Systematic review report for questions 3b

PICO Question 3b

For HPV-positive women with a referral cytology finding of p/dHSIL and who have an unsatisfactory colposcopy, what is the safety and effectiveness of conservative management compared with diagnostic excision of the transformation zone?

Population	Study design	Intervention	Control	Outcomes
HPV positive women who have undergone colposcopy and the colposcopy was unsatisfactory and cytology was: p/d HSIL	Randomized or pseudo- randomized controlled trial	Conservative management: Co-testing at 3-6 months or repeat HPV test at 12 months	Diagnostic 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

An unsatisfactory colposcopy is a colposcopy in which the transformation zone is not fully visible (Jordon et al., (2008) European guidelines for quality assurance in cervical cancer screening: recommendation for clinical management of abnormal cervical cytology, part 1. Cytopathology 19: 432-354).

1. METHODS

1.1 Searches for existing relevant guidelines

Relevant recent (2005 onwards) guidelines were identified by scanning citations identified from 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, as well as meeting 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

The same strategy was used to identify studies potentially relevant to question 3a and question 3b. 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. Database searches for HPV were combined with searches for unsatisfactory colposcopy and cervical cytology, and where possible, database-specific filters for identifying randomized controlled trials and systematic reviews/meta-analyses of 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.

Inclusion criteria for Question 3b

Selection criteria	Inclusion criteria
Study type	Intervention
Study design	Randomised controlled trial (RCT) or pseudo-randomised controlled trial or Systematic reviews or meta-analyses of RCTs or pseudo-randomised controlled trials
Population	HPV positive women who had undergone colposcopy and the colposcopy was **unsatisfactory** and their cytology was p/d HSIL
Intervention	Conservative treatment; contesting or repeat HPV test
Comparator	Diagnostic excision of the transformation zone
Outcomes	Cervical cancer mortality or Cervical cancer diagnosis or CIN3+ detection
Language	English
Publication period	After 31st December 2003 and before1st September 2015

CIN3+ = cervical intraepithelial neoplasm grade 3 or worse; HSIL = high-grade squamous intraepithelial lesion; pHSIL = possible HSIL

Conference proceedings other than those from the EUROGIN 2015 were not included for either question.

2 RESULTS

2.1. Results of Guidelines Searches

Three sets of guidelines (listed in Appendix C) were identified that contained potentially relevant recommendations. These recommendations either were not based systematic reviews of the evidence, or it was unclear as to whether they were based on systematic reviews of the evidence. Thus, they were not adopted as the pre-specified AGREE II criteria for adoption were not met.

2.2 Results of Literature Searches

Figure 1 outlines the process of identifying relevant articles for the systematic reviews. The searches identified a total of 124 citations. Titles and abstracts were examined, however none of the articles identified were potentially relevant to either of the PICO questions. Thus no studies were found that directly answered the clinical questions and met the inclusion criteria for this systematic review. 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	33	0	0	NA

HTA and DARE	2	0	0	NA
Cochrane database of systematic reviews	73	0	0	NA
EUROGIN 2015 abstracts	16	N/A	0	NA
Total	**124**	**0**	**0**	**NA**

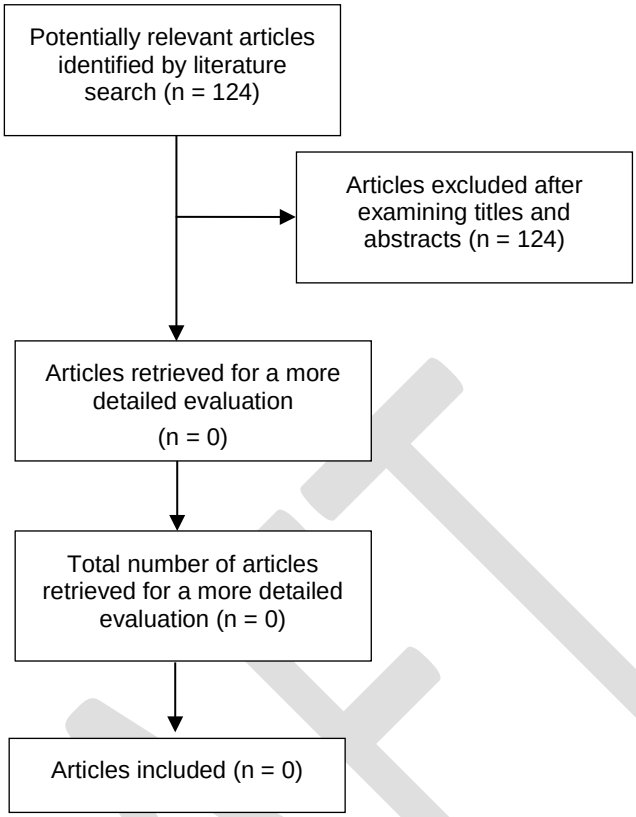

Figure 1. Process of inclusion and exclusion of studies

3 Appendices

Appendix A: 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	squamocolumnar junction.mp.
18	transformation zone.mp.
19	SCJ.mp.
20	(colposcop* adj5 (unsatisfactory or satisfactory or adequate)).mp.
21	17 or 18 or 19 or 20
22	randomized controlled trial.pt.
23	controlled clinical trial.pt.
24	placebo.ab.
25	randomi?ed.ab.
26	randomly.ab.
27	trial.ab.
28	groups.ab.
29	22 or 23 or 24 or 25 or 26 or 27 or 28
30	7 and 13 and 16 and 21 and 29
31	limit 30 to english language
32	limit 31 to humans [Limit not valid in CCTR; records were retained]
33	limit 32 to yr="2004 - 2015"
34	remove duplicates from 33

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 Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessments (HTA) 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	squamocolumnar junction.mp.
18	transformation zone.mp.
19	SCJ.mp.
20	(colposcop* adj5 (unsatisfactory or satisfactory or adequate)).mp.
21	17 or 18 or 19 or 20
22	7 and 13 and 16 and 21

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	Organisation	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
2008 & 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 recommendations were based on systematic reviews – full document no longer available at published website