Cervical screening - Management

Scenario: When to offer cervical screening

Which age groups should be offered cervical screening and how often?

- **All women between the ages of 25 years and 64 years are eligible for cervical screening in England [NHS Cancer Screening Programmes, 2004a]:**

  - Age 25 years: first invitation. (In Wales, Scotland, and Northern Ireland, the first invitation is at 20 years of age.)
  - Age 25–49 years: screening every 3 years.
  - Age 50–64 years: screening every 5 years.

- **Women 65 years of age or older should be screened** if:

  - They have not had a cervical screening test since 50 years of age.
  - A recent cervical cytology sample is abnormal.

- Before recall ceases because of age, a woman who has had mild dyskaryosis or borderline change should have had at least three negative cytology results.
- A transgender man who has retained their cervix should be included in the national cervical screening programme unless they have made an informed decision to opt out.

Basis for recommendation

Age of first invitation for screening

- See Basis for recommendation in the section Under 25s.

Screening intervals

- These screening intervals are the expert opinion of the guideline developers for the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010] who based their decision on evidence from the UK audit of screening histories that has shown that the most effective screening intervals change with a woman's age [Sasieni et al, 2003].
- The recommendations for these screening intervals have been accepted by the Advisory Committee on Cervical Screening and have been implemented in the national programme for cervical screening in England [NHS Cancer Screening Programmes, 2004a]. In Scotland, Wales, and Northern Ireland, the age at the first invitation is 20 years.

Screening women older than 65 years of age

- The recommendation to cease screening after 65 years of age is from the *Guidelines for the NHS cervical screening programme* and is based on a review of the available evidence (however, no details of the quality and interpretation of the trials were given). The guideline developers concluded that [NHS Cancer Screening Programmes, 2010]:
  - The prevalence of invasive cancer and cervical intraepithelial neoplasia in previously screened women older than 50 years of age is low.
  - Women who were diagnosed with invasive cervical cancer after 50 years of age had not participated adequately in the cervical screening programme.
  - Screening women older than 65 years of age who had not participated adequately in the cervical screening programme still caused a reduction in the subsequent rate of cervical cancer.

Ceasing screening because of age in a woman who has had mild dyskaryosis or borderline change

- This recommendation is based on expert opinion in the national guideline *Achievable standards, benchmarks for reporting, and criteria for evaluating cervical cytopathology* [NHS Cancer Screening Programmes, 2000].

Transgender men

- The importance of including transgender men in the screening programme, if they have retained their cervix and have not made an informed decision to opt out, was stressed by one CKS expert reviewer.

How do I take a liquid-based cytology sample?

- **Unless you think that the woman will not re-attend, do not take a cervical sample in the following circumstances:**
  - During menstruation.
  - If the woman is less than 12 weeks post-natally.
  - If there is discharge or infection. Treat the infection and take the sample on another occasion.
  - If the woman is pregnant and she is up to date with routine cytology. For more information, see Pregnant woman.
- **To take the sample:**
  - Fully visualize the cervix by using a speculum.
  - Insert the central bristles of the Cervex-Brush® into the endocervical canal so that the shorter outer bristles contact the ectocervix fully.
  - Rotate the brush 360 degrees five times in a clockwise direction using pencil pressure (the brush is designed to collect cells in clockwise direction only).
- **If a wide ectropion is present:**

- Use a Cervex-Brush® to collect the sample.
- If necessary, a second Cervex-Brush® can be used to sweep the transformation zone in accordance with advice from the liquid-based cytology equipment supplier.
- Both samples should be fixed in the same vial, and the fact that two samples are present should be noted on the cytology request form.

- **An endocervical brush (such as the EndoCervex Brush®) should be used in the following circumstances in conjunction with a Cervex-Brush®:**

- If it is difficult to insert the Cervex-Brush® into the os (for example if the os is narrow or stenosed).
- If the woman is being followed up for previous borderline changes in endocervical cells.
- If the woman is being followed up (this should take place in the colposcopy clinic) for a previously treated endocervical glandular abnormality and all of the following apply:
- She has not had a hysterectomy or radiotherapy.
- A previous sample was inadequate because of the absence of endocervical cells.

- **If using an endocervical brush:**

- Take the EndoCervex Brush® sample after the Cervex-Brush® sample.
- Insert the EndoCervex Brush® gently into the os, with the lower bristles remaining visible, and rotate clockwise through one whole turn.
- Fix both samples in the same vial.

- **Fix the sample immediately** before withdrawing the speculum. There are two systems used in the NHS cervical screening programme:

- **ThinPrep®**
- Using a vigorous swirling motion, rinse the brush into the fixative vial.
- Push the brush into the bottom of the vial at least 10 times, forcing the bristles apart. It is important to use firm pressure to prevent the cells clinging to the brush.
- Inspect the brush for any residual material and remove any remaining by passing the brush over the edge of the fixative vial.
- Ensure that the material reaches the liquid or it will not be preserved.
- Tighten the cap so that the torque line passes the torque line on the vial.
- If there is any material on the edge of the vial, give it a shake.
- Label the vial.

- **SurePath®**
- Remove the head of the brush from the stem and place into the vial of fixative.
- Screw the lid on and label the vial.

Basis for recommendation

These recommendations are based on expert advice in the resource pack for trainers: *Taking samples for cervical screening* [NHS Cancer Screening Programmes, 2006b].

When is routine cervical screening not recommended?

- The following women should not be screened routinely:
- Women younger than 25 years in England and younger than 20 years of age in Scotland and Wales. See Under 25s.
- Women 65 years of age or older who have had three consecutive negative cytology results.
- Women who have had a total hysterectomy.
- Women who are virgins may choose not to have cervical screening, as their risk of cervical cancer is low.

Basis for recommendation

Women older than 65 years of age

- If a woman 65 years of age or older has had three consecutive negative cytology results, it is highly unlikely that she will develop cervical cancer [NHS Cancer Screening Programmes, 2010].
- The guideline developers of the *Guidelines for the NHS cervical screening programmes* [NHS Cancer Screening Programmes, 2010] reviewed a retrospective case analysis study of 23,440 women aged 50–60 years of age who had ever had a cervical screen in the Grampian region [Cruickshank et al, 1997]. This study found that the prevalence of invasive cancer and cervical intraepithelial neoplasia 3 in women older than 50 years of age was low in women who had been adequately screened: 11 per 100,000 women (95% CI 4.5 to 17.5) who were previously well screened, and 59 per 100,000 women in the whole cohort (95% CI 43.9 to 74.1) over a 5-year period.

Women who are virgins

- A systematic review of the evidence on the causes of cervical cancer [NHS Cancer Screening Programmes, 2005] concluded that:
- Human papillomavirus (HPV) DNA is detected only in cervical specimens from sexually active women.

- Non-sexually transmitted low-risk HPV infection, although possible, is rare in women who are virgins. Low-risk HPV (mostly types 6 and 11) usually cause genital warts and are not implicated in the development of cervical cancer [Koliopoulos et al. 2003].
- Non-sexually transmitted HPV infection is rare or nonexistent in adolescent girls.

Should I ever do unscheduled cervical screening?

- **Unscheduled cervical screening is *not* recommended in any situation, including the following:**
- **Women younger than 25 years of age in England and younger than 20 years of age in Scotland and Wales.** See Under 25s.
- **Women older than 65 years of age who have had three negative samples.** See Screening programme.
- **If the woman has symptoms of possible gynaecological cancer.** This includes:
- **Postmenopausal bleeding.** If the woman has postmenopausal bleeding and has attended regular screening, do not take a cervical sample. Examine and refer urgently (within 2 weeks) to a gynaecologist.
- **Suspicious-looking cervix** — urgently refer the woman (within 2 weeks) to a gynaecologist. A cervical sample may be taken and suspicious looking cervix recorded on the form. The cervical cytology result may confirm cancer, but a negative result does not exclude cancer.
- **Abnormal bleeding** (post-coital bleeding, intermenstrual bleeding, and blood-stained vaginal discharge) **—** urgently refer the woman (within 2 weeks) to a gynaecologist.
- **If the woman presents with:**
- **Genital warts.**
- **Vaginal discharge**.
- **Pelvic inflammatory disease.**
- **If the woman requests contraception or hormone replacement therapy (HRT),** including:
- Starting or continuing to take an oral contraceptive.
- Insertion of an intrauterine contraceptive device.
- Starting or continuing HRT.
- **If the woman is pregnant** antenatally or post-natally or after termination unless a previous screening test was abnormal.
- **If the woman has social or behavioural risk factors:**
- Multiple sexual partners.

- Heavy cigarette smoker.

Basis for recommendation

Postmenopausal bleeding

- These recommendations are based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].
- A cervical sample is not an appropriate investigation for postmenopausal bleeding.

Abnormal-looking cervix

- Expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010] is that women with an abnormal-looking cervix should always have a gynaecological examination with onward referral to colposcopy if gynaecological cancer is suspected. An abnormal-looking cervix may be associated with invasive cancer. A negative smear does not rule out cervical cancer.

Women with symptoms of cervical cancer

- These recommendations are based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010] and referral guidelines for suspected cancer from NICE (National Institute for Health and Clinical Excellence) [National Collaborating Centre for Primary Care, 2005].
- Symptoms of cervical cancer include postcoital bleeding, intermenstrual bleeding and vaginal discharge [National Collaborating Centre for Primary Care, 2005].
- An unscheduled cervical sample is also not recommended by SIGN (Scottish Intercollegiate Guidelines Network) [SIGN, 2008].
- A retrospective study of 314 women with post-coital bleeding found that nine women had cervical cancer, one woman had vaginal cancer, and two women had endometrial cancer [Rosenthal et al, 2001].

Genital warts, vaginal discharge, and pelvic inflammatory disease

- These recommendations are based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].
- There is no evidence to suggest that cervical screening every 3 years is less protective in women with genital warts than for other women.

Unscheduled cervical screening at other times

- All of these recommendations are from the *Guidelines for the NHS cervical screening programme* and are based on a review of the available evidence (however, no details of the quality and interpretation of the trials were given) [NHS Cancer Screening Programmes, 2010]. The guideline developers concluded that additional screening is not justified provided the woman has had a screening test within the previous 3–5 years. This is because:
  - A mathematical simulation model found that a cervical sample taken 1 year after the first ever cervical sample gave no benefit in terms of person-years saved.
  - There is no available evidence to suggest that social or behavioural risk factors reduce the length of time in which it is possible to detect preclinical cervical cancer.
  - It is not possible to reliably predict which women will develop high-grade cervical intraepithelial neoplasia.
  - Intensive screening of women with a history of multiple sexual partners and early onset of first intercourse is not cost-effective.

Should women under 25 years of age be offered cervical screening?

- **In England, do not offer cervical screening to women younger than 25 years of age.**
  - Invasive cancer is rare in women younger than 25 years of age.
  - There is no current evidence that screening women younger than 25 years of age reduces the incidence of invasive cancer.
  - It is believed that screening in this age group may result in over-treatment and do more harm than good.
- **In Scotland and Wales, do not offer cervical screening to women younger than 20 years of age.**

Basis for recommendation

Policy in England

- Women younger than 25 years of age are no longer offered cervical screening in England. This recommendation is based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010] who have reviewed the evidence and stated:
  - **Cervical cancer is rare in women younger than 25 years of age.** In 2007, in women 15–25 years of age in England and Wales, there were 56 women with cervical cancer and three deaths from cervical cancer.
  - Cervical screening in this age group may do more harm than good.
  - **Abnormal cervical cytology is common in this age group.** One in every six samples is abnormal. Many of these changes resolve spontaneously.
  - **There is no evidence that screening women younger than 25 years of age reduces the incidence of invasive cancer [NHS Cancer Screening Programmes, 2010].**

- Good evidence from a population-based case-control study indicates that cervical screening in women 20–24 years of age has little or no effect on rates of invasive cervical cancer up to the age of 30 years. Screening women 40 years of age or older is very effective and leads to a large reduction in incidence and mortality from cervical cancer.
- **There is no evidence that screening is effective in women aged 20–24 years. Women younger than 25 years of age who develop cervical cancer are as likely to have been screened as unscreened [Sasieni et al, 2009].**
- **Evidence indicates that harms outweigh benefits because of over-treatment.**
- There is evidence from a meta-analysis and a cohort study that cone biopsy increases the risk of premature birth and also infant death in the perinatal period.
- A retrospective cohort study that included 5548 women who had given birth found that cone biopsy, loop electrosurgical excision procedure and diathermy were all associated with preterm birth. Laser ablation did not increase the risk of a preterm birth [Bruinsma et al, 2007].
- A critical review of the literature concluded that women who are treated for cervical lesions prior to childbearing are at increased risk of preterm delivery [Sasieni et al, 2010].

- In 2003, in England, the cervical screening programme was reorganized to invite women for cervical screening only when they reached 25 years of age. This decision has remained controversial since.
- In 2009, a formal review of the evidence was carried out by the independent Advisory Committee on Cervical Screening [Advisory Committee on Cervical Screening, 2009]. After this meeting, a written ministerial statement was issued on the subject 'Cervical screening for women aged under 25 years' [DH, 2009]. It stated that:

- No new evidence was presented to the review meeting to support the reintroduction of screening in women younger than 25 years of age.
- New evidence was presented indicating that screening is of little or no benefit in women younger than 25 years of age.
- Evidence indicated that treatment after screening in this age group increased the risk of a subsequent premature birth (increasing the risk of babies dying or having severe disabilities).
- There was evidence that there had been no significant increase in the number of women younger than 25 years of age contracting or dying of cervical cancer since the policy change in 2004.

Policy in Scotland and Wales

- In Scotland and Wales, women are invited for screening from 20 years of age.
- The Academic Department of Obstetrics and Gynaecology, Wales College of Medicine was asked to advise on the age at which to commence cervical screening. They reviewed the evidence [Rieck et al, 2006] and made the following points:

- The NHS cervical screening programme in England changed the age at which women are invited for screening to 25 years in 2003. The rationale for this was largely based on a case control study [Sasieni et al, 2003] which assessed the effectiveness of screening intervals at different ages. However, this study did not look at micro-invasive cancer.
- Knife cone biopsy is rarely used and, large loop excision of the transformation zone is now the treatment of choice for high-grade cervical intraepithelial neoplasia. A meta-analysis of five studies [Crane, 2003] found that pre-term birth was more common in women who had loop electrosurgical excision (odds ratio 2.53, CI 1.42 to 1.49, p = 0.001) compared with women who had not had the procedure.
- The incidence of CIN 3 has continued to increase slowly in women in Wales since 1999.
- Deaths from cervical cancer seems to have fallen in women in Wales from 0.5 case per year in the period 1981–1988 to 0.2 cases per year for 1999–2003. This fall may have been due to the introduction of an organized cervical screening programme.
- Ten women aged 20–24 years had cervical cancer during 1999–2003 in Wales: eight were diagnosed by cervical screening and two because of postcoital bleeding. The eight women who had cervical cancer detected by screening were all asymptomatic and early detection would almost certainly have led to a better prognosis.
- Cervical screening detects microinvasive cancer as well as invasive cancer. Each year, screening will detect one new case of cervical cancer and two cases of micro-invasive cancer in women 20–24 years of age in Wales.
- The Academic Department of Obstetrics and Gynaecology, Wales College of Medicine, concluded that:
- 'In Wales we recommend that women continue to be invited for cervical screening from 20 years of age. This will provide the information required to compare the incidence and stage at diagnosis of cervical cancer in young women invited for first time cervical screening at different ages across the UK, and allow time for improved data collection on the outcome of colposcopy.'

Should a pregnant woman be offered cervical screening?

- **If the woman has been called for routine screening and the previous result was normal,** postpone the cervical sample until 12 weeks after delivery.
- **If a previous test result was abnormal** and the woman has become pregnant since this test was done, offer to obtain a cervical sample in the mid-trimester.
- Seek specialist advice if the routine ultrasound scan has suggested a low lying placenta.
- The manufacturers of the Cervex-Brush® do not advise its use after 10 weeks of pregnancy. However they have had no reports of problems with its use in pregnancy.

Basis for recommendation

Advice on when to take a smear in pregnancy

- These recommendations are based on expert opinion from the guideline *Taking samples for cervical screening* [NHS Cancer Screening Programmes, 2006b] and the expert opinion of the guideline developers in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].

Women with a low lying placenta

- The recommendation to seek specialist advice before taking a cervical cytology sample from a woman with a low lying placenta is based on advice from CKS expert reviewers.

Use of Cervex-Brush® after 10 weeks of pregnancy

- The information about the use of Cervex-Brush® is based on personal communication with the manufacturer [Zwart, Personal Communication, 2010].

Should women who have had a hysterectomy be offered cervical screening?

- **Advise women on routine recall with no cervical intraepithelial neoplasia (CIN) in their hysterectomy specimen that they do not need further follow up.**
- **Advise women not on routine recall with no CIN in their hysterectomy specimen** that they should have vault cytology 6 months after surgery.
  - If this is negative, no further screening is necessary.
- **Women with CIN which has been completely excised** should be offered:
  - Vault cytology 6 and 18 months after surgery.
  - If test results are negative at both time points, no further follow up is necessary.
- **Women with CIN which has not been completely excised, or excision is uncertain,** should be offered:
  - If high-grade disease (CIN 2 or CIN 3): cytology at 6 and 12 months, followed by annual cytology for 9 years. Then, return to routine screening.
  - If low-grade disease (CIN 1): cytology at 6, 12, and 24 months. If results are negative at all time points, return to routine screening.
- **Women who have had a subtotal hysterectomy** should be advised that:
  - They still have a cervix and should continue in the National Screening Programme.

Basis for recommendation

Hysterectomy after benign disease

- These recommendations are based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].
- The risk of cervical cancer in a woman who has had a hysterectomy for benign disease is rare. A systematic review [Hartmann et al, 2003] of the evidence found:
  - In a nested case-control study of 172 women within a cross-sectional study of 21,152 women 50 years of age or older, dysplasia and cancer were identified in 1.6 women per 1000 women screened who had not had a hysterectomy and in 0.18 woman per 1000 women screened who had had a hysterectomy [Fox et al, 1999].
  - In a study of 6265 women who had had hysterectomies for benign disease. At 2-year follow up, three women were found to have vaginal intraepithelial neoplasia and one woman was found to have squamous-cell carcinoma [Pearce et al, 1996].

Hysterectomy in women with cervical intraepithelial neoplasia (CIN)

- These recommendations are based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers commented that:
  - Women with CIN who have had a hysterectomy are at risk of developing vaginal intraepithelial neoplasia.
  - After hysterectomy, the risk of developing cancer is similar to that in women who have had localized destruction or excision biopsy. It is unclear whether the development of cancer is due to recurrence or incomplete treatment.
  - Recurrence is unlikely to be a cause if the whole of the cervix (including the transformation zone) has been removed.
  - Therefore, if no transformation zone remains and two follow-up vaginal cytology samples show no dyskaryosis, then it is reasonable to assume that the risk of developing cancer is so small that surveillance beyond 18 months is not justified.
- The guideline developers from the *Guidelines for the NHS cervical screening programme* reviewed the available evidence and found [NHS Cancer Screening Programmes, 2010]:
  - A retrospective longitudinal review [Gemmell et al, 1990].
  - The review identified 341 women who had CIN 3 and had undergone hysterectomy. Of these, 219 (64%) were followed up for 10 years. Only two women developed vaginal intraepithelial neoplasia. Of the 79 women followed up for 15 years, only one developed vaginal intraepithelial neoplasia. No women developed invasive vaginal carcinoma during the 15 years of follow up.
  - The authors additionally identified 60 women with vaginal cancer from the gynaecology cancer register, which covered a 30 year period (1957–1987). Only one of these women had had a previous diagnosis of CIN 3 at hysterectomy.
  - The authors proposed screening every 6 months during the first post-hysterectomy year and then at 2 years. If these cytology samples were normal, the woman could then revert to the normal screening programme.

- A case series of 177 women with CIN treated by hysterectomy. Only seven women (4%) developed subsequent vaginal intraepithelial neoplasia [Burghardt and Holzer, 1980].

Subtotal hysterectomy

- This recommendation is based on expert consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].

Do women who are immunosuppressed need increased surveillance?

- **For women aged 25–65 years who have renal failure and require renal transplantation:**
  - Offer cervical screening at the time they are put on the transplant list if they have not been screened within 3 years if aged 25–49 years, or 5 years if aged 50–64 years.
  - Offer cervical screening within the year after renal transplantation as persistent infection with human papillomavirus would put them at increased risk of developing cervical intraepithelial neoplasia (CIN).
  - Treat any abnormality on cervical screening as a high-grade abnormality and refer promptly for colposcopy.
- **For women who are starting cytotoxic drugs for rheumatological disorders:**
  - Offer cervical screening if they have not been screened within 3 years if aged 25–49 years, or 5 years if aged 50–64 years.
  - Refer to colposcopy if there is any cytological abnormality.
- **Offer women who are HIV positive:**
  - Cervical cytology and ideally colposcopy at diagnosis.
  - Annual cervical screening.
- **There is no indication for increased surveillance** in women taking:
  - Post-transplantation immunosuppressive treatment after the first year in women with no history of cervical intraepithelial neoplasia. However, a woman with an abnormal cervical cytology result should be referred promptly for colposcopy. (Women with a previous history of cervical intraepithelial neoplasia will have increased surveillance.)
  - Cytotoxic drugs for rheumatological disorders.
  - Cytotoxic chemotherapy for non-genital cancers.
  - Long-term steroids.
  - Oestrogen antagonists, such as tamoxifen.

Basis for recommendation

These recommendations (with the exception of recommendations about screening women requiring renal transplantation) are from the *Guidelines for the NHS cervical screening programme* and are based on a review of the available evidence; however, no details of the quality and interpretation of the trials were given. The guideline developers conclusions are summarized in each section [NHS Cancer Screening Programmes, 2010].

- Women who are immunosuppressed are at an increased risk of cervical intraepithelial neoplasia (CIN). Any cytology result other than normal (that is, borderline or worse) should be referred even if the abnormal result would not instigate a colposcopy referral in a woman who does not have renal failure.

Women requiring renal transplantation

- The recommendations for cervical screening are based on clarification from an expert reviewer [Patnick, Personal Communication, 2010].
- Good evidence indicates that women requiring dialysis or renal transplantation are at an increased risk of CIN and cervical cancer (probably at least a five-fold risk compared with the normal population).
- Some evidence indicates that cervical cytology is insensitive and CIN could be missed. Therefore, there should be early referral to colposcopy.

Women taking cytotoxic drugs for rheumatological disorders

- Although there is concern that cytotoxic drugs may increase a woman's risk of CIN, there is a lack of good evidence to support this. Therefore, healthcare professionals should stress to women on cytotoxic drugs the importance of having cervical screening at the standard intervals.

Women who are HIV positive

- Cross-sectional, case-control, and cohort studies indicate an increased prevalence of squamous intraepithelial lesions, ranging from 20–40% in women who are HIV positive compared with 3% in women who are HIV negative. Furthermore:
  - In HIV-positive women, regression of low-grade lesions is rare and high-grade lesions may respond poorly to standard treatment.
  - Evidence indicates that women who are HIV positive have an increased risk of false-negative cytology.
  - In one study, the recurrence rate in women with CD4 counts of less than 200/mm^3 was 87%, compared with less than 10% in immunocompetent women. The reason for this may be lack of immune activity against human papillomavirus.
  - Even in people treated with antiretroviral therapy, there is a high risk of an abnormal cervical cytology result, although the treatment may facilitate regression of low-grade lesions (CIN 1).

Women taking immunosuppressive drugs after transplantation

- Data on the long-term management of this group of women are insufficient. Limited evidence from cross-sectional studies and one small longitudinal study suggests that there is no benefit of decreasing the screening interval.

Women who are immunosuppressed owing to chemotherapy for non-genital cancers

- There is no evidence to suggest that these women are at increased risk of CIN.

Women who are on long-term treatment with corticosteroids

- There is no evidence to suggest that these women are at increased risk of CIN.

Women who are taking oestrogen antagonists such as tamoxifen

- There is no evidence to suggest that these women are at increased risk of CIN.

How often should women who have been treated for CIN be offered cervical screening?

- Follow up for woman treated for cervical intraepithelial neoplasia (CIN) is by cervical cytology and should start between 6 and 9 months after treatment.
- Women treated for CIN 1 should be offered cervical screening at 6, 12, and 24 months after treatment. If the cervical cytology results are negative, they then return to the normal recall system.
- Women treated for CIN 2, CIN 3, or cervical glandular intraepithelial neoplasia should be offered cervical screening at 6 and 12 months after treatment and then annually for 9 years (that is, 10-year follow up).
- If women do not have a negative test following treatment, they should be offered repeat colposcopy at least once during the following 12 months.
- It is important to encourage women to attend follow up.

Basis for recommendation

- All of these recommendations are from the *Guidelines for the NHS cervical screening programme* and are based on a review of the available evidence; however, no details of the quality and interpretation of the trials were given. The guideline developers concluded that [NHS Cancer Screening Programmes, 2010]:

- Treated women are between two and five times more likely to develop cervical cancer than the general population. Much of this is due to poor adherence to screening, and case series show that more than 50% of cases of cervical cancer develop in women who are lost to follow up.
- Most recurrent disease is detected in the first 24 months after treatment.
- There is long-term risk of invasive cancer for at least 10 years and possibly for 20 years after treatment.

- Histological examination of the biopsy specimen can determine risk factors for residual disease. Women at increased risk will require more intensive surveillance.
- Although the risks are probably greater for women with high-grade disease, the relative risk for different grades of cervical intraepithelial neoplasia (CIN) are not known.

- A systematic review of 25 studies that investigated the success rate of the treatment of CIN showed that the risk of invasive cancer remained at about 56 per 100,000 woman-years for at least 20 years after treatment [Soutter et al, 2006].

How should women with cervical stenosis be managed?

- Refer women to the colposcopy clinic for consideration of cervical dilatation.

Basis for recommendation

This recommendation is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers state that:

- Severe cervical stenosis is usually the result of previous surgery.
- It may be impossible to obtain a cervical sample that represents the whole transformation zone.
- If the woman has a history of high-grade cervical intraepithelial neoplasia, cervical glandular intraepithelial neoplasia, or unexplained high-grade cytology, then cervical dilatation or hysterectomy is recommended to exclude an abnormality distal to the stenosis which may lead to the cancer if left untreated.
- If these options are not possible, then the lead colposcopist may recommend withdrawal from the screening programme.

Scenario: Managing cervical cytology results

What should happen following a normal cervical cytology result?

- A woman with a normal result will be recalled at the standard interval of the Cervical Screening Programme. This is based on:
  - Her age.
  - Previous abnormal results.
- **There is no need to refer a woman for colposcopy who has contact bleeding** at the time that a cervical sample is obtained in the absence of other symptoms or an abnormal result.
- **If the woman has symptoms of cervical cancer, such as post-coital bleeding (particularly if she is older than 40 years of age), intermenstrual bleeding, or persistent vaginal bleeding** — urgently refer (within 2 weeks) to a gynaecologist for assessment and urgent onward referral for colposcopy if cervical cancer is suspected, even if the cervical cytology sample is reported as negative.
- **If the woman has an abnormal-looking cervix** and cervical cancer is suspected — urgently refer (within 2 weeks) to a gynaecologist, even if the cervical cytology sample is reported as normal.

Basis for recommendation

Contact bleeding at the time of the cervical cytology sample

- This recommendation is based on expert consensus in *Guidelines for the NHS screening programme* [NHS Cancer Screening Programmes, 2010].

Referral of women with symptoms

- The guideline developers recommend that if other symptoms are present, then the woman should be referred to a gynaecologist experienced in the management of cervical disease and onward referral for colposcopy if cancer is suspected [NHS Cancer Screening Programmes, 2010]. The guideline developers identified one study that reviewed 314 women with post-coital bleeding retrospectively and found that nine women had cervical cancer, one woman had vaginal cancer, and two women had endometrial cancer [Rosenthal et al, 2001]. The guideline developers also commented that [NHS Cancer Screening Programmes, 2010]:

- Although post-coital bleeding is a significant symptom, cancer is unlikely.
- Chlamydia infection and problems with contraception are likely causes in younger women.

Abnormal cervix

- The guideline developers in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010] based this recommendation on good clinical practice. An abnormal cervix may be associated with invasive cancer.

What should happen following an inadequate cervical cytology sample?

- If the cervical cytology sample is reported to be inadequate, repeat.
- If three consecutive cervical cytology samples are reported to be inadequate, refer for colposcopy.

Basis for recommendation

This recommendation is based on expert consensus in the *Guidelines for the NHS cervical screening programme.* This is because it is necessary to exclude invasive cancer, which is associated with inflammatory processes and may bleed on contact [NHS Cancer Screening Programmes, 2010].

What should happen following an abnormal cervical cytology result?

- **Urgently refer the woman to a gynaecologist (within 2 weeks)** if she has symptoms of cervical cancer (post-coital bleeding [particularly if she is older than 40 years of age], intermenstrual bleeding, and persistent vaginal bleeding) or an abnormal-looking cervix, regardless of the test result.
- **Urgently refer the woman for colposcopy (within 2 weeks)** if the the cervical sample is reported as showing:
  - Possible invasive cancer.
  - Glandular neoplasia.
- **Urgently refer the woman for colposcopy (within 4 weeks)** if the the cervical sample is reported as showing:
  - Moderate or severe dyskaryosis after one test.
- **Urgently refer the woman to a gynaecologist (within 2 weeks) if the test shows atypical endometrial cells,** regardless of the woman's age, menopausal status, and whether or not she has irregular vaginal bleeding. This result will be classified as 'query glandular neoplasia' but will state that the appearance of the cells suggests endometrial origin. These cells may be associated with:

- An endometrial polyp.
- Chronic endometritis.
- An intrauterine contraceptive device.
- Endometrial hyperplasia.
- Endometrial carcinoma.

- **Seek specialist advice about whether to refer urgently if the test shows benign endometrial cells, particularly if the woman has symptoms and is:**

- Postmenopausal.
- Aged 40 years or older and menstruating or having withdrawal bleeds if the smear was done after the 14th day of the menstrual cycle. There may be a small risk of serious underlying disease unless the woman:
- Is taking oral contraception, *or*
- Is taking hormone replacement therapy, *or*
- Has an intrauterine contraceptive device in situ, *or*
- Is taking tamoxifen.

- **Refer women for colposcopy** (within 4 weeks) if the cervical sample shows:

- Borderline glandular change (nuclear change in endocervical cells) after one test.

- **Refer women for colposcopy** if the cervical sample shows:

- **An abnormal result of any grade on three tests in any 10-year period.** This applies to women who have been returned to the normal routine recall system.
- **Borderline nuclear changes** in squamous cells on three consecutive tests.
- **Mild dyskaryosis** on one test (although it remains acceptable to repeat the test before referral in accordance with local protocols).
- **Previous treatment for cervical intraepithelial neoplasia,** and the woman has not been returned to routine recall and a subsequent test is reported as mild dyskaryosis or worse.

Basis for recommendation

Possible invasive cervical cancer

- The recommendation to urgently refer women with possible invasive cervical cancer is based on expert opinion in *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers based their opinion on evidence from a cross-sectional study of 527 cervical cytology samples that found that the positive predictive value of invasive cervical cancer if the sample [Johnson and Wadehra, 2001]:

  - Suggests frank invasion was 56% (on the basis of results from 121 cervical cytology samples).
  - Indicates a suspicion of invasion was 22% (on the basis of results from 236 cervical cytology samples).
  - Indicates a suspicion of micro-invasion was 17.2% (on the basis of results from 170 cervical cytology samples).

Possible glandular neoplasia (includes cervical and non-cervical glandular neoplasia)

- This recommendation to urgently refer women with possible glandular neoplasia is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers based their opinion on evidence from:

  - A retrospective review of the clinical management of 80 women with abnormal glandular cells on a cervical cytology sample. The predictive value of a cervical cytology sample with abnormal glandular cells for cancer was 42.5% and for pre-cancer was 28.8%. Thirteen women had cervical intraepithelial neoplasia (CIN), 13 women had endometrial cancer, 10 women had cervical adenocarcinoma, and eight women had cervical intraepithelial glandular neoplasia [Cullimore and Scurr, 2000].
  - A retrospective study of 89 women with abnormal glandular cytology found that 15 women had CIN without glandular abnormality, one woman had vaginal intraepithelial neoplasia, and one woman had cervical adenocarcinoma. Eleven women had cervical carcinoma, and 22 women had endometrial carcinoma. The authors recommended that all women with glandular neoplasia should have cone biopsy and endometrial sampling even if the colposcopy is normal [Leeson et al, 1997].

Severe dyskaryosis

- *Guidelines for the NHS cervical screening programme* currently recommend that women with severe dyskaryosis are referred for colposcopy within 4 weeks, based on evidence from case series that reported a high incidence (80–90%) of CIN 2 or CIN 3 at colposcopy [NHS Cancer Screening Programmes, 2010]. No details of the quality or the interpretation of the trials were given.

- However, one CKS expert reviewer who was a member of the editorial group for the *Guidelines for the NHS cervical screening programme* recommends referral within 2 weeks [Patnick, Personal Communication, 2010].

Moderate dyskaryosis

- This recommendation to refer women with moderate dyskaryosis within 4 weeks is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers based their opinion on evidence from:

- A cross-sectional analysis (within a randomized prospective study of 913 women) of 82 women with moderate dyskaryosis: 73% of the women had either CIN 2 or CIN 3 [Anderson et al, 1992].

- Case series that also reported an incidence of 74–77% of CIN 2 or CIN 3 at colposcopy. No details of the quality or the interpretation of the trials were given.

- The guideline developers based their opinion on evidence that included three case series that showed that many women who have a cervical cytology sample showing borderline endocervical change will have either invasive or premalignant disease.

- One case series analysed the case notes of 48 women with borderline glandular changes. Five women were excluded from the analysis (three because their case notes were not available, one because of severe dyskaryosis, and one because of recurrent glandular cells during pregnancy). More than half of the women had clinically significant lesions: seven women had cancer (six had cervical cancer and one had endometrial cancer), seven women had intraepithelial neoplasia, and 19 women had either no abnormality or insignificant abnormalities [Mohammed et al, 2000].

- One case series of 136 women with atypical glandular cells found an association with substantial underlying uterine pathology: at least 4% (95% CI 0.8% to 11.0%) invasive cancers and 13% (95% CI 6.4% to 22.6%) precancerous lesions [Kennedy et al, 1996].

- One case series of 127 women with cytology samples reported as showing glandular changes found that 25 women had cervical lesions: 12 women had low-grade CIN, six women had high-grade CIN, three women had endocervical atypia, one woman had adenocarcinoma in situ, and three women had invasive adenocarcinoma. One woman had ovarian cancer [Zweizig et al, 1997].

Presence of abnormal endometrial cells

- The recommendation to urgently refer women with abnormal endometrial cells is from *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010] and is based on what the guideline development group considers to be good clinical practice. After reviewing the available evidence the guideline developers stated that:

- More than a third of women with atypical endometrial cells have significant endometrial disease.
- Studies (no details given) have shown that 80% of postmenopausal women with atypical endometrial cells have endometrial disease: 13–18% have endometrial cancer, and 6–7% have high-grade dysplasia and squamous-cell carcinoma.

Benign endometrial cells

- The recommendations for referral of woman with benign endometrial cells in cervical cytology samples are based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. These guidelines state that:
- In women younger than 40 years of age, the presence of benign endometrial cells has no significance.
- The prevalence of benign endometrial cells is higher in cervical cytology samples obtained by the liquid-based cytology method that with conventional cytology. *Guidelines for the NHS cervical screening programme* recommend that if benign endometrial cells are present, the cervical cytology result should be reported as negative, but the report will include a note to the effect that 'endometrial cells are present in a woman older than 40 years of age. Such cells may be associated with endometrial pathology, particularly if out of phase or after the menopause. Referral for a gynaecological opinion should be considered in the light of the menstrual, drug, and clinical history'.
- After reviewing the evidence, the guideline developers stated that:
- Most women with benign (normal) endometrial cells but who have endometrial abnormalities will have symptoms, such as postmenopausal bleeding.
- Benign (normal) endometrial cells in asymptomatic postmenopausal women have been found to be associated with a low prevalence of premalignant or malignant uterine disease.
- The guidelines reviewers based their recommendations on evidence from a systematic review that investigated the prevalence of normal endometrial cells and also their relationship to significant endometrial pathology [Canfell et al, 2008]. The review found 22 studies that met their inclusion criteria: all of these studies involved retrospective review and were considered to be of low or fair quality. Conclusions were that:
- The estimated prevalence for normal endometrial cells in liquid based cytology samples was 0.9% (95% CI 0.5 to 1.4%).
- The proportion of women with normal endometrial cells in liquid based cytology samples who had significant endometrial pathology was 2%. Half of these (1%) had endometrial cancer.
- Most women with significant endometrial pathology will have abnormal uterine bleeding.

- The decision whether or not to refer women aged over 40 years who are asymptomatic is a clinical one.

Borderline glandular changes (nuclear changes in endocervical cells)

- The recommendation to urgently refer women with borderline glandular changes is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].

- The guideline developers based their opinion on evidence that included three case series that showed that many women who have a cervical cytology sample showing borderline endocervical change will have either invasive or premalignant disease.

- One case series analysed the case notes of 48 women with borderline glandular changes. Five women were excluded from the analysis (three because their case notes were not available, one because of severe dyskaryosis, and one because of recurrent glandular cells during pregnancy). More than half of the women had clinically significant lesions: seven women had cancer (six had cervical cancer and one had endometrial cancer), seven women had intraepithelial neoplasia, and 19 women had either no abnormality or insignificant abnormalities [Mohammed et al, 2000].

- One case series of 136 women with atypical glandular cells found an association with substantial underlying uterine pathology: at least 4% (95% CI 0.8% to 11.0%) invasive cancers and 13% (95% CI 6.4% to 22.6%) precancerous lesions [Kennedy et al, 1996].

- One case series of 127 women with cytology samples reported as showing glandular changes found that 25 women had cervical lesions: 12 women had low-grade CIN, six women had high-grade CIN, three women had endocervical atypia, one woman had adenocarcinoma in situ, and three women had invasive adenocarcinoma. One woman had ovarian cancer [Zweizig et al, 1997].

Abnormal result of any grade on three tests in any 10-year period.

- This recommendation to refer women with an abnormal result of any grade on three tests in any 10-year period is based on professional consensus in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].

Borderline nuclear change in squamous cells

- This recommendation to refer women with borderline nuclear change in squamous cells on three consecutive tests is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers based their opinion on evidence that included:

- One arm of a randomized trial that found that the incidence of high-grade cervical intraepithelial neoplasia after a single smear reporting borderline changes was 11% [Solomon et al, 2001].

- A retrospective study of 437 women with borderline changes who were followed up for 13–106 months found that 98 (22.4%) developed high-grade dyskaryosis [Hirschowitz et al, 1992].

Mild dyskaryosis

- This recommendation to refer women with mild dyskaryosis is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010]. The guideline developers based their opinion on evidence that included the following studies:

- A cross-sectional survey of 146 women with mild dyskaryosis that found that 78% had either CIN 2 or CIN 3 [Anderson et al, 1992].

- An analysis of five studies that included 3903 women with mild dyskaryosis and found an average incidence rate of invasive cancer of 208 per 100,000 woman-years [Soutter and Fletcher, 1994].

- A prospective study of 91 women with mild dyskaryosis or koilocytosis that found that of the 38 women with mild dyskaryosis, eight (18%) had CIN 2 and eight (21%) had CIN 3 [Bolger and Lewis, 1988].

- A cross-sectional study of 29 women with mild dyskaryosis that found that 49% of the women had CIN 2, CIN 3, or invasive cancer [Soutter et al, 1986].

- Recently, a multicentre randomized controlled trial examined the effectiveness of cytological surveillance every 6 months in primary care compared with immediate colposcopy in women with a low-grade cytological abnormality (borderline nuclear abnormalities or mild dyskaryosis) [TOMBOLA Group, 2009]. 1476 of the 4439 women in the trial had mild dyskaryosis. All were followed up for 3 years.

- As expected, immediate referral for colposcopy detected more women with CIN 2 or worse initially, but this may have led to over-treatment, as some cases of CIN 2 may have regressed spontaneously.

- Initial colposcopy led to a large number of referrals of women in whom no CIN 2 or worse was found. There were also more adverse effects than with cytological surveillance.

- The authors concluded that referral for immediate colposcopy after low-grade cervical abnormalities resulted in no benefit compared with cytological surveillance and caused more adverse effects.

Previous treatment for CIN

- This recommendation to refer women with previous treatment for CIN is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].

- The guideline developers stated that women who have been treated for CIN have an increased risk of developing cervical cancer.

How do I manage someone who has organisms reported on their cervical cytology result?

Note that incidental organisms are no longer routinely reported as part of screening but are instead reported to the sample taker for consideration of further action according to local protocols.

- **If *Candida* is present,** offer treatment if the woman is symptomatic. For further information, see the CKS topic on Candida - female genital.
- **If bacterial vaginosis is present,** offer treatment if the woman is symptomatic. For further information, see the CKS topic on Bacterial vaginosis.
- **If herpes simplex type 2 is present:**
  - Refer to a service specializing in sexual health.
  - Prescribe aciclovir 200 mg five times a day for 5 days, if there appears to be active infection.
  - For further information, see the CKS topic on Herpes simplex - genital.
- **If *Trichomonas vaginalis* is present:**
  - Refer the woman to a service specializing in sexual health so that diagnosis can be confirmed by microscopic examination or culture of vaginal secretions.
  - For further information, see the CKS topic on Trichomoniasis.
- **If actinomyces-like organisms (ALOs) are present:**
  - Ask the woman to make an appointment to be seen.
  - Explain that ALOs usually need no intervention.
  - Most people with ALOs will have an intrauterine contraceptive device or the levonorgestrel-releasing intrauterine system (Mirena®) in situ.
  - Ask about pelvic pain, deep dyspareunia, vaginal discharge, dysuria, and intermenstrual bleeding continuing beyond 6 months after the device was inserted.
  - Perform an abdominal examination to look for pelvic tenderness.

- If the woman is asymptomatic:
- Warn her about the small possibility of developing pelvic actinomycosis and to return if she develops symptoms.
- If an intrauterine device or the levonorgestrel-releasing intrauterine system (Mirena®) is in situ, it does not need to be removed.
- No follow up is required.
- If the woman is symptomatic, look for other causes of pelvic inflammatory disease.
- Obtain endocervical swabs for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. For further information on the investigation of pelvic inflammatory disease, see the section on Investigations in the CKS topic on Pelvic inflammatory disease.
- Urgently seek specialist advice regarding treatment.
- If an intrauterine device or the levonorgestrel-releasing intrauterine system (Mirena®) is in situ, consider its removal: if removed, send the device for culture.
- For more information, see the section on IUD in situ in the CKS topic on Pelvic inflammatory disease.

Basis for recommendation

Candida, bacterial vaginosis, and herpes simplex type 2 infection

- These recommendations are from the *Guidelines for the NHS cervical screening programme* and are based on expert opinion [NHS Cancer Screening Programmes, 2010].

Trichomoniasis

- Advice in guidelines from the British Association of Sexual Health and HIV states that cervical cytology may detect *Trichomonas vaginalis* as an incidental finding, with a weighted mean sensitivity of 58%. However, the false-positive rate is around 30% with Papanicolaou (Pap) smear and may be less with liquid-based cytology, so diagnosis should be confirmed by microscopic examination or culture of vaginal secretions [BASHH, 2007].
- This advice was based on studies of the Pap smear, which is no longer used in the UK. An analysis of 12 studies that fulfilled all three of the authors' inclusion criteria found that the pooled specificity of the Pap smear for the diagnosis of trichomoniasis was 98% (95% CI 93% to 100%), and the sensitivity was 57% (95% CI 51% to 63%). In areas where the

prevalence of trichomoniasis is medium (about 10%), this translated into a likelihood ratio for a positive cytology sample of 68% [Wiese et al, 2000].

- *Trichomonas* infection is also identified by liquid-based cytology.

  - A cross-sectional study of 203 consecutive women who had liquid-based cytology found that 28 women (13.8%) were positive for trichomoniasis on their cervical cytology sample, but 44 women (21.6%) were positive on culture. There was a sensitivity of 61.4%, a specificity of 99.4%, a positive predictive value of 96.4%, and a negative predictive value of 90.8%. However when the results of the wet mount and the culture were combined, there was a sensitivity of 50%, a specificity of 93%, a positive predictive value of 77%, and a negative predictive value of 80% [Lara-Torre and Pinkerton, 2003].

  - A cross-sectional study of 51 cervical cytology samples that were positive for *T vaginalis* found that trichomoniasis was confirmed in 50 of the 51 samples. giving a specificity of 99%, a sensitivity of 96.2%, a positive predictive value of 98%, and a negative predictive value of 99% [Aslan et al, 2005].

Presence of actinomyces-like organisms (ALOs) in a woman with an intrauterine contraceptive device or the levonorgestrel-releasing intrauterine system (Mirena®).

- Expert opinion in guidelines from the Faculty of Sexual and Reproductive Healthcare is that [FSRH, 2007]:

  - The role of ALOs in infection in women using intrauterine contraception is unclear. *Actinomyces israelii* is a commensal organism in the female genital tract, and although these organisms may be found on cervical cytology samples or swabs, their presence is not diagnostic or predictive of disease. Therefore, there is no need to remove intrauterine contraceptive devices if the woman does not have symptoms.

  - If pelvic inflammatory disease is suspected in a woman who has a history of ALOs on a cervical cytology sample, it is important to consider that the infection may be due to other organisms.

  - Removal of intrauterine contraceptive devices may be considered if the woman has pelvic pain and ALOs have been identified on swabs.

What advice should I give pregnant women who have been referred to colposcopy?

- Explain to the woman that it is very important to attend for colposcopy even if she is pregnant. Explain that:

  - The aim of colposcopic assessment is to exclude invasive disease. If no invasive disease is found, biopsy or treatment will be deferred until after delivery.

- If cervical intraepithelial neoplasia (CIN) 1 or less is suspected, then the colposcopic examination should be repeated 3 months after delivery.
- If CIN 2 or CIN 3 is suspected, then repeat colposcopy will be done at the end of the second trimester or 3 months after delivery if the pregnancy has advanced beyond the second trimester.
- If invasive disease is suspected clinically or colposcopically, then cone, wedge, or diathermy loop biopsy will be offered.
- Explain that the woman will be called for colposcopic assessment post-natally, and it is essential that she attends.

Basis for recommendation

Safety of delaying treatment until after delivery if there is no invasive disease

- This recommendation is from the *Guidelines for the NHS cervical screening programme* and is based on a review of the available evidence; however, no details of the quality and interpretation of the trials were given. The guideline developers reviewed [NHS Cancer Screening Programmes, 2010]:
  - Cohort and retrospective uncontrolled studies and concluded that the incidence of invasive cervical disease during pregnancy and after delivery are low and pregnancy does not affect the prognosis.

Necessity of a biopsy if invasive disease is suspected (clinically or colposcopically)

- This recommendation is from the *Guidelines for the NHS cervical screening programme* and is based on expert opinion from the guideline developers [NHS Cancer Screening Programmes, 2010], who state that:
  - Punch biopsies do not reliably exclude invasion.
  - Cone, wedge, or diathermy loop biopsy is essential. However, all are associated with a risk of haemorrhage of about 25% (evidence from case series).

The importance of colposcopic assessment after delivery

- This recommendation is from the *Guidelines for the NHS cervical screening programme* and is based on a review of the available evidence; however, no details of the quality and interpretation of the trials were given [NHS Cancer Screening Programmes, 2010]. The guideline developers stated that:
  - It is essential that all women with abnormal cytology or cervical intraepithelial neoplasia proven on biopsy are reviewed postpartum.

- Excision biopsy in pregnancy cannot be considered therapeutic, and colposcopic assessment is necessary postpartum.

- The guideline developers reviewed the available evidence.

- Retrospective uncontrolled studies showed that preinvasive cervical cancer does not usually regress during pregnancy.

- A retrospective study of pregnant women treated by cone biopsy for high-grade cervical intraepithelial neoplasia and micro-invasion reported high rates of persistent disease.

What should I advise a woman with abnormal cervical cytology about the use of contraception?

- Advise women that an abnormal cervical cytology result does not influence the choice of contraception.

- Some women with an intrauterine contraceptive device or the levonorgestrel-releasing intrauterine system (Mirena®) in situ may be advised by the colposcopy clinic that their device may need to be removed and they will need to use alternative contraception.

- An intrauterine contraceptive device or the levonorgestrel-releasing intrauterine system (Mirena®) does not have to be removed for local treatment.

Basis for recommendation

Use of oral contraception

- This recommendation is based on expert opinion in the *Guidelines for the NHS cervical screening programme* [NHS Cancer Screening Programmes, 2010].

- The guideline developers based their opinion on a review of the evidence; however, no details of the quality and interpretation of the trials were given. They reviewed:

- A large prospective study that found no association between cervical cancer and past and present use of oral contraception.

- A systematic review of studies of women who use oral contraception for up to 10 years (controlled for human papillomavirus [HPV] status).

- Nested case-control studies that found a small increase in the relative risk of cervical intraepithelial neoplasia in women using oral contraception long term, after compensating for HPV infection.

- The guideline developers commented that there was no evidence that stopping oral contraception will change the course of the disease.

Use of the intrauterine device or the levonorgestrel-releasing intrauterine system (Mirena®)

- The guideline developers stated that they based this recommendation on good clinical practice [NHS Cancer Screening Programmes, 2010].