Systematic review report for question 16

PICO Question 16: For women have been treated for a high grade precancerous squamous lesion what is the safety and effectiveness of testing with HPV test and cytology at 12 months after treatment and discharging if double-negative compared with testing at 12 and 24 months and discharging if double-negative at both 12 and 24 months?

Population	Study design	Intervention	Control	Outcomes
Women who have been treated for high grade precancerous squamous lesions	Randomized or pseudo-randomized controlled trial	Cytology and HPV testing 12 months after treatment with discharge if double negative	Cytology and HPV testing 12 and 24 months after treatment with discharge if double negative on both occasions	Cervical cancer mortality Cervical cancer diagnosis Precancerous high grade lesion detection

1. METHODS

1.1. Guidelines

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 Search

Medline including articles in process, 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 HPV were combined with searches for cervical lesions or cancer and their treatments, 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 term “HPV”, and abstracts for the 2015 EUROGIN conference were searched using the term “intraepithelial”. Reference lists of relevant articles and guidelines were checked for additional potentially relevant articles.

1.3. Inclusion Criteria

Selection criteria	Inclusion criteria
Study type	Intervention
Study design	Randomised controlled trial or pseudo-randomised controlled trial or Systematic reviews or meta-analyses of RCTs or pseudo-randomised controlled trials
Population	Women who have been treated for high grade precancerous squamous lesions
Intervention	Cytology and HPV testing 12 months after treatment with discharge if double negative
Comparator	Cytology and HPV testing 12 and 24 months after treatment with discharge if double negative on both occasions
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

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

2. RESULTS

2.1 Results of Guidelines Searches

Seven sets of guidelines (listed in Appendix C) were identified that contained potentially relevant recommendations. These recommendations either did not directly address the clinical question, were not based systematic reviews of the evidence or it was unclear as to whether they were based on systematic reviews of the evidence and thus were not adopted as they did not meet the pre-specified AGREE II criteria for adoption.

2.2 Results of Literature Searches

Figure 1 outlines the process of identifying relevant articles for the systematic review. The searches identified a total of 305 citations. Titles and abstracts were examined and 2 articles were retrieved for a more detailed evaluation. Neither met the inclusion criteria for the PICO question. Thus no studies were found that directly answered the clinical question 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.

The retrieved articles that were not included and the reasons for their exclusion are documented in Appendix C. In summary, they were excluded because either they did not compare co-testing at 12 months only with 12 and

24 month co-testing or they were systematic reviews that reportedly found no RCTs addressing the clinical question.

Database or Source	Number of Citations	Number of Articles Collected	Number of Articles Included	ATSI filter results
Medline, PreMedline, CENTRAL and Embase	224	1	0	0
HTA and DARE	7	0	0	N/A
Cochrane database of systematic reviews	74	1	0	N/A
EUROGIN 2015 abstracts	0	N/A	0	N/A
Snowballing	0	0	0	N/A
TOTAL	**305**	**2**	**0**	**0**

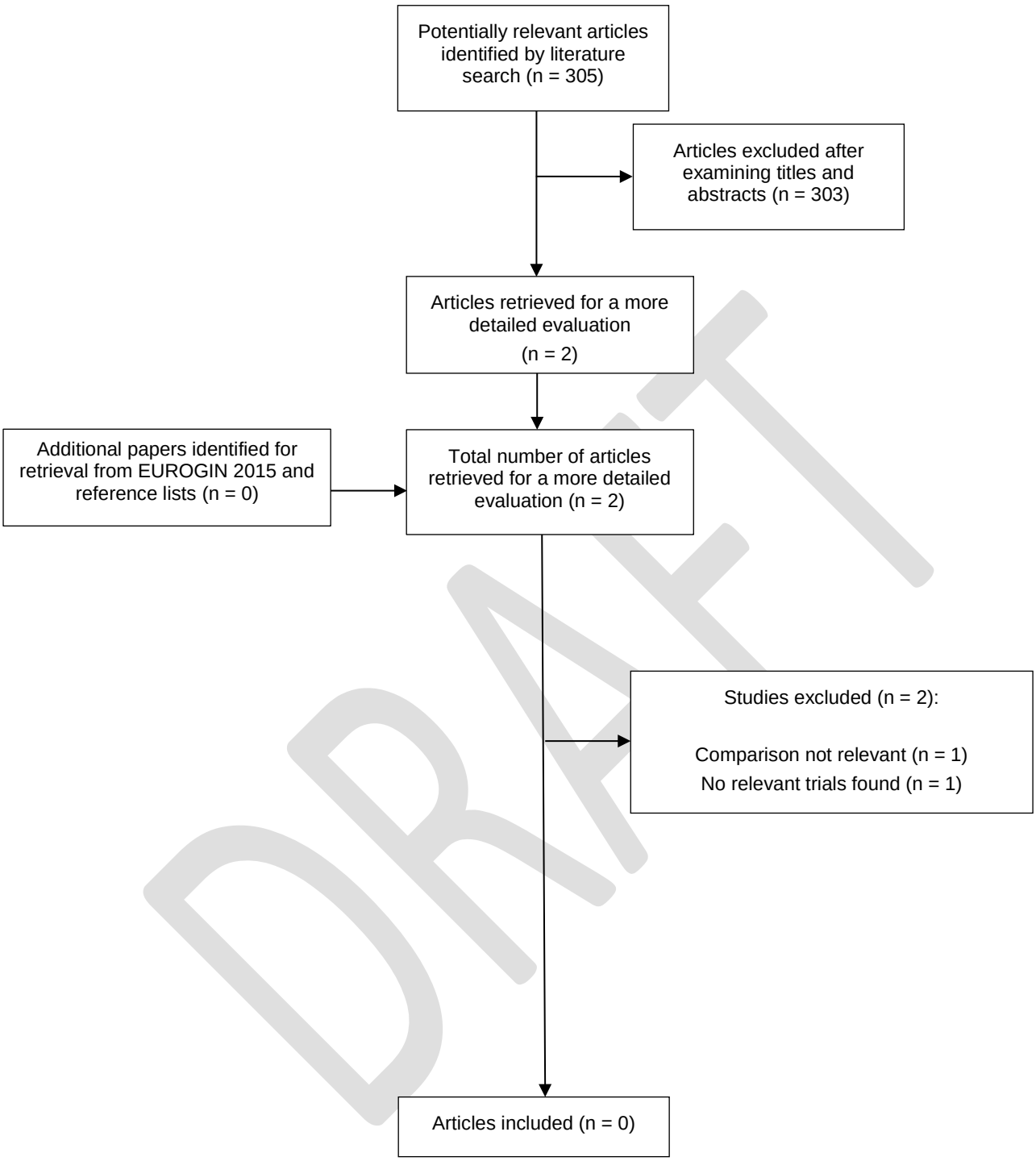

Figure 1. Process of inclusion and exclusion of studies

APPENDICES

Appendix A: Search strategies used

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

#	Searches
1	Uterine Cervical Neoplasms/
2	Cervical Intraepithelial Neoplasia/
3	CIN*.mp.
4	(cervi* adj5 (cancer* or tumor* or tumour* or malignan* or neoplas* or carcinoma* or adenocarcinoma* or precancer* or pre-cancer*)).mp.
5	AIS.mp.
6	Adenocarcinoma in Situ/
7	(adenocarcinoma* adj5 endocervi*).mp.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	excision*.mp.
10	surg*.mp.
11	cone biops*.mp.
12	(cone adj3 biops*).mp.
13	coni?ation.mp.
14	(LEEP or LLETZ or SWETZ or NETZ).mp.
15	loop electro-excisional procedure.mp.
16	laser.mp.
17	Fischer cone.mp.
18	electro-surg*.mp.
19	recurrent.mp.
20	"test of cure".mp.
21	(treat* adj5 surveillance).mp.
22	(post-treatment or posttreatment).mp.
23	(treat* adj5 follow*).mp.
24	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25	HPV.mp.
26	papillomavir*.mp.
27	hr$HPV.mp.
28	exp Papillomavirus Infections/
29	exp Papillomaviridae/
30	25 or 26 or 27 or 28 or 29
31	8 and 24 and 30
32	randomized controlled trial.pt.
33	controlled clinical trial.pt.
34	placebo.ab.
35	randomi?ed.ab.
36	randomly.ab.

37	trial.ab.
38	groups.ab.
39	32 or 33 or 34 or 35 or 36 or 37 or 38
40	31 and 39
41	limit 40 to (english language and female and humans and yr="2004 -Current")
42	vaccine.mp.
43	41 not 42
44	remove duplicates from 43

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	Uterine Cervical Neoplasms/
2	Cervical Intraepithelial Neoplasia/
3	CIN*.mp.
4	(cervi* adj5 (cancer* or tumor* or tumour* or malignan* or neoplas* or carcinoma* or adenocarcinoma* or precancer* or pre-cancer*)).mp.
5	AIS.mp.
6	Adenocarcinoma in Situ/
7	(adenocarcinoma* adj5 endocervi*).mp.
8	1 or 2 or 3 or 4 or 5 or 6 or 7
9	excision*.mp.
10	surg*.mp.
11	cone biops*.mp.
12	(cone adj3 biops*).mp.
13	coni?ation.mp.
14	(LEEP or LLETZ or SWETZ or NETZ).mp.
15	loop electro-excisional procedure.mp.
16	laser.mp.
17	Fischer cone.mp.
18	electro-surg*.mp.
19	recurrent.mp.
20	"test of cure".mp.
21	(treat* adj5 surveillance).mp.
22	(post-treatment or posttreatment).mp.

23	(treat* adj5 follow*).mp.
24	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25	HPV.mp.
26	papillomavir*.mp.
27	hr$HPV.mp.
28	exp Papillomavirus Infections/
29	exp Papillomaviridae/
30	25 or 26 or 27 or 28 or 29
31	8 and 24 and 30

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	American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology	Screening guidelines for the prevention and early detection of cervical cancer.	Does not directly address the clinical question
2012	American College of Obstetricians and Gynecologists	Screening for cervical cancer.	Unclear as to whether recommendations were based on systematic reviews – appear to be based on other guidelines
2012	Society of Obstetricians and Gynaecologists of Canada	Colposcopic management of abnormal cervical cytology and histology.	Does not directly address the clinical question
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, Part 2	Unclear as to whether recommendations were based on systematic reviews – full document no longer available at published website
2013	University of Michigan Health System	Cancer screening	Based on other existing guidelines
2010	NHS	Colposcopy and Programme Management Guidelines for the NHS Cervical Screening Programme	Unclear as to whether recommendations were based on systematic reviews

Excluded studies

Study	Reason for Exclusion
Bais 2008	No relevant comparison
Van der Heijden 2015	No relevant data - Found no evidence from RCTs to inform decision about best surveillance strategy following treatment for CIN

References: Excluded studies

1. Bais AG, Eijkemans MJ, Rebolj M et al. Post-treatment CIN: randomised clinical trial using hrHPV testing for prediction of residual/recurrent disease. *International Journal of Cancer*. 2009;124:889-895.

2. van der Heijden E, Lopes AD, Bryant A, Bekkers R, Galaal K. Follow-up strategies after treatment (large loop excision of the transformation zone (LLETZ)) for cervical intraepithelial neoplasia (CIN): Impact of human papillomavirus (HPV) test. *Cochrane Database of Systematic Reviews* 2015, Issue 1. Art. No.: CD010757. DOI: 10.1002/14651858.CD010757.pub2.