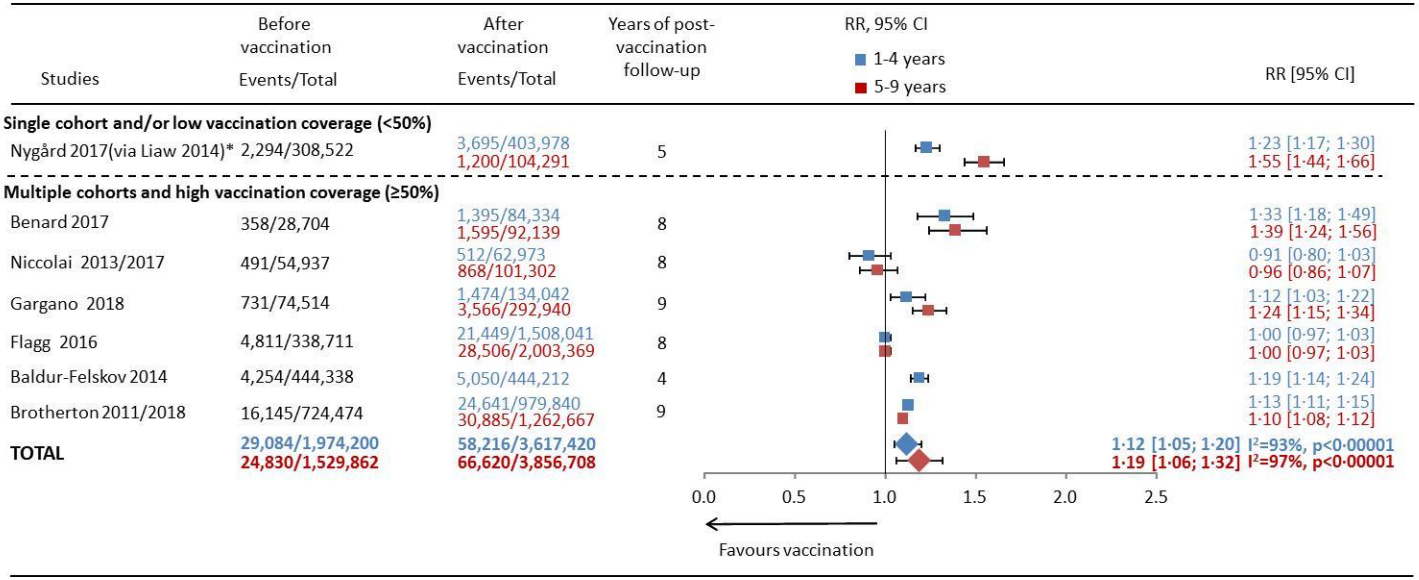
A) Girls aged 15-19 years old



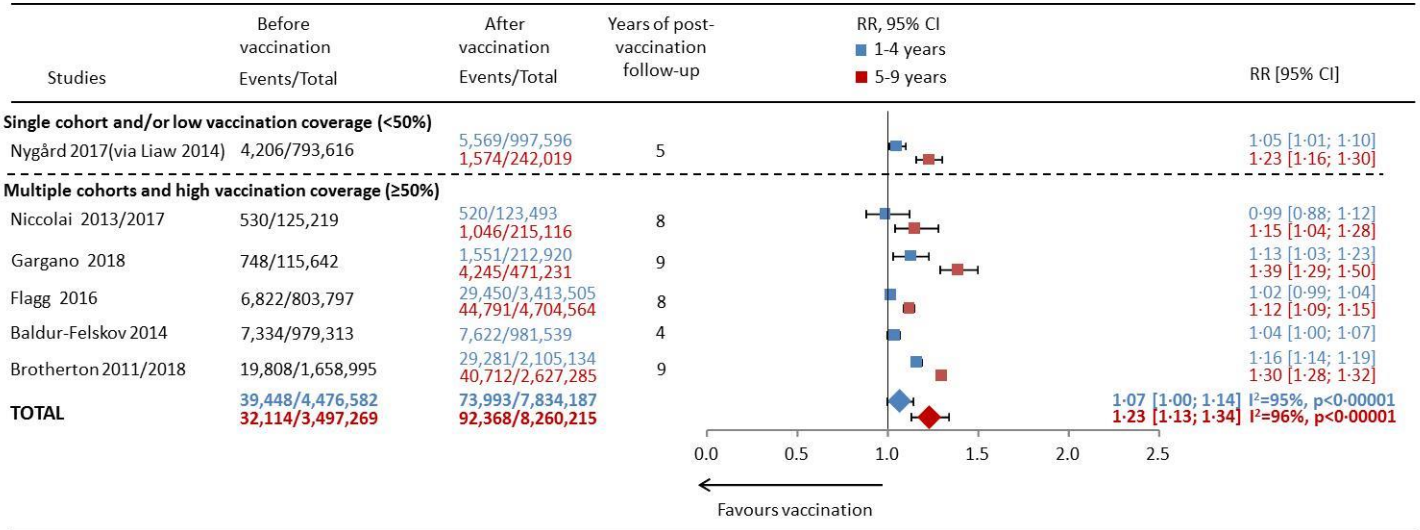
B) Women aged 20-24 years old



C) Women aged 25-29 years old



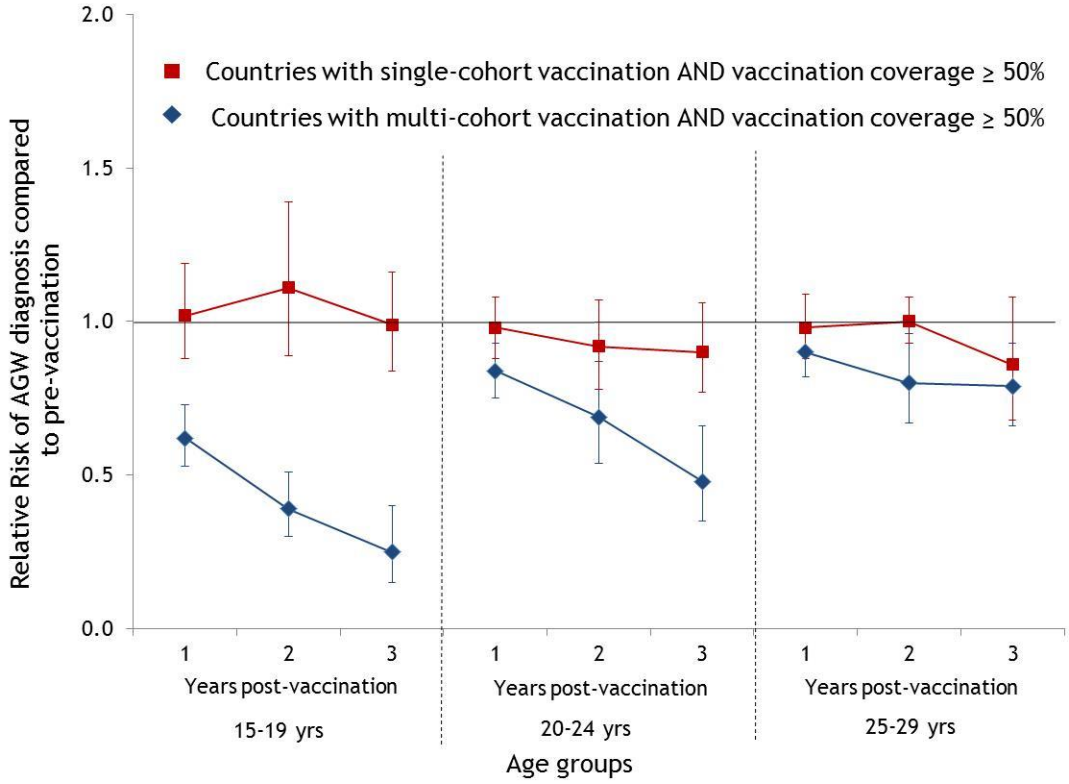
D) Women aged 30-39 years old



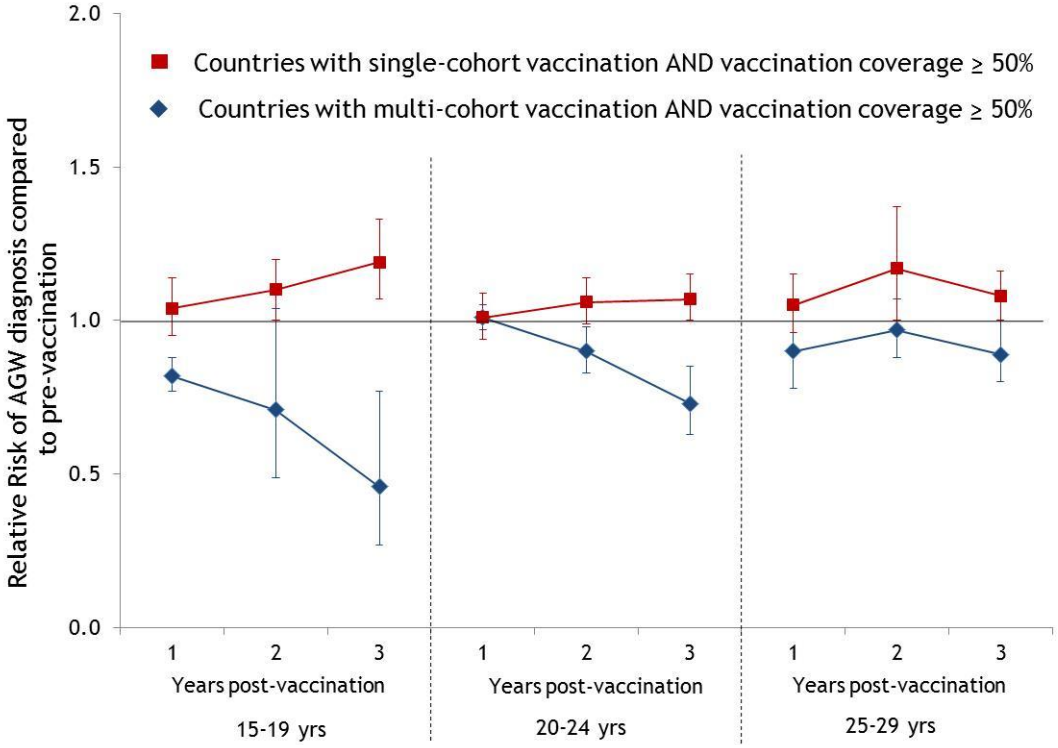
* CIN2+ data from Norway were identified in the article by Liaw et al 2014 and were provided by Mari Nygård (personal communication)

Figure S4. Sensitivity analysis: changes in anogenital warts comparing countries with multi-cohort and single-cohort vaccination, restricted to countries with high routine vaccination coverage.

A) Girls and Women



B) Boys and Men



■ Canada-Manitoba (Kliewer 2012/Thompson 2016), Canada-Ontario (Guerra 2016), Italy (Cocchio 2017)

◆ Australia (Ali 2013/Chow 2015, Smith 2015, Harrison 2014, Liu 2014); Denmark (Baandrup 2013/Bollerup 2016); New Zealand (Oliphant 2011/2017), Canada-Québec (Steben 2018)

Data were available for more than 2 studies per age group only for the first 3 years after the introduction of HPV vaccination.