General review for Question 3a

PICO question 3a

For HPV positive women currently not in treatment follow-up and have negative or LSIL cytology who have undergone colposcopy and the colposcopy was unsatisfactory what is the safety and effectiveness of repeat HPV test at 12 months compared with repeat cytology and HPV testing in 12 months?

Population	Study design	Intervention	Control	Outcomes
HPV positive women who have undergone colposcopy and the colposcopy was unsatisfactory and cytology was: i. negative, ii. p/d LSIL	Randomized or pseudo- randomized controlled trial	Repeat HPV test at 12 months; Colposcopy (and reflex LBC test) if positive and if negative HPV test in 12 months	Repeat cytology and HPV testing at 12 month; Colposcopy if HPV positive test or if cytology pHSIL or worse, and another 12 months follow-up if HPV negative p/dLSIL; repeat HPV and cytology test in 12 months if HPV negative and cytology p/dLSIL or negative	Cervical cancer mortality Cervical cancer diagnosis Precancerous high grade lesion detection

pLSIL = possible LSIL; dLSIL = definite LSIL; LSIL = low-grade squamous intraepithelial lesion

Definitions

An unsatisfactory colposcopy is a colposcopy in which the transformation zone is not fully visible (Jordon et al., (2008) European guidelines for quality assurance in cervical cancer screening: recommendation for clinical management of abnormal cervical cytology, part 1. Cytopathology 19: 432-354).

Background to this general review

A systematic search of the literature found no studies that directly addressed this question (Please see Question 3a and b technical report). As a result it was decided to undertake a general review of the literature on the management of women with LSIL cytology and an unsatisfactory colposcopy to inform the drafting of relevant consensus-based recommendations.

GENERAL REVIEW OF THE LITERATURE

Existing guidelines

1. **Current (2005) Australian guidelines**

For women with LSIL cytology - If the colposcopic assessment is unsatisfactory, consideration should be given to repeating the Pap test in 6–12 months. In asymptomatic women and in the absence of any cytologic, colposcopic or histologic suggestion of high-grade disease, further diagnostic procedures, such as cone biopsy or loop excision, are not indicated. ***(Consensus)***

2. Other existing potentially relevant guidelines

Title	Organisation	Evidence-based?	Recommendation
2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors	American Society for Colposcopy and Cervical Pathology.	Consensus based on literature searches and Kaiser Permanente Northern California data	For women with **ASC-US or LSIL cytology** endocervical sampling is preferred for women with an inadequate colposcopy (AII)

Search Strategy

Medline, Premedline and Embase databases were searched from 2004 onwards for studies reporting outcomes for women with unsatisfactory or inadequate colposcopies. We examined these studies for any relevant data for women with normal cytology and HPV positive, or a possible or definite LSIL diagnosis on initial cytology

Results

Question 3a: Results for women with normal cytology and HPV positive, or a possible or definite LSIL diagnosis on initial cytology

Longitudinal studies following-up women with p/dLSIL initial cytology and an unsatisfactory colposcopy– **No studies found**

Cross-sectional studies of women with p/dLSIL initial cytology and an unsatisfactory colposcopy – **3 studies (Table 1)**

Table 1: Characteristics and results of studies of women with **p/dLSIL** initial cytology and an unsatisfactory colposcopy

Study	Study design	Population	Results
Women underwent endocervical curettage			
Goksedef 2013 (Turkey)	Retrospective cohort Cross-sectional	Women with ASC-US (52.7%) or LSIL cytology who underwent colposcopy with **endocervical curettage** between 2003 and 2011 N = 846 Median age = 42 years (21-75 years) and the **colposcopy was unsatisfactory (**entire squamocolumnar junction not visible) N = 427 HPV status not reported Endocervical curettage often undertaken when transformation zone or proximal extent of a lesion not adequately visualised	**Women with unsatisfactory colposcopy n = 427** 4.2% (n = 18) diagnosed with CIN2+ lesions of the endocervical canal 8/18 endocervical canal CIN2+ lesions in women who did not undergo cervical biopsy or whose cervical biopsy was < CIN2 0.5% (n = 2) diagnosed with invasive cancer of the endocervical canal (both women were CIN2+ on cervical biopsy) *Subgroup with **normal** colposcopy n = 256* 1.2% (n = 3) diagnosed with CIN2+ lesions of the endocervical canal No endocervical canal cancers diagnosed *Subgroup with **abnormal** colposcopy n = 171* 8.8% (n = 15) diagnosed with CIN2+ lesions of the endocervical canal 1.2% (n = 2) diagnosed with invasive cancer of the endocervical canal
Poomtavorn 2014 (Thailand)	Retrospective cohort Cross-sectional	Women with ASC-US (58.5%) or LSIL cytology who underwent colposcopy with **endocervical curettage** between 2010 and 2012 N = 260 Mean age = 37 years and the **colposcopy was unsatisfactory (**entire squamocolumnar junction not visible or visible lesion not seen in its entirety) N = 118 HPV status not reported Reasons for endocervical curettage not described – authors reported " in selected cases"	**Women with unsatisfactory colposcopy n = 118** 15.3% (n = 18) diagnosed with CIN2+ disease (all detected on biopsy, no additional patients detected on curettage) 6/18 had endocervical as well as ectocervical disease No cervical cancers diagnosed by either biopsy or curettage

Women with CIN1 on colposcopy biopsy who underwent cone biopsy			
Day 2008 (USA)	Retrospective cohort Cross-sectional	Women with normal (9%), ASCUS (17%) or LSIL (70%) cytology who underwent colposcopy and endocervical sampling between 1999 and 2005 and the **colposcopy was unsatisfactory (**entire squamocolumnar junction not visible or visible lesion not seen in its entirety) and was followed by **cervical cone biopsy** N = 23 Median age = 33 years 25% HIV-positive HPV status not reported Cervical cone biopsy (LEEP or Fischer cone biopsy) undertaken for CIN2/3, cytological/histological discrepancy, persistent CIN1 and, after 2001, CIN1 in the setting of unsatisfactory colposcopy	**Women with CIN1 and unsatisfactory colposcopy n = 23** 4.3% (n = 1) diagnosed with CIN2+ disease on cervical cone biopsy No cervical cancers diagnosed on cervical cone biopsy

ASC-US = atypical squamous cell of undetermined significance (Bethesda 2001); ASCUS = atypical squamous cell of undetermined significance (Bethesda pre 2001); CIN = cervical intraepithelial neoplasia; CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; LEEP = loop electrosurgical excision procedure; LSIL= low-grade squamous cell lesions

References

1. Day T, Weitzen S, Cooper AS et al. Should unsatisfactory colposcopy necessitate treatment of cervical intraepithelial neoplasia 1? *J Low Genit Tract Dis*. 2008;12:11-15.

2. Goksedef BP, Akbayir O, Numanoglu C et al. Evaluation of endocervical canal in women with minimal cervical cytological abnormalities. *J Low Genit Tract Dis*. 2013;17:261-266.

3. Poomtavorn Y, Suwannarurk K, Thaweekul Y et al. Diagnostic value of endocervical curettage for detecting dysplastic lesions in women with atypical squamous cells of undetermined significance (ASC-US) and low grade squamous intraepithelial lesion (LSIL) Papanicolaou smears. *Asian Pac J Cancer Prev*. 2014;15:3461-3464.