



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.

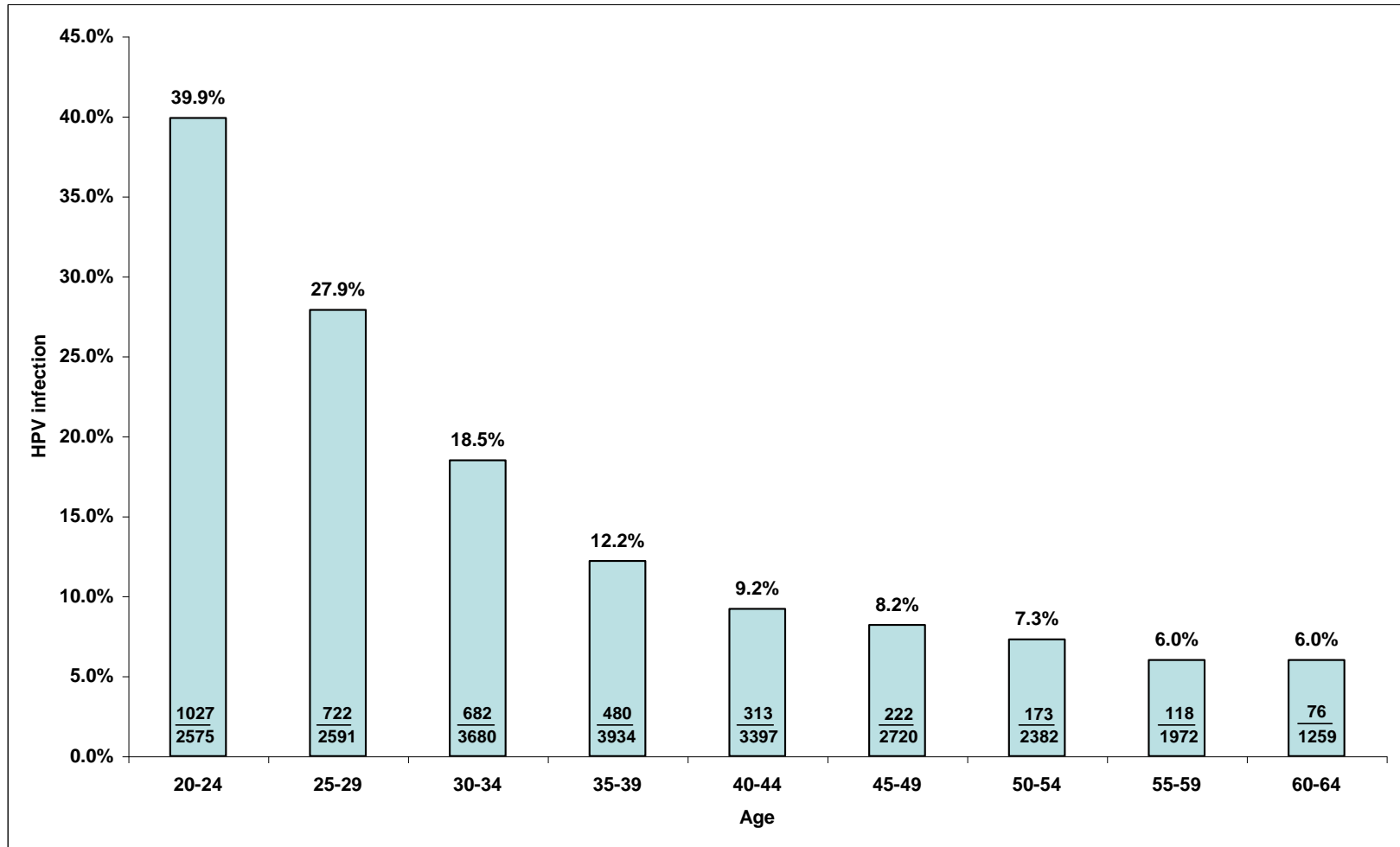
# HPV in cervical screening

- 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](https://www.gov.uk/phe/screening)

## **Professional guidance**

[www.gov.uk/government/collections/cervical-screening-professional-guidance](https://www.gov.uk/government/collections/cervical-screening-professional-guidance)

## **Information for women**

[www.gov.uk/government/collections/cervical-screening-information-leaflets](https://www.gov.uk/government/collections/cervical-screening-information-leaflets)

## **Sample taker training**

[cpdscreening.phe.org.uk/csp](https://cpdscreening.phe.org.uk/csp)