General review for Questions 2b

PICO question 2b

For women who are HPV positive with p/dHSIL referral cytology and p/dLSIL or less after cytologic review and colposcopy is negative, what is the safety and effectiveness of conservative management compared with excision of the transformation zone?

<table>
<thead>
<tr>
<th>Population</th>
<th>Study design</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcome</th>
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</table>
| HPV positive women who have undergone colposcopy and the colposcopy was negative and referral cytology was p/d HSIL and review cytology was p/d LSIL or less | Randomized or pseudo randomized controlled trial | Conservative management | Excision of the transformation zone | Cervical cancer mortality  
Cervical cancer diagnosis  
Precancerous high grade lesion detection |

Definitions

A negative colposcopy is a colposcopy in which no abnormalities are seen: it does not include the subsequent reports on any biopsy taken.

Background to this general review

A systematic search of the literature found no studies that directly addressed this question (Please see Question 2b systematic review report). As a result it was decided to undertake a general review of the literature on the management of women with p/dHSIL cytology and a negative colposcopy to inform the drafting of relevant consensus-based recommendations.
GENERAL REVIEW OF THE LITERATURE

Existing guidelines


Women with possible high-grade squamous lesions - If the cervical TZ is fully visible and is found to be normal, then an option is to closely observe the patient (Figure 7.1 – Pap and colposcopy repeated at 3-6 months) –
(Comment - not an actual recommendation)

2. Other existing potentially relevant guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Organisation</th>
<th>Evidence-based?</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors</td>
<td>American Society for Colposcopy and Cervical Pathology</td>
<td>Consensus based on literature searches and Kaiser Permanente Northern California data</td>
<td>Management of Women With CIN 1 or No Lesion Preceded by ASC-H or HSIL When CIN 2+ is not identified histologically, either a diagnostic excisional procedure or observation with co-testing at 12 months and 24 months is recommended, provided in the latter case that the colposcopic examination is adequate and the endocervical sampling is negative. (BIII).</td>
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<tr>
<td>2012 Colposcopic management of abnormal cervical cytology and histology</td>
<td>Society of Obstetricians and Gynaecologists of Canada</td>
<td>Unclear as to evidence base</td>
<td>Managing HSIL on referral for colposcopy In the absence of an identifiable lesion at colposcopy, whether satisfactory or unsatisfactory, an endocervical curettage and directed biopsies should be performed. (III-B) With an ASC-H Pap smear, the finding of negative colposcopy does not automatically warrant a diagnostic excisional procedure. (III-E)</td>
</tr>
<tr>
<td>2009 European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, Parts 1 and 2</td>
<td>European Cancer Screening Network and European Cancer Network</td>
<td>Unclear if evidence based</td>
<td>If colposcopy is satisfactory and colposcopy and biopsy rule out the presence of high-grade CIN, a review of cytology and histology is recommended. Management should be decided according to the reviewed diagnosis. If the cytological interpretation of HSIL is upheld, excision of the TZ is recommended provided the woman is not pregnant. Cyto-colposcopic discrepancies – high grade abnormal cytology confirmed on review A second colposcopy is required. If the SCJ is visible and no colposcopic abnormality is apparent, the investigation should be completed by a detailed examination of the vagina. If again there is no obvious lesion, the endocervical canal should be assessed as thoroughly as possible. If no abnormality can be seen, then the TZ should be excised in its entirety; this should be combined with an endocervical curettage. Where the presence of HSIL is suspected (ASC-H), and the colposcopy is negative, and when a diagnosis of ASC-US is agreed after review of cytology, colposcopy and histology, a repeat smear at 6 and 12 months or hrHPV DNA test at 12 months is recommended. (Wright 2002 consensus guidelines)</td>
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Search Strategy

This review focused on negative colposcopies and drew on the articles collected as a result of systematic searches of Medline, Premedline and Embase databases from 2004 onwards that were designed to identify all studies reporting negative or normal colposcopies. We examined these studies for any data for women with an HSIL diagnosis on initial cytology.
Results

Studies following-up women with p/dHSIL initial cytology following a negative colposcopy and review cytology either LSIL or HSIL – None found

Studies following-up women with p/dHSIL initial cytology following a negative colposcopy – None found

Studies of women with p/dHSIL initial cytology and a negative colposcopy – 1 study found (Table 1)

Table 1: Characteristics and results of studies of women with p/dHSIL initial cytology and a subsequent negative colposcopy – 1 study

<table>
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<th>Study</th>
<th>Study design</th>
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| Lerma Puertas  | Prospective cohort? Cross-sectional | Women with no history of abnormal smears who underwent cytology screening between 2000 and 2007 and were diagnosed with HSIL and underwent colposcopy (N = 340) and the colposcopy was normal N = 17  
No information as to whether LSIL or HSIL on review cytology  
Age not reported  
N = 9 underwent biopsy (endocervical curettage for at least 4) despite normal colposcopy | Women with normal colposcopy n = 17  
11.8% (n = 2) diagnosed with cervical adenocarcinoma  
11.8% (n = 2) diagnosed with cervical adenocarcinoma in situ  
Results for the other 13 women not reported  
HPV status not reported  
Women with HSIL who underwent biopsy n = 331  
4 were diagnosed with cervical adenocarcinoma or cervical adenocarcinoma in situ – all 4 had negative colposcopies |

HSIL = high-grade squamous cell lesion (Bethesda); LSIL= low-grade squamous cell lesions
Less relevant or irrelevant studies?

Studies of women with p/dHSIL initial cytology and a negative biopsy – 1 study found (Table 2)

Studies of women with p/dHSIL initial cytology and CIN2+ disease examining the contribution of endocervical curettage and random biopsies of normal cervical quadrants to the diagnosis of CIN2+ disease – 1 study found (Table 3)

Table 2: Characteristics and results of studies of women with p/dHSIL initial cytology and a subsequent negative biopsy

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<td>Lanneau 2007</td>
<td>Retrospective</td>
<td>Women who had undergone LEEP (N = 32) or LEEP cone (N = 27) as a result of HSIL cytology and a normal biopsy (N = 34) or CIN1 (n = 25) histology (2-step discrepancy)</td>
<td>Normal cervical biopsy: 14/34 (41%) CIN3 on excisional biopsy CIN1 on cervical biopsy: 16/25 (64%) CIN3 on excisional biopsy OR (95% CI) 4.05 (1.1 – 14.6) of CIN3 on LEEP for CIN1 biopsy vs normal histology on biopsy</td>
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<tr>
<td>(USA)</td>
<td>Cross-sectional</td>
<td></td>
<td>HPV status not reported</td>
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Table 3: Characteristics and results of studies of women with p/dHSIL initial cytology and CIN2+ disease examining the contribution of endocervical curettage and random biopsies of normal cervical quadrants to the diagnosis of CIN2+ disease

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<td>Pretorius 2004</td>
<td>Cases only</td>
<td>Women with CIN2+ diagnosis between 2000 and 2002 as a result of a satisfactory colposcopy in which normal quadrants were randomly biopsied and which included endocervical curettage HSIL or cancer smear N = 196 Maximum age range 32-50 years</td>
<td>Women with CIN2+ disease and HSIL or cancer smear 290/689 (42.1%) of targeted biopsies were CIN2+ 97/551 (17.6%) of random biopsies of normal cervical quadrants were CIN2+ 75/196 (38.3%) were CIN2+ on endocervical curettage For women with HSIL do not report what % CIN2+ diagnosed by random biopsy or endocervical curettage</td>
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<tr>
<td>(China)</td>
<td>Cross-sectional</td>
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CIN = cervical intraepithelial neoplasia; CIN2+ = cervical intraepithelial neoplasia grade 2 or worse; HSIL = high-grade squamous cell lesion (Bethesda)
References


