

## Systematic review report for question 9

**PICO Question 9:** For women who are at higher risk of cervical cancer due to immunosuppression 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
Organ transplant recipient women Or HIV-positive women	Screening randomized or pseudo-randomized controlled trial	Modified recommended screening strategy: starting at an age <25 years and/or screening intervals less than 5 years and/or referring all HPV positive women to colposcopy irrespective of reflex cytology result	Recommended screening strategy 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](http://www.cancerview.ca)) and consulting experts in the field. 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

##### 1.2.1. Organ transplantation

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 31<sup>st</sup> August 2015, using text terms and, where available, database-specific subject headings. In these databases searches for organ transplantation were combined with searches for HPV and cervi\*, 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 immunosuppression, immunocompromised and transplant. Reference lists of relevant articles and guidelines were checked for additional potentially relevant articles.

### 1.2.2. HIV

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 31<sup>st</sup> August 2015, using text terms and, where available, database-specific subject headings. In these databases searches for HIV were combined with searches for HPV and cervi\*, 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 HIV. Reference lists of relevant articles and guidelines were checked for additional potentially relevant articles.

## 1.3. Inclusion Criteria

### 1.3.1. Organ transplantation

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	Organ transplant recipient women
Intervention	Modified recommended screening strategy: Starting at an age <25 years and/or Screening intervals less than 5 years and/or Referring all HPV positive women to colposcopy irrespective of reflex cytology result
Comparator	Recommended screening strategy: 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
Outcomes	Cervical cancer mortality or Cervical cancer diagnosis or CIN3+ detection
Language	English
Publication period	After 31 <sup>st</sup> December 2003 and before 1 <sup>st</sup> September 2015

### 1.3.2. HIV

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	HIV-positive women

Intervention	Modified recommended screening strategy: Starting at an age <25 years and/or Screening intervals less than 5 years and/or Referring all HPV positive women to colposcopy irrespective of reflex cytology result
Comparator	Recommended screening strategy: 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
Outcomes	Cervical cancer mortality or Cervical cancer diagnosis or CIN3+ detection
Language	English
Publication period	After 31 <sup>st</sup> December 2003 and before 1 <sup>st</sup> September 2015

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

## 2. RESULTS

### 2.1. Guidelines

Nine 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 on 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

#### 2.2.1. Organ transplantation

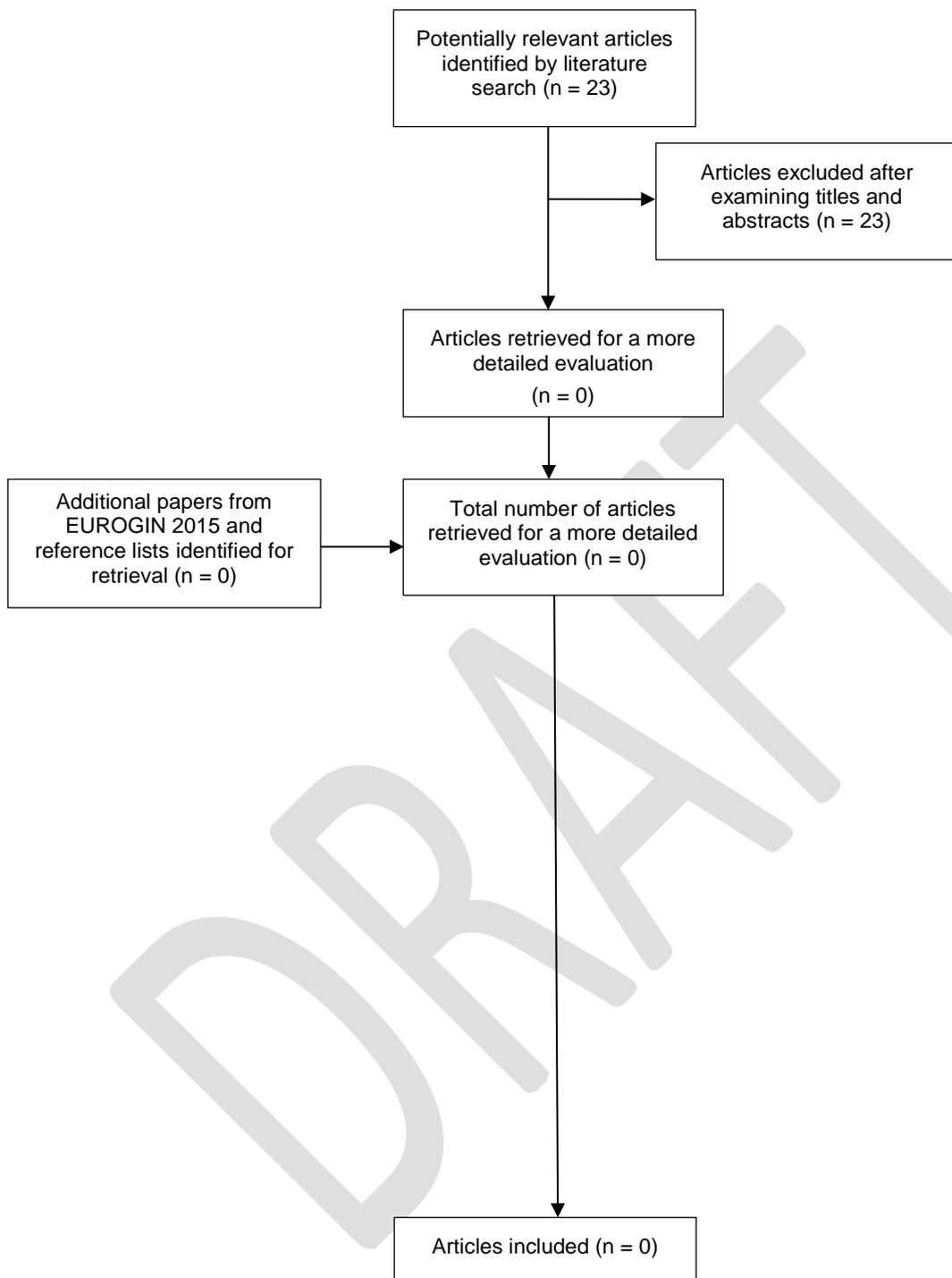
Figure 1 outlines the process of identifying relevant articles for the systematic review. The searches identified a total of 23 citations. Titles and abstracts were examined however none of the articles identified were potentially relevant to the systematic review. Thus no studies were found that directly 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 + Embase	23	0		0
HTA + DARE	0			
EUROGIN 2015 abstracts	0			
Snowballing	0			

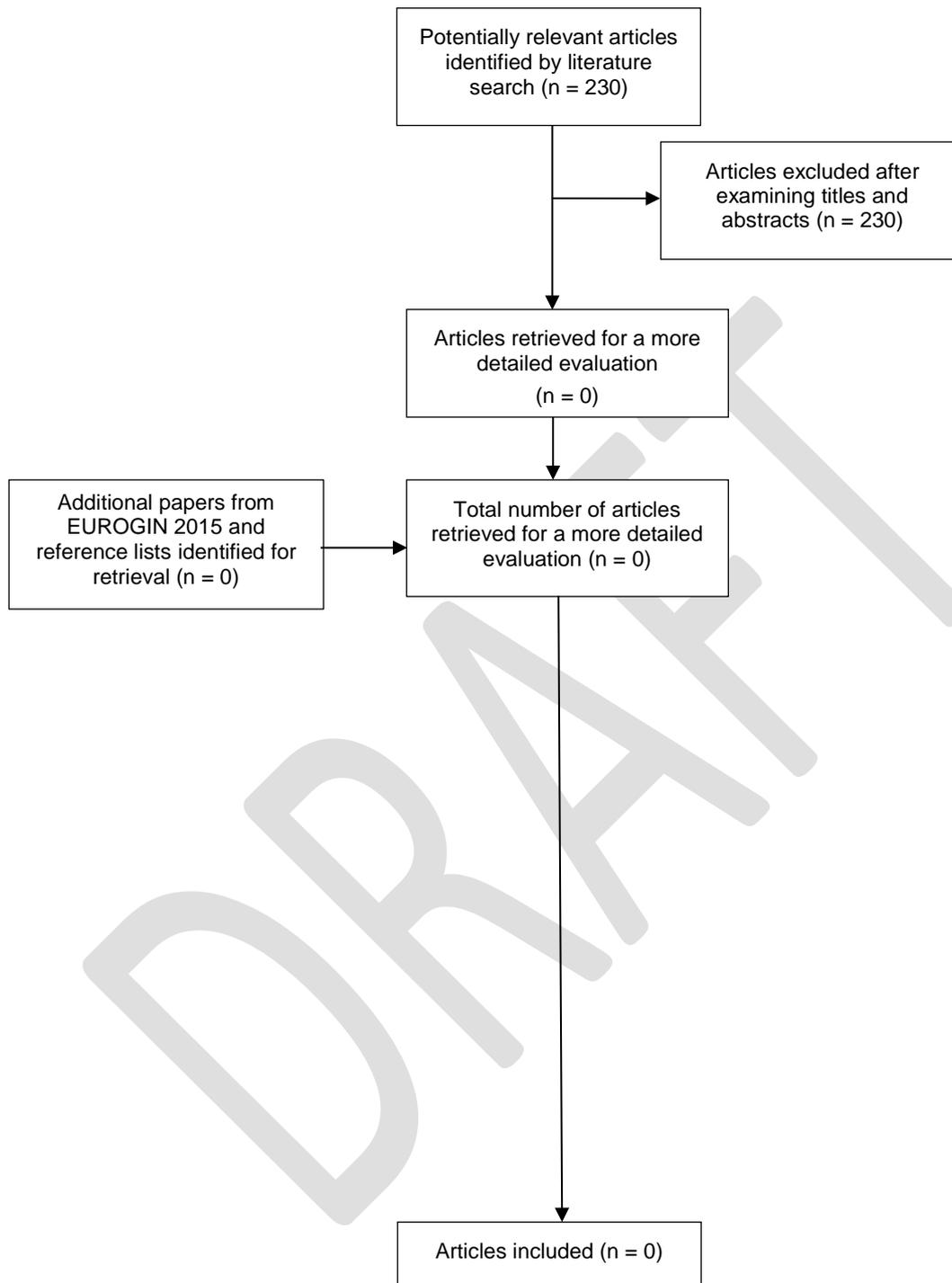
### 2.2.2. HIV

Figure 2 outlines the process of identifying relevant articles for the systematic review. The searches identified a total of 230 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	228	0		0
HTA + DARE	2	0		
EUROGIN 2015 abstracts	0			
Snowballing	0			



**Figure 1.** Process of inclusion and exclusion of studies: Organ transplantation



**Figure 2.** Process of inclusion and exclusion of studies: HIV

## APPENDICES

### Appendix A: Search strategies used:

#### 1. Organ transplantation

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 Papillomaviridae/
6	exp DNA Probes, HPV/
7	1 or 2 or 3 or 4 or 5 or 6
8	cervi*.mp.
9	exp Transplants/
10	organ transplant*.mp.
11	(transplant* and immunosuppress*).mp.
12	9 or 10 or 11
13	7 and 8 and 12
14	randomized controlled trial.pt.
15	controlled clinical trial.pt.
16	placebo.ab.
17	randomi?ed.ab.
18	randomly.ab.
19	trial.ab.
20	groups.ab.
21	14 or 15 or 16 or 17 or 18 or 19 or 20
22	13 and 21
23	limit 22 to english language

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	cervi*.mp.
9	exp Transplants/
10	organ transplant*.mp.
11	(transplant* and immunosuppress*).mp.
12	9 or 10 or 11
13	7 and 8 and 12

## 2. HIV

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	cervi*.mp.
8	exp HIV/
9	human immunodeficiency virus.mp.
10	HIV.mp.
11	8 or 9 or 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	6 and 7 and 11 and 19
21	limit 20 to english language
22	limit 21 to yr="2005 -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)

#### 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	cervi*.mp.
9	exp HIV/
10	human immunodeficiency virus.mp.
11	HIV.mp.
12	9 or 10 or 11
13	7 and 8 and 12
14	limit 13 to (english language and yr="2005 -Current") [Limit not valid in DARE; records were retained]

## 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: <ul style="list-style-type: none"><li>- Phase II clinical trial</li><li>- Non-randomised, experimental trial<sup>9</sup></li><li>- Controlled pre-test/post-test study</li><li>- Adjusted indirect comparisons</li><li>- Interrupted time series with a control group</li><li>- Cohort study</li><li>- Case-control study</li></ul> or a meta-analysis/systematic review of level III-2 studies
III-3	A comparative study without concurrent controls: <ul style="list-style-type: none"><li>- Phase I clinical trial</li><li>- Historical control study</li><li>- Two or more single arm study<sup>10</sup></li><li>- Unadjusted indirect comparisons</li><li>- Interrupted time series without a parallel control group</li></ul> 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
2015	European AIDS Clinical Society	European AIDS Clinical Society Guidelines version 8.0	Did not directly address PICO as to whether HIV-positive women should be screened using strategies other than those recommended for the general population.
2012	American College of Obstetricians and Gynecologists (ACOG).	Screening for cervical cancer. Washington (DC); 2012 Nov. 17 p. (ACOG practice bulletin; no. 131).	Unclear if evidence based. Appear to be based on other guidelines
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	Reportedly evidence based (unable to find documentation)
2012	University of Michigan Health System.	Cancer screening. Ann Arbor (MI): 2012 Oct. 18 p. [21 references] Based on : Saslow et al 2012 ACS/ ASCCP/ ASCP guidelines ACOG 2009 guidelines NCCN 2012 guidelines NCI guidelines 2010 USPSTF guidelines 2012	Not evidence based
2010	American College of Obstetricians and Gynecologists (ACOG).	Gynecologic care for women with human immunodeficiency virus. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2010 Dec. 18 p. (ACOG practice bulletin; no. 117).	Consensus based, not evidence based
2010	Kaiser Permanente Care Management Institute.	Cervical cancer screening clinical practice guideline. Oakland (CA): Kaiser Permanente Care Management Institute; 2010 Oct. 152 p.	Consensus based, not evidence based
2010	NHS	Colposcopy and Programme Management Guidelines for the NHS Cervical Screening Programme Second edition 2010	Unclear if evidence based (based on evidence, otherwise consensus)
2009	CDC, the National Institutes of Health and the HIV Medicine Association of the Infectious Disease Society of America	Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. MMWR Recomm. Rep. 2009, 58, 1–207.	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	Unclear if evidence based