Systematic review report for Question 1a

Primary PICO question 1a

For women who are positive for HPV types other than 16 or 18 and have pLSIL/dLSIL reflex liquid based cytology (intermediate risk), what is the safety and effectiveness of immediate colposcopy compared to colposcopy delayed by 12 months based on later HPV test results (assuming referral to colposcopy if any HPV positive at 12 months)?

Population	Study design	Intervention	Control	Outcome
Women who are positive for HPV types other than 16 or 18 and have pLSIL/dLSIL (ASC-US/LSIL – Bethesda) liquid based cytology (intermediate risk)	Randomised or pseudo randomized controlled trial	Immediate Colposcopy	Repeat HPV test in 12 months; Colposcopy if positive	Cervical cancer mortality Cervical cancer diagnosis Precancerous high grade lesion detection

ASC-US = Atypical squamous cells, undetermined significance (Bethesda 2001); dLSIL = definite LSIL; LSIL = Low-grade squamous intraepithelial lesion; pLSIL = possible LSIL

Randomised and pseudo-randomised controlled trials directly address primary PICO question 1a. In the event that no relevant randomised or pseudo-randomised controlled trials were identified an indirect approach was planned with a secondary PICO question focussing on benchmarking ie examining the risk of high grade lesions in women who are positive for hr-HPV types other than 16 or 18 with possible or definite LSIL (pLSIL/dLSIL) or normal cytology, and comparing these with current risk thresholds for immediate colposcopy and 12-month follow-up/later colposcopy. Definite LSIL cytology was chosen as the benchmark for the level of risk for 12-month follow-up as 12-month follow-up is recommended for definite LSIL cytology in the current guidelines. Two benchmarks were considered for the level of risk at which immediate colposcopy is recommended:

i) possible or definite HSIL (pHSIL/dHSIL) cytology (representing a benchmark from the current guidelines);

ii) HPV16/18+ (representing a benchmark from planned management under the renewed program from 2017).

Secondary PICO 1a: For women undergoing routine cervical screening what is the risk of CIN3+ for women who are positive for HPV oncogenic types other than 16 and 18 and have **pLSIL/dLSIL** cytology compared with women who have dLSIL cytology regardless of HPV status, pHSIL/dHSIL cytology regardless of HPV status, or are HPV 16/18+ regardless of cytology?

Population	Study design	Exposure	Comparator	Outcome
Women undergoing routine cervical screening	Longitudinal or cross-sectional prognostic cohort studies	Positive for HPV oncogenic types other than 16 and 18 and have pLSIL/dLSIL cytology	dLSIL or pHSIL/dHSIL or HPV 16/18+	CIN3+ CIN2+

CIN 3+ = cervical intraepithelial neoplasia grade 3 or worse; CIN 2+ = cervical intraepithelial neoplasia grade 2 or worse; dHSIL = definite HSIL; dLSIL = definite LSIL; HSIL = high-grade squamous intraepithelial lesion; LSIL = Low-grade squamous intraepithelial lesion; pHSIL = possible HSIL; pLSIL = possible LSIL

1. Methods

1.1. Search for existing relevant guidelines that could be adopted

Relevant recent (2005 onwards) guidelines were identified by scanning the citations identified by the literature search and searching the National Guideline Clearinghouse (http://guideline.gov/) and the Guidelines Resource Centre (www.cancerview.ca).

To be considered for adoption guidelines had to be directly relevant, based on systematic reviews of the evidence and meet the pre-specified criteria of scores of greater or equal to 70% for the domains rigour of development, clarity of presentation and editorial independence of the AGREE II instrument (http://www.agreetrust.org/resource-centre/agree-ii/).

1.2 Literature searches

In 2013 systematic reviews were undertaken by the NHMRC Clinical Trials Centre (CTC) to provide the evidence base for the assessment by the Medical Services Advisory Committee (MSAC) of cervical screening strategies for the renewal of the National Cervical Screening Program (http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/E6A211A6FFC29E2CCA257CED007FB678/$File/Review%20of%20Evidence%20notated%2013.06.14.pdf).

One of the CTC systematic reviews addressed the question,

What is the comparative safety and effectiveness of undertaking a colposcopy immediately in comparison to delaying the test in women who have pLSIL/dLSIL cytology and a positive HPV test? (MSAC Question 3.3).

This CTC review would include any studies relevant to primary question 1a. Given that this review was based on searches using detailed and comprehensive search strategies of multiple databases up until December 2012 and the application of precise and transparent inclusion criteria, it was used as the source of evidence up until the end of 2011. To identify subsequent relevant publications, Medline, the Cochrane Central Register of Controlled Trials (CENTRAL), Embase, PreMedline, Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessments (HTA) databases were searched for articles published from 2012 until 31st August 2015, using text terms and, where available, database-specific subject headings. In these databases searches for cervical cytology were combined with searches for HPV and colposcopy, and where possible, database-specific filters for identifying randomized controlled trials. To identify studies which considered Aboriginal and Torres Strait Islander (ATSI) peoples these searches were then coupled with search terms for ATSI peoples. A complete list of the terms used for search strategies are included as Appendix A. The Cochrane systematic review database was also searched for relevant systematic reviews or meta-analyses using the terms, HPV and colposcopy, and abstracts from the 2015 EUROGIN conference were scanned for relevant studies using the term “colpos”. Reference lists of relevant articles and guidelines were checked for additional potentially relevant articles.

To identify publications that addressed the secondary PICO question the Medline, PreMedline, Embase, and CENTRAL databases were searched for articles published from 2004 until 31st August 2015, using the same search strategies with the randomised controlled trial filters removed, and the

results of the DARE, HTA, the Cochrane systematic review database and the EUROGIN 2015 abstracts searches undertaken for the primary PICO question were reassessed against the broader inclusion criteria of the secondary PICO. A complete list of the terms used for these search strategies are included in Appendix A.

1.3. Inclusion criteria

Inclusion criteria for primary PICO question 1a

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Women undergoing screening who are positive for oncogenic HPV types other than 16 or 18 and have either pLSIL (ASC-US – Bethesda 2001) or dLSIL (LSIL - Bethesda) cytology	Conducted in referred population and do not specifically exclude women undergoing follow-up following treatment For HPV test used • In-situ hybridization or • p16 immunostaining or • Tests of viral load or • Hybrid Capture I or HPV test detected oncogenic HPV types other than those detected by the Cobas test
Study type	Screening intervention	
Study design	Randomised or pseudo-randomised controlled trials or Systematic review/meta-analyses thereof	Reviews, editorials Conference proceedings other than 2015 EUROGIN conference proceedings
Intervention	Immediate colposcopy	
Comparison	Colposcopy dependent on repeat HPV testing at 12 (+/- 6 months) with discharge to screening if hr-HPV negative	Repeat HPV test delayed to 24 months^^
Outcomes	Cervical cancer mortality or Cervical cancer diagnosis or CIN3+^ diagnosis or CIN2+ diagnosis	
Search period	1st January 2004 – 31st August 2015	
Language	English	

ASC-US = Atypical squamous cells, undetermined significance (Bethesda 2001); CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; dLSIL = definite LSIL; LSIL = Low-grade squamous intraepithelial lesion; pLSIL = possible LSIL

^ MSAC states “Cervical cancer is rare in screened populations and therefore trials designed to detect differences in incidence and mortality of cervical cancer in these populations are unfeasible. Reduced CIN3+ is considered as an acceptable proxy outcome of trials evaluating new preventative strategies (Arbyn et al. 2009).”

^^The ARTISTIC study modelling showed that the risk of CIN2+ is higher in women who are referred at 24 months instead of 12 months and is not safe for women positive for HPV at baseline.

Inclusion criteria for secondary PICO question 1a

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Women undergoing routine screening	Conducted in referred population and do not specifically exclude women undergoing follow-up following treatment
Study type	Prognostic	
Study design	Cohort: Longitudinal or cross-sectional	Case-control studies in which absolute risk cannot be calculated Reviews, editorials Conference proceedings other than 2015 EUROGIN conference proceedings
Exposure	Positive for oncogenic HPV types other than 16 or 18 and have either pLSIL (ASC-US – Bethesda 2001) and/or dLSIL (LSIL - Bethesda) cytology	For HPV test used • In-situ hybridization or • p16 immunostaining or • Tests of viral load or • Hybrid Capture I or HPV test detected oncogenic HPV types other than those detected by the Cobas test pLSIL potentially included some pHSIL eg ASC or ASCUS pre 2001
Comparator	dLSIL (LSIL) cytology regardless of HPV status or pHSIL or dHSIL cytology regardless of HPV status or HPV 16/18 positive regardless of cytology	Exposed and comparators assessed in a different age groups No exit colposcopy for all participants and follow-up differed for exposed and comparators ie reference standard of colposcopy and/or biopsy not systematically applied to both exposed and comparator Assessed only a subgroup of comparators eg HPV+ve LSIL or HPV16/18+ve LSIL
Outcomes	Cervical cancer diagnosis or CIN3+ diagnosis or CIN2+ diagnosis	
Search period	1st January 2004 – 31st August 2015	
Language	English	

ASC = Atypical squamous cells (pre Bethesda 2001- includes pHSIL); ASCUS = Atypical squamous cells, undetermined significance (pre Bethesda 2001 includes pHSIL); ASC-US = Atypical squamous cells, undetermined significance (Bethesda 2001); CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; dLSIL = definite LSIL; HSIL = High-grade squamous intraepithelial lesion; LSIL = Low-grade squamous intraepithelial lesion; pHSIL = possible HSIL pLSIL = possible LSIL

2. Results

2.1. Results of Guidelines Search

The American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology 2012 *Screening guidelines for the prevention and early detection of cervical cancer* contained potentially relevant recommendations regarding cervical screening protocols using partial HPV genotyping. These recommendations were included in the American Society for Colposcopy and Cervical Pathology's 2012 *Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors* and the American College of Obstetricians and Gynecologists' 2012 *Screening for cervical cancer guidelines*

They were not adopted as they were concerned with HPV-positive women with negative not possible LSIL or definite LSIL and thus did not specifically address the primary PICO question.

2.2. Results of Literature Search

Primary PICO

The CTC systematic review did not include any studies that met the inclusion criteria for primary PICO question 1a. Figure 1 outlines the Figure 1 outlines the steps undertaken to identify relevant published from 2012 onwards. Searches of the Medline, PreMedline, Embase and CENTRAL databases identified 156 citations, DARE and HTA databases another 22 citations, the Cochrane database of systematic reviews 73 citations and EUROGIN abstracts, 16 citations; a total of 134 citations. Titles and abstracts were examined and 15 articles were retrieved for a more detailed evaluation.

None met the inclusion criteria for the primary PICO thus **no studies were found that directly addressed the primary PICO question**.

There were no studies of Aboriginal and/or Torres Strait Islander women that met the inclusion criteria.

The retrieved articles that were not included and the reason for their exclusion are documented in Appendix C. The main reasons for exclusion were an absence of outcomes specifically for women with pLSIL or dLSIL cytology who were positive for oncogenic HPV types other than 16 or 18, did not identify for women with pLSIL or dLSIL cytology who were positive for oncogenic HPV types other than 16 or 18 or were not randomised or pseudo-randomised controlled trials.

Database or Source	Number of Citations	Number of Articles Collected	Number of Articles Included	ATSI filter results
Medline and PreMedline and CENTRAL	116	9	0	NA
Embase	40	4	0	NA
Cochrane database of systematic reviews	73	0	0	NA
HTA and DARE	22	2	0	NA
EUROGIN	16	NA	0	NA
TOTAL	**267**	**15**	**0**	**NA**

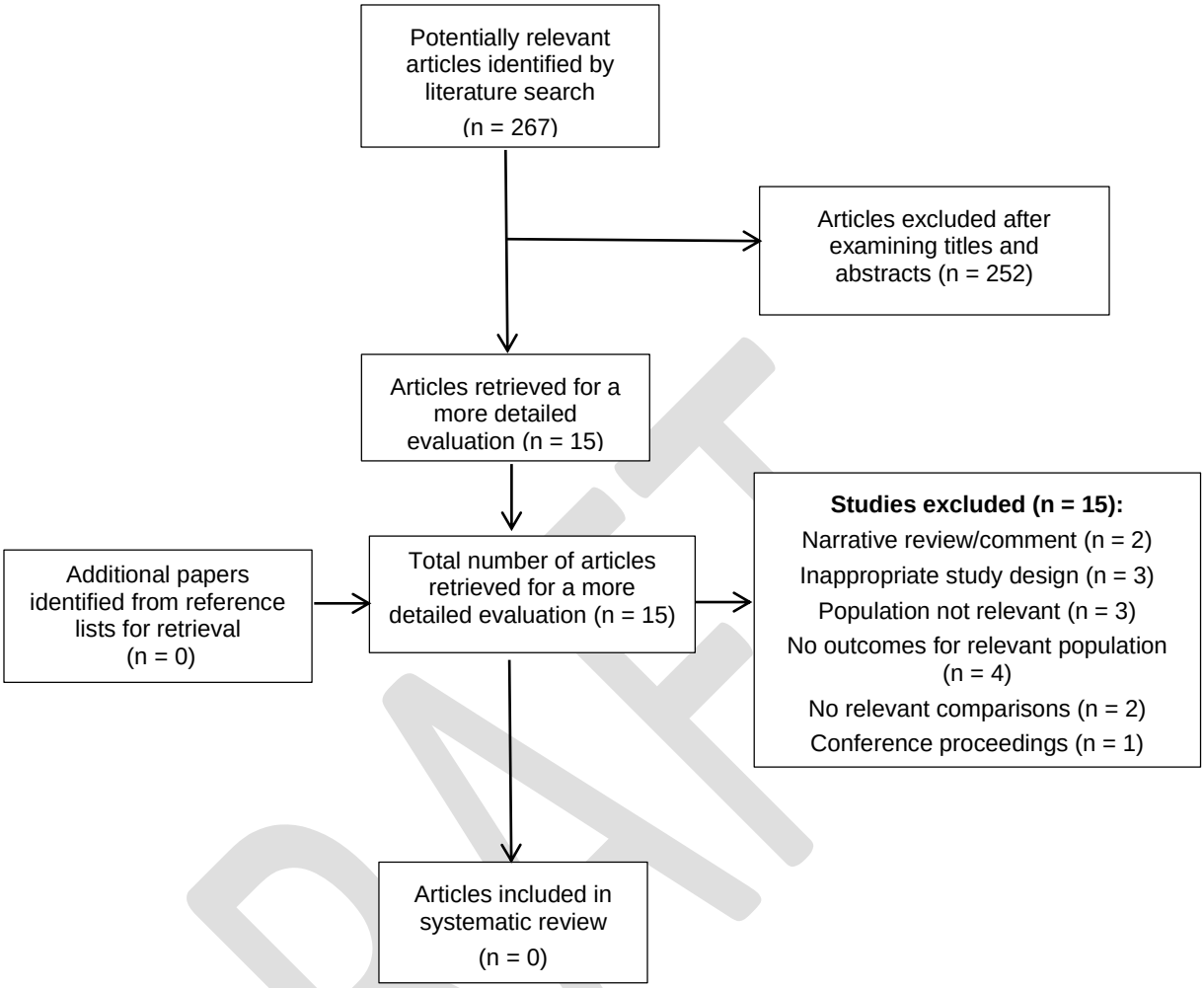

Figure 1. Process of inclusion and exclusion of studies for primary PICO questions

Secondary PICO

Searches were then broadened as pre-planned to identify studies that might address the secondary PICO question. Figure 2 outlines the steps undertaken to identify relevant articles for the systematic review. Searches of the Medline, Embase, PreMedline and CENTRAL databases with the RCT filter removed identified 2,551 citations. When combined with those identified by HTA and DARE database and 2015 EUROGIN abstracts searches, a total of 2,671 citations were identified. Titles and abstracts were examined and 413 articles were retrieved for a more detailed evaluation. An additional 9 potential citations were identified from the reference list of retrieved articles resulting in a total of 422 retrieved articles.

A total of 6 studies reported in 11 articles (5 publications for 1 study and 2 publications for another study) met the inclusion criteria for the secondary PICO question systematic review. There were no studies of Aboriginal and/or Torres Strait Islander women that met the inclusion criteria.

The retrieved articles that were not included and the reason for their exclusion are documented in Appendix C. The main reason for exclusion was an absence of outcomes for women positive for oncogenic HPV types other than 16 and /or 18 with pLSIL or dLSIL cytology.

Database or Source	Number of Citations	Number of Articles Collected	Number of Articles Included	ATSI filter results
Medline and PreMedline and CENTRAL	1,550	9 + 354	9	0
Embase	1,001	48	1	0
Cochrane database of systematic reviews	73	0	0	NA
HTA and DARE	22	2	0	NA
EUROGIN	16	NA	0	NA
snowballing	NA	9	1	NA
TOTAL	**2,662**	422	**11**	**0**

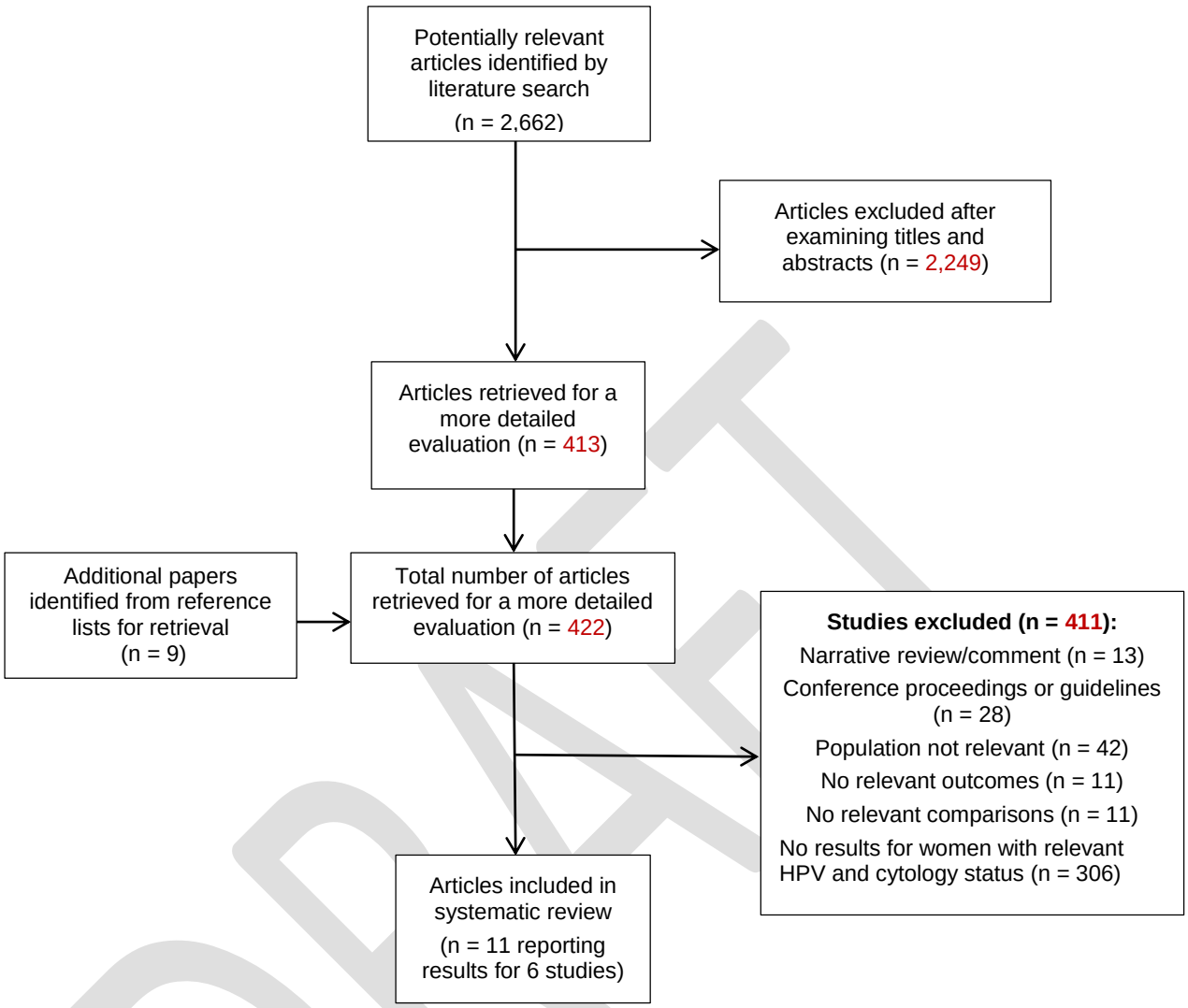

Figure 2. Process of inclusion and exclusion of studies for secondary PICO

2.3 Characteristics of included studies addressing secondary PICO question 1a

Table 1: Characteristics of **longitudinal studies** reporting risks of high grade cervical neoplasia or worse with differing baseline HPV statuses and cytology types

Study	Study design	Population	Exposure	Comparator	Outcome	Comments
ASCUS-LSIL Triage Study (ALTS) Gage 2013 (USA)	Prospective cohort Longitudinal	Participants in a randomised controlled trial recruited between 1997-1998 at 4 clinical centres with LSIL N = 1,572 with no known history of ablative or excisional therapy to the cervix Randomised to immediate colposcopy regardless (n = 673) or if HPV positive or HSIL at enrolment (85% of n = 224), or if HSIL at enrolment (14% of n = 675) Aged 18 – 88 years Mean age = 25 years	LSIL positive for hr-HPV types other than 16 or 18	LSIL	CIN3+ CIN2+ Follow-up = 2 years	Post hoc analysis Active follow-up: Cytology at 6, 12 and 18 months and colposcopy referral if HSIL Exit colposcopy at 24 months (~80% underwent exit colposcopy) Colposcopically-directed biopsies taken of any suspicious lesion and endocervical curettage if transformation zone or extent of lesion not adequately visualised ASCUS included ASC-US and ASC-H Histological diagnoses of CIN2+ treated with LEEP HPV status for clinical management determined by HC2 test (13 hr-HPV types) HPV genotyping for analysis undertaken using Line Blot Assay (14 hr-HPV types)
Kaiser Permanente Portland Castle 2012 *(USA)*	Prospective cohort Longitudinal	Women presenting for routine annual cytology screening between 1989-1990 recruited at Kaiser Permanente Portland aged $\geq$ 16 years who had no previous history of HSIL/CIN2+ or hysterectomy **18-years follow-up** N = 19,512 with valid baseline tests At enrolment NILM N = 18,450 ASCUS N = 630 LSIL N = 381 HSIL N = 51 Mean age = 35.8 years	LSIL positive for hr-HPV types other than 16 or 18	LSIL	CIN3+ CIN2+ Follow-up = 18 years	Only some participants underwent colposcopy ie those with a specific abnormal cytology ASCUS included ASC-US and ASC-H Follow-up and indications for colposcopy as per screening program but not specified and may have varied as participants were enrolled in 1989–1990 thus comparisons could only be made within a given grade of cytology Women who were treated for lesions were censored Authors note substantial losses to follow-up and as a result risk estimates maybe underestimated HPV testing undertaken using HC2 (13 hr-HPV types) however authors note sensitivity may be impaired due to using lavage rather than exfoliation to collect cells Partial genotyping undertaken using HPV16 and 18 RNA probes

ASC = atypical squamous cells; ASCUS = atypical squamous cell, undetermined significance (pre Bethesda 2001); CIN 3+ = cervical intraepithelial neoplasia grade 3 or worse; CIN 2+ = cervical intraepithelial neoplasia grade 2 or worse; HC2= Hybrid Capture II; HSIL = high-grade squamous intraepithelial lesion; LSIL = low -grade squamous intraepithelial lesion; NILM = negative for intraepithelial lesion or malignancy

Table 2: Characteristics of **cross-sectional studies** reporting risks of high grade cervical neoplasia or worse with differing baseline HPV statuses and cytology types

Study	Study design	Population	Exposure	Comparator	Outcome	Comments
ATHENA Castle 2011; Cox 2013; Cuzick 2013; Stoler 2011; Wright 2011 (USA)	Prospective cohort Cross-sectional	Women presenting for routine screening between 2008-2009 recruited at 61 clinical centres who had not received treatment for CIN in last 12 months aged ≥ 21 years N = 45,864 with valid tests At enrolment ASC-US N = 1,918 LSIL N = 1,084 *Subgroups:* Aged ≥ 25 years N = 40,901 with valid tests Aged ≥ 30 years N = 34,254 eligible Mean age = 44.7 years NILM N = 32,260	NILM positive for hr-HPV types other than 16 or 18 OR ASC-US positive for hr-HPV types other than 16 or 18 OR LSIL positive for hr-HPV types other than 16 or 18	ASC-US OR LSIL OR Positive for hr-HPV types 16 or 18 OR ASC-H OR HSIL	CIN3+ CIN2+	Colposcopy if: aged ≥ 25 years and cytology ≥ ASC-US or HPV positive on Amplicor or Linear Array HPV test aged 21 -24 years and cytology ≥ ASCUS If no lesions seen on colposcopy a random biopsy was taken. Endocervical curettage if unsatisfactory colposcopy A random sample of women with NILM cytology and HPV negative underwent colposcopy At enrolment samples taken for liquid-based cytology and HPV testing and genotyping HPV testing and partial genotyping undertaken included Cobas HPV test (14 hr-HPV types) Amplicor test was more sensitive than Cobas test
Cervista Trial Einstein 2010 & 2011 (USA)	Prospective cohort Cross-sectional	Women presenting for routine screening recruited between 2006 and 2007 at 89 sites aged ≥ 18 years referred for colposcopy as a result of an ASC-US cytology N = 1,514 Mean age = 33.7 years N = 1,312 with HPV partial genotyping and colposcopy results	ASC-US positive for hr-HPV types other than 16 or 18	ASC-US	CIN3+ CIN2+	Colposcopy if ASC-US cytology Biopsy at discretion of colposcopist HPV testing undertaken on residual cytology samples HPV testing undertaken using Cervista HPV HR (14 hr-HPV types) test and Cervista HPV 16/18 test
CLEAR Castle 2015 (USA)	Prospective cohort Cross-sectional	Women presenting for routine screening recruited at 19 clinical centres aged ≥ 21 years referred for colposcopy as a result of an ASC-US cytology who had no previous history of cervical disease or an abnormal cervical cytology in last 12 months N = 988 Mean/median age not reported	ASC-US positive for hr-HPV types other than 16 or 18	ASC-US	CIN2+	Excluded women who reported prior vaccination against HPV Colposcopy if ASC-US cytology Biopsied each quadrant: directed biopsy if lesion seen , random biopsy if no lesion seen At colposcopy (mean 33.7 days after screening test) samples taken for HPV testing and genotyping HPV testing undertaken included Cobas HPV test (14 hr-HPV types)

Predictors 1 & 2 Mesher 2013 (UK)	Prospective cohort Cross-sectional	Women presenting for routine screening aged 18 - 67 years who had not received treatment for CIN referred for colposcopy as a result of a borderline or single mildly dyskaryotic smear N = 1,228 Median age = 29 years *Subgroup:* Participants with mild dyskaryosis and tested with Cobas test N = 486	Mild dyskaryosis positive for hr-HPV types other than 16 or 18	Mild dyskaryosis	CIN3+ CIN2+	Colposcopy if borderline or mildly dyskaryotic cytology Biopsy at discretion of colposcopist 63% of those referred with borderline cytology had multiple borderline smears – not included At colposcopy samples taken for repeat cytology, HPV testing and genotyping HPV testing and partial genotyping undertaken included Cobas HPV test (14 hr-HPV types) **Included histology results within 9 months of initial colposcopy – follow-up not described** – assumed colposcopies in subsequent 9 months rare and not based on cytology or HPV status and that results reflect those for baseline colposcopy not 9 months follow-up

ASC = atypical squamous cells; ASC-H = atypical squamous cells, cannot exclude HSIL; ASC-US = atypical squamous cell, undetermined significance (Bethesda 2001); ASCUS = atypical squamous cell, undetermined significance (pre Bethesda 2001); CIN 3+ = cervical intraepithelial neoplasia grade 3 or worse; CIN 2+ = cervical intraepithelial neoplasia grade 2 or worse; HC2=

2.4 Assessment of risk of bias of included studies addressing secondary PICO question 1a

Methodological quality of included cohort studies is described in Tables 3-4.

Table 3: Risk of bias for the included **cohort** studies (n = 6)

Quality Category	N (%)
Selection of the exposed and non-exposed cohorts	
Low risk of bias	6 (100)
Moderate risk of bias	0 (0)
High risk of bias	0 (0)
Measurement of exposure	
Low risk of bias	3 (50.0)
Moderate risk of bias	3 (50.0)
High risk of bias	0 (0)
Measurement of outcome	
Low risk of bias	4 (66.7)
Moderate risk of bias	1 (16.7)
High risk of bias	1 (16.7)
Participation rate	
Low risk of bias	6 (100)
Moderate risk of bias	0 (0)
High risk of bias	0 (0)
Completeness of follow-up	
Low risk of bias	3 (50.0)
Moderate risk of bias	2 (33.3)
High risk of bias	1 (16.7)
Accuracy of dates of outcome or censoring	
Low risk of bias	5 (83.3)
Moderate risk of bias	1 (16.7)
Difference in follow-up between exposed and non-exposed	
Low risk of bias	6 (100)
Moderate risk of bias	0 (0)
High risk of bias	0 (0)
Difference in missing data for exposure between those with or without the outcome	
Low risk of bias	6 (100)
Moderate risk of bias	0 (0)
High risk of bias	0 (0)
Comparability of exposed and non-exposed cohorts with respect to potentially important confounding variables	
Low risk of bias	0 (0)
Moderate risk of bias	0 (0)
High risk of bias	6 (100)

Table 4: Risk of bias for the included **cohort** studies (n = 6)

	ATHENA	Castle 2013	Castle 2012 (KP Portland)	Einstein 2010	Gage 2013 (ALTS)	Mesher 2013
Selection of the exposed and non-exposed cohorts	Low	Low	Low	Low	Low	Low
Measurement of exposure	Moderate	Low	Moderate	Low	Moderate	Low
Measurement of outcome	Low	Low	Moderate	Low	High	Low
Participation rate	Low	Low	Low	Low	Low	Low
Completeness of follow-up	Moderate	Low	High	Low	Moderate	Low
Accuracy of dates of outcome or censoring	Low	Low	Moderate	Low	Low	Low
Difference in follow-up between exposed and non-exposed	Low	Low	Low	Low	Low	Low
Difference in missing data for exposure between those with or without the outcome	Low	Low	Low	Low	Low	Low
Comparability of exposed and non-exposed cohorts with respect to potentially important confounding variables[1]	High	High	High	High	High	High
Overall risk of bias	**High**	**High**	**High**	**High**	**High**	**High**

[1]*Age, smoking and vaccination status*

Key to overall rating
High risk of bias – high risk of bias in any domain
Moderate risk of bias – moderate or low risk of bias in all domains
Low risk of bias – all domains low risk of bias

2.5 Results from included studies addressing secondary PICO question 1a

I CIN3+ DETECTION

Longitudinal studies

Table 5 Results of longitudinal studies comparing risk associated with differing HPV statuses and cytology types: **cervical intraepithelial neoplasia grade 3 or worse**

Study	Population	Cytology	HPV status	N	Length of follow-up	CIN3+ n	CIN3+ risk % (95% CI)
Women aged ≥ 30 years							
ALTS (Gage 2013)	Women with genotyping results	LSIL	Hr-HPV other than 16/18 positive	94	2 years	8	8.5
		LSIL	**Positive or negative**	**261**		**33**	**12.6**
Women aged 18-29 years							
ALTS (Gage 2013)	Women with genotyping results	LSIL	Hr-HPV other than 16/18 positive	581	2 years	58	10.0
		LSIL	**Positive or negative**	**1,291**		**200**	**15.5**
Women aged ≥ 18 years							
ALTS (Gage 2013)	Women with genotyping results	LSIL	Hr-HPV other than 16/18 positive	675	2 years	66	9.8
		LSIL	**Positive or negative**	**1,552**		**233**	**15.0**
Women aged ≥ 16 years							
Kaiser Permanente Portland (Castle 2012)	Women with valid tests including those who had not undergone colposcopy – assume same follow-up for all LSIL	LSIL	Hr-HPV other than 16/18 positive	183	18 years	NR	2.7 (1.1 - 6.5)*
		LSIL	**Positive or negative**	**381**	**18 years**	**NR**	**7.4 (5.1 - 10.7)***

CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; CI = confidence interval; hr-HPV = high risk HPV type; LSIL = low -grade squamous intraepithelial lesion; NR = not reported
Bold indicates results for benchmark: LSIL (Bethesda) equivalent to definite LSIL benchmark for follow-up tests at 12 months
** Cumulative incidence rate calculated using Kaplan Meier method*

Cross-sectional studies

Table 6 Results of longitudinal studies comparing risk associated with differing HPV statuses and cytology type: **cervical intraepithelial neoplasia grade 3 or worse**

Study	Population	Cytology	HPV status	N	CIN3+ n	CIN3+ risk % (95% CI)
Women aged ≥ 50 years						
ATHENA (Cuzick 2013)	Women who underwent colposcopy with valid results for all 3 HPV tests and valid	LSIL	Hr-HPV other than 16/18 positive	26	1	3.8
		LSIL	**Positive or negative**	**70**	**2**	**2.9**
Women aged ≥ 40 years						
ATHENA (Cox 2013; Cuzick 2013)	Women who underwent colposcopy with valid results for all 3 HPV tests and valid	LSIL	Hr-HPV other than 16/18 positive	91	7	7.7
		LSIL	**Positive or negative**	**220**	**10**	**4.5**
Women aged ≥ 30 years						
ATHENA (Cox 2013; Cuzick 2013; Wright 2011)	Women who had undergone all tests and a colposcopy	ASC-US	Hr-HPV other than 16/18 positive	172	10	5.8
		Any including NILM	**Hr-HPV 16/18 positive**	**580**	**101**	**17.4**
	Women who underwent colposcopy with valid results for all 3 HPV tests and valid	NILM	Hr-HPV other than 16/18 positive	NR	NR	2.4 (1.6 - 3.3)
		LSIL	Hr-HPV other than 16/18 positive	195	13	6.7
		LSIL	**Positive or negative**	**438**	**27**	**6.2**
Women aged ≥ 25 years						
ATHENA (Castle 2011; Cuzick 2013)	Hr-HPV positive women with valid results for all tests who underwent colposcopy with valid biopsy	ASC-US	Hr-HPV other than 16/18 positive	255	15	5.9
		LSIL	Hr-HPV other than 16/18 positive	301	17	5.6
		LSIL	**Positive or negative**	**656**	**38**	**5.8**
		Any including NILM	**Hr-HPV 16/18 positive**	**966**	**150**	**15.5 (14.0-17.1)**

Women aged ≥ 21 years						
ATHENA (Stoler 2011; Cuzick 2013)	Women with valid results for all tests who underwent colposcopy with valid biopsy	ASC-US	Hr-HPV other than 16/18 positive	338	15	4.4 (2.7-7.2)
		ASC-US	Positive or negative	1,578	46	2.9
		LSIL	Hr-HPV other than 16/18 positive	436	17	3.9 (2.4-6.2)
		LSIL	**Positive or negative**	**925**	**48**	**5.2**
		ASC-H	**Positive or negative**	**53**	**18**	**34.0**
		HSIL	**Positive or negative**	**126**	**58**	**46.0**
Women aged ≥ 18 years						
Cervista (Einstein 2010 & 2011)	Women with results for all tests and colposcopy	ASC-US	Hr-HPV other than 16/18 positive	500	5	1.0
		ASC-US	Positive or negative	1,312	22	1.7
Predictors 1 & 2 (Mesher 2013)	Women with results for Cobas test and colposcopy	Mild dyskaryosis	Hr-HPV other than 16/18 positive	239	10	4.2
		Mild dyskaryosis	**Positive or negative**	**486**	**35**	**7.2**

ASC-H = atypical squamous cells, cannot exclude HSIL; ASC-US = atypical squamous cell, undetermined significance (Bethesda 2001); CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; CI = confidence interval; HSIL = high-grade squamous intraepithelial lesion; hr-HPV = high risk HPV type; LSIL = low -grade squamous intraepithelial lesion; NILM = negative for intraepithelial lesion or malignancy

Bold indicates results for benchmarks: LSIL (Bethesda) and mild dyskaryosis equivalent to definite LSIL benchmark for follow-up tests at 12 months; HSIL (Bethesda), ASC-H (Bethesda 2001) and Hr-HPV 16/18 positive benchmarks for immediate colposcopy

II CIN2+ DETECTION

Longitudinal studies

Table 7 Results of longitudinal studies comparing risk associated with differing HPV statuses and cytology types: **cervical intraepithelial neoplasia grade 2 or worse**

Study	Population	Cytology	HPV status	N	Length of follow-up	CIN2+ n	CIN2+ risk % (95% CI)
Women aged ≥ 30 years							
ALTS (Gage 2013)	Women with genotyping results	LSIL	Hr-HPV other than 16/18 positive	94	2 years	22	23.4
		LSIL	**Positive or negative**	**261**		**53**	**20.3**
Women aged 18-29 years							
ALTS (Gage 2013)	Women with genotyping results	LSIL	Hr-HPV other than 16/18 positive	581	2 years	122	21.0
		LSIL	**Positive or negative**	**1,291**		**340**	**26.3**
Women aged ≥ 18 years							
ALTS (Gage 2013)	Women with genotyping results	LSIL	Hr-HPV other than 16/18 positive	675	2 years	144	21.3
		LSIL	**Positive or negative**	**1,552**		**393**	**25.3**
Women aged ≥ 16 years							
Kaiser Permanente Portland (Castle 2012)	Women with valid tests including those who had not undergone colposcopy – assume same follow-up for all LSIL	LSIL	Hr-HPV other than 16/18 positive	183	18 years	NR	12.0 (8.1-17.8)*
		LSIL	**Positive or negative**	**381**	**18 years**	**NR**	**17.6 (14.0-21.9)***

CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; CI = confidence interval; hr-HPV = high risk HPV type; LSIL = low -grade squamous intraepithelial lesion; NR = not reported
Bold indicates results for benchmark: LSIL (Bethesda) equivalent to definite LSIL benchmark for follow-up tests at 12 months
** Cumulative incidence rate calculated using Kaplan Meier method*

Cross-sectional studies

Table 8 Results of longitudinal studies comparing risk associated with differing HPV statuses and cytology type: **cervical intraepithelial neoplasia grade 2 or worse**

Study	Population	Cytology	HPV status	N	CIN2+ n	CIN2+ risk % (95% CI)
Women aged ≥ 50 years						
ATHENA (Cuzick 2013)	Women who underwent colposcopy with valid results for all 3 HPV tests and valid	LSIL	Hr-HPV other than 16/18 positive	**26**	**1**	**3.8**
		LSIL	**Positive or negative**	**70**	**3**	**4.3**
Women aged ≥ 40 years						
ATHENA (Cuzick 2013)	Women who underwent colposcopy with valid results for all 3 HPV tests and valid	LSIL	Hr-HPV other than 16/18 positive	91	12	13.2
		LSIL	**Positive or negative**	**220**	**19**	**8.6**
Women aged ≥ 30 years						
ATHENA (Cox 2013; Cuzick 2013; Wright 2011)	Women who had undergone all tests and a colposcopy	ASC-US	Hr-HPV other than 16/18 positive	172	16	9.3
		Any including NILM	**Hr-HPV 16/18 positive**	**580**	**122**	**21.0**
	Women who underwent colposcopy with valid results for all 3 HPV tests and valid	NILM	Hr-HPV other than 16/18 positive	NR	NR	4.6 (3.5 – 5.7)
		LSIL	Hr-HPV other than 16/18 positive	195	24	12.3
		LSIL	**Positive or negative**	**438**	**48**	**11.0**
Cervista (Einstein 2010 & 2011)	Women with results for all tests and colposcopy	ASC-US	Hr-HPV other than 16/18 positive	235	8	3.4
		ASC-US	Positive or negative	701	29	4.1
Women aged ≥ 25 years						
ATHENA (Castle 2011; Cuzick 2013)	Hr-HPV positive women with valid results for all tests who underwent colposcopy with valid biopsy	ASC-US	Hr-HPV other than 16/18 positive	255	25	9.8
		LSIL	Hr-HPV other than 16/18 positive	301	41	13.6
		LSIL	**Positive or negative**	**656**	**79**	**12.0**
		Any including NILM	**Hr-HPV 16/18 positive**	**966**	**197**	**20.4 (18.6-22.3)**

Women aged ≥ 21 years						
ATHENA (Stoler 2011; Cuzick 2013)	Women with valid results for all tests who underwent colposcopy with valid biopsy	ASC-US	Hr-HPV other than 16/18 positive	338	29	8.6 (6.0-12.1)
		ASC-US	Positive or negative	1,578	80	5.1
		LSIL	Hr-HPV other than 16/18 positive	436	50	11.5 (8.8-14.8)
		LSIL	**Positive or negative**	**925**	**107**	**11.6**
		ASC-H	**Positive or negative**	**53**	**22**	**41.5**
		HSIL	**Positive or negative**	**126**	**72**	**57.1**
CLEAR (Castle 2015)	Women who underwent colposcopy	ASC-US	Hr-HPV other than 16/18 positive	292	35	12.0
		ASC-US	Positive or negative	988	94	9.5
Women aged 18 – 29 years						
Cervista (Einstein 2010 & 2011)	Women with results for all tests and colposcopy	ASC-US	Hr-HPV other than 16/18 positive	265	12	4.5
		ASC-US	Positive or negative	611	40	6.6
Women aged ≥ 18 years						
Cervista (Einstein 2010 & 2011)	Women with results for all tests and colposcopy	ASC-US	Hr-HPV other than 16/18 positive	500	20	4.0 (2.6 – 6.1)
		ASC-US	Positive or negative	1,312	69	5.3
Predictors 1 &2 (Mesher 2013)	Women with results for Cobas test and colposcopy	Mild dyskaryosis	Hr-HPV other than 16/18 positive	239	34	14.2
		Mild dyskaryosis	**Positive or negative**	**486**	**95**	**19.5**

ASC-H = atypical squamous cells, cannot exclude HSIL; ASCUS = atypical squamous cell, undetermined significance (Bethesda 2001); CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; CI = confidence interval; HSIL = high-grade squamous intraepithelial lesion; hr-HPV = high risk HPV type; LSIL = low -grade squamous intraepithelial lesion; NILM = negative for intraepithelial lesion or malignancy

Bold indicates results for benchmarks: LSIL (Bethesda) and mild dyskaryosis equivalent to definite LSIL benchmark for follow-up tests at 12 months; HSIL (Bethesda), ASC-H (Bethesda 2001) and Hr-HPV 16/18 positive benchmarks for immediate colposcopy

3. Body of Evidence

CIN3+ Risk – Longitudinal studies

Name of study	Study type	Population (N)	Level of evidence*	Risk of bias**	Length of follow-up	Risk of CIN3+ (95% CI)		Relevance of evidence*
						Exposure	Benchmark	
						hr-HPV other+ LSIL	all LSIL	
ALTS (Gage 2013)	Prospective cohort	Aged ≥ 30 years N = 261	II	High	2 years	8.5	12.6	1
		Aged ≥ 18 years N = 1,552	II	High	2 years	9.8	15.0	1
		Aged 18-29 years N = 1,291	II	High	2 years	10.0	15.5	1
Kaiser Permanente Portland (Castle 2012)	Prospective cohort	Aged ≥ 16 years N = 381	II	High	18 years	2.7 (1.1 - 6.5)^	7.4 (5.1 - 10.7)^	1

CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; CI = confidence interval; hr-HPV = high risk HPV type; LSIL = low-grade squamous intraepithelial lesion (Bethesda)
^Cumulative incidence rate of CIN3+ calculated using Kaplan Meier method

**Refer to appendix B for detailed explanations of rating scores; ** See Tables 3 - 4 for appraisals of risk of bias*

Clinical significance of size of effect is addressed in the assessment of clinical impact in the NHMRC evidence statement form.

CIN3+ Risk on immediate colposcopy

Name of study	Study type	Population age	Level of evidence*	Risk of bias**	Risk of CIN3+ (95% CI)		Relevance of evidence*
					Exposure	Benchmark	
					hr-HPV other+ LSIL/mild dyskaryosis	**all HPV 16/18+**	
ATHENA (Castle 2011)	Prospective cohort	≥ 25 years	II	High	5.6 n = 301	15.5 (14.0-17.1) n = 966	1
						all HSIL	
ATHENA (Cuzick 2013)	Prospective cohort	≥ 21 years	II	High	3.9 (2.4-6.2) n = 436	46.0 n = 126	1
						all LSIL/mild dyskaryosis	
ATHENA (Cuzick 2013)	Prospective cohort	≥ 21 years	II	High	3.9 (2.4 - 6.7)	5.2 n = 925	1
		≥ 25 years	II	High	5.6	5.8 n = 656	1
		≥ 30 years	II	High	6.7	6.2 n = 438	1
		≥ 40 years	II	High	7.7	4.5 n = 220	1
		≥ 50 years	II	High	3.8	2.9 n = 70	1
Predictors 1 & 2 (Mesher 2013)	Prospective cohort	≥ 18 years	II	High	4.2	7.2 n = 486	1

					hr-HPV other[+] ASC-US	**all HPV 16/18+**	
ATHENA (Castle 2011)	Prospective cohort	≥ 25 years	II	High	5.9 n = 255	15.5 (14.0-17.1) n = 966	1
(Cox 2013)		≥ 30 years	II	High	5.8 n = 172	17.4 n = 580	1
						All HSIL	
ATHENA (Stoler 2011; Cuzick 2013)	Prospective cohort	≥ 21 years	II	High	4.4 (2.7-7.2) n = 338	46.0 n = 126	1
						All LSIL	
ATHENA (Stoler 2011; Cuzick 2013)	Prospective cohort	≥ 21 years	II	High	4.4 (2.7-7.2)	5.2 n = 925	1
(Castle 2011; Cuzick 2013)		≥ 25 years	II	High	5.9	5.8 n = 656	1

ASC-US = atypical squamous cell, undetermined significance (Bethesda 2001); CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; CI = confidence interval; hr-HPV = high risk HPV type; LSIL = low-grade squamous intraepithelial lesion (Bethesda); HSIL = high-grade squamous intraepithelial lesion (Bethesda)

**Refer to appendix B for detailed explanations of rating scores; ** See Tables 3 – 4 for appraisals of risk of bias*

Clinical significance of size of effect is addressed in the assessment of clinical impact in the NHMRC evidence statement form.

References: Included Studies

1. Castle PE, Stoler MH, Wright TC, Jr. et al. Performance of carcinogenic human papillomavirus (HPV) testing and HPV16 or HPV18 genotyping for cervical cancer screening of women aged 25 years and older: a subanalysis of the ATHENA study. *Lancet Oncology*. 2011;12:880-890.

2. Castle PE, Glass AG, Rush BB et al. Clinical human papillomavirus detection forecasts cervical cancer risk in women over 18 years of follow-up. *J Clin Oncol*. 2012;30:3044-3050.

3. Castle PE, Eaton B, Reid J et al. Comparison of human papillomavirus detection by Aptima HPV and cobas HPV tests in a population of women referred for colposcopy following detection of atypical squamous cells of undetermined significance by Pap cytology. *J Clin Microbiol* . 2015;53:1277-1281.

4. Cox JT, Castle PE, Behrens CM et al. Comparison of cervical cancer screening strategies incorporating different combinations of cytology, HPV testing, and genotyping for HPV 16/18: results from the ATHENA HPV study. *American Journal of Obstetrics & Gynecology*. 2013;208:184.

5. Cuzick J, Thomas CJ, Zhang G et al. Human papillomavirus testing for triage of women with low-grade squamous intraepithelial lesions. *International journal of cancer*. 2013;132:959-966.

6. Einstein MH, Martens MG, Garcia FA et al. Clinical validation of the Cervista HPV HR and 16/18 genotyping tests for use in women with ASC-US cytology. *Gynecol Oncol*. 2010;118:116-122.

7. Einstein MH, Garcia FA, Mitchell AL et al. Age-stratified performance of the Cervista HPV 16/18 genotyping test in women with ASC-US cytology. *Cancer Epidemiology, Biomarkers & Prevention*. 2011;20:1185-1189.

8. Gage JC, Schiffman M, Solomon D et al. Risk of precancer determined by HPV genotype combinations in women with minor cytologic abnormalities. *Cancer Epidemiology, Biomarkers & Prevention*. 2013;22:1095-1101.

9. Mesher D, Szarewski A, Cadman L et al. Comparison of human papillomavirus testing strategies for triage of women referred with low-grade cytological abnormalities. *European Journal of Cancer*. 2013;49:2179-2186.

10. Stoler MH, Wright TC, Jr., Sharma A et al. High-risk human papillomavirus testing in women with ASC-US cytology: results from the ATHENA HPV study. *American Journal of Clinical Pathology*. 2011;135:468-475.

11. Wright TC, Jr., Stoler MH, Sharma A et al. Evaluation of HPV-16 and HPV-18 genotyping for the triage of women with high-risk HPV+ cytology-negative results. *American Journal of Clinical Pathology*. 2011;136:578-586.

4. Appendices

Appendix A: Search strategies used

For Medline, Premedline and Cochrane Central Register of Controlled trials databases (Ovid):

#	Searches
1	HPV.mp.
2	hr$HPV.mp.
3	papillomavirus.mp.
4	exp Papillomavirus Infections/
5	exp Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	hybrid capture.mp.
9	HC2.mp.
10	HCII.mp.
11	(hybrid adj5 capture).mp.
12	realtime.mp.
13	cervista.mp.
14	amplicor.mp.
15	cobas 4800.mp.
16	linear array.mp.
17	(linear adj3 array).mp.
18	papillocheck.mp.
19	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20	exp Polymerase Chain Reaction/
21	pcr.mp.
22	20 or 21
23	7 or 19 or 22
24	exp Vaginal Smears/
25	((cervi* or vagina*) and (smear* or screening* or test*)).tw.
26	(pap adj5 smear).tw.
27	papanicolaou.tw.
28	LBC.mp.
29	cytolog$.mp.
30	exp Uterine Cervical Dysplasia/
31	cervical dysplasia.mp.
32	(cervi* adj5 dysplasia).mp.
33	(dyskaryosis or dyskariosis).mp.
34	ASCUS.mp.
35	ASC US.mp.
36	ASC$US.mp.

37	ASC R.mp.
38	(atypical squamous adj4 cervi$).mp.
39	atypical endocervical.mp.
40	atypical gland$.mp.
41	AGUS.mp.
42	((borderline or low-grade) adj3 abnormal$).mp.
43	((borderline or low-grade) adj3 cytology).mp.
44	SIL.mp.
45	LSIL.mp.
46	L-SIL.mp.
47	LGSIL$.mp.
48	pLSIL$.mp.
49	dLSIL$.mp.
50	low-grade squamous intraepithelial.mp.
51	possible low-grade squamous intraepithelial.mp.
52	definite low-grade squamous intraepithelial.mp.
53	24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52
54	exp Colposcopy/
55	colposcop$.mp.
56	54 or 55
57	Surveillance.mp.
58	56 or 57
59	23 and 53 and 58
60	randomized controlled trial.pt.
61	controlled clinical trial.pt.
62	placebo.ab.
63	randomi?ed.ab.
64	randomly.ab.
65	trial.ab.
66	groups.ab.
67	60 or 61 or 62 or 63 or 64 or 65 or 66
68	59 and 67
69	limit 68 to english language

Used the Cochrane sensitivity maximizing filter for identifying randomized controlled trials (http://handbook.cochrane.org, accessed 12/09/2015)

ATSI search terms used

#	**Searches**
1	((exp Australia/ OR Australia$.ti,ab) AND (Oceanic ancestry group/ OR aborigin$.ti,ab. OR indigenous.mp.)) OR torres strait$ islander$.ti,ab

From the Lowitja Institute at http://www.lowitja.org.au/litsearch-background-information accessed 30/09/2013)

For Embase database (Embase):

#	Searches
1.	'hpv 16'/exp OR 'hpv 16'
2.	'hpv18'/exp OR 'hpv18'
3.	'hpv31'/exp OR 'hpv31'
4.	'hpv33'/exp OR 'hpv33'
5.	'hpv35'/exp OR 'hpv35'
6.	'hpv45'/exp OR 'hpv45'
7.	'hpv 52'/exp OR 'hpv 52'
8.	'hpv 58'/exp OR 'hpv 58'
9.	'hpv'/exp OR 'hpv'
10.	'human papillomavirus'/exp OR 'human papillomavirus'
11.	'human papillomavirus test'
12.	hr*hpv
13.	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
15.	'vagina smear'/exp OR 'vagina smear'
16.	'uterine cervix cytology'/exp OR 'uterine cervix cytology'
17.	'uterine cervix dysplasia'/exp OR 'uterine cervix dysplasia'
18.	cervi* OR vagina* AND (smear* OR screen* OR test*)
19.	pap* NEAR/5 smear*
20.	papanicolaou
21.	'papanicolaou test'/exp OR 'papanicolaou test'
22.	lbc
23.	cytolog*
24.	cervi* NEAR/5 dysplasia
25.	dyskaryosis OR dyskariosis
26.	ascus OR 'asc us' OR 'asc r'
27.	'asc-us' OR 'asc-r'
28.	atypical AND squamous NEAR/4 cervi*
29.	'atypical endocervical'
30.	atypical NEXT/1 gland*
31.	agus
32.	(borderline OR 'low-grade') NEAR/3 abnormal*
33.	(borderline OR 'low-grade') NEAR/3 cytology
35.	sil* OR lsil* OR 'l-sil' OR lgsil* OR plsil* OR dlsil* OR 'p/dlsil'

36.	'low-grade squamous intraepithelial'
37.	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32OR #33 OR #35 OR #36
38.	'colposcopy'/exp
39.	colposcop*
40.	surveillance
41.	#38 OR #39 OR #40
42.	rct
43.	'randomized controlled trial'/de
44.	'randomised controlled trial' OR 'randomized controlled trial' OR 'randomised controlled trials' OR 'randomized controlled trials'
45.	'random allocation' OR 'randomly allocated'
46.	'randomization'/de
47.	allocated NEAR/2 random
48.	'double blind procedure'/de
49.	'single blind procedure'/de
50.	single NEXT/1 blind*
51.	double NEXT/1 blind*
52.	(treble OR triple) NEXT/1 blind*
53.	placebo
54.	'placebo'/de
55.	'prospective study'/de
56.	'crossover procedure'/de
57.	'clinical trial'/de
58.	#42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57
59.	'case study'/de
60.	'case report'
61.	'abstract report'/de
62.	'letter'/de
63.	#59 OR #60 OR #61 OR #62
64.	#58 NOT #63
65.	#13 AND #37 AND #41 AND #64
66.	#13 AND #37 AND #41 AND #64 AND [2013-2015]/py
67.	#13 AND #37 AND #41 AND #64 AND [2013-2015]/py AND [english]/lim
68.	#13 AND #37 AND #41 AND #64 AND [2013-2015]/py AND [english]/lim AND [embase]/lim

69.	#13 AND #37 AND #41 AND #64 AND [2013-2015]/py AND [english]/lim AND [embase]/lim AND [medline]/lim
70.	#67 NOT #69

Used the SIGN filter for identifying randomized controlled trials (www.sign.ac.uk/methodology/filters.html#systematic accessed 20/02/2013)

ATSI search terms used

#	Searches
1	'australia'/exp OR australia*:ab,ti
2	'aborigine'/exp OR aborigin*:ab,ti OR indigenous:de,ab,ti
3	'torres strait islander':ab,ti OR 'torres strait islanders':ab,ti
4	#1 AND #2 OR #3

For Health Technology Assessments (HTA) and Database of Abstracts of Reviews of Effects (DARE) databases (Ovid):

#	**Searches**
1	HPV.mp.
2	hr$HPV.mp.
3	papillomavirus.mp.
4	exp Papillomavirus Infections/
5	exp Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	hybrid capture.mp.
9	HC2.mp.
10	HCII.mp.
11	(hybrid adj5 capture).mp.
12	realtime.mp.
13	cervista.mp.
14	amplicor.mp.
15	cobas 4800.mp.
16	linear array.mp.
17	(linear adj3 array).mp.
18	papillocheck.mp.
19	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20	exp Polymerase Chain Reaction/
21	pcr.mp.
22	20 or 21
23	7 or 19 or 22
24	exp Vaginal Smears/
25	((cervi* or vagina*) and (smear* or screening* or test*)).tw.

26	(pap adj5 smear).tw.
27	papanicolaou.tw.
28	LBC.mp.
29	cytolog$.mp.
30	exp Uterine Cervical Dysplasia/
31	cervical dysplasia.mp.
32	(cervi* adj5 dysplasia).mp.
33	(dyskaryosis or dyskariosis).mp.
34	ASCUS.mp.
35	ASC US.mp.
36	ASC$US.mp.
37	ASC R.mp.
38	(atypical squamous adj4 cervi$).mp.
39	atypical endocervical.mp.
40	atypical gland$.mp.
41	AGUS.mp.
42	((borderline or low-grade) adj3 abnormal$).mp.
43	((borderline or low-grade) adj3 cytology).mp.
44	SIL.mp.
45	LSIL.mp.
46	L-SIL.mp.
47	LGSIL$.mp.
48	pLSIL$.mp.
49	dLSIL$.mp.
50	low-grade squamous intraepithelial.mp.
51	possible low-grade squamous intraepithelial.mp.
52	definite low-grade squamous intraepithelial.mp.
53	24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52
54	exp Colposcopy/
55	colposcop$.mp.
56	54 or 55
57	Surveillance.mp.
58	56 or 57
59	23 and 53 and 58
60	limit 59 to english language

For Cochrane Database of Systematic Reviews:

#	**Searches**
1	colposcop$.mp.
2	HPV.mp.
3	1 or 2

Appendix B:

Level of evidence rating criteria – Risk assessment studies

Level	Study design
I	Meta-analysis or a systematic review of level II studies
II	Prospective cohort studies
III-1	All or none
III-2	Retrospective cohort studies
III-3	Case control studies
IV	Cross-sectional studies or case series

According to the standards of the National Health and Medical Research Council

Relevance of the Evidence

Rating	Relevance
1	Evidence of an effect on patient-relevant clinical outcomes including benefits and harms, quality of life and survival.
2	Evidence of an effect on a surrogate outcome* that has been shown to be predictive of patient-relevant outcomes for the same intervention.
3	Evidence of an effect on proven surrogate outcomes but for a different intervention.
4	Evidence of an effect on proven surrogate outcomes but for a different intervention and population.
5	Evidence confined to unproven surrogate outcomes.

**'surrogate outcome' refers to reasonable indicators of whether there has been some effect (e.g. blood pressure measurements or levels of serum cholesterol)*

Points for considering patient-relevant outcomes:
i) The goal of decision making in health care is to choose the intervention(s) (which may include doing nothing) that is (are) most likely to deliver the outcomes that patients find desirable.
ii) Surrogate outcomes (such as blood pressure measurements or levels of serum cholesterol) may be reasonable indicators of whether there has been some effect. However, they should not be the basis for clinical decisions unless they reliably predict an effect on the way the patient feels, otherwise they will not be of interest to the patient or their carers.
iii) All possible outcomes that are of most interest to patients (particularly harms) should be identified and evaluated.

Adapted from table 1.10 of: National Health and Medical Research Council. How to use the evidence: assessment and application of scientific evidence. Canberra: NHMRC; 2000.
http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/cp69.pdf

Appendix C:

Excluded Studies

Primary PICO question

Study	Reason for Exclusion
Bergeron 2015	Does not include women with relevant HPV and cytology status
Blatt 2015	Does not include women with relevant HPV and cytology status
Cruickshank 2015	No relevant comparison
Cuzick 2013	Not randomised or pseudo-randomised controlled trial
Del Mistro 2014	Does not include women with relevant HPV and cytology status
Dijkstra 2014	No relevant comparison
Gage 2013	Not randomised or pseudo-randomised controlled trial
Kececioglu 2013	No results for women with relevant HPV and cytology status
Kitchener 2014	No results for women with relevant HPV and cytology status
McIntosh 2012	Review
Nakamura 2015	Not randomised or pseudo-randomised controlled trial
Reid 2015	No results for women with relevant HPV and cytology status
Ronco 2014	No results for women with relevant HPV and cytology status
Van Le 2015	Summary of a published study
Wright 2013	Conference proceedings 2013

Secondary PICO question

Study	Reason for Exclusion
Adamopoulou 2009	No results for women with relevant HPV and cytology status
Agodi 2009	No results for women with relevant HPV and cytology status
Agorastas 2005	No results for women with relevant HPV and cytology status
Agorastos 2015	No relevant comparators
Aksu 2011	Conference proceedings
Alameda 2014	Conference proceedings
Alamonte 2007	No results for women with relevant HPV and cytology status
Allia 2015	No results for women with relevant HPV and cytology status
Annappa 2015	Conference proceedings
Antonishyn 2008	No results for women with relevant HPV and cytology status
Antonishyn 2009	No results for women with relevant HPV and cytology status
Arbyn 2004	No results for women with relevant HPV and cytology status
Arbyn 2009	No results for women with relevant HPV and cytology status
Arbyn 2012	No results for women with relevant HPV and cytology status
Atkins 2006	Does not assess women with relevant HPV and cytology status
Ault 2011	Participants women with AIS
Badano 2011	No results for women with relevant HPV and cytology status
Bais 2005	No results for women with relevant HPV and cytology status

Balbi 2012	No results for women with relevant HPV and cytology status
Bapir 2013	Conference proceedings
Barcelos 2011	No results for women with relevant HPV and cytology status
Barzon 2011	No results for women with relevant HPV and cytology status
Basu 2011	Cervical cancer specimens only
Bekkers 2004	No results for women with relevant HPV and cytology status
Belinson 2010	No results for women with relevant HPV and cytology status
Belinson 2011	No results for women with relevant HPV and cytology status
Bello 2009	No results for women with relevant HPV and cytology status
Benevolo 2011	No results for women with relevant HPV and cytology status
Benevolo 2011b	No results for women with relevant HPV and cytology status
Benoy 2011	No results for women with relevant HPV and cytology status
Bergeron 2015	Does not include women with relevant HPV and cytology status
Berkhof 2006	No results for women with relevant HPV and cytology status
Bhatla 2007	No results for women with relevant HPV and cytology status
Bhatla 2008	No results for women with relevant HPV and cytology status
Bian 2013	Unclear as to whether results for women with relevant HPV and cytology status
Bjerre 2008	No results for women with relevant HPV and cytology status
Blatt 2015	Does not include women with relevant HPV and cytology status
Boardman 2006	Does not include women with relevant HPV and cytology status
Boldrini 2014	No results for women with relevant HPV and cytology status
Bollmann 2006	Post treatment follow-up population
Bourgain 2011	Conference proceedings
Bratti 2004	No results for women with relevant HPV and cytology status
Brink 2006	No results for women with relevant HPV and cytology status
Bulk 2007	No results for women with relevant HPV and cytology status
Bulkmans 2007	No results for women with relevant HPV and cytology status
Bulkmans 2007b	No results for women with relevant HPV and cytology status
Campari 2015	No results for women with relevant HPV and cytology status
Canda 2009	No results for women with relevant HPV and cytology status
Carozzi 2005	No results for women with relevant HPV and cytology status
Carozzi 2006	No results for women with relevant HPV and cytology status
Carozzi 2013	No results for women with relevant HPV and cytology status
Carozzi 2013b	No results for women with relevant HPV and cytology status
Carter 2010	No results for women with relevant HPV and cytology status
Castle 2004	Commentary
Castle 2007	Participants women with CIN2 histology on colposcopy
Castle 2008	No results for women with relevant HPV and cytology status
Castle 2009	No results for women with relevant HPV and cytology status
Castle 2009 short	No results for women with relevant HPV and cytology status
Castle 2009c	No outcomes of interest
Castle 2009d	No results for women with relevant HPV and cytology status

Castle 2010	Does not include women with relevant HPV and cytology status
Castle 2011b	No results for women with relevant HPV and cytology status
Castle 2011c	Participants women who have CIN1 or less
Castle 2015	No results for women with relevant HPV and cytology status
Castle 2015 Reliability	No results for women with relevant HPV and cytology status
Cattani 2009	No results for women with relevant HPV and cytology status
Chao 2008	No results for women with relevant HPV and cytology status
Chao 2010	No results for women with relevant HPV and cytology status
Chen 2006	No results for women with relevant HPV and cytology status
Chen 2015	No results for women with relevant HPV and cytology status
Chevarie-Davis 2013	No results for women with relevant HPV and cytology status
Chiang 2013	No results for women with relevant HPV and cytology status
Chivukula 2006	Does not include women with relevant HPV and cytology status
Cho 2015	No results for women with relevant HPV and cytology status
Chranioti 2012	No results for women with relevant HPV and cytology status
Cilingir 2013	Colposcopy referral population and unclear if follow-up patients excluded
Ciotto 2004	No results for women with relevant HPV and cytology status
Clad	Includes post treatment follow-up population
Clarke 2014	Conference proceedings
Cobo 2009	No results for women with relevant HPV and cytology status
Confortini 2010	No results for women with relevant HPV and cytology status
Corneanu 2011	No results for women with relevant HPV and cytology status
Correa 2012	No results for women with relevant HPV and cytology status
Cottier 2009	No results for women with relevant HPV and cytology status
Cotton 2010	No results for women with relevant HPV and cytology status
Cruickshank 2014	Results for only a subgroup of women with relevant HPV and cytology status
Crum 2004	Participants women with CIN2/CIN3
Cuschieri 2014	No results for women with relevant HPV and cytology status
Cuzick 2008	No results for women with relevant HPV and cytology status
Cuzick 2010	No results for women with relevant HPV and cytology status
Dalla Palma 2008	Participants women with CIN histology
Dalstein 2004	No results for women with relevant HPV and cytology status
Dane 2009	No results for women with relevant HPV and cytology status
Daponte 2006	No results for women with relevant HPV and cytology status
de Vuyst 2005	No results for women with relevant HPV and cytology status
Del Mistro 2010	No results for women with relevant HPV and cytology status
Del Mistro 2014	Does not include women with relevant HPV and cytology status
Denny 2010	No results for women with relevant HPV and cytology status
Depuydt 2011	No results for women with relevant HPV and cytology status
Desteli 2004	No results for women with relevant HPV and cytology status
Diaz Montes 2007	Not relevant population - AGUS or AGC cytology
Dijkstra 2013	No results for women with relevant HPV and cytology status
Dillner 2008	No results for women with relevant HPV and cytology status

Dillner 2011	No results for women with relevant HPV and cytology status
Dinc 2010	No results for women with relevant HPV and cytology status
Ding 2011	Participants women treated for CIN2 histology
Ding 2014	No results for women with relevant HPV and cytology status
Discacciati 2014	Not a cervical screening population - women with CIN2
Dockter 2009	Includes follow-up population
Du 2011	No results for women with relevant HPV and cytology status
Dufresne 2011	No results for women with relevant HPV and cytology status
Elfgren 2005	No results for women with relevant HPV and cytology status
Eltoum 2005	No results for women with relevant HPV and cytology status
Filho 2005	No results for women with relevant HPV and cytology status
Fokom-Domgue 2015	No results for women with relevant HPV and cytology status
Froberg 2008	No results for women with relevant HPV and cytology status
Gage 2010	ASCUS/LSIL: <=CIN1 on immediate colposcopy
Gage 2014	No results for women with relevant HPV and cytology status
Geng 2011	Conference proceedings
Geraets 2013	No results for women with relevant HPV and cytology status
Gilani 2013	No results for women with relevant HPV and cytology status
Giorgi Rossi 2010	No results for women with relevant HPV and cytology status
Giorgi Rossi 2011	No results for women with relevant HPV and cytology status
Giorgi Rossi 2013	No results for women with relevant HPV and cytology status
Giovannelli 2005	No results for women with relevant HPV and cytology status
Girianelli 2006	No results for women with relevant HPV and cytology status
Gold 2013	No results for women with relevant HPV and cytology status
Gonzalez- Bosquet 2006	No results for women with relevant HPV and cytology status
Gonzalez-Bosquet 2008	No results for women with relevant HPV and cytology status
Gonzalez-Losa 2004	No results for women with relevant HPV and cytology status
Goodrich 2014	No relevant comparator
Gravitt 2010	No results for women with relevant HPV and cytology status
Grisaru 2008	Not a cervical screening population - included women undergoing post treatment follow-up
Guo 2014	No results for women with relevant HPV and cytology status
Gurumurthy 2014	Participants women with CIN1
Gutierrez-Delgado 2014	Conference proceedings
Haidopoulos 2009	No results for women with relevant HPV and cytology status
Haldorsen 2015	No results for women with relevant HPV and cytology status
Halfon 2010	No results for women with relevant HPV and cytology status
Halfon 2013	No results for women with relevant HPV and cytology status
Hariri 2015	Population women with CIN2
Hariri 2015b	Population women with CIN2
HooKim 2014	Does not include women with relevant HPV and cytology status
Hopenhayn 2014	Not a cervical screening population - women with cervical cancer
Hou 2012	No results for women with relevant HPV and cytology status
Hoyer 2005	No results for women with relevant HPV and cytology status
Hu 2011	No results for women with relevant HPV and cytology status

Huang 2006	No results for women with relevant HPV and cytology status
Huang 2009	No results for women with relevant HPV and cytology status
Hughes 2005	No results for women with relevant HPV and cytology status
Huh 2015	Clinical guidelines
Ibanez 2014	No results for women with relevant HPV and cytology status
Iftner 2015	No results for women with relevant HPV and cytology status
Ikenberg 2013	No results for women with relevant HPV and cytology status
Inoue 2007	No results for women with relevant HPV and cytology status
Jakobsson 2012	Participants women with recurrent cytological abnormalities
Jariene 2012	No results for women with relevant HPV and cytology status
Jentschke 2013	No results for women with relevant HPV and cytology status
Jeronimo 2015	No results for women with relevant HPV and cytology status
Jiang 2011	No results for women with relevant HPV and cytology status
Johnson 2008	No results for women with relevant HPV and cytology status
Jones 2011	Editorial
Jovanovic 2012	No results for women with relevant HPV and cytology status
Kakti 2011	No results for women with relevant HPV and cytology status
Kakti 2013 Benchmarking	No results for women with relevant HPV and cytology status
Kakti 2013 CIN1	Participants women with HPV infection or abnormal cytology and histology <CIN2
Kares 2014	Conference proceedings
Katki 2013 LSIL	No results for women with relevant HPV and cytology status
Katki 2013d neg	No results for women with relevant HPV and cytology status
Katki 2013f ASCUS	No results for women with relevant HPV and cytology status
Kececioglu 2013	No results for women with relevant HPV and cytology status
Keegan 2014	Participants women with recurrent cytological abnormalities
Kelly 2011	No results for women with relevant HPV and cytology status
Khan 2005	Participants included women with prior history of HSIL/CIN2+ diagnosis
Kim 2013	No results for women with relevant HPV and cytology status
Kitchener 2008	Post treatment population
Kitchener 2011	No results for women with relevant HPV and cytology status
Kitchener 2014	No results for women with relevant HPV and cytology status
Ko 2011	No results for women with relevant HPV and cytology status
Kocken 2012	No results for women with relevant HPV and cytology status
Kotaniemi-Talonen 2005	No results for women with relevant HPV and cytology status
Kotaniemi-Talonen 2008	No results for women with relevant HPV and cytology status
Kovacic 2008	No results for women with relevant HPV and cytology status
Krambeck 2008	No results for women with relevant HPV and cytology status
Kroupis 2007	No results for women with relevant HPV and cytology status
Kulasingam 2006	No results for women with relevant HPV and cytology status
Lai 2008	No relevant comparator
Lazcano-Ponce 2010	No results for women with relevant HPV and cytology status
Le Donne 2013	No results for women with relevant HPV and cytology status
Lee 2004	No results for women with relevant HPV and cytology status
Lee 2006	No results for women with relevant HPV and cytology status

Lee 2009	No results for women with relevant HPV and cytology status
Lee 2015	No comparator
Leeson 2014	Discussion article
Leinonen 2013	No results for women with relevant HPV and cytology status
Li 2015	No results for women with relevant HPV and cytology status
Liao 2014	No results for women with relevant HPV and cytology status
Lin 2011	No results for women with relevant HPV and cytology status
Liou 2015	No results for women with relevant HPV and cytology status
Litjens 2013	No results for women with relevant HPV and cytology status
Litjens 2014	Particpants women with CIN3 who were previously CIN1
Littell 2011	No results for women with relevant HPV and cytology status
Liu 2014	No results for women with relevant HPV and cytology status
Liverani 2012	No results for women with relevant HPV and cytology status
Loiacono 2012	Conference proceedings
Louvanto 2010	No results for women with relevant HPV and cytology status
Louwers 2010	No results for women with relevant HPV and cytology status
Luttmer 2015	No results for women with relevant HPV and cytology status
Maenpaa 2014	Conference proceedings
Massad 2013	Consensus guidelines
Massad 2014	Review
Maucourt-Boulch 2009	No results for women with relevant HPV and cytology status
Mayrand 2007	No results for women with relevant HPV and cytology status
McDonald 2014	No results for women with relevant HPV and cytology status
McIntosh 2012	Review
McKenna 2014	No results for women with relevant HPV and cytology status
Medeiros 2005	No results for women with relevant HPV and cytology status
Mendoza 2011	No results for women with relevant HPV and cytology status
Mentzelopoulou 2014	Conference proceedings
Menzo 2008	No relevant outcomes reported
Michelli 2011	No results for women with relevant HPV and cytology status
Michelli 2013	No relevant outcomes reported
Mijit 2015	No results for women with relevant HPV and cytology status
Min 2015	Conference proceedings
Moarcas 2014	No results for women with relevant HPV and cytology status
Monsonego 2008	No results for women with relevant HPV and cytology status
Monsonego 2008b	No results for women with relevant HPV and cytology status
Monsonego 2011	No results for women with relevant HPV and cytology status
Monsonego 2012	No results for women with relevant HPV and cytology status
Moore 2010	No results for women with relevant HPV and cytology status
Moss 2006	No results for women with relevant HPV and cytology status
Moy 2010	No results for women with relevant HPV and cytology status
Musa 2011	No relevant outcomes reported
Muwonge 2014	No results for women with relevant HPV and cytology status
Nakamura 2015	Colposcopy referral population and unclear if treatment follow-up patients excluded
Nam 2008	Participants women with CIN diagnosis

Namugenyi 2013	No results for women with relevant HPV and cytology status
Nasioutziki 2011	No results for women with relevant HPV and cytology status
Naucler 2007	No results for women with relevant HPV and cytology status
Naucler 2007 Human	No results for women with relevant HPV and cytology status
Naucler 2009	No results for women with relevant HPV and cytology status
Ngugi 2015	No results for women with relevant HPV and cytology status
Niccolai 2013	No results for women with relevant HPV and cytology status
Nomelini 2007	No results for women with relevant HPV and cytology status
Nomelini 2012	No results for women with relevant HPV and cytology status
Nygard 2014	No results for women with relevant HPV and cytology status
O'Connor 2008	No results for women with relevant HPV and cytology status
Ogilvie 2010	No results for women with relevant HPV and cytology status
Ogilvie 2012	No results for women with relevant HPV and cytology status
Okadome 2014	Particpants women with CIN2 histology
Ovestad 2011	No results for women with relevant HPV and cytology status
Paba 2012	No results for women with relevant HPV and cytology status
Pacchiarotti 2014	No results for women with relevant HPV and cytology status
Padalko 2013	No results for women with relevant HPV and cytology status
Paengchit 2014	No comparator
Pajtler 2010	No results for women with relevant HPV and cytology status
Pan 2013	No results for women with relevant HPV and cytology status
Pan 2014	No results for women with relevant HPV and cytology status
Pasquale 2015	No results for women with relevant HPV and cytology status
Perksanusak 201	No results for women with relevant HPV and cytology status
Perrons 2005	No results for women with relevant HPV and cytology status
Petry 2011	No results for women with relevant HPV and cytology status
Petry 2012	No results for women with relevant HPV and cytology status
Petry 2013	No results for women with relevant HPV and cytology status
Piccolo 2008	No results for women with relevant HPV and cytology status
Pity 2012	No results for women with relevant HPV and cytology status
Possati-Resende 2015	No results for women with relevant HPV and cytology status
Pouliakis 2015	No results for women with relevant HPV and cytology status
Pretorius 2013	No results for women with relevant HPV and cytology status
Pruski 2012	No results for women with relevant HPV and cytology status
Qiao 2014	No results for women with relevant HPV and cytology status
Rabelo-Santos 2009	No results for women with relevant HPV and cytology status
Ramzan 2015	Review
Rao 2013	No results for women with relevant HPV and cytology status
Ratnam 2010	No results for women with relevant HPV and cytology status
Ratnam 2011	No results for women with relevant HPV and cytology status
Rebolj 2011	Commentary
Rebolj 2014	No results for women with relevant HPV and cytology status
Rebolj 2015	No results for women with relevant HPV and cytology status
Reid 2015	No results for women with relevant HPV and cytology status
Riera 2013	Conference proceedings

Rijkaart 2012	No results for women with relevant HPV and cytology status
Rijkaart 2012	No results for women with relevant HPV and cytology status
Rijkaart 2012	No relevant comparator similarly followed up
Rodriguez 2008	No results for women with relevant HPV and cytology status
Rodriguez 2010	No results for women with relevant HPV and cytology status
Rokita 2012	No results for women with relevant HPV and cytology status
Ronco 2010	No results for women with relevant HPV and cytology status
Ronco 2014	No results for women with relevant HPV and cytology status
Saccardi 2014	No results for women with relevant HPV and cytology status
Safaeian 2009	No results for women with relevant HPV and cytology status
Sahasrabuddhe 2014	No results for women with relevant HPV and cytology status
Sahasrabuddhe 2014b	No results for women with relevant HPV and cytology status
Samarawardana 2010	No results for women with relevant HPV and cytology status
Sankaranarayanan 2009	No results for women with relevant HPV and cytology status
Saslow 2012	No results for women with relevant HPV and cytology status
Sauer 2011	Conference proceedings
Sauter 2014	No results for women with relevant HPV and cytology status
Schettino 2014	No results for women with relevant HPV and cytology status
Schiffman 2011	Discussion article
Schiffman 2011b	No results for women with relevant HPV and cytology status
Schiffman 2015	No relevant comparators similarly followed up
Schiffman 2015a	No results for women with relevant HPV and cytology status
Schiffman 2015b	No results for women with relevant HPV and cytology status
Schlichte 2014	Review
Schnatz 2009	Not relevant population - AGC cytology
Sellors 2011	No results for women with relevant HPV and cytology status
Selvaggi 2015	No results for women with relevant HPV and cytology status
Seo 2006	No results for women with relevant HPV and cytology status
Shahid 2015	No results for women with relevant HPV and cytology status
Shastri 2005	No results for women with relevant HPV and cytology status
Shen 2013	No results for women with relevant HPV and cytology status
Shen-Gunther 2011	Does not discuss multiple infections
Shi 2009	No results for women with relevant HPV and cytology status
Shipitsyna 2011	No results for women with relevant HPV and cytology status
Shwe 2015	No results for women with relevant HPV and cytology status
Siebers 2014	No results for women with relevant HPV and cytology status
Sigurdsson 2009	No results for women with relevant HPV and cytology status
Sikon 2014	Conference proceedings
Silva 2014	No relevant outcomes reported
Sodhani 2006	Not a screening population - women with non specific gynecological symptoms
Sole-Sedeno 2015	Conference proceedings
Solomon 2015	Conference proceedings
Song 2006	No results for women with relevant HPV and cytology status
Sorboye 2011	No results for women with relevant HPV and cytology status

Sorbye 2013	No results for women with relevant HPV and cytology status
Sorbye 2014	No results for women with relevant HPV and cytology status
Soto 2014	No colposcopy/biopsy/histology results
Spathis 2012	No results for women with relevant HPV and cytology status
Spinillo 2009	No results for women with relevant HPV and cytology status
Spinillo 2014	No results for women with relevant HPV and cytology status
Spinillo 2014b	No results for women with relevant HPV and cytology status
Stanculescu 2013	No results for women with relevant HPV and cytology status
Stanczuk 2015	No results for women with relevant HPV and cytology status
Stoler 2013	No results for women with relevant HPV and cytology status
Stoler 2015	Commentary
Sultana 2015	No outcomes of interest
Supho 2014	No comparator
Sycuro 2008	No results for women with relevant HPV and cytology status
Szarewski 2007	No results for women with relevant HPV and cytology status
Szarewski 2008	No results for women with relevant HPV and cytology status
Szarewski 2011	Commentary
Szarewski 2012	No results for women with relevant HPV and cytology status
Tempfer 2007	No results for women with relevant HPV and cytology status
Tinelli 2013	Participants either women at high-riskof HPV infection or women who have been treated for CIN2+ diagnosis
Tokmak 2014	No results for women with relevant HPV and cytology status
Tornsello 2007	No results for women with relevant HPV and cytology status
Tornsello 2011	No relevant outcomes reported
Trimble 205	Population women with CIN2/3 diagnosis
Trope 2012	No results for women with relevant HPV and cytology status
Tsai 2009	No results for women with relevant HPV and cytology status
Tsiodras 2010	No results for women with relevant HPV and cytology status
Tsiodras 2011	Conference proceedings
Tsoumpou 2011	Results for only a subgroup of women with relevant HPV and cytology status
Twiggs 2011	Discussion article
Twu 2011	No results for women with relevant HPV and cytology status
Uijterwaal 2014	No results for women with relevant HPV and cytology status
Uijterwaal 2015	No relevant comparator
Ursu 2011	No relevant outcomes reported
van der Marel 2014	No results for women with relevant HPV and cytology status
van der Marel 2015	No results for women with relevant HPV and cytology status
Van Le 2015	Summary of a published study
Verdoodt 2013	No results for women with relevant HPV and cytology status
Vidal 2013	Conference proceedings
Vidal 2014	No results for women with relevant HPV and cytology status
Vink 2014	Modelling effect of increasing screening interval
Wahlstrom 2007	No results for women with relevant HPV and cytology status
Walavalkar 2015	No results for women with relevant HPV and cytology status

Walker 2006	Participants women with cytological abnormalities and histology < CIN2
Walmer 2013	No results for women with relevant HPV and cytology status
Wang 2009	No results for women with relevant HPV and cytology status
Wang 2013	No results for women with relevant HPV and cytology status
Watson 2015	No results for women with relevant HPV and cytology status
Wei 2014	No results for women with relevant HPV and cytology status
Wentzensen 2009	Analysis restricted to women with CIN
Wentzensen 2009b	No results for women with relevant HPV and cytology status
Wentzensen 2010	No results for women with relevant HPV and cytology status
Wentzensen 2015	No results for women with relevant HPV and cytology status
Werner 2007	No results for women with relevant HPV and cytology status
Wheeler 2006	No results for women with relevant HPV and cytology status
Wheeler 2009	No relevant outcomes reported
Wheeler 2014	No results for women with relevant HPV and cytology status
White 2013	No results for women with relevant HPV and cytology status
Whitlock 2011	No results for women with relevant HPV and cytology status
Winer 2005	No results for women with relevant HPV and cytology status
Winsley 2014	No results for women with relevant HPV and cytology status
Wong 2008	No relevant outcomes reported
Woodard 2014	Conference proceedings
Woodard 2015	No results for women with relevant HPV and cytology status
Wright 2006	No results for women with relevant HPV and cytology status
Wright 2007a	Consensus guidelines (superseded)
Wright 2007b	Consensus guidelines (superseded)
Wright 2013	Conference proceedings
Wright 2014	Conference proceedings
Wright 2014	No results for women with relevant HPV and cytology status
Wright 2015	No comparable comparative data
Wu 2005	No results for women with relevant HPV and cytology status
Wu 2010	No results for women with relevant HPV and cytology status
Wu 2012	No results for women with relevant HPV and cytology status
Yao 2014	Conference proceedings
Ye 2010	No results for women with relevant HPV and cytology status
Yetimalar 2011	No results for women with relevant HPV and cytology status
You 2013	No results for women with relevant HPV and cytology status
Yuan 2011	No results for women with relevant HPV and cytology status
Zappacosta 2013	No results for women with relevant HPV and cytology status
Zeferino 2011	No results for women with relevant HPV and cytology status
Zeng 2011	No results for women with relevant HPV and cytology status
Zhang 2013	No results for women with relevant HPV and cytology status
Zhang 2014	Participants women with persistent HPV infection
Zhao 2013	No results for women with relevant HPV and cytology status
Zorzi 2013	No results for women with relevant HPV and cytology status

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