Systematic review report for Questions 2c

PICO question 2c

For women who are HPV positive with p/dHSIL referral cytology and p/dHSIL after cytologic review and colposcopy is negative, what is the safety and effectiveness of cytologic and colposcopic follow-up at 3-6 months compared with excision of the transformation zone?

Population	Study design	Intervention	Control	Outcome
HPV positive women who have undergone colposcopy and the colposcopy was **negative** and referral and review cytology was p/d HSIL	Randomized or pseudo randomized controlled trial	Conservative management; cytologic and colposcopic follow-up at 3-6 months	Excision of the transformation zone	Cervical cancer mortality Cervical cancer diagnosis Precancerous high grade lesion detection

dHSIL = definite HSIL; HSIL = high-grade squamous intraepithelial lesion; pHSIL = possible HSIL

Definitions

A negative colposcopy is a colposcopy in which no abnormalities are seen: it does not include the subsequent reports on any biopsy taken.

1. Methods

1.1. Searches for existing relevant guidelines

Relevant guidelines from 2005 onwards 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/).

1.1. Literature searches

To identify publications that addressed the PICO questions Medline, PreMedline, Embase, CENTRAL, Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) databases, were searched for articles published from 2004 until 31st August 2015, using text terms and, where available, database-specific subject headings. In these databases searches for cytology testing were combined with searches for HPV and negative or normal 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.

1.2. Inclusion criteria

Inclusion criteria for secondary PICO question 2c

Selection criteria	Inclusion criteria	Exclusion criteria
Population	Women who have p/d HSIL cytology and who have undergone colposcopy and the colposcopy was negative and cytology review remains p/d HSIL	Conducted in referred population and do not specifically exclude women undergoing follow-up following treatment
Study type	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
Exposure	Conservative management: cytology and colposcopy at 3-6 months	
Comparator	Excision of the transformation zone	
Outcomes	Cervical cancer mortality or Cervical cancer diagnosis or CIN3+ diagnosis or CIN2+ diagnosis or AIS diagnosis	
Search period	1st January 2004 – 31st August 2015	Case reports, reviews, editorials Conference proceedings other than 2015 EUROGIN conference proceedings
Language	English	

AIS = adenocarcinoma in situ; CIN = cervical intraepithelial neoplasia; CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; CIN3+ = cervical intraepithelial neoplasia grade 3 or worse; dHSIL = definite HSIL; HSIL = high-grade squamous intraepithelial lesion; pHSIL = possible HSIL

2. Results

2.1. Results of Guidelines Search

Three guidelines were identified that contained potentially relevant recommendations regarding negative colposcopies. These recommendations were not adopted as either they were not or it was unclear as, to whether they were based on a systematic review. These guidelines and the reason why they were not adopted are listed in Appendix C.

2.2. Results of Literature Search

Figure 1 outlines the process of identifying relevant articles for the systematic reviews. Searches of the Medline, PreMedline, Embase and CENTRAL databases identified 40 citations, DARE and HTA databases another 5 citations, the Cochrane database of systematic reviews 73 citations and EUROGIN abstracts, 16 citations; a total of 134 citations.

All were excluded after examining titles and abstracts thus **no studies were found that directly addressed the PICO question**. As such, there were no studies of Aboriginal and/or Torres Strait Islander women that met the inclusion criteria.

Database or Source	Number of Citations	Number of Articles Collected	Number of Articles Included	ATSI filter results
Medline, PreMedline, CENTRAL and Embase	40	0	0	N/A
Cochrane database of systematic reviews	73	0	0	N/A
HTA and DARE	5	0	0	N/A
EUROGIN	16	N/A	0	N/A
TOTAL	**134**	**0**	**0**	**N/A**

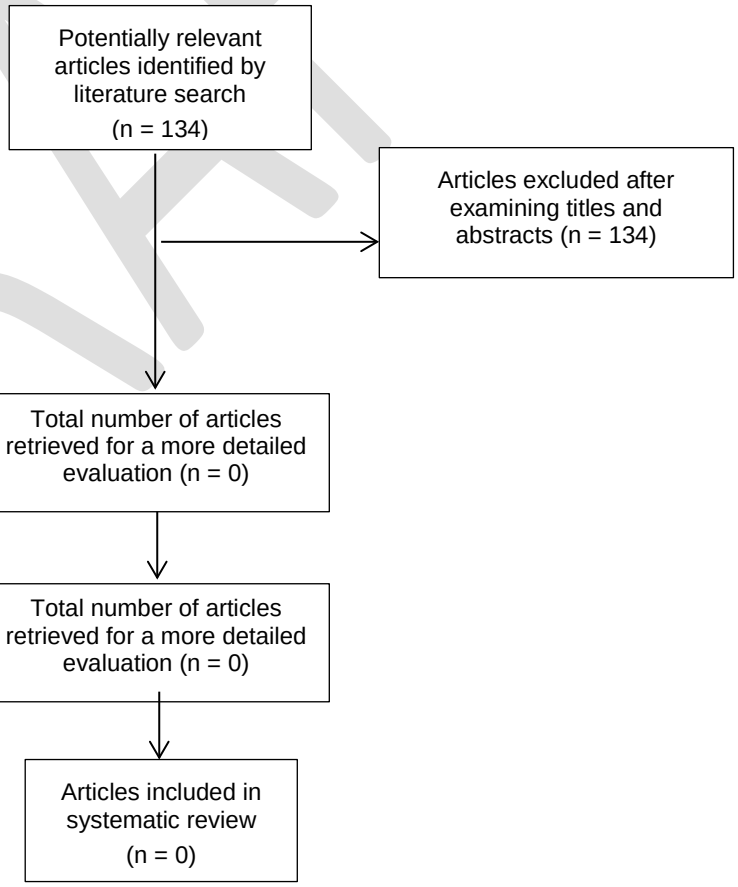

Figure 1. Process of inclusion and exclusion of studies for PICO questions 2b and c

3 Appendices

Appendix A: Search strategies

1. Primary PICO search strategies

For Medline, Premedline, Embase and CENTRAL databases (via Ovid):

#	Searches
1	HPV.mp.
2	hr$HPV.mp.
3	papillomavirus.mp.
4	exp Papillomavirus Infections/
5	exp Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	exp Vaginal Smears/
9	((cervi* or vagina* or pap) and (smear* or screen* or test*)).tw.
10	papanicolaou.tw.
11	LBC.mp.
12	cytolog$.mp.
13	8 or 9 or 10 or 11 or 12
14	exp Colposcopy/
15	colposcop$.mp.
16	14 or 15
17	randomized controlled trial.pt.
18	controlled clinical trial.pt.
19	placebo.ab.
20	randomi?ed.ab.
21	randomly.ab.
22	trial.ab.
23	groups.ab.
24	17 or 18 or 19 or 20 or 21 or 22 or 23
25	7 and 13 and 16 and 24
26	(negative adj5 colposcop*).mp.
27	(normal adj5 colposcop*).mp.
28	26 or 27
29	25 and 28
30	limit 29 to english language
31	limit 30 to humans

32	limit 31 to yr="2004 - 2015"
33	limit 32 to (conference abstract or conference paper or conference proceeding or "conference review" or editorial)
34	32 not 33
35	remove duplicates from 34

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

#	Searches
1	HPV.mp.
2	hr$HPV.mp.
3	papillomavirus.mp.
4	exp Papillomavirus Infections/
5	exp Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	exp Vaginal Smears/
9	((cervi* or vagina* or pap) and (smear* or screen* or test*)).tw.
10	papanicolaou.tw.
11	LBC.mp.
12	cytolog$.mp.
13	8 or 9 or 10 or 11 or 12
14	exp Colposcopy/
15	colposcop$.mp.
16	14 or 15
17	(negative adj5 colposcop*).mp.
18	(normal adj5 colposcop*).mp.
19	17 or 18
20	7 and 13 and 16
21	19 and 20

For Cochrane Database of Systematic Reviews:

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

Appendix B:

NHMRC Evidence Hierarchy for Intervention studies

Level	Study design
I	Meta-analysis or a systematic review of level II studies
II	Randomised controlled trial or a phase III/IV clinical trial
III-1	Pseudo-randomised controlled trial or a meta-analysis/systematic review of level III-1 studies
III-2	Comparative study with concurrent controls: - Phase II clinical trial - Non-randomised, experimental trial9 - Controlled pre-test/post-test study - Adjusted indirect comparisons - Interrupted time series with a control group - Cohort study - Case-control study or a meta-analysis/systematic review of level III-2 studies
III-3	A comparative study without concurrent controls: - Phase I clinical trial - Historical control study - Two or more single arm study10 - Unadjusted indirect comparisons - Interrupted time series without a parallel control group or a meta-analysis/systematic review of level III-3 studies
IV	Case series with either post-test or pre-test/post-test outcomes or a meta-analysis/systematic review of level IV studies

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

Appendix C:

Potentially relevant guidelines identified and reason why not adopted

Year	Organization	Title	Reason why not adopted
2012	American Society for Colposcopy and Cervical Pathology.	Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors	Consensus based on literature searches and KPNC data
2012	Society of Obstetricians and Gynaecologists of Canada	Colposcopic management of abnormal cervical cytology and histology	Consensus based
2009	European Cancer Screening Network and European Cancer Network	European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, Parts 1 and 2	Unclear as to whether based on systematic reviews – full document no longer available at published website