High-risk human papillomavirus (HPV) testing as triage for women with mild or borderline cytology abnormalities

What is an evidence note

Evidence notes are rapid reviews of published secondary clinical and cost-effectiveness evidence on health technologies under consideration by decision makers within NHSScotland. They are intended to provide information quickly to support time-sensitive decisions and are produced in an approximately 3 month period. Evidence notes are not comprehensive systematic reviews. They are based on the best evidence that Healthcare Improvement Scotland could identify and retrieve within the time available. The reports are subject to peer review but do not undergo external consultation. Evidence notes do not make recommendations for NHSScotland.

Introduction

Within the Scottish Cervical Screening Programme women aged 20–60 years are offered routine screening by means of a smear test using liquid based cytology (LBC) every 3 years. Routine screening cytology showing low-grade squamous cell abnormalities are reported as mild dyskaryosis or borderline nuclear abnormalities (BNA; some authors use the term borderline dyskaryosis). Women with low-grade abnormalities are currently offered repeat smears at regular intervals (cytological follow up) and referral to colposcopy after three consecutive borderline or two mild dyskaryosis smears have been reported. An unsatisfactory LBC sample is one that cannot be properly assessed microscopically due to poor quality or too few cells or too little material. Women for whom this is applicable are currently offered cytological follow up at 3-monthly intervals and referral to colposcopy after three consecutive unsatisfactory results.

The British Society of Clinical Cytology (BSCC) system of classification for cervical cytological abnormalities differs from systems used in other countries, including The Bethesda System (TBS) developed in the United States of America (USA) that is widely used in the research literature. The current Bethesda System categorises low-grade abnormalities as ‘Atypical Squamous Cells—Undetermined Significance’ (ASC–US) and ‘Low-grade Squamous Intraepithelial Lesions’ (LSIL). Prior to 2001, the category ASCUS (TBS 1991) included a higher risk subcategory that was subsequently reclassified, so ASCUS as used in earlier studies is a somewhat higher risk grouping than ASC–US. A BNA result in the United Kingdom (UK) is similar to ASCUS/ASC–US, and mild dyskaryosis is similar to LSIL.

Human papillomavirus (HPV) is present in over 99% of cervical cancers. Persistent infection with a high-risk (oncogenic) genotype of HPV is associated with...
an increased risk of cervical intraepithelial neoplasia (CIN) or precancer. The risk of progression from CIN to invasive cancer depends on the level of dysplasia: mild (CIN1), moderate (CIN2) or severe (CIN3). High grade disease is defined as CIN2 or worse (variously designated as CIN2/3, CIN2+ and CIN3+). Approximately 60% of CIN1 lesions will regress to normal with only 10% likely to progress to CIN3 and 1% to cervical cancer. About 40% of CIN2 lesions are likely to regress whereas 20% will progress to CIN3 and 5% to cancer. More than 12% of CIN3 lesions are likely to progress to cervical cancer with only 33% expected to regress to normal.

HPV triage is the use of HPV testing to discriminate women with low-grade cytology abnormalities who are at risk for CIN and require referral to colposcopy from those not at risk who can return to routine screening.

HPV triage has been incorporated in the National Health Service Cervical Screening Programme (NHSCSP) in England for implementation in 2011–2012 following pilot feasibility studies and sentinel sites evaluation. HPV triage is not currently undertaken as part of the Scottish Cervical Screening Programme.

High-risk HPV co-testing with cytology follow up after treatment for cervical neoplasia (test of cure) is scheduled for national implementation in Scotland in 2012 (C Mckenzie, Consultant Gynaecologist, NHS Tayside. Personal communication, 2 Nov 2011). The HPV reference group is assessing the potential for further use of HPV testing within the Scottish Cervical Screening Programme including primary screening and triage of women with mild or borderline cytology abnormalities, or unsatisfactory smears.

This evidence note addresses high-risk HPV triage for screen detected low-grade squamous cell abnormalities and unsatisfactory smears. Healthcare Improvement Scotland has produced a separate evidence note on high-risk HPV testing in primary screening.

**Health technology description**

High-risk HPV testing utilises laboratory assays to detect the presence of any of a range of high-risk types of HPV in cervical cell samples. The HPV test can be taken directly from the LBC medium in response to the abnormal screening cytology result (reflex HPV triage) or performed at a later date (delayed triage).

The Digene Hybrid Capture II (HC2) High-Risk HPV deoxyribonucleic acid (DNA) test (QIAGENE, Gaithersburg, MD, USA) is the most widely used commercially available test. The HC2 assay detects 13 high-risk types of HPV. It produces luminescence with an intensity that is proportional to the amount of HPV DNA in the sample and expressed in relative light units (RLU): the test positivity cut-off recommended by the manufacturer is 1.0 RLU, which is equivalent to 1 pg/ml HPV DNA. Other currently available assays use different technologies and detect different arrays of high-risk HPV genotypes. The NHSCSP has accepted several other technologies in addition to the HC2 assay for high-risk HPV triage and selection of the HPV testing platform will be a local choice.

**Epidemiology**

Cervical screening saves around 5,000 lives in the UK every year and prevents 8 out of 10 cervical cancers from developing. In Scotland, 326 new cases of cervical cancer were diagnosed and 107 deaths from cervical cancer were recorded in 2009.

The Scottish Cervical Screening Programme processed 390,194 LBC cervical screening tests in 2010–2011, of which 2.8% (n=10,839) were unsatisfactory. Of the 97.2% satisfactory quality tests, 5.7% (n=21,508) had borderline squamous cell abnormalities and 2.1% (n=8,136) had mild dyskaryosis.

Cervical biopsy results for all referrals to colposcopy from the Scottish Cervical Screening Programme in 2010 (n=9,266 biopsies) reported 21.3% CIN1, 24.5% CIN2, and 26.9% CIN3. The prevalence of high-risk HPV in Scotland has not yet been established at the screening population level. The prevalence of high-risk HPV in 3,444 randomly selected residual LBC specimens from women attending routine screening in Edinburgh and Lothian was 15.7%, including 71.9% of women with borderline dyskaryosis and 86.8% with mild dyskaryosis.

The introduction of HPV vaccination in Scotland in 2008 will have an impact on the future epidemiology of cervical cancer which may necessitate a comprehensive re-evaluation of the optimal role for HPV testing in the cervical screening programme.
Clinical effectiveness

HPV triage for mild and borderline cytology abnormalities

Meta-analysis

Arbyn et al.23 recently added the NHSCSP sentinel sites data13 to a previous meta-analyses of HC2 test positivity rates from reflex HPV triage studies published to 200724. The previous meta-analysis24 had included five primary studies from the UK, including data from the NHSCSP pilot studies11. The NHSCSP pilot studies used a test positivity threshold of 3.0 RLU, the sentinel sites used 2.0 RLU, and the other studies used 1.0 RLU as recommended by the manufacturer. The studies were pooled in subgroups according to the cytological classification system that they used, ie atypical cytology defined as ASCUS, ASC–US, or borderline dyskaryosis; and low-grade cytology defined as LSIL or mild dyskaryosis23. The pooled estimates are summarised in table 1.

The results showed similar pooled HPV positivity rates in each atypical cytology subgroup (ASCUS, ASC-US, borderline dyskaryosis) in studies published to 200723,24. There was, however, marked statistical heterogeneity between studies in every subgroup (I², a measure of the amount of heterogeneity that is not due to chance, =96.9%, 89.9% and 90.7%, respectively; all p<0.001)23,24. Meta-analysis also showed similar but higher pooled HPV positivity rates in each low-grade cytology subgroup (LSIL, mild dyskaryosis) in studies published to 2007. Again, statistical heterogeneity was significant in each subgroup (I²=95.0%; p<0.001 and 63.3%; p=0.042, respectively)23,24.

HPV positivity rates observed at the NHSCSP sentinel sites were among the highest reported in the literature on HPV triage of low-grade abnormalities23. There was considerable variation in positivity rates between the six sentinel sites, from 34.8–73.3%13 (I²=98.9%; p<0.00123) of borderline cases and 73.4–91.6%13 (I²=94.3%; p<0.00123) for mild dyskaryosis cases13. These differences remained after the rates were standardised for age13.

Meta-analysis showed consistently higher positivity rates between LSIL/mild dyskaryosis and ASCUS/borderline dyskaryosis based on 15 studies published to 2007 and the sentinel sites23. The overall pooled difference was 32% (95% CI 27 to 37; I²=93.5%; p<0.001)23.

In a previous meta-analysis, Arbyn et al. derived pooled estimates of sensitivity and specificity from reflex HC2 triage studies (published 1999–2006) for the detection of histologically confirmed underlying CIN2+ and CIN3+ in cases of ASCUS and LSIL25. The included studies used a test positivity cut-off of 1.0 RLU. The pooled estimates are summarised in table 2.

Table 1 HC2 test positivity results from meta-analysis of triage studies23

<table>
<thead>
<tr>
<th>Cytology</th>
<th>Number of studies</th>
<th>Test positivity rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCUS</td>
<td>20</td>
<td>43% (95% CI 38 to 48)</td>
</tr>
<tr>
<td>ASC-US</td>
<td>6</td>
<td>43% (95% CI 38 to 48)</td>
</tr>
<tr>
<td>Borderline dyskaryosis: studies published to 2007</td>
<td>6</td>
<td>43% (95% CI 34 to 52)</td>
</tr>
<tr>
<td>Borderline dyskaryosis: NHSCSP sentinel sites</td>
<td>6 sites</td>
<td>56% (95% CI 45 to 68)</td>
</tr>
<tr>
<td>LSIL</td>
<td>12</td>
<td>75% (95% CI 69 to 82)</td>
</tr>
<tr>
<td>Mild dyskaryosis: studies published to 2007</td>
<td>4</td>
<td>78% (95% CI 73 to 84)</td>
</tr>
<tr>
<td>Mild dyskaryosis: NHSCSP sentinel sites</td>
<td>6 sites</td>
<td>85% (95% CI 80 to 90)</td>
</tr>
</tbody>
</table>

*Confidence interval (CI)

Table 2 Sensitivity and specificity results from meta-analysis of HC2 triage studies25

<table>
<thead>
<tr>
<th>Cytology</th>
<th>CIN2+</th>
<th>CIN3+</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of studies</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>ASCUS</td>
<td>20</td>
<td>92.5% (95% CI 90.1 to 94.9)</td>
</tr>
<tr>
<td>LSIL</td>
<td>10</td>
<td>97.2% (95% CI 95.6 to 98.9)</td>
</tr>
</tbody>
</table>
The results showed high sensitivity for ASCUS and LSIL, considerably lower specificity for ASCUS and very low specificity for LSIL. Most women (58–85%) with LSIL in the included studies had a positive HC2 result (pooled test positivity rate=76.6%; 95% CI 70.9 to 82.3)25. Between study heterogeneity was not statistically significant for sensitivity but highly significant for specificity25.

Meta-analysis of seven studies that evaluated both HC2 and repeat cytology as triage methods for ASCUS showed that the sensitivity of HC2 was on average 14% higher than repeat cytology for detection of CIN2+ using ‘ASCUS or worse’ as the cut-off to define a positive repeat cytology result, with similar specificity (pooled sensitivity ratio=1.14; 95% CI 1.08 to 1.20; pooled specificity ratio=0.99; 95% CI 0.88 to 1.10)25.

Arbyn et al. concluded that their findings indicated improved accuracy of HPV triage for ASCUS cases compared with repeat cytology for detection of high-grade CIN2, but that reflex high-risk HPV triage was insufficiently discriminative in cases of LSIL23,24.

These meta-analyses, and their earlier versions26,27, have methodological shortcomings — primarily the lack of assessment of the quality of the included studies and their potential for bias, and inadequate handling of heterogeneity. Arbyn et al. are currently completing a Cochrane systematic review of the diagnostic accuracy of high-risk HPV triage using robust methods24,28.

UK randomised controlled trial

The Trial of Management of Borderline and Other Low-grade Abnormal smear (TOMBOLA)3 was a multicentre randomised controlled trial (RCT) nested in the cervical screening programmes in Scotland (Grampian, Tayside) and England (Nottingham) that considered whether HPV status was helpful in making decisions on management3,29–31. Women with borderline nuclear abnormalities or mild dyskaryosis (predominantly on conventional smears) were randomised to immediate colposcopy or cytological surveillance, stratified by age, cytology result, recruitment centre and baseline HPV status3,29. HPV testing was done using a noncommercial high-risk HPV PCR enzyme immunoassay2. Women allocated to immediate colposcopy were subsequently randomised in the same strata to immediate large loop excision of the transformation zone (LLETZ) or biopsy with selective recall for LLETZ. The primary clinical outcome was the cumulative incidence of CIN2+ at 3-years follow up. The analysis concluded that while a single HPV test could be useful in determining which women >40 years of age with low-grade cytological abnormalities should be referred for colposcopy (using a negative HPV test to rule out further investigation) it would not be useful in younger women or to determine the most effective management strategy at colposcopy29,31.

Effect of age

The NHSCSP sentinel sites data showed a statistically significant decreasing trend in HPV positivity rates and positive predictive value (PPV) for CIN2+ with increasing age in both borderline and mild dyskaryosis categories (p<0.0001)13.

Age-stratified analysis of TOMBOLA data suggested that a single HPV test could be useful in women >40 years of age because high negative predictive values (NPV) could be used to rule out further investigation, but not in younger women29. The NPV for CIN2+ exceeded 90% in women aged 40–59 years with mild dyskaryosis but not in younger age groups; in women with BNA the NPV exceeded 90% in all age groups over 25 years29. The NPV for CIN3+ exceeded 90% in the 40–59 and 20–24 years age groups with mild dyskaryosis, and in all age groups with BNA29.

A recent study of ASC–US among women attending organised screening in Italy32 showed that HC2 sensitivity for CIN2+ did not differ by age whereas specificity was better than repeat cytology in women ≥35 years but tended to be lower than repeat cytology in younger women33.

In the ASCUS-LSIL Triage Study (ALTS) conducted in the USA, subgroup analysis suggested that for ASC–US restricting HPV triage to women aged ≥29 years may provide higher sensitivity to detect CIN3 compared with a single repeat cytology test34.

ALTS provided insufficient evidence to inform conclusions on the relative effectiveness of HPV triage by age in women with LSIL34. Using meta-analysis, Arbyn et al. concluded that while reflex high-risk HPV triage could be useful in older women with LSIL, no obvious age threshold could be defined due to the lack of reporting of age-specific data24.
Impact on colposcopy referral

The NHSCSP pilot studies of reflex HPV triage provide before and after data on colposcopy referrals\(^\text{11}\). The HC2 test positivity threshold of 3.0 RLU was three times higher than recommended by the manufacturer\(^\text{13}\). The initial protocol, in which all women who tested HPV positive were referred for immediate colposcopy, was revised in some centres because it led to too many referrals. The revised protocol only referred younger women (20–34 years) if they remained HPV positive at 6 months or if cytology showed mild dyskaryosis or worse. For BNA, referral to colposcopy increased from 15% before the pilot to 44% in the initial protocol period and 29% in the revised protocol period. For mild dyskaryosis referral increased from 37% to 80% and 60%, respectively\(^\text{11}\). Over the entire period, referral rates among women aged 35–64 years more than doubled for both BNA (from 12% to 27%) and mild dyskaryosis (from 34% to 75%)\(^\text{11}\).

In the subsequent NHSCSP sentinel sites evaluation, reflex HC2 triage using a test positivity cut-off of 2.0 RLU allowed approximately one third of all women (ie those who tested negative for HPV) aged 25–64 years with borderline and mildly dyskaryotic results to return immediately to routine recall (at 3 or 5 years depending on age)\(^\text{13}\). Of the 64.4% (6,470/10,051) of women who tested positive (53.7% of BNA cases and 83.9% of mild dyskaryosis cases) and were referred to colposcopy, 90.2% (5,838/6,470) attended. The overall PPV was 6.1% for CIN2+ and 16.3% for CIN3+\(^\text{13}\). The variation in HPV positivity rates between sites indicated the variable impact on colposcopy workload expected on wider rollout of HPV triage\(^\text{13}\).

A recent health technology assessment (HTA) appraised three studies that reported on the impact on colposcopy referrals of a single HC2 triage test at a positivity cut-off of 1.0 RLU compared with repeat cytology alone among women with ASCUS or LSIL\(^\text{34}\). ALTS and one observational study reported a statistically significant reduction in colposcopy referral rates in favour of HPV triage of ASCUS, whereas another observational study showed no difference\(^\text{34}\). One study (ALTS) showed no significant difference in referral rates between HPV triage and repeat cytology among women with LSIL: both strategies resulted in high colposcopy referral rates across all age groups\(^\text{34}\).

Theoretical estimates based on longitudinal data from ALTS indicated that for ASC–US a management strategy of two repeat cytology tests at 6-month intervals, with a colposcopy referral threshold of ASC–US, would provide similar sensitivity compared with reflex HPV triage to detect CIN3+. There was also a statistically significant increase in the colposcopy referral rate from 53% to 67%\(^\text{34}\). In the case of LSIL, repeat cytology at a threshold of ASC–US would require >80% referral to colposcopy even with a single repeat cytology. If the threshold for colposcopy referral was raised to LSIL, three repeat cytology tests would be required to provide similar sensitivity to HPV triage for detection of CIN3+ and would lower colposcopy referral from 84% to 69%\(^\text{34,35}\).

Reflex versus delayed HPV triage

A recent HTA failed to identify studies that compared repeat cytology alone with delayed HPV testing conducted with repeat cytology 12 months after an index cytology result of ASCUS or LSIL\(^\text{34}\). Two studies provided evidence that immediate HPV triage and delayed HPV triage combined with repeat cytology within 6 months of an index cytology result of ASCUS or LSIL were both more sensitive and less specific than repeat cytology alone\(^\text{34}\).

Effect of HPV vaccination status

None of the HPV triage studies identified included HPV-vaccinated women.

HPV triage for unsatisfactory smears

There is limited published evidence on the use of high-risk HPV testing to triage women with unsatisfactory LBC results. One retrospective study reported that 5/11 (45%) women with unsatisfactory LBC and positive HPV (HC2 assay) results had CIN1 diagnosed on repeat cytology and colposcopy compared with 1/205 (0.5%) women with unsatisfactory LBC and HPV-negative results who had repeat cytology\(^\text{36}\).

Safety

High-risk HPV testing uses the same procedure for collecting cervical cell samples as for LBC, and can be performed using the same sample. Sample collection does not, therefore, introduce additional risks\(^\text{34}\). No adverse effects due to the collection of cervical cells for HPV testing were reported in eight studies comparing HPV triage with repeat cytology (two studies used LBC)\(^\text{34}\).

The low specificity of high-risk HPV testing to detect high-grade disease among women with low-grade squamous cell abnormalities carries a risk of unnecessary colposcopy. There are few complications associated with the colposcopy procedure, although there is some evidence of long-term effects on obstetric outcomes, anxiety, sexual dysfunction and quality of life; this is an area of ongoing research\(^\text{37}\).
There is evidence from observational studies that women who test positive for HPV report higher levels of anxiety and distress and greater concerns about their sexual health in the short term compared with women who test negative. One observational study of women attending routine screening at centres taking part in the NHSCSP pilot studies found no difference in anxiety, distress or quality of life at 6-month follow up, suggesting that these effects do not persist. A qualitative study in England representative of women aged 20–64 years from various ethnic and socioeconomic groups highlighted the importance of providing adequate information to minimise the potential adverse social and psychological impact of HPV testing in cervical screening.

An RCT of HPV triage of ASC-US among women attending family planning clinics in Australia randomised to HPV testing, repeat cytology at 6-months, or informed choice of either option found lower levels of distress and greater satisfaction with care in the HPV test group at 1-year follow up and no difference in anxiety, sexual health concerns or quality of life. The longer wait for repeat cytology results was suggested as the reason for higher distress and lower satisfaction.

**Cost effectiveness**

The most recent HTA identified reviewed published (2002–2008) studies of the cost effectiveness of HPV triage as an alternative to repeat cytology for women with low-grade cytological abnormalities. One of eight studies that estimated incremental cost-effectiveness ratios (ICER), the NHSCSP pilot studies analysis, simulated cohorts of women requiring low-grade abnormality follow up from an LBC screening platform in a UK setting. Cost-effectiveness data from the NHSCSP sentinel sites are yet to be published.

The NHSCSP pilot studies analysis used the results from three participating centres to populate a Markov model to predict the lifetime effects, costs and cost effectiveness of using high-risk HPV testing to triage women aged 25–64 years with mild or borderline cytology to colposcopy. The analysis was from the NHS perspective. It compared conventional cytology screening with strategies using LBC alone and four combined LBC and high-risk HPV triage strategies with different age cut-offs and follow up. The combined strategies were 1) LBC and HPV triage of all mild or borderline results, immediate referral of positive HPV cases to colposcopy and recall of negative cases for repeat cytology and HPV testing at 6 months; 2) as strategy 1 except HPV positive women <35 years are not referred to colposcopy but recalled for repeat combined testing at 6 and (if HPV negative again) 12 months; 3) as strategy 1 for women ≥35 years, and LBC surveillance at 6 months for HPV positive women <35 years; 4) as strategy 1 but without HPV testing in repeat tests.

Transition probabilities between health states were taken from the literature on the natural history of HPV infection and cervical cancer. Local data on survival from invasive cancer and mortality from other causes were used to adapt the model to the UK. Data from the pilot sites were used to estimate attendance rates for repeat cytology and colposcopy. Estimates of sensitivity and specificity were based on one published UK study for conventional cytology and a published meta-analysis for HPV testing using the HC2 assay. Estimates of the improvement in sensitivity and specificity of LBC over conventional cytology to detect CIN1 were based on published studies, and PPVs in the pilot studies were used to estimate the improvement in sensitivity to detect CIN2/3. The model assumed that 90% of cases of invasive cancer are detected at each screening round for all strategies; all colposcopies are 100% sensitive and specific; all abnormalities found at colposcopy are treated and treatment is 90% (range 80–100%) effective; and that 90% (range 0–100%) of women return to a healthy state with no HPV.

Data from the pilot sites were used to calculate unit costs of conventional cytology, LBC and HPV testing (HC2 assay). Testing equipment and consumables costs were NHS based, and primary care unit costs were taken from the literature. Staff time was estimated from records for a random sample of smear takers and all smear readers. Laboratory staff costs were estimated from mid-point staff salaries. Cytology costs were adjusted to incorporate inadequate results as reported in the pilot studies. The model assumed that HPV test kits were used at full capacity. All costs were converted to 2001–2002 NHS prices. Audit data provided costs associated with CIN and costs of invasive cancer over 5 years. Costs and benefits were discounted in the analysis at 3.5% for the first 30 years and 3% thereafter.

The most cost-effective strategy was LBC with adjunctive HPV testing to triage women with mild or borderline results aged ≥35 years to immediate colposcopy, repeat cytology and HPV testing at 6-months for HPV negative cases, and LBC surveillance at 6-months for HPV positive women <35 years. The predicted ICER was £3,735 per life year saved.

Extending HPV triage to all ages increased the ICER to £18,605 per life year saved. Replacing...
combined cytology and HPV testing at 6-months for HPV negative women ≥35 years with repeat cytology alone had an ICER of £4,233 per life year saved. The model predicted that HPV triage strategies would reduce lifetime repeat smears by 52–86% and increase lifetime colposcopies by 64–138%12.

One-way sensitivity analysis identified the extent to which preinvasive cancer developed to high-grade disease and the sensitivity of cytology to detect CIN2/3 as key areas of uncertainty12. The key cost drivers were LBC, HPV and colposcopy costs. Probabilistic sensitivity analysis showed considerable uncertainty in both the incremental costs and gains from HPV triage in the model. Cost-effectiveness acceptability curves showed that if decision makers are willing to pay between £7,500 and £30,000 per life year gained, strategies utilising HPV testing to triage all women with mild or borderline LBC to immediate colposcopy provide the greatest net health benefit12.

The study concluded that HPV triage was likely to be cost effective in the NHSCSP, and most cost effective if restricted to women aged ≥35 years12. There was, however, a trade-off between reduced repeat cytology and increased referrals to colposcopy associated with the four combined LBC and high-risk HPV triage strategies compared with LBC alone12.

Conclusion

Evidence from meta-analysis of cross-sectional studies indicates that high-risk HPV testing is more sensitive and has similar specificity to repeat cytology to triage women with borderline dyskaryosis to colposcopy, but is insufficiently discriminative in women with mild dyskaryosis. The impact on colposcopy workload of high-risk HPV triage of borderline and mild dyskaryosis regardless of age in the NHSCSP sentinel sites evaluation varied widely between sites. There is limited evidence on the clinical effectiveness of delaying HPV triage in women with low-grade abnormalities or the utility of HPV triage in women with unsatisfactory smears. None of the HPV triage studies identified included vaccinated women. HPV testing and positive test results can have adverse effects on women’s wellbeing. HPV triage of low-grade cytology abnormalities is likely to be cost effective in the NHSCSP context, and most cost effective if restricted to women aged ≥35 years.

Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The evidence note process has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org

About evidence notes

For further information about the evidence note process, see www.healthcareimprovementscotland.org

To propose a topic for an evidence note, email evidencenotes.HCIS@nhs.net

References can be accessed via the internet (where addresses are provided), via the NHS Knowledge Network http://www.knowledge.scot.nhs.net, or by contacting your local library and information service.

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