Total hysterectomy after adenocarcinoma in situ (AIS)

Systematic review report

PICO

This systematic review addresses the following PICO which is summarised in detailed in Table 1

For women who have had a total hysterectomy after adenocarcinoma in situ (AIS)

i. who have been treated for AIS by excision with clear margins and are under surveillance, and subsequently had a total hysterectomy (either as completion therapy or for other benign indications) OR

ii. who have had incomplete excision of AIS with clear margins on total hysterectomy OR

iii. who had a total hysterectomy as initial treatment for AIS with clear margins on hysterectomy

AND have had i. 2 consecutive negative annual HPV and cytology co-tests ii. 10 consecutive negative annual HPV and cytology co-tests, what is the safety of cessation of annual co-testing compared to continued annual co-testing?

Table 1. PICO components

Population	***Study design***	***Intervention***	***Control***	***Outcomes***
Women who have had a total hysterectomy after adenocarcinoma in situ (AIS) who: i. have been treated for AIS by excision with clear margins and are under surveillance, and subsequently had a total hysterectomy (either as completion therapy or for other benign indications) ii. following incomplete excision of AIS using cold-knife cone biopsy or diathermy excision (or other excisional treatment), with clear margins on total hysterectomy iii. who had a total hysterectomy as initial treatment for AIS with clear margins on hysterectomy	Screening randomized or pseudorandomized **controlled trial**	Cessation of annual co-testing after i. 2 consecutive negative annual HPV and cytology co-tests (test of cure) ii. 10 consecutive negative annual HPV and cytology co-tests	Indefinite annual HPV and cytology co-testing	Cervical or vaginal cancer diagnosis Cervical or vaginal cancer mortality

AIS = adenocarcinoma in situ; HPV = human papillomavirus

1. METHOD

1.1 Selection Criteria

Table 2. Selection criteria.

	Inclusion criteria	***Exclusion criteria***
Study type	Intervention	
Study design	Screening randomized or pseudorandomized controlled trial	Cohort studies Case-control studies
Population	Women who have had a total hysterectomy after adenocarcinoma in situ (AIS) who: i. have been treated for AIS by excision with clear margins and are under surveillance, and subsequently had a total hysterectomy (either as completion therapy or for other benign indications) ii. following incomplete excision of AIS using cold-knife cone biopsy or diathermy excision (or other excisional treatment), with clear margins on total hysterectomy iii. who had a total hysterectomy as initial treatment for AIS with clear margins on hysterectomy	
Intervention	Cessation of annual co-testing after i. 2 consecutive negative annual HPV and cytology co-tests (test of cure) ii. 10 consecutive negative annual HPV and cytology co-tests	
Comparator	Indefinite annual HPV and cytology co-testing	No comparator
Outcome	Cervical or vaginal cancer diagnosis Cervical or vaginal cancer mortality	
Publication date	2015 onwards	
Publication type	Peer-reviewed journal article or letter or comment that reports original data	Conference abstract Editorial Letter or article that does not report original data
Language	English	

AIS = adenocarcinoma in situ; HPV = human papillomavirus

1.2 Definitions and terminology

For the purposes of this review:

Cervical cancer refers to primary cervical cancer

1.3 Guidelines

Relevant recent (2015 onwards) guidelines were identified by scanning the citations identified by the literature search (described in section 1.4 below) and by searches of the following websites and databases in February and March:

- International Health Technology Assessment (HTA) database
- Guidelines International Network (GIN) database
- National Institute for Health and Care Excellence (NICE) Guidelines website
- Scottish Intercollegiate Guidelines Network (SIGN) website
- NHS England website
- Public Health Wales website

- World Health Organisation website
- The American Cancer Society website
- The American college of Obstetricians and Gynecologists website
- U.S. Preventive Services Task Force website
- University of Michigan Rogel Cancer Centre website
- The American Society of Clinical Oncology website
- NCCN Clinical Practice Guidelines in Oncology website
- British Columbia Medical Association website
- Health Canada
    - Canadian Task Force on Preventive Health Care (CTFPHC) Guidelines (2016) website
- Toward Optimized Practice (TOP Alberta doctors) website
- Cancer Care Ontario website
- European Society of Medical Oncologists (ESMO) website
- The Danish Health and Medicines Authority website
- Haute Autorite de Sante website

To be considered for adoption by the Working Party, guidelines had to be evidence-based and meet the pre-specified criteria of scores of greater or equal to 70% for the following domains: rigour of development, clarity of presentation and editorial independence of the AGREE II instrument (http://www.agreetrust.org/resource-centre/agree-ii/). Guidelines were not considered for adoption if they were not based on systematic reviews of the evidence i.e. did not report using systematic methods to search for evidence, did not clearly describe the criteria for selecting the evidence or did not assess the risk of bias or where this is not possible, appraise the quality of the evidence.

1.4 Literature searches

Medline (including MEDLINE Epub Ahead of Print, I-Process & Other Non-Indexed Citations), Embase and CENTRAL databases were searched on 8th May 2023 combining text terms and database-specific subject headings for adenocarcinoma in situ, hysterectomy, and randomised controlled trial. Searches were limited to articles published in English from 1st January 2015 onwards and were designed to identify potentially relevant trials in populations that included Aboriginal and Torres Strait Islander peoples. A complete list of the terms used is included as Appendix A. On 3rd March 2023 the Cochrane Database of Systematic Reviews was searched from inception using the search terms “human papilloma virus” and “adenocarcinoma in situ” and the INAHTA database was searched from 2005 onwards using the search term “hysterectomy”. Reference lists of included articles, recent relevant guidelines and systematic reviews were checked for potential additional articles.

1.5 Risk of bias assessments

For included studies risk of bias assessments using the Cochrane Collaboration Risk of Bias-II tool (Sterne 2019) were planned.

1.6 GRADE assessment of the certainty of the evidence

GRADE assessments were planned to assess the certainty of the body of evidence for each outcome. (https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-certainty-evidence).

2. RESULTS

2.1 Guidelines searches

Twenty-eight potentially relevant guidelines were identified. At least some recommendations in six of these were based on systematic reviews published in English. Of these, none included recommendations that addressed the question of interest (Appendix B).

2.2 Literature searches

Figure 1 outlines the process of identifying relevant articles for this systematic review update. The combined Medline, Embase and CENTRAL search identified 152 citations and the search of the Cochrane Database of Systematic Reviews and INHATA database identified 109 citations, resulting in a total of 261 citations. Titles and abstracts were examined by one reviewer, and no articles were retrieved for a more detailed evaluation. No randomised controlled trials were found that met the inclusion criteria. No trials that included Aboriginal or Torres Strait Islander peoples were identified.

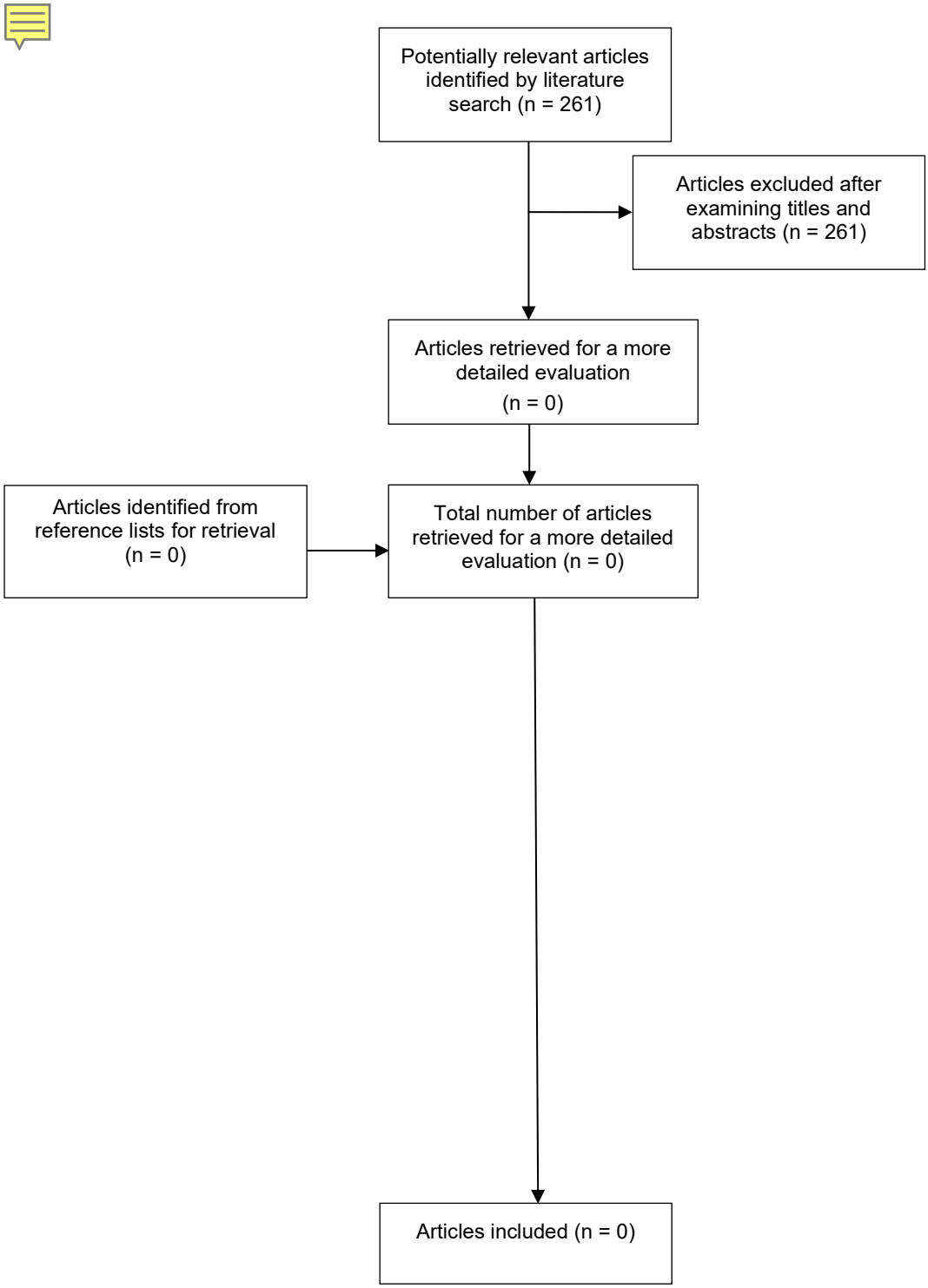

Figure 1. Process of inclusion and exclusion of studies for the systematic review update.

REFERENCES:

Sterne JA, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019; 366: l4898.

APPENDICES

Appendix A: Medline Embase and CENTRAL database (via Ovid platform) search strategy

Database(s): **Embase Classic+Embase** 1947 to 2023 May 05**, Ovid MEDLINE(R) ALL** 1946 to May 04, 2023**, EBM Reviews - Cochrane Central Register of Controlled Trials** April 2023
Search Strategy:

#	Searches
1	AIS.tw.
2	Adenocarcinoma in Situ/
3	adenocarcinoma in situ.tw.
4	(adenocarcinoma adj3 situ).tw.
5	(adenocarcinoma* adj3 (cervi* or endocervix*)).tw.
6	gland*.tw.
7	1 or 2 or 3 or 4 or 5 or 6
8	exp Hysterectomy, Vaginal/ or exp Hysterectomy/
9	(hysterectomy or post-hysterectomy).tw.
10	8 or 9
11	7 and 10
12	randomized controlled trial.pt.
13	controlled clinical trial.pt.
14	placebo.ab.
15	randomi?ed.ab.
16	randomly.ab.
17	trial.ab.
18	groups.ab.
19	12 or 13 or 14 or 15 or 16 or 17 or 18
20	11 and 19
21	limit 20 to (english language and yr="2015 -Current")
22	remove duplicates from 21

Used the Cochrane sensitivity maximizing filter for identifying randomized controlled trials in Medline (https://training.cochrane.org/handbook/current/chapter-04-technical-supplement-searching-and-selecting-studies accessed 8/03/2023).

Appendix B: Potentially Relevant Guidelines reportedly based on systematic reviews

Developer	*Publication or link*	*Title*	*Year*	*Reasons for not adopting*
U.S. Preventive Services Task Force	https://jamanetwork.com/journals/jama/fullarticle/2697704 https://www.ncbi.nlm.nih.gov/books/NBK526306/	Screening for cervical cancer	2018	No relevant recommendations
WHO	https://www.who.int/publications/i/item/9789240030824	WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition	2021	No relevant recommendations
WHO	Santesso N, Mustafa RA, Schunemann HJ et al. (2016) Int J Gynaecol Obstet: 132(3):252-8	World Health Organization Guidelines for treatment of cervical intraepithelial neoplasia 2-3 and screen-and-treat strategies to prevent cervical cancer	2016	No relevant recommendations
NICE	https://www.nice.org.uk/guidance/dg32	Adjunctive colposcopy technologies for assessing suspected cervical abnormalities	2018	No relevant recommendations
Saudi Arabia Ministry of Health	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6074318/	Clinical Practice Guidelines on the Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention in Saudi Arabia	2016	No relevant recommendations
Italian Group on Cervical Screening	https://www.imrpress.com/journal/EJGO/42/5/10.31083/j.ejgo4205157	Evidence-based guidelines for follow up of women treated for cervical intraepithelial neoplasia grade 2 or 3 (CIN2/3) in Italian screening programmes	2021	No relevant recommendations