Systematic review report for question 11

PICO Question 11: For women who were exposed to diethylstilboestrol (DES) in utero and their daughters what is the safety and effectiveness of screening using strategies other than those recommended for the general population compared to those recommended for the general population?

Population	Study design	Intervention	Control	Outcome
Asymptomatic women exposed in utero to DES and their daughters	Screening randomized or pseudo-randomized controlled trial	Current practice: Annual vaginal examination, cervical and vaginal cytology test, HPV test and colposcopy of the lower genital tract	Recommended screening strategy for general population: Primary HPV screening every 5 years from ages 25–69 years using partial genotyping with women positive for HPV16/18 referred to colposcopy and women positive for other oncogenic types undergoing cytology triage	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 diethylstilbestrol were combined with searches for vaginal or cervical neoplasms, 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 all search strategies are included as Appendix A. Abstracts for the 2015 EUROGIN conference were searched using the term “diethylstilbestrol”. 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 screening trial or Systematic reviews or meta-analyses of RCTs or pseudo-randomised controlled screening trials
Population	Asymptomatic women exposed in utero to DES and/or their daughters
Intervention	Screening protocol
Comparator	Another screening protocol
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

Two sets of guidelines (listed in Appendix C) were identified that contained potentially relevant recommendations. These recommendations were either 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 26 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 men that met the inclusion criteria.

Database or Source	Number of Citations	Number of Articles Collected	Number of Articles Included	ATSI filter results
Medline, CENTRAL and Embase	18	0	0	N/A
HTA and DARE	8	0	0	N/A
EUROGIN	0	0	0	N/A
Total	**26**	**0**	**0**	**N/A**

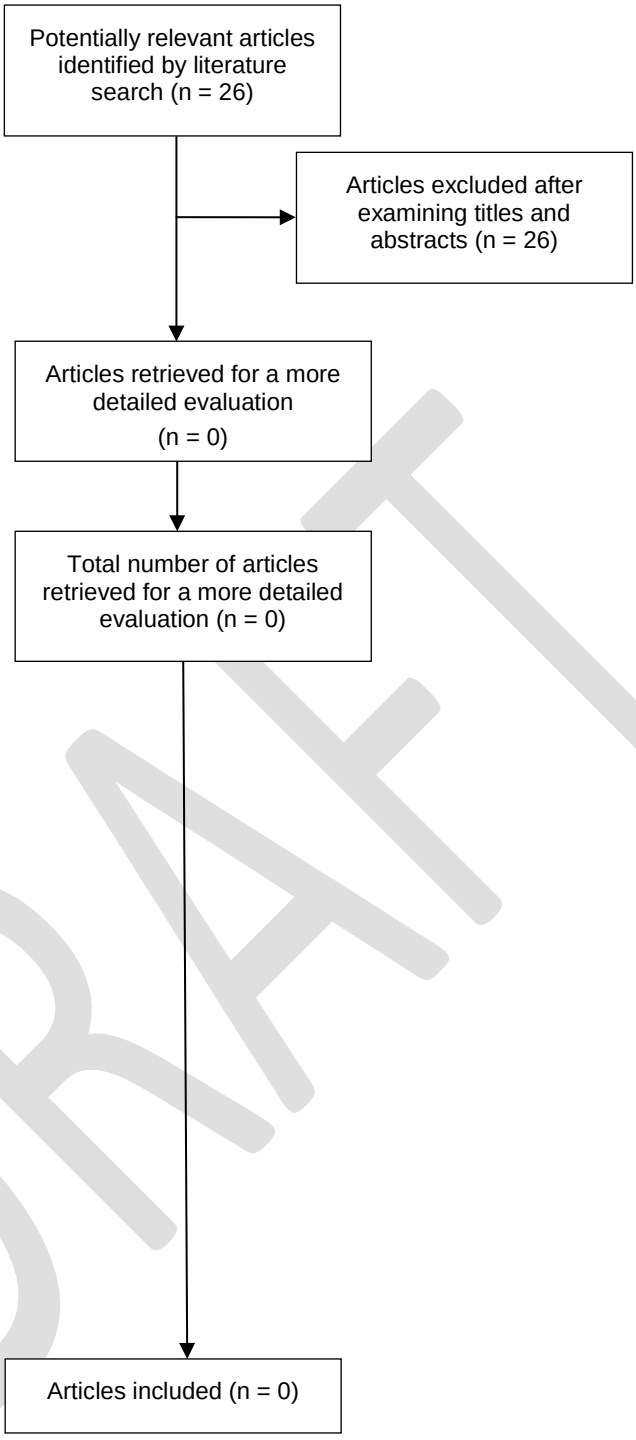

Figure 1. Process of inclusion and exclusion of studies

APPENDICES

Appendix A: Search strategies used

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

#	Searches
1	DES.mp.
2	Diethylstilbestrol.mp.
3	Diethylstilboestrol.mp.
4	Diethylstilbestrol/
5	1 or 2 or 3 or 4
6	Cervi*.mp.
7	Vagina*.mp.
8	uterine cervical neoplasms/ or vaginal neoplasms/
9	6 or 7 or 8
10	5 and 9
11	randomized controlled trial.pt.
12	controlled clinical trial.pt.
13	placebo.ab.
14	(randomised or randomized).ab.
15	randomly.ab.
16	trial.ab.
17	groups.ab.
18	11 or 12 or 13 or 14 or 15 or 16 or 17
19	exp animals/ not humans.sh.
20	18 not 19
21	10 and 20
22	limit 21 to (english language and yr="2004 -Current")
23	remove duplicates from 22

Used the Cochrane sensitivity maximizing filter for identifying randomized controlled trials (http://handbook.cochrane.org, accessed 12/09/2015).

For Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessments (HTA) databases (via OvidSP):

#	Searches
1	DES.mp.
2	Diethylstilbestrol.mp.
3	Diethylstilboestrol.mp.
4	Diethylstilbestrol/
5	1 or 2 or 3 or 4
6	Cervi*.mp.
7	Vagina*.mp.
8	uterine cervical neoplasms/ or vaginal neoplasms/
9	6 or 7 or 8
10	5 and 9

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 College of Obstetricians and Gynecologists (ACOG)	Screening for cervical cancer.	Unclear as to whether based on systematic review of the evidence
2012	University of Michigan Health System.	Cancer screening	Not based on a systematic review of the evidence