Systematic review report for question 4

PICO Question 4: For HPV positive women currently not in treatment follow-up who have undergone colposcopy (without treatment) with colposcopy LSIL and CIN 1 or less on biopsy, what is the safety and effectiveness of excisional treatment or testing with repeat HPV test at 12 months when compared with repeat cytology and HPV testing in 12 months?

Population	Study design	Intervention	Control	Outcome
HPV positive women, who have undergone colposcopy and colposcopy LSIL, confirmed by biopsy CIN1 or less, and referral cytology was: i. negative or p/d LSIL or ii. p/dHSIL	Randomized or pseudo randomized controlled trial	Excisional treatment or Repeat HPV test at 12 months	**i. Negative cytology or p/dLSIL:** Repeat cytology and HPV testing at 12 months: Colposcopy if HPV positive test or if cytology pHSIL or worse; If HPV negative and cytology negative or p/dLSIL: repeat HPV and cytology test at 24 months **ii. p/dHSIL:** repeat cytology and colposcopy in 6 months	Cervical cancer mortality Cervical cancer diagnosis Precancerous high grade lesion detection

CIN1: cervical intraepithelial neoplasia grade one; dLSIL = definite LSIL; LSIL = low-grade squamous intraepithelial lesion; pLSIL = possible LSIL; HSIL: high-grade intraepithelial lesion

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 CIN1 were combined with searches for HPV and colposcopy, 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. Abstracts for the 2015 EUROGIN conference were searched using the

terms CIN1 and colposcopy. 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 (RCT) or pseudo-randomised controlled trial or Systematic reviews or meta-analyses of RCTs or pseudo-randomised controlled trials
Population	HPV positive women, who have undergone colposcopy and colposcopy LSIL, confirmed by biopsy CIN1 or less and referral cytology was: i. negative or p/d LSIL or ii. p/dHSIL
Intervention	Excisional treatment or Repeat HPV test at 12 months
Comparator	i. negative or p/dLSIL Repeat cytology and HPV testing in 12 months ii. p/dHSIL Repeat cytology and colposcopy in 6 months
Outcomes	Cervical cancer mortality or Cervical cancer diagnosis or CIN3+ detection
Language	English
Publication period	After 31st December 2003 and before1st September 2015

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

2. RESULTS

2.1. Guidelines

Three 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 Search

Figure 1 outlines the process of identifying relevant articles for the systematic review. The searches identified a total of 92 citations. Titles and abstracts were examined however none of the articles identified were potentially relevant to the systematic review. 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.

Database or Source	Number of Citations	Number of Articles Collected	Number of Articles Included	ATSI filter results
Medline + CENTRAL + Embase	91	0		0
HTA + DARE	1	0		
EUROGIN 2015 abstracts	0			
Snowballing	0			

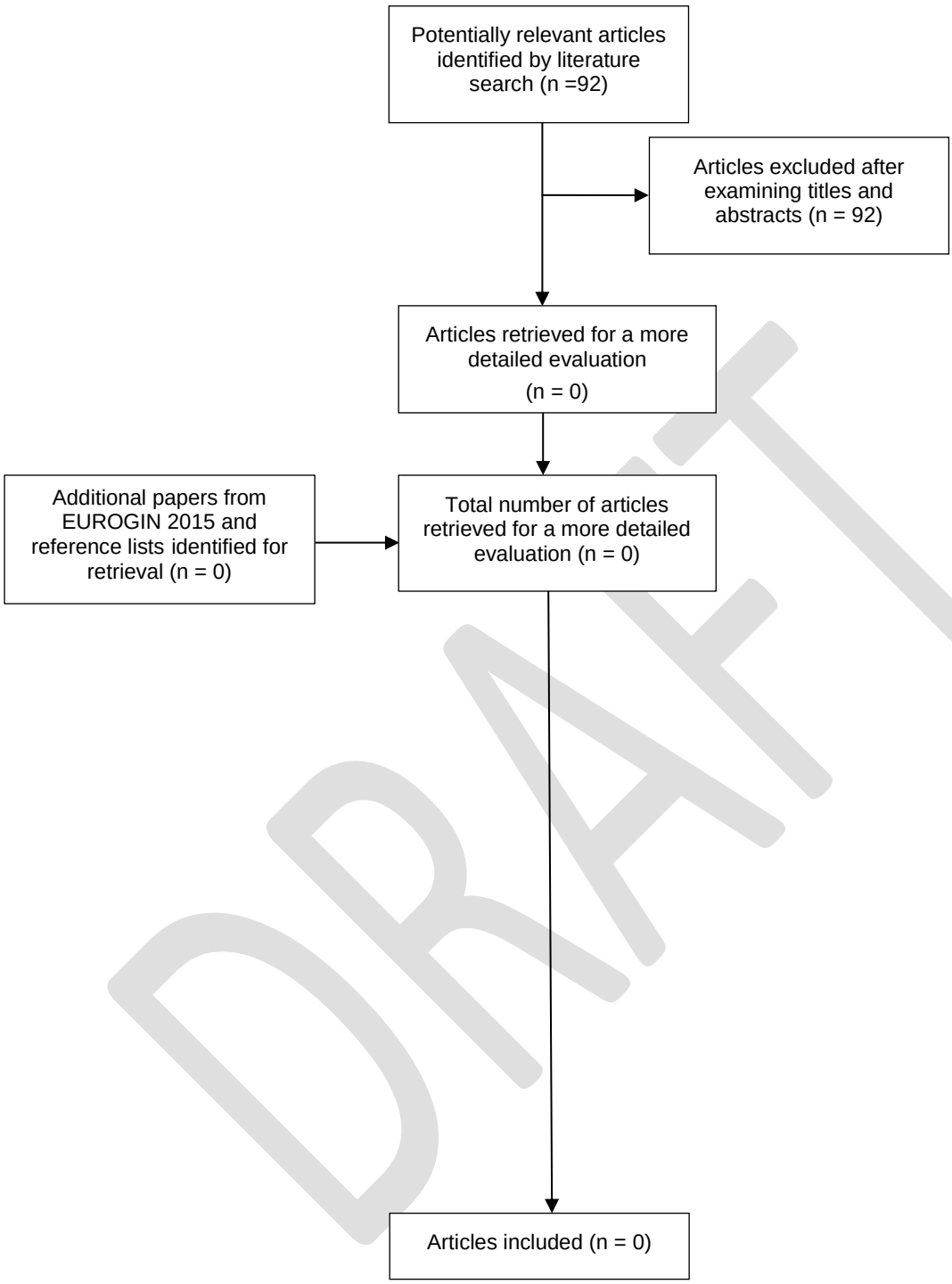

Figure 1. Process of inclusion and exclusion of studies

APPENDICES

Appendix A: Search strategies used

For Medline including articles in process, Embase and CENTRAL databases (via OvidSP):

#	Searches
1	HPV.mp.
2	hr$HPV.mp.
3	papillomavirus.mp.
4	exp Papillomavirus Infections/
5	exp DNA Probes, HPV/
6	1 or 2 or 3 or 4 or 5
7	CIN 1.mp.
8	CIN1.mp.
9	cervical intraepithelial neoplasia 1.mp.
10	cervical intraepithelial neoplasia grade 1.mp.
11	cervical intraepithelial neoplasia one.mp.
12	cervical intraepithelial neoplasia grade one.mp.
13	low grade neoplas$.mp.
14	low-grade neoplas?.mp.
15	LG neoplas$.mp.
16	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17	colposcop$.mp.
18	6 and 16 and 17
19	randomized controlled trial.pt.
20	controlled clinical trial.pt.
21	placebo.ab.
22	randomi?ed.ab.
23	randomly.ab.
24	trial.ab.
25	groups.ab.
26	19 or 20 or 21 or 22 or 23 or 24 or 25
27	18 and 26
28	limit 27 to (english language and yr="2005 -Current")
29	remove duplicates from 28

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:

#	Searches
1	HPV.mp.
2	hr$HPV.mp.
3	papillomavirus.mp.
4	exp Papillomavirus Infections/
5	exp Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	CIN1.mp.
9	CIN 1.mp.
10	cervical intraepithelial neoplasia 1.mp.
11	cervical intraepithelial neoplasia grade 1.mp.
12	cervical intraepithelial neoplasia one.mp.
13	cervical intraepithelial neoplasia grade one.mp.
14	low grade neoplas$.mp.
15	low-grade neoplas?.mp.
16	LG neoplas$.mp.
17	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
18	colposcop$.mp.
19	7 and 17 and 18

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**.	**2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors** Massad et al., for the 2012 ASCCP Consensus guidelines conference (2013). 2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Lower Genital Tract Disease 17(5): S1 – S27	Consensus based
2012	**Society of Obstetricians and Gynaecologists of Canada**	**Colposcopic management of abnormal cytology and histology 2012** Bentley et al., (2012) Colposcopic management of abnormal Cervical Cytology and histology J Obstet Gynaecol Can 34 (12) 1188-1202	Unclear if evidence based
2009	**Jordan et al**	**European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, Part 2 2009** Jordan et al., (2009) Cytopathology 20:5-16	Unclear if evidence