Primary High Risk HPV Testing with Cytology Triage

NHS Cervical Screening Programme

Public Health England leads the NHS Screening Programmes
Human papillomavirus (HPV)

- High risk (HR) HPV is associated with cervical intraepithelial neoplasia (CIN) and is found in 99.7%* of cervical cancer cases
- Persistent infection with HR-HPV is a necessary but insufficient cause of cervical cancer
- Persistent HR-HPV infection increases the risk of women developing cervical cancer
- Transient HR-HPV infection is common

HPV in cervical screening

• HR-HPV testing picks up more cervical abnormalities (more sensitive) than cytology, but more women without abnormalities test positive for HR-HPV (not as specific)

• Women who test negative for HR-HPV have no significant cervical abnormalities (CIN2+) in 99.8%* of cases

• Most women with high-grade abnormalities will be identified by HR-HPV testing

HPV in cervical screening

• HPV triage and test of cure have been implemented across the NHS cervical screening programme (NHSCSP) since 2011

• As the HR-HPV test is more sensitive but less specific than cytology, primary HR-HPV testing coupled with cytology triage offers a more appropriate screening strategy, especially in an HPV-vaccinated population

• The primary HR-HPV testing protocol reverses the current HR-HPV triage protocol
ARTISTIC trial

• ARTISTIC stands for ‘A Randomised Trial in Screening to Improve Cytology’ (NIHR funded)

• The aim of the trial was to evaluate the effectiveness of HPV primary screening

• The trial was based in Manchester and recruited 24,510 women

• The trial compared liquid-based cytology (LBC) and HR-HPV testing
ARTISTIC trial – age at entry

<table>
<thead>
<tr>
<th>Age</th>
<th>HPV Infection</th>
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<tbody>
<tr>
<td>20-24</td>
<td>39.9%</td>
</tr>
<tr>
<td>25-29</td>
<td>27.9%</td>
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<tr>
<td>30-34</td>
<td>18.5%</td>
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<tr>
<td>35-39</td>
<td>12.2%</td>
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<tr>
<td>40-44</td>
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<td>55-59</td>
<td>6.0%</td>
</tr>
<tr>
<td>60-64</td>
<td>6.0%</td>
</tr>
</tbody>
</table>
ARTISTIC trial

Over 3 screening rounds primary HR-HPV screening:

- Showed improved sensitivity compared to liquid based cytology testing
- Gave women longer term protection following a negative HR-HPV test result than a normal cytology result
Pilot of primary HR-HPV testing

Primary HR-HPV testing commenced at 6 English pilot sites in 2013.

The aims of the pilot are to assess:

• Feasibility of using primary HR-HPV testing
• Clinical protocols for patient management
• Acceptability of HR-HPV testing to women
• Cost effectiveness
Pilot of primary HR-HPV testing

- Data from the pilot has confirmed the benefits of primary HR-HPV testing in improving sensitivity in the NHSCSP.
- In January 2016 the UK National Screening Committee recommended the adoption of primary HR-HPV testing to replace primary cytology screening.
- In July 2016 ministerial announcement confirmed the implementation of primary HR-HPV testing across England.
Primary HR-HPV testing

• All women aged between 25 and 64 (on routine and early recall) are eligible
• Information on primary HR-HPV testing will be included in the invitation for screening, along with a corresponding HPV leaflet
• The cervical sample will be taken as normal
• The sample will be tested for HR-HPV first
• Samples that are positive for HR-HPV will then be processed for cytological examination (cytology triage)
• Women who are HIV+ will be screened annually with the HR-HPV test in accordance with programme guidelines
Primary HR-HPV testing algorithms

The current versions of the NHSCSP HPV primary screening protocol and colposcopy management recommendations algorithms can be found on the GOV.UK website.

**HPV primary screening protocol algorithm**


**HPV primary screening pilot: colposcopy management recommendations algorithm**

Possible results

- HR-HPV not detected: return to normal recall (3 or 5 years)
- HR-HPV detected, cytology negative (no abnormal cells): recall 12 months
- HR-HPV detected, cytology positive (abnormal cells found): refer for colposcopy
- Inadequate result: repeat in 3 months
Possible results (cont.)

Some HR-HPV tests also tell us if the women has HPV 16/18 genotypes.

Currently 4 pilot sites are using genotyping for HPV 16/18 to inform the management of women.

• The HPV 16/18 result will be recorded for HR-HPV positive/cytology negative women

• Women testing HPV 16/18 positive/cytology normal at baseline and again at their first 12 month follow up test can be referred to colposcopy without further repeat tests
Women in follow up

• Women in follow up for treatment of CIN will be given a 3-year recall if HR-HPV negative 6 months after treatment, and will be referred to colposcopy if HR-HPV positive(any grade of cytology)

• Women in follow up after adequate treatment for CGIN/SMILE will be given a 3-year recall if HR-HPV negative at both 6 and 18 months after treatment

• Women in follow up for cervical cancer (still with cervix) and CGIN/SMILE (without complete excision margins) will be screened annually with the HR-HPV test (instead of cytology) for 10 years
Other considerations

- Local call/recall software has been adapted to cope with an HR-HPV negative result only
- Primary HR-HPV test results will be available throughout the country
- Letters have been revised to accommodate changes in terminology and results
- Colposcopy activity will be monitored carefully
- Electronic GP links will remain the same
- HR-HPV negative read codes are included in the Quality Outcomes Framework(QOF) cytology ruleset
Sample taker training/monitoring

- A cytology slide will be prepared for all samples taken by trainees regardless of the HR-HPV result.
- This enables feedback to be given to the trainee on the cytological quality of the sample.
- Women will be managed on the results of both the HR-HPV and cytology test.
Women with symptoms

- HR-HPV is associated with cancer of the cervix
- The NHSCSP is a screening programme to prevent cervical cancer. It is inappropriate to take a cervical sample to assess symptomatic women
- Women with symptoms should be referred to gynaecology or colposcopy as appropriate
- Non-cervical lesions may not be detected by HR-HPV testing
Possible symptoms

Symptoms of cervical cancer can include:

- Post-menopausal bleeding
- Suspicious cervix
- Post-coital bleeding
- Inter-menstrual bleeding
Further information

Population screening programmes

gov.uk/phe/screening

Professional guidance

www.gov.uk/government/collections/cervical-screening-professional-guidance

Information for women


Sample taker training

cpdscreening.phe.org.uk/csp