Public Health England

NHS

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

* Walboomers JM(1), Jacobs MV, Manos MM, Bosch FX. J Pathol. 1999 Sep;189(1):12-9. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide.

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

*Kitchener et al. Lancet Oncol 2009, Ronco et al. Lancet Oncol 2006, Ronco et al. JNCI 2006, Rijkaart et al. Lancet Oncol 2012.

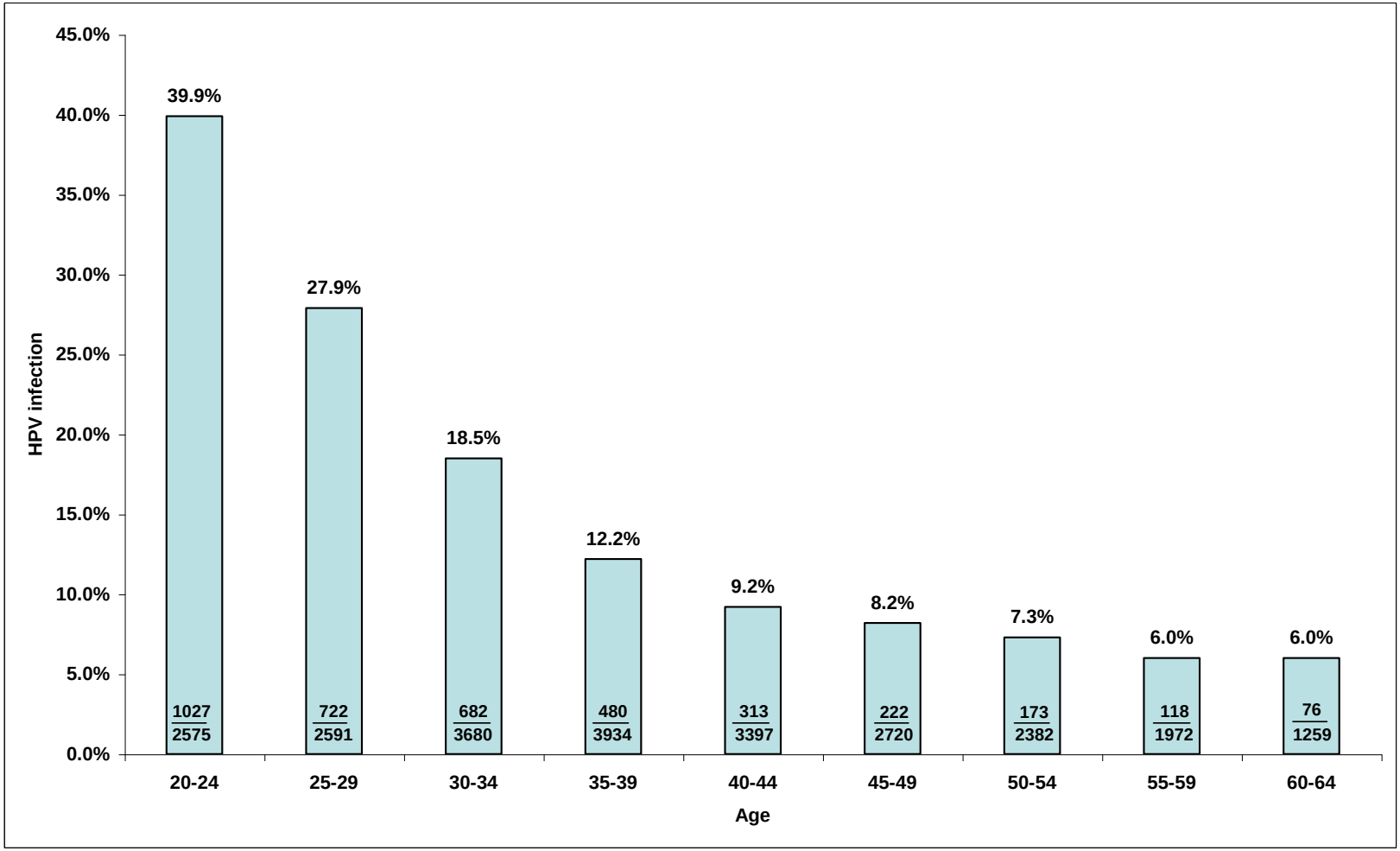
HPV in cervical screening

- 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



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

https://www.gov.uk/government/publications/human-papillomavirus-hpv-primary-screening-protocol

HPV primary screening pilot: colposcopy management recommendations algorithm

https://www.gov.uk/government/publications/human-papillomavirus-hpv-primary-screening-colposcopy-management

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

www.gov.uk/government/collections/cervical-screening-information-leaflets

Sample taker training

cpdscreening.phe.org.uk/csp