# Systematic review report for question 7

**PICO Question 7:** For women who are HPV positive with adenocarcinoma in situ (AIS) or possible high-grade glandular lesion cytology or biopsy confirmed AIS, what is the safety and effectiveness of large loop excision of the transformation zone (LLETZ), Fischer cone, laser cone or straight wire/needle excision of the transformation zone (SWETZ/NETZ) compared with cold knife cone biopsy?

| Population | Study design | Intervention | Control | Outcomes |
|---|---|---|---|---|
| Women who are HPV positive with AIS or possible high-grade glandular lesion cytology or biopsy confirmed AIS | Randomized or pseudo-randomized controlled trial | LLETZ or Fischer cone or laser cone or SWETZ/ NETZ or any electro-surgery of the transformation zone | Cold knife cone biopsy | Cervical cancer mortality<br>Cervical cancer diagnosis<br>CIN3+ detection<br>Recurrent AIS detection<br>Completeness of excision<br>Depth of excision |

*AIS = adenocarcinoma in situ; CIN3+ = cervical intraepithelial neoplasm grade 3 or worse*

## 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 glandular abnormalities and/or cervical adenocarcinoma were combined with searches for excisional techniques, 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 “gland”, “AIS” and “cone”. 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<br>or<br>Systematic reviews or meta-analyses of RCTs or pseudo-randomised controlled trials |
| Population | Women who are HPV positive with<br>AIS or possible high-grade glandular lesion cytology or biopsy confirmed AIS |
| Intervention | LLETZ<br>or<br>Fischer cone<br>or<br>laser cone<br>or<br>SWETZ/NETZ<br>or<br>Any electro-surgery of the transformation zone |
| Comparator | Cold knife cone biopsy |
| Outcomes | Cervical cancer mortality<br>or<br>Cervical cancer diagnosis<br>or<br>CIN3+ detection<br>or<br>Recurrent AIS detection<br>or<br>Completeness of excision<br>or<br>Depth of excision |
| Language | English |
| Publication period | After 31st December 2003 and before1st September 2015 |

*AIS = adenocarcinoma in situ; CIN3+ = cervical intraepithelial neoplasm grade 3 or worse*

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

## 2. RESULTS

### 2.1. Guidelines

Two sets of guidelines (listed in Appendix C) were identified that contained potentially relevant recommendations. Neither directly addressed the clinical question and thus were not adopted.

### 2.2. Results of Literature Search

Figure 1 outlines the processes of identifying relevant articles for the systematic review. The searches identified a total of 27 citations. Titles and abstracts were examined but no studies were found that directly answered the clinical questions and met the inclusion criteria for the 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 | Number of | Number of Articles | ATSI filter results |
|---|---|---|---|---|

| | Citations | Articles Collected | Included | |
|---|---|---|---|---|
| Medline, Premedline, CENTRAL and Embase | 25 | 0 | 0 | 0 |
| HTA and DARE | 2 | 0 | 0 | N/A |
| EUROGIN 2015 abstracts | 0 | 0 | 0 | N/A |
| **Total** | **27** | **0** | **0** | **0** |

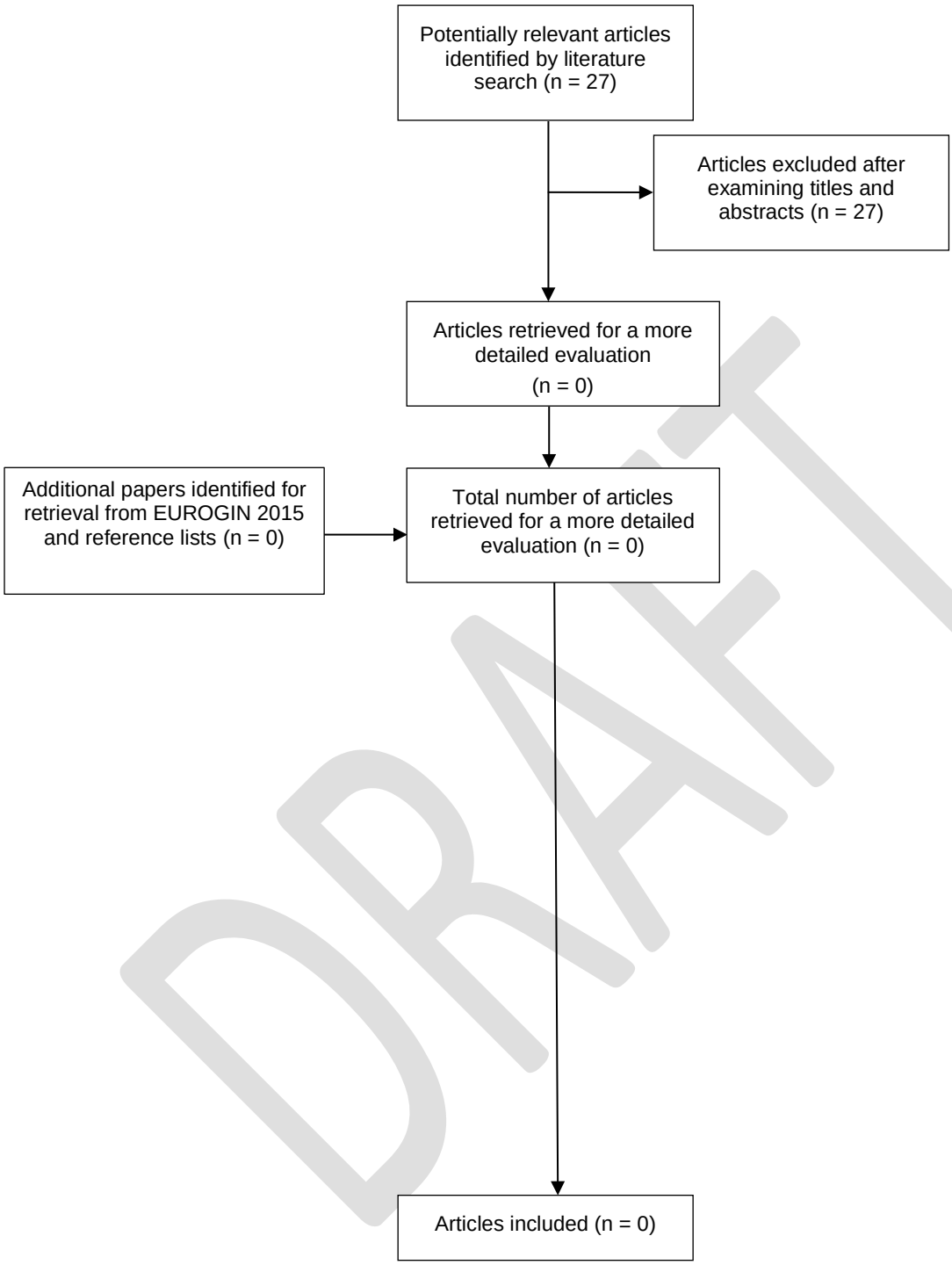




**Figure 1.** Process of inclusion and exclusion of studies

# APPENDICES

### Appendix A: Search strategies used

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

| # | Searches |
|---|---|
| 1 | (adenocarcinoma adj5 cervi*).mp. |
| 2 | (adenocarcinoma adj5 endocervi*).mp. |
| 3 | exp Adenocarcinoma in Situ/ |
| 4 | AIS.mp. |
| 5 | ACIS.mp. |
| 6 | HGGA.mp. |
| 7 | HGGL.mp. |
| 8 | atypical endocervi*.mp. |
| 9 | atypical gland*.mp. |
| 10 | (gland* adj5 (dysplas* or abnormal* or lesion*)).mp. |
| 11 | 9 or 10 |
| 12 | (endocerv* or cervi*).mp. |
| 13 | 11 and 12 |
| 14 | AGUS.mp. |
| 15 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 13 or 14 |
| 16 | excision*.mp. |
| 17 | cone biops*.mp. |
| 18 | (cone adj3 biops*).mp. |
| 19 | coni?ation.mp. |
| 20 | CKC.mp. |
| 21 | LEEP.mp. |
| 22 | loop electro-excisional procedure.mp. |
| 23 | LLETZ.mp. |
| 24 | SWETZ.mp. |
| 25 | NETZ.mp. |
| 26 | laser con*.mp. |
| 27 | laser excis*.mp. |
| 28 | Fischer cone.mp. |
| 29 | electro-surg*.mp. |
| 30 | 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 |
| 31 | randomized controlled trial.pt. |
| 32 | controlled clinical trial.pt. |
| 33 | placebo.ab. |
| 34 | randomi?ed.ab. |
| 35 | randomly.ab. |
| 36 | trial.ab. |
| 37 | groups.ab. |

| | |
|---|---|
| 38 | 31 or 32 or 33 or 34 or 35 or 36 or 37 |
| 39 | 15 and 30 and 38 |
| 40 | limit 39 to english language |
| 41 | limit 40 to yr="2004 -Current" |
| 42 | remove duplicates from 41 |

*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 | (adenocarcinoma adj5 cervi*).mp. |
| 2 | (adenocarcinoma adj5 endocervi*).mp. |
| 3 | exp Adenocarcinoma in Situ/ |
| 4 | AIS.mp. |
| 5 | ACIS.mp. |
| 6 | HGGA.mp. |
| 7 | HGGL.mp. |
| 8 | atypical endocervi*.mp. |
| 9 | atypical gland*.mp. |
| 10 | (gland* adj5 (dysplas* or abnormal* or lesion*)).mp. |
| 11 | 9 or 10 |
| 12 | (endocerv* or cervi*).mp. |
| 13 | 11 and 12 |
| 14 | AGUS.mp. |
| 15 | 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 13 or 14 |
| 16 | excision*.mp. |
| 17 | cone biops*.mp. |
| 18 | (cone adj3 biops*).mp. |
| 19 | coni?ation.mp. |
| 20 | CKC.mp. |
| 21 | LEEP.mp. |
| 22 | loop electro-excisional procedure.mp. |
| 23 | LLETZ.mp. |
| 24 | SWETZ.mp. |
| 25 | NETZ.mp. |
| 26 | laser con*.mp. |

| | |
|---|---|
| 27 | laser excis*.mp. |
| 28 | Fischer cone.mp. |
| 29 | electro-surg*.mp. |
| 30 | 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 |
| 31 | 15 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:<br>- Phase II clinical trial<br>- Non-randomised, experimental trial9<br>- Controlled pre-test/post-test study<br>- Adjusted indirect comparisons<br>- Interrupted time series with a control group<br>- Cohort study<br>- Case-control study<br>or a meta-analysis/systematic review of level III-2 studies |
| III-3 | A comparative study without concurrent controls:<br>- Phase I clinical trial<br>- Historical control study<br>- Two or more single arm study10<br>- Unadjusted indirect comparisons<br>- Interrupted time series without a parallel control group<br>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 |
|---|---|---|---|
| **2008** | 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 | Did not address PICO as to whether LLETZ, Fischer cone, laser cone or NETZ/SWETZ or other improved patient outcomes compared to cold knife cone biopsy |
| **2012** | Society of Obstetricians and Gynaecologists of Canada | Colposcopic management of abnormal cervical cytology and histology | Did not address PICO as to whether LLETZ, Fischer cone, laser cone or NETZ/SWETZ or other improved patient outcomes compared to cold knife cone biopsy |