Cervical Screening (Cervical Smear Test)

The benefits of screening

Cervical cancer is the third or fourth most common female malignancy worldwide, causing an approximate 529,828 new cases each year.\(^1\) It occurs much more frequently in developing countries. In the UK it is now the 17th most common female cancer, and accounts for 1% of female deaths from cancer.\(^2\) Age-standardised mortality rate for the UK was 2.2 per 100,000 in 2012 (2.1 in England and Wales, 2.2 in Northern Ireland, and 3.2 in Scotland).\(^2\)

The cervical screening programme has not been without its critics, but there is no doubt that screening significantly reduces incidence and mortality.\(^3\) Incidence of cervical cancer in the UK fell by 43% between 1987-89 and 1997-99, apparently attributable to the screening programme introduced in the late 1980s.\(^2\) Three-yearly screening up to 39 years of age prevents 41% of cancers. Five-yearly screening between 40 and 54 years of age prevents 63% of cancers.\(^5\) It has also been shown that the cervical screening programme is associated with improved rate of cure of invasive cervical cancer.\(^6\) The challenge is to choose the most cost-effective screening programme to deliver the maximum benefit. Methods of screening and ages of women screened still differ between nations as this continues to undergo research.

Cervical screening is currently a rapidly changing field. This is due to recognition of the fact that human papillomavirus (HPV) causes the vast majority of cases of cervical cancer, the introduction of widespread HPV vaccination in many developed countries including the UK, and understanding of the benefits of HPV testing in screening for cervical cancer. Further changes in the way the screening process occurs are expected as studies of HPV testing report.

Coverage of the programme

Standard call and recall schedule\(^7\)

- First invitation for screening:
  - Age 25 in England, Wales and Northern Ireland.
  - Age 20 in Scotland.

- Routine recall:
  - England, Wales and Northern Ireland: routine three-yearly recall between ages 25-49, then five-yearly recall until aged 65.
  - Scotland: routine three-yearly recall from age 20 until aged 60.

- Women over the age of 65 are only screened if they have not been screened since the age of 50 or have had recent abnormal tests.

Current evidence shows that cervical screening in women aged 20-24 has little or no impact on rates of invasive cervical cancer up to the age of 30.\(^8\) Uncertainty remains regarding its impact on advanced-stage tumours in women under the age of 30. Screening older women, however, leads to a substantial reduction in incidence of, and mortality from, cervical cancer.\(^5\)

Uptake

A study of non-engaging women in Sweden concluded that the reasons women did not attend for smears were complex and affected by personal circumstances. Women who chose not to attend often felt healthy and cited other priorities. A negative body image, low self-esteem, feelings of discomfort when confronted with the gynaecological examination and fear of the results also influenced their non-attendance.\(^9\)
Latest statistics show uptake rates in the UK as follows:

- In England: as of 31 March 2013, 78.3% of eligible women had been screened at least once in the previous five years.\[^{10}\]
- In Scotland: as of 31 March 2014, 70.7% of eligible women had been screened in the previous 3.5 years.\[^{11}\]
- In Wales: as of 31 March 2013, 76.3% of eligible women had been screened at least once in the previous five years.\[^{12}\]
- In Northern Ireland: as of 31 March 2011, 77.3% of eligible women had been screened at least once in the previous five years.\[^{13}\]

### The screening process

A speculum made from disposable plastic (or from metal, which should be warmed) should be inserted vaginally to view the squamocolumnar junction of the cervix. Liquid-based cytology (LBC) is now the method of choice.\[^{14}\]

A brush is used rather than a spatula, which is rotated against the squamocolumnar junction (usually in the cervical canal). Two systems for LBC are in use. Both systems use brushes which look similar. In one, the head of the brush that contains the cells is broken off into a pot that contains special preservative liquid. The brush head is sent to the laboratory in the pot (this is the SurePath\(^{\text{®}}\) brand method). In the other system, the brush is rinsed in the preservative to wash the cells into the pot. The brush is then discarded (this is the ThinPrep\(^{\text{®}}\) brand).

LBC is now used nationally. It has significantly reduced numbers of inadequate smears, as the liquid is spun and treated to remove other cells such as pus or blood. Numbers of inadequate smears dropped from over 9% to 2.8% when LBC was introduced.\[^{5}\] As a result, fewer repeats are needed, which benefits both women and laboratories. Reporting time is reduced and results are available and sent to the patient in approximately two weeks.

Older methods include the Papanicolaou (Pap) smear test which uses a brush or the Ayre spatula to sample the ectocervix, by rotating it twice through 360°. In both these methods, the material obtained is smeared on to a microscope slide, which is then sprayed with or immersed in a fixative solution prior to transporting to the laboratory.

### Interpreting smear results

Cells are analysed to look for abnormalities in the appearance of the nucleus and other aspects of cell morphology (dyskaryosis). There is some lack of standardisation among laboratories, but basically one can expect to see one of the following results on a report:\[^{10}\]

- **Negative** - approximately 94% of tests in England in 2012-13. Endocervical cells with normal nuclei are seen.
- **Inadequate** - 2.2% of smears in England in 2012-13. Inadequate smears may be caused by insufficient or unsuitable material sampled (vaginal cells, endocervical cells, insufficient cells) unlabelled specimens or by inadequate fixation/poor spreading of the material on the slide in the laboratory.
- **Borderline** - 3.4% of smears in England in 2012-13. Cells are seen with abnormal nuclei, but the pathologist cannot say for certain that they are indicative of dyskaryosis. Many patients revert to normal smears eventually. Very few of these patients go on to develop cancer.
- **Mild dyskaryosis** - 1.5% of smears in England in 2012-13. Again, many women with this finding eventually revert to normal smears. Strictly speaking, the cervical intraepithelial neoplasia (CIN) grading system should not be used on smears but on cervical biopsy material obtained during colposcopy. However, mild dyskaryosis usually equates to CIN 1. Cancer is very unlikely.
- **Moderate dyskaryosis** - 0.4% of smears in England in 2012-13. This usually equates to CIN 2 and is seen in approximately 1% of samples. CIN 2 is considered a pre-cancerous condition with an intermediate probability of developing into cancer.
- **Severe dyskaryosis** - 0.6% of smears in England in 2012-13. This usually equates to CIN 3. It is at the higher risk end of the cancer spectrum. Less than 0.1% of smears will show nuclear and other cellular changes suggestive of carcinoma, sometimes referred to as carcinoma in situ.
- **Glandular neoplasia** - less than 0.1% of smears in England in 2012-13. Occasionally, abnormalities of glandular cells are seen, suggestive of adenocarcinoma in situ, adenocarcinoma of the cervix, endometrial adenocarcinoma, or adenocarcinoma of an organ outside the uterus.
Management of results[^15][^16]

With the advent of HPV testing, management of abnormal results is in a process of reassessment and change. Currently there are differences across the UK, with further change likely to occur over the next few years.

**Negative (normal)**  
It is appropriate to:

- Investigate and manage incidental findings - eg, infections.  
- Ensure that the patient is informed of the result.  
- Recall as appropriate for a negative result, depending on age and previous screening history.

**Inadequate**  
- Repeat sample immediately after treating any infection, preferably within three months.  
- Repeat sample as soon as convenient if technically inadequate.  
- If persistent (three inadequate samples), advise assessment by colposcopy.

**Borderline changes and mild dyskaryosis**

In some areas of the UK, samples from women with borderline or mild dyskaryotic changes go on to have an HPV DNA test. This is known as HPV triage. The test is done on the original sample used for the cytology test. Women who test positive for high-risk types of HPV are referred for a colposcopy straightaway. Research has shown that HPV DNA testing leads to earlier detection of clinically relevant CIN grade 2 or worse, which when adequately treated, improves protection against CIN grade 3 or worse and cervical cancer.[^17] A 2003 Cochrane review found HPV testing to be more accurate than repeat cytology.[^18] High-risk HPV types (16, 18, 31, 33) have been found to be present in close to 100% of all cervical cancers. Equally, women with a mild or borderline smear result, who have no evidence of high-risk HPV infection are very unlikely to develop cervical cancer.[^15] HPV testing is not currently recommended for primary screening, but this may well change.

- In England and Northern Ireland, borderline smears and those with mild dyskaryosis are now automatically tested for HPV:  
  - If HPV is negative, women are returned to normal recall. They do not require referral for colposcopy.  
  - If the HPV test is inadequate or unreliable, they are advised to have a repeat smear/HPV test in six months time.  
  - If HPV is positive, women are referred for colposcopy.

- In Scotland and Wales, women who have borderline smears or mild dyskaryosis have a repeat after six months or are referred for colposcopy. They do not return to normal recall unless they have had two smears six months apart which are negative, or a normal colposcopy.

**Moderate dyskaryosis**

Refer for colposcopy.

**Severe dyskaryosis**

Refer for colposcopy.

**Management following colposcopy and/or treatment of abnormal cells**

Across the UK women who have had treatment for abnormal smear results will have an HPV test along with cytology done on their follow-up smear, called a "test of cure". This is carried out six months after initial treatment. If HPV is negative, they are returned to normal recall. If HPV is positive, or there is moderate/severe dyskaryosis, the woman is referred back to colposcopy for further treatment.

Women who have untreated CIN 1 at colposcopy, are followed up at 12 months with cytology and HPV testing. At this point, again, if HPV is negative, they can then be returned to normal recall. If HPV is positive, they are referred for colposcopy, irrespective of the cytological changes. If there are high-grade cytological changes, HPV testing is not done, and they are referred back to colposcopy.
For women who have had results showing cervical glandular intraepithelial neoplasia (CGIN) and had treatment, follow-up is set at six months. Test of cure is carried out with or without colposcopy. The tests are repeated again after 12 months, even if the test of cure showed normal cytology and was negative for HPV.

The detailed flowchart considering all eventualities is available on the NHS cancer screening websites in the individual nations.\[^{19}\]

### Future developments

HPV vaccination was introduced in September 2008 for girls aged 12-13 but it will be many years before this programme has an effect on the incidence of cervical cancer.

HPV testing as a means of screening for cervical cancer is attracting increasing interest and is the subject of much research. It may be that HPV testing is as effective as cytology, or even more so.\[^{20}\]\[^{21}\] Accuracy of self-sampling of vaginal swabs has been explored.\[^{22}\] It has recently been demonstrated that a urinary test for HPV is effective in detecting cervical HPV.\[^{23}\] This has potential to be a less expensive option which is likely to be more acceptable to women.

### Further reading & references

2. Cervical cancer - UK mortality statistics; Cancer Research UK
5. NHS Cervical Screening Website
7. UK Screening Programmes; UK Screening Portal
9. Oscarsson MG, Wijma BE, Benzein EG; ‘I do not need to... I do not want to... I do not give it priority...’—why women choose not to attend cervical cancer screening. Health Expect. 2008 Mar;11(1):26-34.
11. Cervical screening; Information Services Division (ISD) Scotland
12. Cervical Screening Wales; Public Health Wales
13. Cervical screening publications; HSC Northern Ireland Public Health Agency
15. Colposcopy and Programme Management; Guidelines for the NHS Cervical Screening Programme, May 2010
19. NHS Cervical Screening Programme Screening Protocol Algorithm for HPV Triage and TOC; Public Health England
23. Pathak N et al; Accuracy of urinary human papillomavirus testing for presence of cervical HPV: systematic review and meta-analysis, BMJ, 16 September 2014

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