KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1 - Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++ High quality systematic reviews of case control or cohort studies
   High quality case control or cohort studies with a very low risk of confounding or bias and a
   high probability that the relationship is causal
2 + Well conducted case control or cohort studies with a low risk of confounding or bias and a
   moderate probability that the relationship is causal
2 - Case control or cohort studies with a high risk of confounding or bias and a significant risk that
   the relationship is not causal
3 Non-analytic studies, eg case reports, case series
4 Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the
recommendation is based. It does not reflect the clinical importance of the recommendation.

A At least one meta-analysis, systematic review, or RCT rated as 1++,
and directly applicable to the target population; or
A body of evidence consisting principally of studies rated as 1+,
directly applicable to the target population, and demonstrating overall consistency of results

B A body of evidence including studies rated as 2++,
directly applicable to the target population, and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 1++ or 1+

C A body of evidence including studies rated as 2+,
directly applicable to the target population and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 2++

D Evidence level 3 or 4; or
Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINTS

☑ Recommended best practice based on the clinical experience of the guideline development group.

NHS Quality Improvement Scotland (NHS QIS) is committed to equality and diversity. This
guideline has been assessed for its likely impact on the six equality groups defined by age, disability,
gender, race, religion/belief, and sexual orientation.

For the full equality and diversity impact assessment report please see the “published guidelines”
section of the SIGN website at www.sign.ac.uk/guidelines/published/numlist.html. The full report
in paper form and/or alternative format is available on request from the NHS QIS Equality and
Diversity Officer.
Management of cervical cancer
A national clinical guideline

January 2008
Introduction

1.1 THE NEED FOR A GUIDELINE

Despite the presence of a well established UK screening programme for detecting cervical pre-invasive disease there are approximately 2,800 cases of cervical cancer per annum and 1,000 women still die from cervical cancer each year. In Scotland there were 282 new cases diagnosed in 2004 and 127 deaths from the disease in 2005. The five-year relative survival rate in Scotland between 1997 and 2001 was 70.6%.

Only 30% of cervical cancers are screen detected, and the majority of cases occur in women who have never had a smear, or have not been regular participants in the screening programme.

The optimal management of cervical cancer involves a multidisciplinary team. The challenge for the team is to individualise treatment. As cervical cancer commonly occurs between the ages of 30 and 45, this includes offering women with early disease the option of having fertility conserving surgery, where appropriate. For those with intermediate or advanced disease the aim is to minimise treatment side effects without compromising the outcome.

1.1.1 CERVICAL SCREENING PROGRAMMES

Cervical cytology detects precancerous changes of the cervix, known as cervical intraepithelial neoplasia (CIN). Abnormal cytology is a possible presentation for cervical cancer.

Population screening has been shown to reduce the incidence of cervical cancer and reduce the proportion of women with advanced disease. It has been estimated that the screening programme in the UK saves approximately 5,000 lives per year.

The Scottish Cervical Screening Programme was established in 1987. More than 90% of tests in the programme are reported as negative. Treatment of women who have CIN has been shown to reduce the incidence of, and mortality from, cervical cancer. To date, both have fallen by more than 40%.

1.1.2 VACCINATION

Any woman who is sexually active is at risk of infection from human papillomavirus (HPV). Over 100 subtypes of HPV have been identified. A significant proportion of HPV disease is attributed to four subtypes: 6,11,16 and 18. HPV subtypes 16 and 18 cause approximately 70% of cervical cancer cases worldwide. HPV subtypes 6 and 11 infections are responsible for genital warts. One or more co-factors that increase the likelihood of persistence of HPV infection are also needed for cervical cancer to develop.

Two HPV vaccines have been developed: Cervarix®, a bivalent HPV (types 16,18) vaccine and Gardasil®, a quadrivalent HPV (types 6,11,16,18) vaccine. Both are prophylactic vaccines that have been shown to be effective in young women prior to HPV exposure.

Following the advice of the Joint Committee on Vaccination and Immunisation (JCVI) the Scottish Government and the Department of Health are to introduce HPV vaccines for girls aged around 12 to 13 years of age, starting from September 2008.
1.2 REMIT OF THE GUIDELINE

This guideline will cover presentation, referral, diagnosis, staging and treatment of cervical cancer. The management of small cell and large cell neuroendocrine carcinomas is not covered.

The aim of this guideline is to ensure that optimal management by a multidisciplinary team minimises the huge social, economic and emotional burden experienced by women with the disease and their families.

1.3 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient’s case notes at the time the relevant decision is taken.

1.3.1 ADDITIONAL ADVICE TO NHSScotLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in the section on implementation.

1.4 REVIEW AND UPDATING

This guideline was issued in 2008 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk.
2 Mutlidisciplinary team working

Patients with cancer often have complex needs that cannot be addressed by a single specialty or discipline. Multidisciplinary team working should ensure a consistent and equitable approach to planning and managing care. No evidence was identified to determine the effect of multidisciplinary working or managed clinical networks (MCN) on the management of patients with cervical cancer.

Cervical cancer is a relatively uncommon tumour and there may be lack of expertise in managing the complex diagnostic, surgical, oncological and palliative issues of patients in a district general hospital setting.

There is some evidence to suggest that diagnostic imaging accuracies in secondary care/district general hospitals may be poorer than from tertiary care/specialist referral centres. All patients with invasive cervical cancer should be referred to a multidisciplinary team to determine optimal management. This should include specialist radiological review of any imaging.

2.1 THE ROLE OF THE CLINICAL NURSE SPECIALIST

The clinical nurse specialist (CNS) is an integral part of an MCN. Key components of the CNS role are to coordinate care between settings and to provide support, advice and information for patients and their carers throughout their illness.

All patients newly diagnosed with cervical cancer should have access at diagnosis to a clinical nurse specialist for support, advice and information.

2.2 CASE VOLUME

With the incidence of cervical cancer declining due to well organised screening programmes, a new set of problems has emerged for the specialist teams involved in delivering care. For pathologists, radiologists and surgeons in particular, the critical issue of what constitutes an adequate volume of cases to maintain specialist skills is pertinent.

In the UK it is now accepted that only gynaecologists who have been appropriately trained should undertake radical hysterectomy and pelvic lymph node dissection. With the fall in the incidence of cervical cancer there will be regions in the UK where recognised gynaecological oncological surgeons will have a very small number of cases. To ensure that women get the best outcome from their surgery, in terms of cure, lowest risk of side effects, and the possibility of appropriate, newer, less radical procedures, particularly where fertility conservation is an issue, it may be necessary to concentrate surgical services for cervical cancer in supraregional centres.
3 Presentation and referral

3.1 SIGNS AND SYMPTOMS

Prior to the introduction of a national cervical cancer screening programme, signs and symptoms were important for indicating referral of women to investigate for possible cervical cancer. The Scottish Cervical Screening Programme was established in 1987 and data predating systematic screening may no longer reflect the current situation.8

The symptoms associated with cervical cancer are common and non-specific (see Table 1), but may indicate significant pathology and should be investigated appropriately. Symptoms are associated with later stage cervical cancers,15 although studies have shown that 15.7-32% of women with early stage disease had symptoms at presentation.16,17

Women should be encouraged to participate in a screening programme.

Table 1: Signs and symptoms that may suggest cervical cancer15

<table>
<thead>
<tr>
<th>Sign or symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>inter-menstrual bleeding (IMB)</td>
</tr>
<tr>
<td>post-coital bleeding (PCB)</td>
</tr>
<tr>
<td>post-menopausal bleeding (PMB)</td>
</tr>
<tr>
<td>abnormal appearance of the cervix (suspicion of malignancy)</td>
</tr>
<tr>
<td>vaginal discharge (blood stained)</td>
</tr>
<tr>
<td>pelvic pain</td>
</tr>
</tbody>
</table>

Many of the signs and symptoms suggestive of cervical cancer are common to genital Chlamydia trachomatis infection. Women presenting with these symptoms or with an inflamed or friable cervix which may bleed on contact should be tested for Chlamydia trachomatis and treated if appropriate.18

Post-menopausal bleeding may also be the presenting symptom of endometrial cancer. Women presenting with PMB require a pelvic examination during their assessment. Examination by a general practitioner (GP) or practice nurse can alter the course of clinical management if it expedites referral on grounds of raised suspicion of malignancy (including cervical carcinoma).19

Abnormal vaginal bleeding, such as IMB and PCB, is common. The point prevalence of PCB in women in the community is 0.7-9%,20 but only a small proportion of these women are seen in secondary care. The probability that a woman under the age of 25 who experiences PCB has cervical cancer is very low (see Annex 1). The probability is higher in women over 35, but is still low.20 Two per cent of women attending secondary care with PCB have cervical cancer.20 The duration and extent of symptoms, such as PCB, are not related to the risk of having a cervical cancer.21 Women referred with PCB where cervical cancer is excluded have no increased risk of cervical cancer in the future.22

A systematic review identified no evidence to support performing a smear when a woman presents with PCB if the smear is not due.20

Annex 2 shows an algorithm for the investigation of PCB.

A woman presenting with symptoms who has negative cytology has a greatly reduced risk of cervical cancer compared to a woman with positive cytology, but the risk is not entirely eliminated.20,23
Pre-menopausal women presenting with abnormal vaginal bleeding should be tested for *Chlamydia trachomatis*.

- Post-menopausal women presenting with abnormal vaginal bleeding should be referred for gynaecological investigation.
- *Chlamydia trachomatis* testing should be done if appropriate.

An unscheduled smear is not recommended outwith the screening programme.

### 3.2 RISK FACTORS

Recognised risk factors for cervical cancer are HPV infection, cigarette smoking and socioeconomic status.\(^{24,25}\) No evidence was identified to stratify patients for investigation based on these risk factors.

### 3.3 REFERRAL

There is no good evidence to suggest to which clinical setting women with PCB should be referred for further investigation.

- If cervical cancer is suspected on examination when a woman attends for cervical screening she should be referred to gynaecology.
- Women with symptoms suggestive of cervical cancer should be referred to gynaecology if cervical cancer is suspected on examination.
4 Diagnosis and staging

4.1 DIAGNOSIS AND PROGNOSIS

4.1.1 HISTOPATHOLOGICAL REPORTING

A diagnosis of cervical cancer is made by the histopathological examination of cervical biopsies. The World Health Organisation (WHO) histological classification of tumours of the uterine cervix is shown in Annex 3. As part of this process it is important for the tissue samples to be prepared appropriately. Guidance is available from the Royal College of Pathologists (www.rcpath.org).

The stage of a cervical cancer and the presence of lymph node metastases are important indicators of prognosis and for determining treatment. Early stage disease is defined by varied histopathological criteria with conflicting evidence as to their significance. By definition, the diagnosis of early stage cervical cancer (International Federation of Gynecology and Obstetrics, FIGO stage IA1 and IA2) requires that the entire tumour is excised completely and is available for histopathological examination.

There are histological features that can be used to stratify women to higher risk or lower risk of metastatic disease. These histological features should be included in a pathology report.

Histological reports should follow the minimum dataset of the Royal College of Pathologists (see Annex 4 for a minimum dataset proforma).

<table>
<thead>
<tr>
<th>Pathology reports of cervical tumours should include the following histological features:</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ tumour type</td>
</tr>
<tr>
<td>▪ tumour size</td>
</tr>
<tr>
<td>▪ extent of tumour (e.g. involvement of the vaginal wall or parametrium)</td>
</tr>
<tr>
<td>▪ depth of invasion</td>
</tr>
<tr>
<td>▪ pattern of invasion (infiltrative or cohesive invasive front)</td>
</tr>
<tr>
<td>▪ lymphovascular space invasion (LVSI)</td>
</tr>
<tr>
<td>▪ status of resection margins (presence of tumour and distance from margin)</td>
</tr>
<tr>
<td>▪ status of lymph nodes (including site and number of nodes involved)</td>
</tr>
<tr>
<td>▪ presence of pre-invasive disease.</td>
</tr>
</tbody>
</table>

When assessing stromal involvement:

▪ all biopsy material should be taken into account
▪ it is important to be aware that a small tumour may be entirely removed by biopsy.

Pathological assessment should be quality assured and standardised, with readily accessible specialist review available if required, following discussion by the multidisciplinary team.

4.1.2 TUMOUR MARKERS

Squamous cell carcinoma antigen (SCCA) belongs to a family of serine and cysteine protease inhibitors. The antigen is present in normal squamous cervical epithelium and its expression is increased in cervical squamous cancers.

Pre-treatment levels of SCCA are related to tumour volume but are insufficiently reliable for identifying patients at risk of having pelvic lymph node metastases or parametrial involvement.
4.2 CLINICAL STAGING
Cervical cancer is clinically staged using the FIGO criteria (see Annex 5). FIGO staging does not take into account results of computerised tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography (PET).

4.2.1 SENTINEL NODE SURGERY
There is evidence from a number of small case studies that it is feasible to identify sentinel lymph nodes during cervical cancer surgery. The evidence that the status of these nodes accurately predicts the status of the remaining pelvic lymph nodes is conflicting. Comparison of the results of these studies is hampered by variable methodology, and there have been no long term studies of follow up.

At present there is no evidence to support the use of sentinel node surgery in preference to pelvic lymphadenectomy in cervical cancer. Larger standardised studies are required.

4.2.2 PELVIC LYMPHADENECTOMY
No evidence was identified to address the adequacy of pelvic lymphadenectomy specifically in cervical cancer. Evidence from many studies indicates that there is considerable variation in the number of lymph nodes obtained from this procedure. There is no evidence relating the number of lymph nodes retrieved to long term outcome. Many of the studies lack information about how the tissue is handled by the pathologist.

This lack of good quality evidence illustrates the need for standardisation of pathological assessment. Further guidance is available from the Royal College of Pathologists (www.rcpath.org).

4.3 RADIOLOGICAL STAGING
Radiological assessment of patients with visible cervical carcinoma is an essential part of the strategy in determining the most appropriate management of patients, both at primary presentation and with relapsed disease or complications of treatment.

Radiological studies often have inherent design weaknesses, which are difficult to eliminate. Some of the disparity of results between individual studies may be dependent on:

- heterogeneity of equipment
- image interpretation and training
- clinical setting (specialist centre compared to district general/community hospital)
- MRI, CT methodology and sequences
- advances in MRI, CT and PET technology.

The staging accuracy (sensitivity and specificity) of MRI, CT, and PET is shown in Table 2.

4.3.1 PRIMARY TUMOUR ASSESSMENT
There is consistent evidence that MRI is more accurate than CT for radiological staging of cervical carcinoma (accuracies 40–97%) and both modalities are more accurate than clinical staging.

For women with contraindications to MRI scanning CT is appropriate. For women with clinically apparent stage IVA or IVB disease, post contrast spiral or multislice CT scans of chest, abdomen and pelvis are more appropriate than MRI.
MRI technique is important in correct staging. Thin section axial and sagittal T2 sequences including axial oblique sections perpendicular to the long axis of the cervix, are of most value in primary tumour assessment. Intravenous non-dynamic contrast in MRI is non-contributory in primary tumour staging.

Ultrasound is not generally reliable in either assessment of primary tumour size or nodal status. Transrectal ultrasound may be of value if undertaken by experienced operators.

PET-CT can assess both the primary tumour and detect metastatic spread. PET-CT has potential for more accurately selecting patients for surgery than PET imaging alone, in addition to contributing to more accurate treatment planning.

4.3.2 PRIMARY TUMOUR VOLUME

Primary tumour volume is best assessed by MRI rather than CT. Tumour diameter less than 5-10 mm cannot be reliably imaged by either modality. Post-biopsy changes may also adversely affect tumour measurement, particularly in small tumours.

Appearances following a loop excision biopsy or cone biopsy cause difficulty in assessing the size and extent of the primary tumour, which may have important staging and prognostic consequences.

There is some evidence that PET scans may also measure tumour volume, but false negative uptake also occurs following excision biopsy.

4.3.3 VAGINAL INVASION

Vaginal invasion is best assessed by MRI, with accuracies ranging from 78-94%. Overstaging errors are reported in association with bulky primary tumours distending the fornices. CT staging accuracies are not available.

4.3.4 PARAMETRIAL STAGING

Involvement of parametrium indicates inoperable FIGO IIB disease.

Studies report variable accuracy for parametrial staging by MRI and CT, but MRI is generally superior to CT, with staging accuracy of 75-90%.

The greatest value of MRI in influencing treatment options lies in the high negative predictive value for parametral invasion (85%). Full thickness disruption of the ring of cervical stroma by tumour on MRI corresponds to FIGO stage IIB disease. Confirmation of an intact ring of cervical stroma, on adequate MRI assessment, confers potentially operable status.

PET imaging alone cannot accurately determine early parametrial involvement. Data are not available comparing the accuracy of PET-CT to MRI.

4.3.5 BLADDER AND RECTAL INVASION

Assessment of bladder and rectal invasion is consistently more accurate with CT and MRI than clinical staging, with the specificity of MRI considerably greater than CT. There is heterogeneity of results from studies assessing detection of tumour involvement, which may be related to both procedure methodology and interpretation criteria in specialist hospitals compared to community/district general hospitals. Several studies show 100% negative predictive values for CT and MRI in bladder, rectal and ureteric invasion.

A normal appearance of bladder and rectum on MRI examination obviates the need for cystoscopy or sigmoidoscopy.

Intravenous urography (IVU) has been superseded as a stand alone investigation, as CT, MRI or ultrasound are as accurate in determining ureteric obstruction secondary to parametrial invasion and give additional information.

Barium enemas are not routinely indicated.
4.3.6 PELVIC OR PARA-AORTIC LYMPH NODES

Although not a part of the FIGO staging criteria, the involvement of pelvic or para-aortic lymph nodes in most histological types of cervical cancer, is the greatest single predictor of long term survival\textsuperscript{72,76} and cannot be assessed by clinical examination alone.

Lymphangiography is not routinely available in many radiology departments in Scotland. Comparable studies with contemporary CT and MRI are not available.

Lymphangiography is probably less sensitive than other contemporary modalities for preoperative assessment with positive predictive values that are variable in cervical carcinoma (14\% to 80\%).\textsuperscript{58} Lymphangiography may interfere with the specificity and interpretation of PET scans.\textsuperscript{77}

There is consistent evidence that both CT and MRI have poor sensitivity for detection of nodal metastases, based on size criteria (generally 1 cm short axis diameter cut off for positive involvement) and node morphology, in both the pelvic and para-aortic nodes. Poor sensitivity is due to the presence of metastases within normal sized lymph nodes. MRI is better than CT.\textsuperscript{57,78}

PET-CT scans may be the most accurate imaging method of detecting involved lymph nodes (see section 4.3.7).\textsuperscript{65,72}

### Table 2: Staging accuracy (sensitivity and specificity) of MRI, CT and PET

<table>
<thead>
<tr>
<th></th>
<th>MRI %</th>
<th>CT %</th>
<th>PET %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary tumour detection</strong> (macroscopic disease)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>93,\textsuperscript{53} 100\textsuperscript{79}</td>
<td>93,\textsuperscript{53} 100\textsuperscript{79}</td>
<td>100\textsuperscript{79}</td>
</tr>
<tr>
<td>Specificity</td>
<td>93,\textsuperscript{53} 100\textsuperscript{79}</td>
<td>93,\textsuperscript{53} 100\textsuperscript{79}</td>
<td>100\textsuperscript{79}</td>
</tr>
<tr>
<td><strong>Parametrial involvement</strong></td>
<td>74,\textsuperscript{57} 85\textsuperscript{56}</td>
<td>55\textsuperscript{57}</td>
<td>n/a</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>85\textsuperscript{56,57}</td>
<td>85\textsuperscript{56,57}</td>
<td>n/a</td>
</tr>
<tr>
<td>Specificity</td>
<td>75\textsuperscript{57}</td>
<td>75\textsuperscript{57}</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Lymph node involvement</strong></td>
<td>60\textsuperscript{57}</td>
<td>43\textsuperscript{57}</td>
<td>84\textsuperscript{49}</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>91\textsuperscript{57}</td>
<td>91\textsuperscript{57}</td>
<td>95\textsuperscript{49}</td>
</tr>
<tr>
<td>Specificity</td>
<td>91\textsuperscript{57}</td>
<td>91\textsuperscript{57}</td>
<td>95\textsuperscript{49}</td>
</tr>
<tr>
<td><strong>Bladder involvement</strong></td>
<td>75\textsuperscript{57}</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>91\textsuperscript{57}</td>
<td>73\textsuperscript{57}</td>
<td>n/a</td>
</tr>
<tr>
<td>Specificity</td>
<td>91\textsuperscript{57}</td>
<td>73\textsuperscript{57}</td>
<td>n/a</td>
</tr>
<tr>
<td><strong>Rectal involvement</strong></td>
<td>71\textsuperscript{57}</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>71\textsuperscript{57}</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Specificity</td>
<td>71\textsuperscript{57}</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

**B** All patients with visible, biopsy proven cervical carcinoma (except those with FIGO IV disease) should have an MRI scan.

**C** The MRI scan should include:
- thin section T2 weighted images perpendicular to the cervix, and
- sequences to include urinary tract and para-aortic nodal areas.

**B** Post contrast spiral CT should be considered as an alternative to MRI in patients who cannot have MRI.

**B** Women who have clinically apparent FIGO stage IV disease should have post contrast spiral or multislice CT scans of chest abdomen and pelvis.

**☑ MRI scans should ideally occur prior to excision biopsy, to avoid inflammatory changes and to allow more accurate measurement of tumour size.**
Ultra-small iron oxide particles for MRI lymphangiography will be available for use in the UK from Spring 2008, which may potentially increase the sensitivity of MRI for detection of nodal metastases.

4.3.7 PET

PET is more accurate than CT\textsuperscript{80} or MRI\textsuperscript{81} in detecting metastatic lymphadenopathy,\textsuperscript{81} having the potential to significantly change patient management\textsuperscript{79} and survival.

Patient numbers in PET studies tend to be small, but there is some evidence that PET is superior to MRI and CT in the detection of metastatic para-aortic nodes, with higher sensitivities and specificities.\textsuperscript{72,82} Sensitivities remain suboptimal, and possibly technique dependent, in nodes less than 10 mm in size.\textsuperscript{82}

There is wide variation in fdg-PET imaging techniques with respect to the administered isotope dose, patient preparation and timing of scans post injection, with consequent heterogeneity in results. PET sensitivity varies from 79%\textsuperscript{83} to 84%\textsuperscript{83} in the pelvic nodes to 35%\textsuperscript{84} to 84%\textsuperscript{83} in the para-aortic nodes, with overall sensitivity for detection of pelvic and para-aortic nodes of 80%.\textsuperscript{80}

False positive nodal fdg-PET uptake may be secondary to inflammatory change from a variety of causes including infection and chronic granulomatous disease.\textsuperscript{65,83,85,86} It is important that metastatic involvement is confirmed by sampling or biopsy before there is a change to the planned treatment regimen.

PET-CT combined is emerging as the most accurate method for detection of nodal metastases in the pelvis and para-aortic nodes, with sensitivities of 75% and 100% respectively.\textsuperscript{65} There is insufficient evidence to support the routine use of PET-CT to confirm operable status in patients staged as IB1 or less, given the limitations of negative predictive values for PET-CT in the detection of pelvic nodal metastases.\textsuperscript{84,65,72}

PET or PET-CT scans do not detect all nodes with micrometastases.\textsuperscript{65} If nodal enlargement is evident on staging MRI scans in patients with clinically operable disease, then PET scanning will determine the extent of potential metastatic involvement.

The greatest benefit from PET-CT is in women with inoperable disease, considered potentially curable with chemoradiotherapy. This group of women is statistically more likely to have nodal or metastatic disease than those women suitable for surgery.

C Patients not suitable for surgery should be considered for a PET scan.

4.3.8 CHEST X-RAY

Limited data are available on the use of chest X-rays in staging. Chest X-ray has identified metastases in 4% of women with clinical stage IIB or greater disease.\textsuperscript{75} In patients with FIGO stage IB disease there is a very low likelihood of pulmonary metastases.\textsuperscript{75}

CT scans are more accurate in comparison to chest X-ray in identifying pleural effusions, thoracic nodal status and parenchymal metastases.\textsuperscript{99}

☐ Routine chest X-rays are not indicated in women with operable disease (FIGO IA1, IA2 and IB1).

4.3.9 THE RELATIVE BENEFIT OF IMAGING OVER OTHER OPTIONS IN PRE-TREATMENT STAGING

Use of MRI or CT in pre-treatment assessment is less invasive, more accurate,\textsuperscript{87} and confers cost/time benefits in determining the preoperative stage of patients.\textsuperscript{13,54,58} compared to conventional FIGO investigations of IVU, cystoscopy, sigmoidoscopy and barium enema. MRI is more accurate than CT in correctly staging patients.\textsuperscript{13,56-58,67}

Cystoscopy and sigmoidoscopy should be reserved for women in whom a normal bladder or rectum cannot be confirmed on clinical or radiological assessment (CT or MRI).\textsuperscript{58,74,87}
Nodal staging, which will determine prognosis, operability and radiotherapy fields, is most effectively determined by PET-CT.\textsuperscript{65}

Lymphangiography is invasive,\textsuperscript{88} probably less sensitive than other contemporary modalities for preoperative assessment and may interfere with the specificity and interpretation of PET scans.\textsuperscript{77}

Assessment of pelvic and para-aortic nodal disease is most accurately determined by laparotomy or laparoscopic surgery.\textsuperscript{89}

These are invasive, morbid procedures requiring a general anaesthetic. The alternative is to use pre-treatment imaging to determine nodal status, despite the limitations in sensitivity and specificities of current techniques (MRI, CT, PET and PET-CT).

- Cystoscopy and sigmoidoscopy should not be routinely performed for staging purposes.
- If imaging cannot exclude bladder or bowel involvement, cystoscopy and sigmoidoscopy should be used for staging.
- Ultrasound, IVU and lymphangiography are not recommended for staging.

4.3.10 CONVEYING THE DIAGNOSIS

The information needs of women diagnosed with cancer and methods of conveying information are covered in sections 3.3-3.5.

- Diagnosis should be conveyed sensitively and in easily understood language.
5 Surgery

For early stage disease surgery conserves ovarian function and avoids the effects of early menopause. Less shortening and fibrosis of the vagina occurs compared to radical radiotherapy which gives better results in terms of residual sexual function. Surgery also allows the status of the pelvic lymph nodes to be assessed accurately. Surgery is the preferred treatment option in young women provided that there are no contraindications. The outcome following surgery is associated with a variety of prognostic factors including size of primary tumour, depth of stromal invasion, presence or absence of LVI; proximity of tumour to vaginal and parametrial margins (see section 4.1).

The relative risks and benefits of different surgical management approaches should be thoroughly discussed with the patient on an individual basis.

5.1 Radical Hysterectomy

Radical hysterectomy (RH) involves the en-bloc removal of uterus, cervix, parametrial tissues and upper vagina. It is usually combined with pelvic lymphadenectomy. The extent of parametrial tissue removed determines whether a class II or class III RH has been done. RH is a more complex procedure than a simple hysterectomy and is undertaken by appropriately trained gynaecologists.

The combined treatment of radical surgery and postoperative radiotherapy increases overall morbidity compared to either alone. To minimise post-surgical morbidity, before doing an RH the size of primary tumour should be accurately assessed radiologically and efforts should be made to ensure that there is no pelvic lymphadenopathy (see sections 4.3.1 and 4.3.6).

The evidence suggests that there is no difference in disease-free survival or overall survival of patients with FIGO IB and IIA disease treated by either class III radical hysterectomy or radical radiotherapy. Class II and class III radical hysterectomies are equally effective for the surgical treatment of FIGO IB and IIA cervical cancer.

The involvement of pelvic lymph nodes in FIGO IB disease is approximately 16%, Where the tumour size is less than 2 cm the incidence of nodal metastases is 6%, For tumours measuring more than 4 cm the incidence of lymph node metastases increases to 36%, which increases the likelihood of using adjuvant chemoradiotherapy to treat positive nodes (see section 6.2.1).

Radical surgery is recommended for FIGO IB1 disease if there are no contraindications to surgery.

RH is not recommended if the tumour measures more than 4 cm to reduce the likelihood of using chemoradiotherapy post-surgery.

No study was identified comparing radical hysterectomy with chemoradiotherapy for treatment of cervical cancer. There is good evidence from more recent studies that chemoradiotherapy is more effective than radiotherapy alone (see section 6.1).

Where positive pelvic nodes are identified at the time of radical hysterectomy, the practice of aborting the hysterectomy has not been tested in a randomised trial. Descriptive studies suggest that there is a beneficial effect on prognosis if the pelvic nodes are removed and the radical hysterectomy completed. Recurrence after completed hysterectomy and removal of lymph nodes was significantly lower than after incomplete lymph node removal (25% compared to 56%). After adjusting for other prognostic factors, completed lymph node removal showed an independent effect on disease-free survival. Survival in patients whose radical hysterectomy was abandoned because grossly positive nodes were found and removed, was significantly worse than that of patients whose node metastases were identified after the operation (58.5% compared to 93.5%).
5.2 TREATMENT OF CERVICAL CANCER AFTER SUBTOTAL HYSSTERECTOMY

In subtotal hysterectomy the cervical stump is not removed. This procedure may be done when difficulties are encountered whilst doing a hysterectomy for benign disease such as endometriosis.

The incidence of cervical cancer in women who have had a subtotal hysterectomy is no different to that in women with an intact uterine cervix. Cancer of the cervical stump behaves like cancer in an intact uterine cervix. Cancer of the cervical stump should be managed in the same way as cervical cancer arising in an intact uterus.

5.3 TREATMENT OF EARLY STAGE DISEASE (FIGO IA1 AND IA2)

5.3.1 PELVIC NODE METASTASES

The risk of pelvic lymph node metastases is no more than 1% for stage FIGO IA1 and 3-6% for FIGO IA2 cervical squamous cell cancer. The FIGO classification for early stage squamous cervical cancer (FIGO IA) is also applicable to early stage adenocarcinomas.

The presence of LVSI is an indicator of prognosis and should be considered when determining whether to perform pelvic lymphadenectomy in early stage cervical cancer. In IA1 disease with LVSI, no good quality evidence was found to support or preclude pelvic lymph node dissection.

Evaluation of tumour depth and horizontal spread is more difficult in early stage adenocarcinomas than in squamous cell cancers. Measurement of depth and horizontal spread (2-dimensional) is as effective as determining tumour volume. In FIGO IA1 and IA2 disease tumour volume exceeding 500 mm$^3$ is a significant adverse prognostic indicator.

Early stage adenocarcinoma with a depth of invasion of $\leq$ 3 mm and horizontal spread of 7 mm or less (FIGO IA1 disease) has little potential for pelvic nodal metastases (less than 1%). The evidence suggests that there is no need to remove pelvic lymph nodes when treating IA1 disease.

Removal of pelvic lymph nodes is not recommended during treatment for FIGO IA1 disease.

Pelvic lymph nodes should be removed if FIGO IA2 disease is present.

In women with FIGO IA1 disease with LVSI the decision to carry out pelvic lymphadenectomy must be individualised taking account of the pattern and extent of invasion.

Diagnosis and measurement of early adenocarcinoma and squamous cell cancer should be done by specialist gynaecological pathologists.

5.3.2 FERTILITY CONSERVATION SURGERY

No randomised controlled trials (RCTs) were identified comparing different methods of fertility sparing/conservation surgery.

Standard treatment for IA1 disease is simple hysterectomy if fertility is not an issue. For IA2 disease it is simple hysterectomy and pelvic lymph node dissection (PLND). For FIGO IB1 disease it is RH with PLND (see section 5.1).

In women for whom preservation of fertility is desirable, an alternative to simple hysterectomy or RH is a radical trachelectomy. This involves vaginal resection of the cervix, the upper 1 to 2 cm of the vaginal cuff and the medial portions of the cardinal and uterosacral ligaments. The cervix is transected at the lower uterine segment and a prophylactic cerclage is placed at the time of surgery.
Radical trachelectomy does not appear to increase the rate of recurrence, provided the tumour diameter is no greater than 2 cm and there is no evidence of LVSI. Radical trachelectomy must be combined with pelvic lymph node dissection for IA2 and IB1 disease.

The safety of radical trachelectomy in women with lesions that are greater than 2 cm in diameter is unclear as the majority of reported cases of radical trachelectomy have been in women with tumours less than 2 cm in diameter.

A recent prospective multicentre study of radical trachelectomy combined with laparoscopic pelvic lymphadenectomy reported three recurrences in 100 treated patients (FIGO IA1, IA2, and IB1). The median follow-up time was 29 months. A meta-analysis of 346 patients with early cervical cancer treated with radical trachelectomy with a median follow up of 44 months reported a recurrence rate of 4.1%.

Following radical trachelectomy the majority of women can anticipate conceiving spontaneously and delivering near term. The rate of first and second trimester miscarriage is comparable to that in the general population. In one study of obstetrical results following RT, 72% of women progressed into the third trimester of pregnancy. Of these, the majority (78%) reached term (>37 weeks of gestation) The pre-term delivery rate was slightly higher than in the general population at 16% compared to 12%. In another study following RT, of 63 women attempting pregnancy there were 28 live births in 19 women. In all studies delivery was usually by caesarean section.

Women requesting fertility conservation should be offered radical trachelectomy and pelvic lymph node dissection, providing the tumour diameter is less than 2 cm and no lymphatic-vascular space invasion is present.

Cold knife conisation or large loop excision of the transformation zone (LLETZ) is adequate treatment for women with IA1 disease where fertility conservation is requested. If LVSI is present PLND needs to be considered (see section 5.3.1).

A study reported that women with cervical cancers of maximum diameter 2 cm and depth of infiltration less than 10 mm had a low risk of parametrial involvement. In this study, of 103 patients who had been treated with radical hysterectomy and PLND only two (1.94%) had parametrial involvement. Both of these patients had LVSI. The study also reviewed literature on 696 patients treated by RH and PLND where the tumour size was less than 2 cm and depth of invasion less than 10 mm and no LVSI was present. Only three (0.43%) had parametrial involvement. The study concluded that for tumours less than 2 cm in diameter and depth of invasion less than 10 mm where pelvic lymph nodes are negative and no LVSI is present the overall risk of parametrial involvement is 0.63%.

Extrapolated evidence suggests that cold knife conisation and PLND or LLETZ and PLND, rather than radical trachelectomy and PLND, is also adequate treatment for women with FIGO IA2 and microscopic FIGO IB1 disease where no LVSI is present.

Diagnosis and measurement of early adenocarcinoma and squamous cell cancer should be done by specialist gynaecological pathologists.

Women who have had LLETZ are more likely than women who have not to have pre-term delivery (11% compared to 7%), low birth weight babies (8% compared to 4%) and premature rupture of the membranes (5% compared to 2%) in a subsequent pregnancy.

Women with early stage disease and no LVSI (FIGO IA2 and microscopic IB1) requesting fertility conservation may be offered cold knife conisation or LLETZ combined with pelvic lymph node dissection.
There is insufficient evidence to recommend cold knife conisation or LLETZ combined with pelvic lymph node dissection when LVSI is present.

- Women with early stage disease (FIGO IA2 and microscopic IB1) and LVSI requesting fertility conservation may be at risk of local recurrence and treatment must be individualised.

As women with early stage IA1/IA2 cancers are diagnosed following LLETZ, the value of MRI for determining tumour volume is debatable (see section 4.3.2). MRI may have a role in assessing the nodes in IA2 and microscopic IB1 disease (see section 4.3.6).

### 5.4 LAPAROSCOPIC-VAGINAL RADICAL HystereCTOMY

Laparoscopic-vaginal radical hysterectomy (LVRH) for the treatment of FIGO IB1 disease appears to be a safe and effective alternative to conventional abdominal RH.\(^{91,113-117}\) Lymph node yield after laparoscopic lymph node dissection is comparable to open surgery.\(^{91,113-117}\) Evidence from a case series reported a non-significant difference in recurrence rate following LVRH compared to RH (8.5% and 2.1% respectively).\(^{115}\) Patients with a large tumour volume (≥ 4.2 cm\(^3\)) undergoing LVRH had a significantly higher recurrence rate (42.9%) than those with small volume disease (2.5%).\(^{115}\) There were, however, only seven patients with large volume disease compared to 40 with small volume disease.\(^{115}\) Descriptive studies show that the mean duration of surgery was longer for LVRH compared to abdominal RH and more intraoperative complications occurred when surgery was carried out by surgeons in training.\(^{113-115}\) Patients’ hospital stay was shorter after LVRH than after RH.\(^{115,116}\)

- **D** Laparoscopic-vaginal radical hysterectomy should not be offered to patients with tumour diameter greater than 2 cm.

- **D** Surgeons wishing to offer laparoscopic-vaginal radical hysterectomy should have appropriate training.

- **✓** MRI should be used to measure tumour volume and diameter.

### 5.5 TOTAL PELVIC EXENTERATION

Total pelvic exenteration (TPE) is covered in section 11.1.1.
6 Non-surgical treatment

Generally chemoradiotherapy is used to treat women with FIGO IB2, IIA, IIB, IIIA, IIIB and IVA disease. Surgery is not offered to this group of women because of the significant risk of positive margins and positive nodes.

6.1 CONCURRENT CHEMORADIOTherapy

Concurrent chemoradiation is better than radiation alone for the treatment of patients with cervical cancer who are considered suitable for radical radiotherapy. There is a significant overall survival benefit for treatment with chemoradiation compared to radiation alone. Survival is increased from 40% to 52% (risk reduction, RR, of death = 29%).

Platinum based chemotherapy is better than non-platinum based chemotherapy. There is more evidence of a beneficial effect in trials using platinum based chemotherapy. A systematic review reported a hazard ratio (HR) for platinum based chemotherapy of 0.70 (95% confidence interval, CI 0.61 to 0.80; p < 0.0001) compared to 0.81 (95% CI 0.56 to 1.16; p = 0.20) for non-platinum based chemotherapy. Chemoradiation with cisplatin alone results in an RR of death of 0.74 (95% CI 0.59 to 0.93) compared to 0.70 (95% CI 0.56 to 0.86) for chemoradiation with cisplatin/5-fluorouracil (5FU).

Chemoradiation for treatment of cervical cancer is associated with increased acute haematological and gastrointestinal toxicity. Genitourinary toxicity is lower after chemoradiotherapy (odds ratio, OR, 0.43; 95% CI 0.2 to 0.92; p = 0.03). There is no difference in neurological and skin toxicity after chemoradiation compared to radiotherapy alone. There is no strong evidence regarding late toxicities but there is no apparent increase.

Any patient with cervical cancer considered suitable for radical radiotherapy treatment should have concurrent chemoradiotherapy with a platinum based chemotherapy, if fit enough.

The balance of risks and benefits must be addressed before offering chemoradiation for treatment of cervical cancer.

6.2 ADJUVANT CHEMORADIOTherapy/RadioTherapy

6.2.1 POSITIVE LYMPH NODES

There are no randomised controlled trials directly comparing chemoradiotherapy after surgery to no further treatment in patients with cervical carcinoma and positive nodes.

Following surgery adjuvant chemoradiotherapy is better than radiotherapy alone for patients with cervical carcinoma and positive nodes. Treatment with adjuvant chemoradiotherapy results in improved overall survival (HR of 1.96; p = 0.007), progression free survival (HR of 2.01; p = 0.003) and a reduction in local and distant recurrence. Four-year survival was 81% for chemoradiotherapy and 71% for radiotherapy alone. Twenty two per cent of patients receiving chemoradiotherapy suffered grade 4 toxicity compared with 3% receiving radiotherapy alone. The majority of the increased toxicity was haematological. Late toxicity was not recorded. A retrospective analysis of this data found the benefit to be greater in patients with tumours larger than 2 cm. The absolute improvement in 5-year survival with the addition of chemotherapy to radiotherapy in patients with tumours ≤ 2 cm was 5% (77% compared to 82%; p = 0.17) and 19% (58% compared to 77%; p = 0.009) for those with tumours > 2 cm. The absolute 5-year survival benefit was less evident among patients with one nodal metastasis (79% compared to 83%; p = 0.438) than when at least two nodes were positive (55% compared to 75%; p = 0.006).

Adjuvant radiotherapy reduces local recurrence in patients with cervical carcinoma and positive nodes following surgery.
Patients who have undergone surgery for cervical carcinoma and have positive nodes should be considered for adjuvant treatment with concurrent chemoradiotherapy with platinum based chemotherapy.

Consideration should be given to the relative risks and benefits of treatment for each individual patient.

6.2.2 NEGATIVE LYMPH NODES

Compared to no further treatment, adjuvant radiotherapy reduces the risk of recurrence in patients with cervical carcinoma with negative lymph nodes following surgery and with at least two of the following risk factors:24

- invasion of more than a third of the total cervical stromal volume
- LVSI, or
- tumour diameter of >4 cm.

The addition of adjuvant radiotherapy reduces overall risk of recurrence from 30.7% to 17.5% (HR 0.54; p = 0.007), local recurrence from 20.7% to 13.95% and distant recurrence from 8.6% to 2.9%.24

Given the body of evidence supporting the superiority of concurrent chemoradiation over radiation alone in other settings (see sections 6.1 and 6.2.1),8,20,24 strong consideration should be given to using concurrent chemoradiation in preference to radiation alone.

Patients who have undergone surgery for cervical carcinoma, have negative nodes and any two of the following risk factors should be considered for adjuvant treatment with radiotherapy, if fit enough:

- greater than a third stromal invasion
- lymphovascular space invasion
- tumour diameter of >4 cm.

Consideration should be given to the relative risks and benefits of treatment for each individual patient.

Concurrent chemoradiation should be considered in preference to radiation alone.

6.3 BRACHYTHERAPY

Brachytherapy is short wave radiotherapy delivered by the insertion of applicators into the uterus via the vagina.

Guidelines from the American Brachytherapy Society indicate that brachytherapy should be considered an essential component of definitive radiotherapy treatment.123,126

Brachytherapy should be considered an essential component of radical radiotherapy or chemoradiotherapy.

- Precise applicator placement is essential for improved local control and reduced morbidity.
- Brachytherapy should be carried out by practitioners experienced in the procedures and dosimetry of brachytherapy.
- If a brachytherapy insertion is not possible then a further boost should be given using external beam radiotherapy.
6.4 NEOADJUVANT CHEMOTHERAPY

No data from RCTs were identified describing the value of using neoadjuvant chemotherapy to make large inoperable tumours surgically resectable. An ongoing randomised phase III study of neoadjuvant chemotherapy followed by surgery compared to concomitant radiotherapy and chemotherapy in patients with FIGO IB2, IIA >4 cm or IIB cervical cancer is addressing this issue.\textsuperscript{127}

6.5 TREATMENT OF STAGE IVB DISEASE

There have been no randomised trials comparing chemotherapy to best supportive care in stage IVB cervical carcinoma. Single-agent cisplatin was the treatment of choice until a recent report demonstrated a modest survival advantage for the combination of topotecan plus cisplatin over cisplatin alone. There are also data indicating that cisplatin plus paclitaxel is an acceptable alternative (see section 11.2).

6.6 TREATMENT OF ANAEMIA

Anaemia during treatment is a stronger indicator of poor prognosis in patients being treated for carcinoma of the cervix than the presence of pre-treatment anaemia.\textsuperscript{128-133} Correction of anaemia by blood transfusion appears to reverse some of the detrimental effect on prognosis.\textsuperscript{130,131}

A meta-analysis of the use of erythropoietin or darbepoetin in patients with cancer was not specifically restricted to patients with cervical cancer and included patients with solid and haematological malignancies.\textsuperscript{134} Treatment with erythropoietin or darbepoetin decreased the relative risk of requiring a blood transfusion (RR 0.64; 95% CI 0.60 to 0.68) and decreased the volume of blood transfusion (on average one unit of blood less than control group).\textsuperscript{134} For patients with a baseline haemoglobin below 12 g/dl, haematological response was observed more often in patients receiving erythropoietin or darbepoetin compared to those not (RR 3.43; 95% CI 3.07 to 3.84).\textsuperscript{134} Treatment also increased the relative risk for thromboembolic complications compared to patients receiving placebo/no treatment (RR 1.67; 95% CI 1.35 to 2.06).\textsuperscript{134} There was no evidence of improved overall survival of patients treated with erythropoietin or darbepoetin.\textsuperscript{134}

Patients with cervical carcinoma undergoing radiotherapy or chemoradiotherapy should have their haemoglobin level monitored and corrected if it falls below 12 g/dl.

Anaemia should be corrected with either blood transfusion or erythropoietin and iron products after consideration of the attendant costs, risks and benefits.

6.7 TREATMENT OF RADIATION INDUCED COMPLICATIONS

During radiation treatment of cervical cancer, other pelvic organs receive a significant radiation dose, resulting in both acute and late toxicity. Late radiation changes occur at least three months after the completion of radiotherapy. Late radiation complications are due to small vessel injury with endothelial damage, inflammation, fibrosis, ischaemia and necrosis. The management of late radiation complications is complex with little high quality evidence to guide practice. Surgical treatment may be required if medical intervention fails.

Patients should have access to specialist multiprofessional teams for treatment and management of severe radiation induced complications.
6.7.1 BLADDER

Symptoms of late radiation effects to the bladder can include urinary frequency, urgency, dysuria, detrusor instability, haematuria, ulceration and the potential for perforation and fistula formation. Radiation ischaemia and necrosis may be a cause of ureteric obstruction in addition to bladder problems.

A Cochrane meta-analysis concluded that the absence of any randomised controlled trials made it impossible to draw any definitive conclusions regarding the treatment of radiation cystitis. Management options included hydration, bladder irrigation, antibiotics to treat infection as required and blood transfusion. Early cystoscopy with diathermy of bleeding points before the cycle of repeated bladder washouts, clot retention and mucosal trauma has started may be beneficial. Nineteen case reports and case series suggested that hyperbaric oxygen was beneficial.

One phase III RCT was identified showing that intravenous treatment with tetrachlorodecaoxyg en (TCDO, or drug WF10) showed no significant difference in objective or subjective symptoms on an intention to treat analysis. Patients should be managed by a urologist with experience of late radiation effects to the bladder, who is able to offer complex reconstructive surgery in the event of severe complications.

6.7.2 RECTUM

Acute radiation proctitis is frequently experienced during pelvic radiotherapy with symptoms including tenesmus, urgency, diarrhoea and occasionally bleeding.

An RCT of 87 patients with prostate cancer showed that sucralfate enemas made no difference compared to placebo for the treatment of acute radiation induced proctitis. Another RCT of 134 patients with prostate cancer randomly assigned to sucralfate (63 patients), mesalazine (8 patients) or hydrocortisone (63 patients) found that mesalazine was detrimental and there was no difference between the sucralfate and hydrocortisone. There was no “no treatment” control arm.

Oral sucralfate showed no benefit over placebo for acute radiation induced proctitis in patients with localised pelvic tumours. Patients receiving sucralfate showed significantly increased diarrhoea at two and six weeks after pelvic radiotherapy (p = 0.49 and p = 0.33 respectively), causing the trial to be stopped.

Rectal or oral sucralfate is not recommended to reduce acute radiation induced proctitis.

Late radiation proctitis can lead to tenesmus, urgency, either diarrhoea or constipation, anal sphincter dysfunction, mucus discharge, bleeding, stricture, ulceration and fistula formation.

Sucralfate enema reduced the duration and severity of late radiation induced proctitis, compared to steroid enema in 11 out of 14 patients (13 of whom had cervical cancer) in a small case series. Another study suggested that combining steroid, sulphasalazine and sucralfate enemas is worse than sucralfate alone. Patients with late appearance of symptoms had a shorter time to healing than patients with an early appearance of symptoms.

Rectal sucralfate may be considered to reduce late radiation induced proctitis.
6.8 HORMONE REPLACEMENT THERAPY

In women with absent ovarian function following surgery and/or radiotherapy for cervical cancer, hormone replacement therapy (HRT) reduces post-menopausal symptoms. HRT significantly reduced long term post-radiation rectal, bladder and vaginal complications (p = 0.01). After five years symptoms persisted in 17% of women taking HRT and in 45% of patients receiving no hormonal therapy.

There is no evidence that HRT increases risk of squamous cell cancer but a small study reported a possible increase in the risk of recurrence in women with adenocarcinoma.

HRT is recommended for women who have lost ovarian function as a result of treatment for cervical cancer.
Treatment during pregnancy

No evidence was identified to suggest that pregnancy accelerates the natural history of cervical cancer.\textsuperscript{94} The prognosis for a pregnant patient with cervical cancer is similar to that of a non-pregnant patient when matched for stage, tumour type and tumour volume.\textsuperscript{94} Disease-specific survival is independent of the trimester of pregnancy in which the diagnosis is made.\textsuperscript{94} The evidence indicates that the choice of therapeutic modality for cervical cancer diagnosed during pregnancy should be decided in the same manner as for non-pregnant patients.\textsuperscript{94}

\begin{itemize}
  \item For pregnant women with cervical cancer, the choice of therapeutic modality should be decided in the same manner as for non-pregnant patients.
  \item The evidence supports immediate treatment for patients diagnosed with cervical cancer at or before 16 weeks of gestation, irrespective of stage.\textsuperscript{46,47,94} After 16 weeks of gestation, in patients with early stage disease (FIGO 1A1, 1A2, 1B), delivery may be delayed until fetal maturity occurs.\textsuperscript{46,47,94}
  \item For pregnant women diagnosed with cervical cancer before 16 weeks of gestation, immediate treatment is recommended.
  \item For pregnant women with early stage disease (FIGO 1A1, 1A2, 1B) diagnosed after 16 weeks of gestation, treatment may be delayed to allow fetal maturity to occur.
  \item An individualised treatment plan should be determined, in consultation with the patient, by the multidisciplinary team, which should include an obstetrician.
  \item For pregnant women with advanced disease (FIGO 1B2 or greater) diagnosed after 16 weeks of gestation, consideration for delay must be based on gestational age at time of diagnosis.
\end{itemize}

For women with late stage disease, there is no good evidence to support delaying treatment to allow fetal maturity as very few cases are described in the literature. No evidence was identified that compared maternal survival after diagnosis at different periods of gestation.

If gestational age is less than 20 weeks at diagnosis of advanced cervical cancer (FIGO 1B2 or greater) a systematic review supports immediate delivery and treatment of the disease. If gestational age is more than 20 weeks, delivery and treatment should be initiated within four weeks of diagnosis.\textsuperscript{94}

\begin{itemize}
  \item No RCTs were identified describing outcomes after delivery by caesarean section compared to vaginal delivery.
  \item Several retrospective studies concluded that there is no statistically different survival benefit given either delivery method.\textsuperscript{46,47,94}
  \item Decisions on the mode and timing of delivery should be made in consultation with the patient and her obstetrician.
\end{itemize}
8 Sexual morbidity

Sexual problems suffered by women with cervical cancer may include loss of libido, change in sexual activity and decreased orgasm. Up to 65% of women experience one or more of these problems due to vaginal dryness, vaginal bleeding, stenosis, dyspareunia, atrophic vaginitis and pain.\textsuperscript{148}

Given the incidence of physical and psychosexual dysfunction following cervical cancer women’s sexual function and concerns need to be assessed prior to treatment. There is no good evidence to suggest when the appropriate time to carry out an assessment is.

☐ The sexual function and concerns of women diagnosed with cervical cancer should be assessed prior to treatment.

8.1 Physical Interventions

A systematic review identified evidence from retrospective studies that vaginal stents/dilators can prevent development of vaginal stenosis and treat vaginal occlusion in patients receiving radiotherapy for cervical or uterine cancer.\textsuperscript{49} Vaginal stenosis was prevented and patency maintained at one-year follow up in 20/35 patients compared to 4/35 patients who had not used a stent.\textsuperscript{49} Vaginal oestrogens appear to be effective for reducing dyspareunia, alterations in the vaginal epithelium and vaginal narrowing. Benzydamine douches appear to be effective for treating acute radiation vaginal mucositis. The included studies were old, small and underpowered and large placebo controlled trials are required.\textsuperscript{49}

☐ Women should be offered a vaginal stent or dilator to prevent post-radiotherapy vaginal complications.

☐ Topical oestrogens or benzydamine douches may be considered to alleviate post-radiotherapy vaginal complications.

A small pilot study suggested that symptoms of sexual dysfunction were reduced with a clitoral therapy device. The results need to be validated in larger controlled trials before the device can be recommended.\textsuperscript{50}

8.2 Psychoeducational Interventions

Compliance with vaginal dilation following pelvic radiotherapy is variable and generally poor. Assistance in overcoming women’s fears and teaching behavioural skills is likely to reduce concerns and improve both knowledge of sexual activity and sexual rehabilitation following pelvic radiotherapy. Consensus guidelines on the use of vaginal dilators in women receiving pelvic radiotherapy are available.\textsuperscript{51}

☐ Women should be offered training and support to maximise the benefit of using a stent or dilator.

Psychoeducational group sessions, guided by the information-motivation-behavioural skills model, provide the necessary information, motivate individuals to engage in the target behaviours and teach behavioural skills for performing specific tasks, such as objective skills and a sense of self efficacy for performing them.\textsuperscript{152} Two one and a half hour sessions significantly reduced women’s fears about their sexuality (p=0.01) and increased their knowledge, particularly in the older age group (over 41.5 years of age, p<0.001) compared with written information alone. The intervention also increased vaginal dilation compliance rates and the ability to have sexual intercourse in younger women.\textsuperscript{152}
In this study group, therapy was delivered at the cancer centre post-radiotherapy. In Scotland it may prove difficult to gather together women who are at the same stage of treatment. The intervention-motivation-behavioural skills model could be used to address issues of concern to women after surgery if tailored to meet the need.

Relaxation and counselling sessions delivered within 24 hours of discharge by a member of the patient’s care team significantly reduce anxiety and moderate depression in the first six weeks after surgery.\textsuperscript{53}

\textbf{B} Information about female sexual function should be offered to patients by a relevantly trained healthcare professional using a model of care that involves addressing motivational issues and teaching behavioural skills.

\textbf{C} Patients should be offered support sessions by a designated member of their care team, as soon as possible after treatment, which may include one or more of the following:
- relaxation
- personalised information about their disease and treatment
- emotional support and care.

☑ Women should be offered one to one sessions if appropriate.
9 Lymphoedema

Lymphoedema, presenting as swelling of one or both lower limbs, is a possible complication of cervical cancer and may be treatment or disease related. Reported incidence rates vary from 3.6-49%.[^14][^15][^16] Studies are not generally comparable due to different patient groups, treatment techniques and lack of standardised reporting of lymphoedema.

Quality of life is affected in patients with lower limb lymphoedema including changes in sensation, appearance, pain[^16]^[161]^[162] and restricted activities[^15]^[163] and distress[^16]^[164]. Treatment may positively influence quality of life.[^165]

- All healthcare professionals involved in the care of patients with cervical cancer should receive education on the identification of lymphoedema.

9.1 RISK FACTORS

Hysterectomy with pelvic node dissection for early stage cervical cancer has been associated with a 7-14% incidence of swelling.[^16]^[163]^[164] Lymphoedema has also been reported in those who had radiotherapy alone[^163]^[166].

The incidence of lymphoedema following pelvic lymph node dissection and radiotherapy for FIGO IB/IIA cervical cancer in a cohort of 99 patients was reported as 19% at one year and 12% at five years.[^156] Similar figures were reported in a cohort of 77 patients.[^167]

A study of women undergoing surgery for cancer of the uterine corpus showed that removal of ≥10 lymph nodes is associated with a greater risk of lymphoedema.[^168]

External radiotherapy doses of >50.4Gy to the low pelvis appear to be associated with an increased risk of complications such as lymphoedema.[^157] A retrospective study of 118 patients showed no difference in the incidence of lymphoedema in those who had irradiation to small pelvic field or whole pelvic field.[^158]

Around one third of patients in one study said they had not received either written or oral information about lymphoedema.[^162] Well timed advice and appropriate written and oral information on lymphoedema risk and management is needed.[^162]^[167]

- Patients with lymphoedema, or at risk of lymphoedema, should have access to appropriate information.

- Information should be delivered by a healthcare professional with relevant training.

Specialist lymphoedema practitioners, usually nurses or physiotherapists, are available in some healthcare settings to provide specialist treatments (see section 9.4). Other healthcare professionals are trained in some aspects of lymphoedema management but may not provide regular, specialist treatments.

- Designated lymphoedema practitioners should be available at all centres treating women with cervical cancer.

9.2 TRIGGER FACTORS

Factors that may trigger the onset of clinical lymphoedema include:[^160]

- injury or trauma, for example, insect bite, cut, injection, sunburn
- extreme temperatures
- air travel
- cellulitis.
9.3 **DIAGNOSIS**

Diagnosis is mainly based on clinical examination and the following criteria have been identified: increase in circumference of the limb; changed sensations such as feelings of fullness, tightness, heaviness, throbbing, shooting pains; reduced flexibility in the limb; palpable changes to the skin or subcutaneous tissue such as fibrosclerosis that may be pitting or non-pitting.

The International Society of Lymphology identifies staging criteria for lymphoedema according to severity (see Annex 6).

Lymphoedema often occurs in the first two years following cancer treatment. Swelling subsides on elevation at early stages but may become chronic, with skin and tissue changes, including thickening, skin folds and fat deposits. Oedema of the trunk can occur in some patients. One study showed that 16% of patients with lymphoedema developed cellulitis requiring antibiotic treatment.

Lymphoedema may be exacerbated if patients gain weight or have concurrent problems such as cardiac failure or medication-related fluid retention. Intrapelvic or intra-abdominal tumours that involve or compress lymphatic or venous return may produce a severe and intractable oedema, particularly near the end of life.

Cancer recurrence should be considered in patients with new onset lymphoedema. The possibility of deep venous thrombosis should also be explored.

Evaluation of lymphoedema risk by healthcare professionals and communication between healthcare teams is essential to ensure early diagnosis and appropriate referral for treatment and to minimise complications.

- Patient review should include identification and recording of lower limb lymphoedema.
- Patients with symptoms suggestive of lymphoedema should be referred early for assessment by a designated lymphoedema practitioner.

9.4 **TREATMENT**

Expert opinion supports the use of conservative physical therapies in lymphoedema management. For some patients this includes decongestive lymphatic therapy (DLT) with compression bandaging and manual lymph drainage (MLD) massage, combined with lymphoedema hosiery, skin care and exercise.

There is evidence from a systematic review to suggest that multi layer bandaging followed by hosiery is more effective in reducing limb volume than hosiery alone.

Early and appropriate antibiotic therapy is important in managing cellulitis and antibiotic prophylaxis may be required for patients with recurrent cellulitis.

- Patients with severe or poorly controlled lymphoedema should be offered DLT with a specialist lymphoedema practitioner.
- Early and appropriate use of antibiotic therapy is recommended for patients with cellulitis.

Prophylactic antibiotic treatment should be considered for patients with more than two episodes of cellulitis in a year.
A consensus report identified no evidence to support the long term use of diuretics to reduce lower limb lymphoedema.\textsuperscript{169}

Two systematic reviews found insufficient evidence to draw conclusions about the effectiveness of selenium or benzopyrones in the treatment of cellulitis or lymphoedema.\textsuperscript{171,172}

Evidence from a non-randomised study, that did not include patients with cervical cancer, suggests that intermittent compression pump therapy may lead to genital oedema.\textsuperscript{173}

\section*{9.5 PATIENT SELF MANAGEMENT}

Patient self management that may include use of lymphoedema hosiery, exercise, skin care and self massage is recognised as important in the effective management of lymphoedema.\textsuperscript{160,169}

A common sense approach to reducing the risk of lymphoedema or preventing complications such as cellulitis has been described including:\textsuperscript{159,169}

\begin{itemize}
  \item taking care of skin and nails and avoidance of interdigital fungal infection
  \item maintaining an optimal body weight
  \item avoiding injury to the affected limb/s including scratches and insect bites
  \item avoiding temperature extremes
  \item protecting the limbs from the sun
  \item wearing comfortable, supportive shoes.
\end{itemize}

Patients with lymphoedema should be supported to self manage by a practitioner qualified in lymphoedema management.
10 Follow up

10.1 POST-TREATMENT SURVEILLANCE

Evidence for the effectiveness of post-treatment surveillance is inconsistent.

In an observational study of 993 patients with FIGO IB disease reviewed after primary surgery or primary radiotherapy, 13% developed recurrent disease (see Table 3). In an observational study of 993 patients with FIGO IB disease reviewed after primary surgery or primary radiotherapy, 13% developed recurrent disease (see Table 3).174 Nine per cent of surgical patients and 17% of radiotherapy patients developed recurrences. All asymptomatic recurrences occurred in the first 16 months of follow up.174 Cervical cytology did not detect a single asymptomatic recurrence.174 Thirty seven of the 993 patients developed recurrent disease in the central pelvis, 21 patients had recurrences in either lung or pelvic side wall and 22 patients had recurrences in the nodes.174 All asymptomatic pelvic recurrences occurred in the first 16 months after completion of treatment. Symptom status at time of recurrence is a significant predictor of survival.174 The median survival from recurrence was 11 months for symptomatic disease and 42 months for asymptomatic.174 Another study reviewed 1,292 women of all FIGO stages after radiotherapy (see Table 3).175 Twenty nine per cent had either local or distant recurrence and around a 10% five-year survival rate.175

In a study of 291 patients followed up for five years after surgery for cervical cancer, 18.2% developed recurrent disease (see Table 3).176 The median time from surgery to recurrence was 17.6 months.176 Recurrent disease was only detected in seven of the 53 patients at routine follow up and two were asymptomatic. Detection of recurrence on routine follow up was not an independent prognostic factor for survival when compared with age, stage and whether the patient received postoperative adjuvant treatment.176

Routine clinical follow up after radical hysterectomy and pelvic lymph node dissection is not a sensitive way of detecting recurrent disease, as a high proportion of patients are found to be symptomatic at the time of detection of recurrence. Sixty three per cent of recurrences occurred before 24 months and 77% before 36 months.174

Table 3: Recurrence detected during follow up

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Number of recurrences</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (Primary treatment)</td>
<td>Total (Type)</td>
<td></td>
</tr>
<tr>
<td>Bodurka-Bevers, 2000</td>
<td>933 surgery 461</td>
<td>40 symptomatic 33</td>
<td>11 months*</td>
</tr>
<tr>
<td></td>
<td>radiotherapy 532</td>
<td>93 symptomatic 81</td>
<td>11 months*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>asymptomatic 7</td>
<td>42 months*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>asymptomatic 12</td>
<td>42 months*</td>
</tr>
<tr>
<td>Hong, 2004</td>
<td>1292 radiotherapy</td>
<td>375 local 162</td>
<td>10% (5-year)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>distant 213</td>
<td>11% (5-year)</td>
</tr>
<tr>
<td>Lim, 2004</td>
<td>291 surgery 53</td>
<td>53 symptomatic 5†</td>
<td>37.5 months*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>asymptomatic 2†</td>
<td>8.3 months*</td>
</tr>
</tbody>
</table>

* median survival post-recurrence
† recurrent disease detected at a planned follow-up clinic

History taking and clinical examination should be carried out during follow up of patients with cervical cancer to detect asymptomatic and symptomatic recurrence.

Cervical cytology or vault smears are not indicated to detect asymptomatic recurrence of cervical cancer.
Although routine follow up after radical hysterectomy or radiotherapy is not a sensitive way of detecting recurrent disease, it is current practice for patients to be followed up because of other benefits, such as detection of treatment complications, and psychosexual and psychosocial morbidity.

☐ Patients should be followed up every four months for at least two years.

☐ Patients with early stage disease who have had fertility conserving surgery should have a smear at six months, 12 months and annually for four years before being returned to the cervical screening programme.

10.2 DETECTION OF RELAPSED DISEASE

Annex 7 shows an algorithm for the detection of relapsed disease.

CT or MRI is more easily available, cheaper and in symptomatic patients is better than PET at differentiating metastatic complications from post-treatment complications, for example, insufficiency fractures of the pelvis.

There is some evidence supporting the use of intravenous contrast in post-therapy MRI scans in symptomatic and asymptomatic patients to differentiate fibrosis post-radiotherapy from recurrent tumour. There is evidence from a small study (19 patients) that PET-CT scans may be more accurate than either postcontrast CT or MRI in differentiating post-treatment fibrosis from recurrent disease.

A whole body PET or PET-CT scan is a sensitive post-therapy surveillance modality for the detection of recurrent and persistent cervical carcinoma in both asymptomatic and symptomatic patients.

There is little evidence to support the optimal timing or frequency of post-therapy scans. In several studies whole body PET scans were generally performed no sooner than three months post primary treatment to avoid false positives associated with post-surgical or radiotherapy oedema or inflammatory response in the pelvis. A PET scan at nine months would be expected to detect the majority of recurrences, whether or not patients are symptomatic. Recurrence may still occur before and after nine months, but rarely after 30 months. A study of 152 patients showed that early persistent post-therapy FDG-PET uptake may be predictive of tumour recurrence and death from cervical cancer.

PET is more accurate in the detection of metastatic or nodal disease than CT or MRI. At the time of publication PET-CT imaging combined is the modality of choice rather than PET scans alone. CT, CT-PET or MRI are more accurate in the detection of recurrent disease than clinical examination alone.

If FDG-PET uptake is positive only in the pelvis and cross-sectional imaging has not been performed, CT or MRI is still required to assess resectibility.

If performed prior to pelvic exenteration, a whole body PET or PET-CT scan can improve selection of operable patients and potentially improve their survival rates and can eliminate unnecessary morbidity associated with salvage procedures in unsuitable patients.

There is no evidence to demonstrate that prior radiotherapy or chemotherapy alters the sensitivity of detection of recurrence.

C MRI or CT should be considered initially to assess potential clinical recurrence in symptomatic patients.

B A whole body PET scan or PET-CT should be performed on all patients in whom recurrent or persistent disease has been demonstrated on MRI or CT and in whom salvage therapy (either pelvic exenteration or radiotherapy) is being considered.

☐ A PET-CT scan at nine months of follow up is recommended in women who have had chemoradiotherapy.
10.2.1 TUMOUR MARKERS

The clinical value of routine SCCA measurement during follow up of patients with early stage cervical cancer treated by radical hysterectomy and PLND with or without radiotherapy has been investigated. SCCA analysis resulted in earlier detection of recurrence in only 14% of patients (in 5/35 who had recurrent disease elevated SCCA was the first measured clinical indicator), but did not contribute to better overall survival.

Routine post-treatment SCCA monitoring is not cost effective for all stages of squamous cervical cancer in the absence of curative treatment for recurrent disease (see section 15.7).

The routine use of SCCA to determine disease recurrence is not recommended.
11 Management of recurrent disease

The prognosis for patients with recurrent disease is six months to two years. In addition, women may experience substantial morbidity from both local recurrence and metastatic disease.

Therapeutic options for those patients with cervical cancer whose first line treatment has failed include:

- surgery (salvage)
- chemotherapy
- palliative treatment only, including best supportive care (see sections 12 and 13), if further surgery or chemotherapy is not appropriate either due to the advanced nature of the tumour, the poor general condition of the patient, or at the patient’s request.

Decisions regarding the appropriate management of recurrent cervical cancer should be made on an individual basis taking into account:

- the patient’s wishes
- the stage of recurrent tumour and its potential resectability
- previous treatment
- likely treatment efficacy
- likely treatment-related morbidity and functional outcome and consequent effects on quality of life
- the patient’s general health.

Decisions regarding the management of recurrent cervical cancer should be made by the multidisciplinary team in consultation with the patient following histological or cytological confirmation of recurrence and full restaging (clinical and radiological).

Patients and their relatives or carers should be carefully counselled about the likely outcome of treatment for recurrent disease, with respect to survival, risk of treatment-related morbidity and mortality and quality of life.

Early referral to palliative care services for symptom control should be considered.

11.1 SURGERY

Following primary treatment for cervical cancer the incidence of isolated relapse confined to the pelvis is infrequent. For women who do present with relapsed disease following biopsy confirmation additional restaging is needed to rule out extrapelvic metastases. The majority of women who develop recurrent disease will have previously received pelvic radiotherapy. For these women the only potentially curative option is pelvic exenteration provided relapsed disease is confined to the central pelvis.

11.1.1 TOTAL PELVIC EXENTERATION

Total pelvic exenteration (TPE) is a high morbidity procedure. Less than 50% of patients survive five years after TPE.

A whole body PET or PET-CT can identify distant nodal and metastatic disease which may not be detected on CT or MRI scans.

If performed prior to pelvic exenteration, a whole body PET or PET-CT scan can improve the selection of operable patients and potentially improve their survival rates, and eliminate unnecessary morbidity associated with salvage procedures in unsuitable patients. CT or MRI is still required to assess resectability.
In one small study, postoperative morbidity following TPE was reported as 35.7%, with reoperations being carried out in 28.6% of patients.\cite{189} Having a dedicated multiprofessional team reduces morbidity and mortality. Recurrence occurred in 50% of cases.\cite{189}

In a phase II trial, the survival and operative mortality rates attainable with TPE for recurrent cervical cancer are comparable to those achieved with chemoradiotherapy.\cite{190}

Urinary diversion represents a fundamental part of surgical reconstruction at the time of TPE. In the UK the most commonly performed procedure is an ileal loop urinary diversion.

A self selected series of patients with prior pelvic irradiation were given an ileocolic continent pouch rather than loop ileal conduit with no apparent increase in morbidity.\cite{191} Good postoperative nutrition, and adequate stenting of the ureteric/intestinal anastomosis site decrease the incidence of complications and increase quality of life.\cite{188}

Reconstruction of the vagina and pelvic floor at the time of pelvic exenteration can be safely done. Surgical time is increased but morbidity is not significantly increased. The rectus abdominal flap is the preferred reconstruction technique. Incidence of flap necrosis was 18.8%.\cite{192}

**Pelvic exenteration should be reserved as salvage surgery for women with recurrent cervical cancer in the central pelvis whose chemoradiotherapy has failed.**

**MRI or CT should be considered initially to assess potential clinical recurrence in symptomatic patients.**

**A whole body PET scan or PET-CT should be performed on all patients in whom recurrent or persistent disease has been demonstrated on MRI or CT and in whom salvage therapy (either pelvic exenteration or radiotherapy) is being considered.**

To minimise mortality and morbidity, a dedicated multiprofessional team should carry out total pelvic exenteration in women with recurrent cervical cancer.

### 11.2 CHEMOTHERAPY

There have been no randomised trials comparing chemotherapy to best supportive care in advanced cervical carcinoma. Cisplatin is the standard chemotherapy despite low response rates.

A trial published in 1985 randomised patients to three different schedules of cisplatin. There was no difference in overall survival or time to progression although response rates were higher with a higher dose of cisplatin.\cite{193} As a result cisplatin at 50 mg/m\(^2\) three weekly has been the standard approach.

Two trials looked at the addition of ifosfamide to cisplatin therapy.\cite{194,195} One closed early due to poor accrual,\cite{194} but no significant differences were seen in survival in either trial. There was an improved progression free survival with cisplatin and ifosfamide but significantly increased toxicity.\cite{195}

The addition of paclitaxel (135 mg/m\(^2\)) to cisplatin resulted in an increase in overall response rate from 19% to 36% and a statistically significant increase in the median progression-free survival of two months from 2.8 months to 4.8 months but there was no improvement in overall survival.\cite{196} Quality of life was the same in both treatment arms.\cite{197}
A statistically significant 2.9 month improvement in median survival was seen with the combination of cisplatin and topotecan (50 mg/m² on day one plus topotecan 0.75 mg/m² on days one to three every three weeks) compared with cisplatin alone (50 mg/m² every three weeks) from 6.5 months to 9.4 months. The unadjusted RR estimate for survival was 0.76 (p = 0.017). The 95% confidence interval comes close to unity (0.593 to 0.979), so the actual overall benefit may be small. When adjusted for covariates of performance status, age, and disease status at entry, the RR estimate is 0.738 (p = 0.0075) favouring cisplatin and topotecan. The greatest benefit was seen in patients who had not previously received chemotherapy, and was poorest in those who received platinum therapy in the previous 12 months.

Increased toxicity, primarily haematological, was associated with the combination regimen. There was an increase in episodes of febrile neutropenia from 7.5% to 17.7% and the incidence of grade 3 or 4 thrombocytopenia increased from 3.4% to 31.3%. There was no reduction in the recorded quality of life of patients treated with the combination regimen despite the increased toxicity.

The SMC has assessed topotecan in combination with cisplatin (see section 14.1.1). 

- Palliative chemotherapy should be offered to women with FIGO stage IVB or recurrent cervical carcinoma, after discussion of the relative benefits and risks, with either:
  - cisplatin 50 mg/m² on day 1 plus topotecan 0.75 mg/m² on days 1 to 3 every 3 weeks, or
  - cisplatin 50 mg/m² on day 1 plus paclitaxel 135 mg/m² every 3 weeks.

- Cisplatin and topotecan combination should be restricted to cisplatin naïve patients.
- Patients of performance status 0-2 should be considered for treatment with cisplatin and topotecan combination.
- Discussion of new drugs in the clinical trial setting should be considered with patients who have relapsed within 12 months.
- Chemotherapy should be prescribed, dispensed, administered and supervised in a safe and effective manner in accordance with the Joint Collegiate Council for Oncology guidelines, clinical oncology good practice guidelines and Scottish Government advice.
11.3 FISTULAE

Fistula formation is a rare but grave feature of cervical cancer. Few women are affected but the distress created by rectovaginal or vesicovaginal fistula development is considerable. The evidence for managing fistulae is poor and management is based on expert opinion.  

Fistulae may occur as a late complication of radiotherapy (with a mean latent time of 17 months to 8.1 years) or as a result of progressive disease. Radiation dose and dose distribution are the main risk factors for the development of post radiation rectovaginal fistulae.

Symptoms include:
- persistent continuous watery discharge
- persistent continuous faeculant discharge with pneumaturia.

For a bowel fistula, after appropriate radiological investigations to establish the site and complexity of the fistula (see section 4.3.5), a treatment option may be stoma formation.

Urological fistulae due to radiotherapy may require temporary diversion by percutaneous nephrostomies or insertion of internal ureteric stents prior to ureteric occlusion and diversion.

Patients with advanced disease who develop fistulae are seldom able to undergo surgery to attempt repair and are constantly reminded of the incurable nature of their condition. Appropriate non-surgical treatments should be offered to maximise comfort and include:

- octreotide, hyoscine butyl bromide or glycopyrronium to reduce volume of discharge
- codeine phosphate or loperamide to firm stool
- barrier creams to protect the perineal skin
- topical steroids, for example, prednisolone foam enemata administered vaginally for local effect
- vaginal moulds
- tampons
- low residue diet.
12 Management of complications in advanced disease

Comprehensive palliative care will be required as the patient’s condition declines and the end of life nears. Symptoms may be challenging and patients may benefit from input from a wide variety of clinical services.

Consideration of every symptom is outwith the scope of this guideline. Guidance on palliative care is available and specialist palliative care advice is available from all Scottish Hospices and Hospital Palliative Care Support Teams. Contact details can be found in the annual Directory of Hospice and Palliative Care Services (www.hospiceinformation.info). Local resources which consider the spiritual and psychosocial aspects of palliative care as well as physical problems are also available, for example, the Forth Valley Palliative Care Resource Pack, (http://intranet.fv.scot.nhs.uk/web/site/Depts/CoreCancer/PalliativeCareResourcePack.asp) and the Lothian Palliative Care Guidelines (www.scan.scot.nhs.uk).

Patients with incurable cervical cancer should be managed on an individual basis.

This section of the guideline addresses distressing problems specifically associated with advanced cervical cancer. These may occur singly or in combination and include:

- pain
- renal failure from bilateral ureteric obstruction
- thrombosis and haemorrhage
- malodorous discharge
- lymphoedema (see section 9)
- fistulae.

12.1 PAIN CONTROL

Pain control in advanced cancer is addressed in SIGN 44: Control of pain in patients with cancer. In advanced cervical cancer the following may also be appropriate:

- early recourse to nerve-blocking procedures in addition to analgesic drugs
- spinal therapy, using combinations of opiates, local anaesthetics and clonidine, to provide regional blockade for pelvic pain, incident neuropathic pain or pain from metastatic disease in the spine or pelvis
- percutaneous cementoplasty for painful lytic bony metastases of the pubic ramus or acetabulum, if pain is refractory to conservative treatment.

12.2 RENAL FAILURE

Renal failure in advanced cervical cancer generally has a post-renal aetiology from lymphadenopathy or direct tumour invasion but concomitant pre-renal and renal causes should be excluded. Ureteric obstruction may initially produce no biochemical evidence of impaired renal function but if left unmanaged will inevitably lead to renal loss.

- Investigations should be performed to exclude additional treatable causes of renal failure.
- There should be a careful assessment of results of the investigations and discussion with the patient.
The management of extrinsic malignant ureteric obstruction is a balance of the patient’s quality of life, renal preservation and the risk of complications in a setting of poor prognosis. There is a lack of consensus on optimal management, and treatment may differ between patients with advanced disease at presentation and those with progressive disease following treatment. Initial management options are:

- no treatment
- percutaneous nephrostomy (PCN), or
- retrograde stenting.

Urology and gynaecology specialists should be involved in any discussion on the best treatment for individual patients.

Advanced decisions taken by the patient should be recorded and respected.

In an emergency situation, and in the absence of an advanced directive, initial treatment should be in favour of life.

An algorithm for the management of renal failure is shown in Annex 8.

PCN can substitute a peaceful uraemic death for a painful, poor quality life with minimal improved survival. Internal stents fail in at least a third of patients within six months. Stent failure is represented by an increase in creatinine by 50% from nadir, pain, infection or hydronephrosis. A retrospective study of cancer patients receiving primary retrograde stents for malignant ureteric obstruction indicated that gross tumour invasion at cystoscopy is a significant risk factor for stent failure and progression to PCN. There is insufficient evidence to compare different types of stent. Long term stents are designed to remain in place for either six or 12 months but some urologists perform more frequent changes to keep the stents patent. The frequency of change depends on the level of ureteric obstruction. If the obstruction is due to pelvic cancer it may be more appropriate to consider PCN. If retroperitoneal lymphadenopathy is the cause of the obstruction, stents will remain patent for considerably longer and will require less frequent change.

If retrograde stent is unsuccessful PCN and/or antegrade stent may be a successful alternative. Consequently open discussion with the patient and relatives is essential.

Retrograde ureteric stents should be changed according to the level of ureteric obstruction (ranging from 3-12 months).

If a retrograde stent is unsuccessful:
- the stent should be changed more frequently
- an alternative stent should be tried
- patients should be offered PCN and/or antegrade stent.

If stent placement permits further treatment, such as radiotherapy or chemotherapy, in patients with advanced disease at presentation, urinary diversion may subsequently become feasible. Patients require careful follow up, with regular monitoring of renal status. Patient selection and counselling are important.

Urinary diversion may be considered in suitable patients.

Patients should have careful follow up and access to counselling.
12.3  THROMBOTIC AND BLEEDING PROBLEMS

Patients with advanced cervical cancer are at risk of both thrombosis and haemorrhage as a consequence of their cancer or metastatic disease.²¹⁸

- Treatment should take account of the patient’s personal views and circumstances. In particular, physical state, prognosis and options for future therapy should be considered.

12.3.1  DEEP VENOUS THROMBOSIS

Risk factors for thrombosis include:
- presence of pelvic masses which compress large veins
- impaired mobility
- effect of treatment
  - radiotherapy
  - surgery
  - chemotherapy.

The frequency of thrombosis is underestimated as concomitant lymphoedema and oedema from hypoalbuminaemia make diagnosis difficult and a high index of suspicion is required (see section 9.3).

The diagnosis of deep venous thrombosis (DVT) is usually made clinically but in mobile patients further investigation, such as whole blood D-dimer testing or ultrasound scanning may be appropriate, but need not delay the initiation of therapy for clinically diagnosed thromboses.²¹⁹

Treatment with low molecular weight heparin (LMWH) was shown to be more effective than an oral anticoagulant in reducing the risk of recurrent thromboembolism, without increasing the risk of bleeding.²²⁰

Patients were shown to find treatment with LMWH acceptable compared to warfarin.²²¹,²²² The duration of treatment should be considered on an individual basis.²²³

- Low molecular weight heparin should be considered for treatment of DVT and prevention of recurrent thromboembolism.

Traditionally bed rest was advocated for mobile patients with acute DVT to reduce the risk of pulmonary thromboembolism (PTE), leg pain and leg swelling. However bed rest can promote stasis and may cause propagation of clot.

Some studies have shown a better clinical outcome when compression garments are used in conjunction with LMWH and early ambulation.²²⁴,²²⁵ The American College of Chest Physicians’ (ACCP) consensus document recommends ambulation as tolerated for DVT and the use of elastic compression stockings to prevent post-thrombotic syndrome.²²⁶

- Compression garments, in conjunction with LMWH and early walking exercises should be considered in patients with DVT.

- All patients with suspected thrombosis should receive symptomatic relief with leg elevation at rest and analgesia.

- Compression garments should be well fitting.
12.3.2 HAEMORRHAGE

Relapsed cervical cancer can present with vaginal bleeding and massive haemorrhage may occur. Bladder or bowel invasion may cause haematuria or rectal bleeding but haemorrhage from thrombocytopenia related to marrow infiltration is unusual in cervical cancer.\textsuperscript{218}

Drugs with antiplatelet activity, for example, non-steroidal anti-inflammatory drugs (NSAIDs) or antithrombotic activity, for example, LMWH may exacerbate bleeding.\textsuperscript{227}

Minor bleeds and/or infection may herald a major haemorrhage.

12.3.3 TREATMENT OF MINOR HAEMORRHAGE

- If a minor haemorrhage occurs:
  - systemic causes of bleeding should be excluded
  - drugs that may exacerbate bleeding should be discontinued
  - antibiotics should be considered if sepsis is present.

Fibrinolytic inhibitors, such as oral tranexamic acid or aminocaproic acid, have been shown to reduce bleeding.\textsuperscript{228} Topical application of tranexamic acid to superficial fungating wounds or by rectal or bladder instillation may also reduce bleeding\textsuperscript{228} as may a single fraction of radiotherapy.\textsuperscript{229}

D Treatment for minor haemorrhage may include:
- oral tranexamic acid or aminocaproic acid
- tranexamic acid applied topically to superficial fungating wound
- tranexamic acid by rectal or bladder instillation
- a single fraction of radiotherapy.

12.3.4 MANAGEMENT OF MAJOR HAEMORRHAGE

A major haemorrhage is defined as arterial blood loss of 1.5 litres in 30 seconds in a patient for whom active treatment is neither appropriate nor possible and which will inevitably be fatal within minutes in the palliative situation.

The aim is to relieve patient distress as quickly as possible. Drugs which are beneficial in this situation are:\textsuperscript{30}
- midazolam for its anxiolytic effect (10 mg subcutaneously or by the buccal route), and
- diamorphine for its hypotensive effect (10 mg subcutaneously if opiate-naïve, two to four times normal breakthrough dose if on regular opiates).

If the patient is peripherally constricted intravenous or intramuscular routes can be used.

- If the patient wishes to be at home to die the risks of anticipated haemorrhage should be explained to the relatives and appropriate support should be offered.
  - If haemorrhage is predictable when at home, dark coloured towels or blankets should be made available to relatives to mask the extent of the haemorrhage.
  - Appropriate drugs should be immediately available by the bedside.
  - If bleeding is due to erosion of a major artery, local pressure with adequate packing should be applied.

- It is important to ensure that the patient is not left alone and, if possible, that a doctor or nurse remains with the patient until death or resolution of the acute event.
12.4 MALODOUR

Malodour and discharge frequently reflect advancing cancer. It is an uncommon but distressing symptom for patients. Malodour has complex significance for a patient with advanced cervical cancer. It impacts on body image, sense of worth and self as a social being and specifically reinforces the fact of ill health.231

Malodorous discharges are usually due to the breakdown of tissue causing loss of fluid from a necrotic tumour or from erosion of the bowel or urinary tract causing leakage of faeces or urine. In addition infection may contribute to malodour.231

☑ A careful history, psychological assessment, physical examination, imaging, microbiological examination and biopsy may all be required to fully assess malodourous discharge.

☑ Management should be tailored to treat infection and reduce or confine fluid loss, while minimising local irritation or discomfort and maximising quality of life.

It may be helpful to use the patient’s estimated prognosis as a guide to discussing appropriate treatment.

Most patients will require non-surgical measures to reduce malodour. If the tumour burden is small, surgery or radiotherapy may be beneficial. A single fraction of radiotherapy may reduce malodour. Surgery may involve:

▪ removal or debridement of necrotic tissue
▪ defunctioning colostomy for fistula-related faecal incontinence
▪ bilateral percutaneous nephrostomies for fistula-related urinary incontinence.

Little published evidence is available on the treatment of malodour, although limited data exist for the treatment of malodourous cutaneous lesions. In a prospective cohort, 4/43 patients with benign or malignant disease treated with topical metronidazole gel assessed at 14 days of treatment reported decreased smell.232

Given the paucity of evidence on malodour, the guideline development group devised a questionnaire, which was sent to all hospices, specialist palliative care units and Gynaecology Specialist Nurses in Scotland, to obtain a view of current practice for non-surgical treatment of malodour and associated symptoms in patients with cervical cancer (see supplementary material, www.sign.ac.uk).

Nine responses out of 17 were received. The results are summarised below:

▪ all units personalised treatment to the individual patient
▪ all units used systemic or topical metronidazole for malodour
▪ seven units used aromatherapy, including eucalyptus and tea tree oils vaporised on a burner for malodour
▪ six units used charcoal outer dressings for malodour
▪ other suggestions were the use of trays of cat litter under the bed to absorb malodour, silver dressings and fragranced tumble dryer sheets as an odour-absorbing outer layer
▪ all units used tranexamic acid for tumour-related vaginal bleeding either orally or topically.
Vaginal tampons were used in five units and one unit described the use of vaginal steroids
▪ tumour-related vaginal discharge was treated by vaginal douche, metronidazole or other antibiotic, antifungal (oral or topical) and topical steroid. Pads and tampons were used as dictated by patient comfort. Barrier creams to prevent skin irritation and excoriation were used
suprapubic catheterisation was suggested for fistula-related urinary incontinence
for fistula-related faecal incontinence subcutaneous octreotide via a syringe driver was used to reduce faecal loss and reduce malodour. Hyoscine butyl bromide to reduce bowel activity, and constipating agents were also used
no unit was able to supply references but all the suggestions above have been recommended on the Association of Palliative Medicine palliative drugs bulletin board (www.palliative-medicine.org, www.bulletinboard@palliativedrugs.com).
13 Psychosocial care and support for patients and carers

Cervical cancer has a significant psychological and psychosocial impact on the individual and it is important to develop strategies to deal with this.\textsuperscript{233}

13.1 PSYCHOLOGICAL AND PSYCHOSOCIAL DISTRESS

Psychological distress is common in patients with all forms of cancer and usually remains undetected.\textsuperscript{234} Regardless of sociodemographic characteristics or clinical characteristics, the well-being of patients with cervical cancer changes during the course of their disease.\textsuperscript{235} A study of 119 patients newly diagnosed with gynaecological cancer evaluated psychological well-being and functions of daily living before surgery, three months after surgery and one year after surgery.\textsuperscript{235} There was a decline in psychological well-being and functions of daily living scores at three months after surgery.\textsuperscript{235} After one year there was a significant improvement in psychological well-being (p<0.05) and no significant difference in functions of daily living compared to before surgery.\textsuperscript{235} In patients treated with surgery, the level of psychological distress may be related to the extent of surgery.\textsuperscript{235}

Patients should be advised that their physical and psychological function is likely to deteriorate in the initial post-treatment period, but that they should anticipate improvement.

13.1.1 IDENTIFYING PSYCHOLOGICAL DISTRESS

A diagnosis of cancer can be difficult to cope with and may lead to psychological distress due to the interplay of a number of factors, including previous history of psychological disorder, coping or adjustment style, and status and characteristics of the disease and its treatment.

Routine screening for psychological distress among people with cancer has been recommended by the US National Comprehensive Cancer Network.\textsuperscript{236} The National Health and Medical Research Council of Australia recommends an approach to screening for significant psychological problems that includes advice to document risk factors for the presence of psychological distress (see Table 4).\textsuperscript{48}

Not all patients who present with risk factors will experience psychological distress and some patients who present with no risk factors will present with very high levels of distress.

An example of a screening tool developed by the US National Comprehensive Cancer Network is shown in Annex 9.\textsuperscript{236}

- The multidisciplinary team (MDT) should routinely screen for the presence of psychological distress and be aware of risk factors for very high levels of psychological distress from the point of diagnosis onwards (including during follow-up review phases).
- Multidisciplinary teams across healthcare settings should have agreed protocols for psychological distress assessment and management. These should include recommendations for referral and care pathways.
- Liaison psychiatry and clinical psychology services should be contacted if the results from distress screening raise concerns about the psychological well-being of a patient.
Table 4: Factors associated with increased risk of psychosocial problems in patients with cancer\textsuperscript{48}

<table>
<thead>
<tr>
<th>Characteristics of the individual</th>
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</thead>
<tbody>
<tr>
<td>Younger</td>
</tr>
<tr>
<td>Single, separated, divorced or widowed</td>
</tr>
<tr>
<td>Living alone</td>
</tr>
<tr>
<td>Children younger than 21 years</td>
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<tr>
<td>Economic adversity</td>
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<tr>
<td>Lack of social support, perceived poor social support</td>
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<tr>
<td>Poor marital or family functioning</td>
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<tr>
<td>History of psychiatric problems</td>
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<tr>
<td>Cumulative stressful life events</td>
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<tr>
<td>History of alcohol or other substance abuse</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Characteristics of disease and treatment</th>
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<tbody>
<tr>
<td>At the time of diagnosis and recurrence</td>
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<tr>
<td>During advanced stage of the disease</td>
</tr>
<tr>
<td>Poorer prognosis</td>
</tr>
<tr>
<td>More treatment side effects</td>
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<tr>
<td>Greater functional impairment and disease burden</td>
</tr>
<tr>
<td>Experiencing lymphoedema</td>
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<tr>
<td>Experiencing chronic pain</td>
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<tr>
<td>Fatigue</td>
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</tbody>
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13.1.2 ISSUES THAT LEAD TO PSYCHOLOGICAL DISTRESS

Many of the psychological, physical and practical challenges facing women with cervical cancer are common to all cancer patients. These include:

- coping with the shock of diagnosis
- pain, nausea, fatigue and disfigurement as a result of treatment
- worries over practical issues such as travel costs and loss of income.

Other issues are specific to patients with cervical cancer. The level of psychological distress experienced will vary between individuals. Table 5 lists issues that are likely to be important for patients with cervical cancer.\textsuperscript{48}

13.2 SUPPORT NEEDS

There is evidence that providing psychological and practical support may have a positive effect on patients' well-being.\textsuperscript{237} Evidence identified in relation to the support needs of cancer patients was from small heterogeneous studies and the types of help offered are very varied.\textsuperscript{238-240} None of the studies was specific to patients with cervical cancer but were generalisable to the cervical cancer population. The interventions included structured psychological support, relaxation techniques, orientation programmes and general psychological support. The interventions reduced anxiety levels and improved quality of life.
Table 5: Summary of issues that may be important for patients with cervical cancer\textsuperscript{48}

<table>
<thead>
<tr>
<th>Psychological issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>• body image</td>
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<tr>
<td>• new relationships post-diagnosis</td>
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<tr>
<td>• sexuality.</td>
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</tbody>
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<tr>
<th>Physical issues</th>
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<tr>
<td>• bowel dysfunction</td>
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<tr>
<td>• fertility</td>
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<tr>
<td>• incontinence</td>
</tr>
<tr>
<td>• lymphoedema</td>
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<tr>
<td>• malnutrition due to lack of appetite</td>
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<td>• odour</td>
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<thead>
<tr>
<th>Practical issues</th>
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</thead>
<tbody>
<tr>
<td>• child care needs</td>
</tr>
<tr>
<td>• difficulties with business dealings</td>
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<tr>
<td>• loss of income</td>
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<tr>
<td>• reconstructive surgery</td>
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<table>
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<tr>
<th>Survival issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>• embryo storage</td>
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<tr>
<td>• guilt</td>
</tr>
</tbody>
</table>

There are many national and local support services, for example, voluntary agencies, clinical nurse specialists, liaison psychiatry, clinical psychologists, local support groups, drop-in centres and day centres (see section 13.5). These support services may offer complementary therapy services, such as yoga, aromatherapy and reiki. It is important that only those services which are mutually agreed to be relevant to the individual are offered.

\begin{itemize}
  \item Patients with cervical cancer should be offered psychological support at the time of diagnosis and at intervals throughout their management.
  \item Information about local support services should be made available to patients.
  \item Voluntary sector agencies should be considered to expand the level of support available to patients.
  \item Women should be assessed for support needs in relation to dependants in their care (children, older adults) and referred to the appropriate support agencies.
\end{itemize}

Partners and children of patients with cancer are also vulnerable to psychological distress. Studies measuring stress levels of patients with colon and prostate cancer and their partners, show that partners experience significantly more distress than patients and receive less support.\textsuperscript{148} Children of parents with cancer are susceptible to levels of stress, dependent on the age and the sex of the child, a key issue being that the child’s usual support sources are often disrupted.\textsuperscript{148}

\begin{itemize}
  \item Carers, families and dependants should be made aware of support available including local and national organisations.
  \item Multidisciplinary teams across healthcare settings should have agreed protocols for offering support for carers, families and dependants of patients with cervical cancer.
\end{itemize}
13.3 INFORMATION NEEDS

Patients diagnosed with cancer for the first time often want information addressing their immediate concerns regarding their disease, treatment options, what they might expect during return appointments and who to go to for information.

Among women with gynaecological cancer, the level of knowledge about their disease has been found to be poor.\textsuperscript{241} Four studies indicate that cancer patients want information on their treatment and prognosis.\textsuperscript{242-245} A cohort study carried out in the West of Scotland highlighted that cancer patients want to know the medical name of their illness, their treatment choices, how treatments work, the likely side effects and the chances of cure.\textsuperscript{243} The preference for, and ability to cope with, information varies between patients.\textsuperscript{246} Some patients do not want extensive information, and the reasons for this may be complex.\textsuperscript{247} Discrepancies between the need for, and actual communication of, information can contribute to difficulties in coping with psychosocial problems.\textsuperscript{246}

A systematic review of studies involving women with gynaecological cancer show that providing patients with information is beneficial, can improve ability to cope and facilitate their participation in treatment decisions.\textsuperscript{241}

C Patients should be offered information throughout their journey of care.

☑ Health professionals should appreciate that information helps patients to understand how their disease may affect them and to anticipate problems and plan their lives.

☑ Patients should be offered the amount of information that is appropriate to their wishes in a way which is sensitive, understandable and accurate.

☑ Multidisciplinary teams across healthcare settings should have agreed protocols for offering information to patients with cervical cancer.

13.4 COMMUNICATION METHODS

Effective communication with patients is a cornerstone of good practice. Poor communication can increase patients’ psychological distress. Complaints from cancer patients about poor communication with healthcare professionals and lack of continuity of care are common.\textsuperscript{248} Communication skills training delivered by expert facilitators results in demonstrable improvements in communication behaviours of participating senior clinicians.\textsuperscript{249}

There is evidence that training programmes for nurses can improve listening and communication skills.\textsuperscript{250} Although the included trials were small and heterogeneous, one systematic review suggested that providing a record of the consultation with a specialist can increase both the amount of information recalled and satisfaction with the information given.\textsuperscript{245} One randomised trial showed that patients preferred information based on their own medical records rather than general information about their type of cancer.\textsuperscript{251}

Patients prefer to receive written information to assist in making an informed choice.\textsuperscript{244}

B Healthcare professionals in cancer care should be trained in listening and communication skills.

B Healthcare professionals in cancer care should consider giving either written summaries or audiotapes of consultations to people who have expressed a preference for them.
13.5 SOURCES OF FURTHER INFORMATION

Many cancer care centres and public libraries have access to the internet. While the internet can provide a vast range of information, patients should be advised to act cautiously as they may not have the means of determining the accuracy or reliability of a site. Healthcare professionals should guide patients to appropriate sites and advise patients that any information found on the internet should be discussed with members of their multidisciplinary team.

3.5.1 ORGANISATIONS SPECIFIC TO CERVICAL CANCER

Jo’s Trust
Weedon Villa, Everdon, Northamptonshire NN11 3BQ
Tel: 01327 341965 • Fax: 01327 349397
www.jotrusted.net • Email: pamela@jotrusted.net
Provides online cervical cancer information and free confidential expert medical advice and support within 12-72 hours.

3.5.2 NATIONAL ORGANISATIONS RELATED TO CANCER

Cancer in Scotland
Scottish Government Health Department, St Andrew’s House, Regent Road, Edinburgh, EH1 3DG
Tel: 0131 244 2364 • Fax: 0131 244 2989
www.show.scot.nhs.uk/sehd/cancerinscotland/ • Email: Cancer@scotland.gsi.gov.uk
Cancer in Scotland identifies the wide range of actions necessary to prevent, detect and improve treatment and care for people with cancer in Scotland.

Cancer Research UK Scotland
Federation House, 222 Queensferry Road, Edinburgh EH4 2BN
Tel: 0131 343 1344
www.cancerresearchuk.org • Email: christine.jason@cancer.org.uk
A free information service for patients with cancer and their families.

Cancer Research UK
PO Box 123, Lincoln’s Inn Fields, London WC2A 3PX
Tel: (Supporter Services) 020 7121 6699 • Tel: (Switchboard) 020 7242 0200
Fax: 020 7121 6700
www.cancerresearchuk.org
A UK based charity dedicated to cancer research, which offers information about all aspects of cancer.

Cancerbackup Scotland
Suite 2, Third Floor, Cranston House, Morrison Court, 104/114 Argyle Street, Glasgow G2 8BH
Tel: 0141 223 7676 • Fax: 0141 248 8422 • Freephone: 0808 800 1234
www.cancerbackup.org.uk
A free one to one service which provides counselling and emotional support for people with cancer and their families and friends. Produces over 60 booklets free of charge.

Macmillan Cancer Support
89 Albert Embankment, London, SE1 7UQ
Cancerline: 0808 808 2020 • Fax: 020 7840 7841
www.macmillan.org.uk • Email: cancerline@macmillan.org.uk
A UK charity which supports people with cancer and their families with specialist information, treatment and care.
Maggie’s provides practical, emotional and social support to people with cancer, their family and friends. Built alongside NHS cancer hospitals and staffed with professional experts, Maggie’s Centres are warm and welcoming, full of light and open space, with a big kitchen table at their heart.

Maggie’s Dundee, Ninewells Hospital, Tom McDonald Avenue, Dundee DD2 1ZV
Tel: 01382 632 999 • Fax: 01382 632998
Email: dundee@maggiescentres.org

Maggie’s Edinburgh, The Stables, Western General Hospital, Crewe Road South, Edinburgh EH6 6AX.
Tel: 0131 537 3131 • Fax: 0131 537 3130
Email: edinburgh@maggiescentres.org

Maggie’s Fife, Victoria Hospital, Kirkcaldy, Fife, KY2 5AH
Tel: 0159 264 3355, ext. 8868 • Fax: 0159 264 8062
Email: ruth@maggiescentres.org

Maggie’s Glasgow, The Gatehouse, Western Infirmary, 10 Dumbarton Road, Glasgow G11 6PA
Tel: 0141 330 3311 • Fax: 0141 330 3363
Email: glasgow@maggiescentres.org

Maggie’s Highlands, Raigmore Hospital, Old Perth Road, Inverness IV2 3UJ
Tel: 01463 706306
Email: highlands@maggiescentres.org

Maggie’s Lanarkshire, c/o Ward 9, Wishaw General, 50 Netherton Street, Wishaw ML2 0DP
Tel: 01698 366 107
Email: mhairi@maggiescentres.org

Marie Curie Cancer Care (Scotland)
29 Albany Street, Edinburgh, EH1 3QN
Tel: 0131 456 3700 • Fax: 0131 456 3701
www.mariecurie.org.uk

Marie Curie Cancer Care, a comprehensive cancer care charity, provides practical nursing care at home and specialist multidisciplinary care through its ten Marie Curie Centres.

Pain Association Scotland
Cramond House, Cramond Glebe Road, Edinburgh EH4 6NS
Tel: 0131 312 7955 • Freephone: 0800 783 6059 • Fax: 0131 312 6007
www.painassociation.com

For all cancer patients suffering from pain. Offers the opportunity for patients and their carers to join support groups.

Tak Tent Cancer Support Scotland
Flat 5, 30 Shelley Court, Gartnavel Complex, Glasgow G12 0YN
Tel: 0141 211 0122 • Fax: 0141 211 0010
www.taktent.org • Email: tak.tent@care4free.net

Promotes the care of cancer patients, their families, friends and the staff involved professionally in cancer care by providing practical and emotional support, information, counselling and therapies as required. Network of local support groups throughout Scotland, including a youth project for 16-25 year olds.
13.5.3 LOCAL ORGANISATIONS RELATED TO CANCER

**Cancer Link Aberdeen and North (CLAN)**
Cancer Support Centre, Clan House, Caroline Place, Aberdeen AB25 2TH
Tel: 01224 647 000 • Freephone: 0800 783 7922• Fax: 01224 640 802
www.clanhouse.org • Email: enquiries@clanhouse.org

Provides emotional support and information through a team of volunteers trained in listening skills; CLAN counsellors, with their personal experience of cancer, provide the opportunity to talk with someone who cares and understands.

**Macmillan Citizens Advice Bureau Partnership**
Raigmore Hospital, Old Perth Road, Inverness, IV2 3UJ
Tel: 01463 706178
Email: macmillan.macmillancab@virgin.net

A service for those living with cancer, their carers and families. It provides advice on many issues including benefits, employment, housing, debt, holiday insurance and community care issues.

**NoSCaN** (North of Scotland cancer network)
Westburn House, Foresterhill, Westburn Road, Aberdeen, AB25 2XG
Tel: 01224 552 745 • Fax: 01224 533 941
www.noscan.scot.nhs.uk • Email: ruth.nisbet@nhs.net

A network of the people in the north of Scotland striving to improve cancer care and improve information to patients, the public and health professionals.

**SCAN** (South East Scotland cancer network)
Deaconess House, 148 The Pleasance, Edinburgh, EH8 9RS
Tel: 0131 536 9304 • Fax: 0131 536 9071
www.scan.scot.nhs.uk • Email: scan@lhb.scot.nhs.uk

Aims to bring together up-to-date, relevant and accurate information about local services for people affected by cancer and healthcare professionals in south east Scotland.

**WoSCAN** (West of Scotland cancer network)
www.woscan.scot.nhs.uk • Email: susan.paton@ggc.scot.nhs.uk

Strives to produce a regional service, which provides equitable access to good quality clinical care for all cancer patients regardless of any geographical or socioeconomic factors.

13.5.4 NATIONAL ORGANISATIONS

**Dipex** (Database of individual experiences)
www.dipex.org

Dipex is a website that reports on a wide variety of personal experiences of health and illness. People can watch, listen to or read interviews, find reliable information on treatment choices and where to find support. The site covers heart disease, epilepsy, screening programmes and cancers.

**Family Planning and Reproductive Health Care**
The Sandyford Initiative, 6 Sandyford Place, Sauchiehall Street, Glasgow G3 7NB
Tel: 0141 211 8130 • Fax: 0141 211 8139
www.sandyford.org/sandyford/pubpages/reproductivehealth/reproductivehealth.html

**Family Planning Association Scotland**
Unit 10, Firhill Business Centre, 76 Firhill Road, Glasgow, G20 7BA
Tel: 0141 576 5088 • Helpline: 0141 576 5088 (Monday to Thursday 9am - 5pm, Friday 9am - 4.30pm)
**Family Planning and Well Woman Services**  
Dean Terrace Clinic, 18 Dean Terrace, Edinburgh, EH4 1NL  
Tel: 0131 332 7941 / 0131 343 6243  
Open: Monday-Thursday: 9.30 am to 7.30 pm; Friday: 9.00 am to 3.30 pm; Saturday: 9.30 am to 12 noon (drop-in clinic for under-25s)

**British Lymphology Society**  
Tracy Hirst-Marsden, Administration Office, British Lymphology Society, PO Box 196, Shoreham, Sevenoaks, Kent TN13 9BF  
Tel: 01959 525524 • Fax: 01959 525524  
www.lymphoedema.org/bls/ • Email: admin@blsac.demon.co.uk  
Aims to promote awareness about lymphoedema to the public and healthcare professionals. Produces guidelines and evidence based standards to underpin treatment for the long term management of lymphoedema.

**Lymphoedema Support Network**  
St Luke’s Crypt, Sydney Street, London, SW3 6NH  
Tel: 020 7351 0990 • Fax: 020 7349 9809 • Helpline: 020 7351 4480  
www.lymphoedema.org/lsn • Email: adminlsn@lymphoedema.freeserve.co.uk  
A national patient-led organisation educating and supporting patients with lymphoedema by providing a high standard of information and promoting self help.

**Samaritans**  
The Upper Mill, Kingston Road, Ewell, Surrey, KT17 2AF  
Tel: 020 8394 8300 • Fax: 020 8394 8301 • Helpline: 08457 90 90 90  
www.samaritans.org.uk • Email: jo@samaritans.org  
Write to: Chris, PO Box 90 90, Stirling, FK8 2SA  
Samaritans is available 24 hours a day to provide confidential emotional support for people who are experiencing feelings of distress or despair, including those which may lead to suicide.

**Well-being of Women**  
27 Sussex Place, Regent’s Park, London, NW1 4SP  
Tel: 020 7772 6400 • Fax: 020 7724 7725  
www.wellbeingofwomen.org.uk • Email: wellbeingofwomen@rcog.org.uk  
Funds research that will translate into patient treatments, increases knowledge amongst experts and publishes widely the outcomes of work funded and improves awareness of obstetric and gynaecological conditions amongst women.

**Women’s Health Concern**  
Women’s Health Concern Ltd, Whitehall House, 41 Whitehall, London, SW1A 2BY  
Helpline: 0845 123 2319 • Fax: 01628 474 042  
www.womens-health-concern.org • Email: info@womens-health-concern.org  
Provides advice through a telephone helpline managed by experienced nurse counsellors, a confidential question-answering service via email and information leaflets and fact sheets on the most common gynaecological conditions.
14 Implementation and recommendations for research

14.1 LOCAL IMPLEMENTATION

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. It is acknowledged that every Board cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

14.1.1 ADVICE TO NHSSCOTLAND FROM THE SCOTTISH MEDICINES CONSORTIUM

The SMC advises that topotecan is accepted for restricted use within NHSScotland in combination with cisplatin for patients with carcinoma of the cervix recurrent after radiotherapy, and for patients with stage IVB disease. It is restricted to patients who are cisplatin-naïve (www.scottishmedicines.org.uk).

Overall survival and progression-free survival are significantly longer for cisplatin plus topotecan compared with cisplatin alone. Topotecan plus cisplatin is cost effective compared to cisplatin alone in cisplatin-naïve patients. The treatment’s cost in relation to its health benefit is not sufficient to be accepted by SMC for use in patients with previous exposure to cisplatin.

14.2 RECOMMENDATIONS FOR RESEARCH

- Only 30% of cervical cancers are screen detected and the majority of cases occur in women who have never had a smear or have not been regular participants in the screening programme. Research is required to explore how to encourage patients who do not attend for screening to take advantage of early detection.
- During radiation treatment of cervical cancer other pelvic organs receive a significant radiation dose resulting in both acute and late toxicity. The management of late radiation complications is complex and requires high quality evidence to guide practice.
- What are the specific support needs of women, who are diagnosed with cervical cancer or who are undergoing treatment, at different stages of their patient journey?
- Research is required on the sexual rehabilitation needs of women following treatment for cervical cancer.
- Compliance with vaginal dilation following pelvic radiotherapy is variable and generally poor. Assistance in overcoming women’s fears and teaching behavioural skills is likely to reduce concerns and improve both knowledge of sexual activity and sexual rehabilitation following pelvic radiotherapy. Research into psychoeducational interventions to aid this is required.
- Less radical forms of surgery for early invasive disease (e.g., cold knife conisation and large loop excision of the transformation zone) need to be evaluated.
- A comparison of ileal loop conduit with other methods of urinary diversion.
- More research is required on the incidence and prevalence of cervical cancer related lymphoedema. Evidence is lacking and studies are not generally comparable due to different patient groups, treatment techniques and lack of standardised reporting of lymphoedema.
Alternative methods of performing post-treatment surveillance. Designing programmes that are more individualised to suit patients’ needs and expectations (including nurse-led follow up compared to hospital-led) are required.

Evaluating the measurement of SCCA after treatment and using elevated levels post-treatment to trigger PET-CT scanning to identify persistent or recurrent disease before it becomes symptomatic.

Evidence is lacking on how to manage malodour. Good quality studies are required to guide practice.
15 Resource implications

This section is based on discussions with the guideline development group regarding current resource use in Scotland and the likely impact of implementing the recommendations made in the guideline. Where current practice will not change as a result of the recommendations it is unlikely there will be resource implications.

15.1 HPV VACCINATION

The introduction of an HPV vaccination programme has a resource implication, but may cause the incidence of cervical cancer to fall in the future, reducing the overall cost of cervical cancer management.

15.2 CROSS-SECTIONAL IMAGING

The use of accurate cross-sectional imaging in staging cervical cancer is more cost effective and less invasive than routine use of FIGO recognised investigations of IVU, barium enemas, cystoscopy and examination under anaesthesia, with cost savings estimated at £1,100 per patient (£2.76 million across the UK, based on UK wide incidence of 2,990 cervical cancer patients annually). It is also a more effective use of the pre-treatment investigative period, without use of day or inpatient beds for anaesthetic/investigative purposes. This strategy should also allow more compliance with government targets of urgent referral by GP to time of treatment of 62 days.

15.3 MRI

The use of MRI in staging is more costly (£144 per patient) and has more limited availability than CT (£101 per patient). The number of patients with invasive carcinoma cervix in 2003 in Scotland was 258 (General Register Office for Scotland; data extracted 2005). This is likely to represent fewer than four patients per week in Scotland requiring initial MRI staging scans, given that stage IA1 disease does not generally require imaging. The diminishing incidence of invasive disease as a result of screening supports the concept of image interpretation by a limited number of experienced radiologists. The Government cancer targets are that patients with initial cancer diagnosis should be imaged within two weeks of referral.

15.4 CT

Patients with clinically advanced FIGO IV disease may be effectively assessed with CT, as this provides more accurate assessment of metastatic spread to lungs, thoracic lymph nodes and other organs not included in routine MRI assessment of pelvis and abdomen. Some patients may require a CT scan following MRI, if unexpected stage IV disease is revealed. This is likely to reflect fewer than six patients per year. The West of Scotland incidence figures for 2005 reported three patients with stage IV disease (available from WoSCAN, see section 13.5.3).

15.5 PET

At the time of publication PET scanning has very limited availability in Scotland. It is likely that the greatest impact of PET in initial staging will be in patients with inoperable FIGO II and III disease. PET scans cannot replace the accuracy of surgical staging as micrometastases in lymph nodes may not be detectable. The detection of possible para-aortic nodal metastases and unexpected distant metastases in patients with inoperable disease may result in changes to the planned radiotherapy fields. While reported sensitivities are variable for detection of metastatic para-aortic nodes with fdg-PET, the alternative gold standard of laparoscopic staging carries significant risk of morbidity and has estimated costs of £1,628-£4,646 per patient compared to approximate NHS costs for PET reported by ISD Scotland and the Scottish Government Health Department of £750. The general reported sensitivity and specificity of fdg-PET still make...
PET imaging a cost-effective alternative to inadequate radiotherapy fields, or inappropriate treatment options.\textsuperscript{83}

False positive results in PET scanning, usually secondary to inflammatory change are recognised, and histological confirmation of metastatic disease is required before implementing a change of treatment.\textsuperscript{65}

The use of fdg-PET in assessing the extent of initial disease extent in patients with FIGO II and III disease would amount to approximately 77 patients annually in Scotland, based on stage at presentation from the West of Scotland incidence figures from 2005, (available from WoSCAN, see section 13.5.3) of 32 patients with FIGO II and III disease extrapolated to the total incidence figures for Scotland (258 patients in 2003). Fewer than 150 patients per year in Scotland will require a nine month PET-CT scan based on these incidence figures.

15.6 CHEST X-RAY
Approximately 30% of women with cervical cancer are screen detected. The majority of these will have operable disease. Not subjecting them to a chest X-ray stops unnecessary exposure to radiation. There will also be a cost saving.

15.7 SQUAMOUS CELL CARCINOMA ANTIGEN
Detection of SCCA is costly and routine post-treatment surveillance costs approx $4,750 per recurrence detected (2001 prices, equivalent to £3,325) with a median of seven samples per patient in a non-selected patient population comprising almost 50% early stage disease.\textsuperscript{87} Routine screening surveillance is not cost effective,\textsuperscript{187} but it may be a cost-effective test in higher risk patients with squamous cell carcinoma to trigger an indication for a PET scan in patients found to have elevated SCCA at pre-treatment assessment. At present this test is not routinely available in the UK.

15.8 SURGERY
As a consequence of the screening programme, in time the incidence of cervical cancer will fall, causing the throughput of patients with operable disease to become too small to maintain the appropriate expertise in some centres.

15.9 CHEMOTHERAPY
The combination of cisplatin and topotecan chemotherapy for palliation of recurrent disease would result in the additional cost of topotecan, of treating a potential increase in the frequency of febrile neutropenia, increased pharmacy preparation time and increased nursing and clinic time administering drugs.

15.10 BRACHYTHErapy
Brachytherapy must be carried out by experienced and skilled practitioners, which will have resource implications for facilities and medical, dosimetry and physics staff.

15.11 SCREENING FOR DISTRESS
Screening for distress, appropriate training to do this, and training in communication skills will all require additional clinician time and funding.
16 Development of the guideline

16.1 INTRODUCTION
SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in “SIGN 50: A Guideline Developer’s Handbook”, available at www.sign.ac.uk

16.2 THE GUIDELINE DEVELOPMENT GROUP

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Ms Anne Williams Cancer Nursing Research Fellow, Napier University, Edinburgh

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive. Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.
16.3 ACKNOWLEDGEMENTS
SIGN is grateful to the following former members of the guideline development group.

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Liaison Radiographer, Glasgow
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Consultant Urologist, Aberdeen Royal Infirmary
Ms Cynthia Tsang  
Medical Student (Year 4), Edinburgh University

16.4 SYSTEMATIC LITERATURE REVIEW
The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer. Databases searched include Medline, Embase, Cinahl, and the Cochrane Library. The year range covered was 1999-2005, although searches for certain questions went back to 1990. Internet searches were carried out on various websites including the New Zealand Guidelines Programme, the Canadian Medical Association, NELH Guidelines Finder, and the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

16.5 CONSULTATION

16.5.1 NATIONAL OPEN MEETING
A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 31st August 2006 and was attended by 130 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

16.5.2 SPECIALIST REVIEW
This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. SIGN is very grateful to all of these experts for their contribution to the guideline.

Dr Mhairi Bender  
General Practitioner, South Beach Surgery, Ardrossan
Dr Esther Black  
Clinical Psychologist in Psychosocial Oncology, Ayrshire Central Hospital, Irvine
Dr Peter Blake  
Consultant Clinical Oncologist, Royal Marsden Hospital, London
Dr Tony Branson  
Consultant Clinical Oncologist, Northern Centre for Cancer Treatment, Newcastle
Dr Laurence Brown  
Consultant Histopathologist and Honorary Senior Lecturer, Leicester Royal Infirmary
Dr Mairi Chong  
General Practitioner, Townhead Practice, Links Health Centre, Montrose
Dr Jo Davis  
Consultant Gynaecological Oncologist, Glasgow Royal Infirmary
As a final quality control check, the guideline was reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers’ comments were addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows:

Dr Keith Brown  
Professor Hillary Capell  
Professor Gordon Lowe  
Dr Safia Qureshi  
Dr Sara Twaddle  

SIGN EDITORIAL GROUP

Royal College of Psychiatrists  
Royal College of Physicians and Surgeons of Glasgow  
Chair of SIGN; Co-Editor  
SIGN Programme Director; Co-Editor  
Director of SIGN; Co-Editor
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5FU</td>
<td>5-fluorouracil</td>
</tr>
<tr>
<td>ACCP</td>
<td>American College of Chest Physicians</td>
</tr>
<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>CIN</td>
<td>cervical intraepithelial neoplasia</td>
</tr>
<tr>
<td>CNS</td>
<td>clinical nurse specialist</td>
</tr>
<tr>
<td>CT</td>
<td>computerised tomography</td>
</tr>
<tr>
<td>DLT</td>
<td>decongestive lymphatic therapy</td>
</tr>
<tr>
<td>DVT</td>
<td>deep venous thrombosis</td>
</tr>
<tr>
<td>fdg-PET</td>
<td>fluorodeoxy glucose positron emission tomography</td>
</tr>
<tr>
<td>FIGO</td>
<td>International Federation of Gynecology and Obstetrics</td>
</tr>
<tr>
<td>GP</td>
<td>general practitioner</td>
</tr>
<tr>
<td>Gy</td>
<td>Gray</td>
</tr>
<tr>
<td>HPV</td>
<td>human papillomavirus</td>
</tr>
<tr>
<td>HR</td>
<td>hazard ratio</td>
</tr>
<tr>
<td>HRT</td>
<td>hormone replacement therapy</td>
</tr>
<tr>
<td>IMB</td>
<td>inter-menstrual bleeding</td>
</tr>
<tr>
<td>ISD</td>
<td>Information Services Division, NHS National Services Scotland</td>
</tr>
<tr>
<td>IVU</td>
<td>intravenous urography</td>
</tr>
<tr>
<td>JCVI</td>
<td>Joint Committee on Vaccination and Immunisation</td>
</tr>
<tr>
<td>LLETZ</td>
<td>large loop excision of the transformation zone</td>
</tr>
<tr>
<td>LMWH</td>
<td>low molecular weight heparin</td>
</tr>
<tr>
<td>LVRH</td>
<td>laparoscopic-vaginal radical hysterectomy</td>
</tr>
<tr>
<td>LVSI</td>
<td>lymphovascular space invasion</td>
</tr>
<tr>
<td>MCN</td>
<td>managed clinical network</td>
</tr>
<tr>
<td>MDT</td>
<td>multidisciplinary team</td>
</tr>
<tr>
<td>MLD</td>
<td>manual lymph drainage</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>MTA</td>
<td>multiple technology appraisal</td>
</tr>
<tr>
<td>NCCN</td>
<td>National Comprehensive Cancer Network</td>
</tr>
<tr>
<td>NHS QIS</td>
<td>NHS Quality Improvement Scotland</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>OR</td>
<td>odds ratio</td>
</tr>
<tr>
<td>PCB</td>
<td>post-coital bleeding</td>
</tr>
<tr>
<td>PCN</td>
<td>percutaneous nephrostomy</td>
</tr>
<tr>
<td>PET</td>
<td>positron emission tomography</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>PET-CT</td>
<td>positron emission tomography-computerised tomography</td>
</tr>
<tr>
<td>PLND</td>
<td>pelvic lymph node dissection</td>
</tr>
<tr>
<td>PMB</td>
<td>post-menopausal bleeding</td>
</tr>
<tr>
<td>PTE</td>
<td>pulmonary thromboembolism</td>
</tr>
<tr>
<td>RH</td>
<td>radical hysterectomy</td>
</tr>
<tr>
<td>RCT</td>
<td>randomised controlled trial</td>
</tr>
<tr>
<td>RR</td>
<td>risk reduction</td>
</tr>
<tr>
<td>SCCA</td>
<td>squamous cell carcinoma antigen</td>
</tr>
<tr>
<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
</tr>
<tr>
<td>SMC</td>
<td>Scottish Medicines Consortium</td>
</tr>
<tr>
<td>TCDO</td>
<td>tetrachlorodecaoxygen</td>
</tr>
<tr>
<td>TPE</td>
<td>total pelvic exenteration</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
</tbody>
</table>
Annex 1

The probability that a woman developing post-coital bleeding in the community has cervical cancer

There is no evidence describing how many women in the community with PCB go on to present to primary care or how many of these women are referred on to secondary care. These probabilities are derived from studies carried out, in part, in secondary care so they may result in a higher positive predictive value for cervical cancer than in women who do not get referred for further investigation.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Annual cumulative incidence of PCB per 100 women (%)</th>
<th>Women with cervical cancer who present with PCB (%)</th>
<th>Annual incidence of cervical cancer in England per 100,000 women</th>
<th>Probability that a woman developing PCB in the community has cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-24</td>
<td>12.6</td>
<td>2.6</td>
<td>1 in 44,000</td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td>7.2</td>
<td>11.7</td>
<td>1 in 56,000</td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>4.8</td>
<td>15.8</td>
<td>1 in 2,800</td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td>3.4</td>
<td>12.7</td>
<td>1 in 2,400</td>
<td></td>
</tr>
</tbody>
</table>
**Annex 2**

Algorithm for the investigation of post-coital bleeding

Women with symptoms suggestive of cervical cancer (e.g., abnormal vaginal bleeding)

- **Clinical suspicion of cancer**
  - **Local cause** (e.g., polyp)
    - Treat or refer to gynaecology
  - **No clinically obvious cancer**
    - **Clinical cancer of the cervix**
      - Refer to gynaecology
  - **Pre-menopausal**
    - Test for *Chlamydia trachomatis*
      - *Chlamydia +ve*
        - Refer to SIGN 42: Management of genital *Chlamydia trachomatis*
        - Treat as appropriate
      - *Chlamydia -ve no local cause*
        - Refer to gynaecology
  - **Post-menopausal**
    - **Refer for a gynaecological investigation**
      - *Chlamydia trachomatis* testing should be done if appropriate

Asymptomatic women attending for cervical screening

- **No clinically obvious cancer**
  - **Clinical cancer of the cervix**
    - Refer to gynaecology

- **Pre-menopausal**
  - Test for *Chlamydia trachomatis*
    - *Chlamydia +ve*
      - Refer to SIGN 42: Management of genital *Chlamydia trachomatis*
      - Treat as appropriate
  - *Chlamydia -ve no local cause*
    - Refer to gynaecology

- **Post-menopausal**
  - **Refer for a gynaecological investigation**
    - *Chlamydia trachomatis* testing should be done if appropriate

- **Annex 2**
  - Algorithm for the investigation of post-coital bleeding

---

*Chlamydia trachomatis* testing should be done if appropriate
### Annex 3

WHO histological classification of tumours of the uterine cervix

<table>
<thead>
<tr>
<th>Epithelial tumours</th>
<th>Squamous tumours and precursors</th>
<th>Mixed epithelial and mesenchymal tumours</th>
<th>Mesenchymal tumours and tumour-like conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcinoma</td>
<td>Endometroid adenocarcinoma</td>
<td>Carcinosarcoma (malignant müllerian mixed tumour)</td>
<td></td>
</tr>
<tr>
<td>Endometroid</td>
<td>Clear cell adenocarcinoma</td>
<td>Adenosarcoma</td>
<td></td>
</tr>
<tr>
<td>adenocarcinoma</td>
<td></td>
<td>Wilm's tumour</td>
<td></td>
</tr>
<tr>
<td>Serous adenocarcinoma</td>
<td></td>
<td>Adenofibroma</td>
<td></td>
</tr>
<tr>
<td>Mesonephric</td>
<td></td>
<td>Adenomyoma</td>
<td></td>
</tr>
<tr>
<td>adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early invasive adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenosquamous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carcinoma variant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glassy cell</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carcinoma variant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoid cystic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carcinoma variant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early invasive (microinvasive) squamous cell carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenofoveal adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocervical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamo transitional</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carcinoma variant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early invasive squamous cell carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocervical</td>
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<td></td>
<td></td>
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<tr>
<td>Intestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamo transitional</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamous cell</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>carcinoma variant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early invasive squamous cell carcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocervical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squamo transitional</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Mixed epithelial and mesenchymal tumours

- Carcinosarcoma (malignant müllerian mixed tumour)
- Adenosarcoma
- Wilm's tumour
- Adenofibroma
- Adenomyoma
- Angiosarcoma
- Malignant peripheral nerve sheath tumour
- Malignant peripheral nerve sheath tumour
- Postoperative spindle cell nodule
Annex 4
National minimum dataset proforma for the histopathological reporting of cervical neoplasia (*see footnote*)

---

### National Minimum Dataset – Cervical Biopsy Histopathology Report

<table>
<thead>
<tr>
<th>Surname</th>
<th>Forenames</th>
<th>Date of birth</th>
<th>Sex</th>
<th>Hospital</th>
<th>Hospital No</th>
<th>NHS No</th>
<th>Date of request</th>
<th>Date of reporting</th>
<th>Report No.</th>
<th>Pathologist</th>
<th>Surgeon</th>
</tr>
</thead>
</table>

#### MACROSCOPY
- Wedge □ Cone □ Loop □ biopsy of cervix measuring .......mm x ....... mm and ....... mm deep
- The cervix was divided into ......... blocks labelled A – .................
- (A) separate fragment(s) labelled ..........., was (were) also received.

#### MICROSCOPY
- Wart virus (HPV) infection | Absent □ Koilocytosis □ HPV-associated features □
- CIN (cervical intra-epithelial neoplasia) | Absent □ Epithelial changes of uncertain significance □
- CIN 1 □ | CIN 2 □ | CIN 3 □
- Endocervical edge | Clear □ | Involved □
- Ectocervical edge | Clear □ | Involved □
- Deep lateral edge | Clear □ | Involved □
- Endocervical epithelium | Normal □ | Low grade CGIN □ | High Grade CGIN □
- Endocervical epithelium at end of canal | Yes □ | No □
- Invasive malignancy | Absent □ Microinvasive □ Squamous cell carcinoma □
- Adenocarcinoma □ | Adenosquamous carcinoma □
- Microinvasive carcinoma, early stromal invasion □
- Microinvasive carcinoma, small confluent tumour □
- Maximum horizontal dimension ....... mm
- Maximum depth of invasion ....... mm
- N.B. If invasive foci are seen in three or more blocks of tissue, the third dimension of the lesion (which is not routinely measured) may exceed 7 mm (i.e. more than Stage IA2).
- Is there lymphovascular space involvement? | Yes □ | No □

#### Comments

**SNOMED codes**
- TB3000 (Cervix) / E3345 (HPV) / M74001 (Koilocytosis) / M74005 (Epithelial changes, uncertain significance)
- *M74008 (CIN 3) / *M74007 (CIN 2) / *M74006 (CIN 1)*
- M80715 (Microinvasive squamous cell carcinoma)
- M80703 (Squamous cell carcinoma) M74009 (CGIN, low or high grade)
- M81402 (Adenocarcinoma *in situ*) / M81403 (Adenocarcinoma)

---

Signature .................................................. Date ............. / ............. / .............

---

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## Annex 4 (continued)
National minimum dataset proforma for the histopathological reporting of cervical neoplasia (see footnote)\(^{38}\)

<table>
<thead>
<tr>
<th>Gross description</th>
<th>Dimensions of uterus: Length ..........mm Transverse ......mm Antero-posterior,......mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal cuff</td>
<td>Present □ Absent □ Length ......mm</td>
</tr>
<tr>
<td>Maximum dimensions of tumour: ...........mm</td>
<td></td>
</tr>
</tbody>
</table>

### Histology

<table>
<thead>
<tr>
<th>Type</th>
<th>squamous carcinoma □ adenocarcinoma □ adenosquamos □ other (please specify) .................................................................</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histological differentiation:</td>
<td>Well □ Moderate □ Poor □</td>
</tr>
<tr>
<td>Tumour size:</td>
<td>maximum horizontal dimension ......mm depth of invasion ......mm distance from closest resection margin (minimum tumour-free rim) ......mm position of this ..........................</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Paracervical involvement:</th>
<th>Yes □ No □</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parametrical involvement:</td>
<td>Yes □ No □</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymphovascular invasion:</th>
<th>Present □ Absent □</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>CIN:</th>
<th>Present □ Grade (please circle) 1 2 3 Absent □</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGIN:</td>
<td>Present □ Grade (please circle) High Low Absent □</td>
</tr>
</tbody>
</table>

### Pelvic nodes

<table>
<thead>
<tr>
<th>Pelvic nodes right left</th>
<th>Common iliac nodes right left</th>
</tr>
</thead>
<tbody>
<tr>
<td>total number of nodes retrieved</td>
<td>total number of nodes retrieved</td>
</tr>
<tr>
<td>lymph nodes with tumour deposits</td>
<td>lymph nodes with tumour deposits</td>
</tr>
<tr>
<td>Extramodal spread Yes □ No □</td>
<td>Yes □ No □</td>
</tr>
</tbody>
</table>

### Para-aortic nodes:

<table>
<thead>
<tr>
<th>Extramodal spread:</th>
<th>not sampled □ positive □ negative □</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Endometrium:</th>
<th>Normal □ Abnormal (please state) ............................................</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myometrum:</td>
<td>Normal □ Abnormal (please state) ............................................</td>
</tr>
<tr>
<td>Right ovary/tube:</td>
<td>Normal □ Abnormal (please state) ............................................</td>
</tr>
<tr>
<td>Left ovary/tube:</td>
<td>Normal □ Abnormal (please state) ............................................</td>
</tr>
</tbody>
</table>

### Comments

<table>
<thead>
<tr>
<th>SNOMED codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>T83000 (Cervix)</td>
</tr>
<tr>
<td>T08000 (Lymph node)</td>
</tr>
<tr>
<td>M80706 (Metastatic squamous carcinoma)</td>
</tr>
</tbody>
</table>

Signature .................................................... Date............./ ............./ .............
## Annex 5

**FIGO staging classification for cancer of the cervix uteri**

<table>
<thead>
<tr>
<th>FIGO stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Carcinoma in situ (pre-invasive carcinoma)</td>
</tr>
<tr>
<td>I</td>
<td>Cervical carcinoma confined to uterus (extension to corpus should be disregarded)</td>
</tr>
<tr>
<td>IA</td>
<td>Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions – even with superficial invasion – are stage IB</td>
</tr>
<tr>
<td>IA1</td>
<td>Stromal invasion no greater than 3.0 mm in depth and 7.0 mm or less in horizontal spread</td>
</tr>
<tr>
<td>IA2</td>
<td>Stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread 7.0 mm or less$^a$</td>
</tr>
<tr>
<td>IB</td>
<td>Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2</td>
</tr>
<tr>
<td>IB1</td>
<td>Clinically visible lesion 4.0 cm or less in greatest dimension</td>
</tr>
<tr>
<td>IB2</td>
<td>Clinically visible lesion more than 4.0 cm in greatest dimension</td>
</tr>
<tr>
<td>II</td>
<td>Tumour invades beyond the uterus but not to pelvic wall or to lower third of the vagina</td>
</tr>
<tr>
<td>IIA</td>
<td>Without parametrial invasion</td>
</tr>
<tr>
<td>IIB</td>
<td>With parametrial invasion</td>
</tr>
<tr>
<td>III</td>
<td>Tumour extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis or non-functioning kidney</td>
</tr>
<tr>
<td>IIIA</td>
<td>Tumour involves lower third of vagina no extension to pelvic wall</td>
</tr>
<tr>
<td>IIIB</td>
<td>Tumour extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney</td>
</tr>
<tr>
<td>IVA</td>
<td>Tumour invades mucosa of bladder or rectum and/or extends beyond true pelvis$^b$</td>
</tr>
<tr>
<td>IVB</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

$a$: The depth of invasion should not be more than 5 mm taken from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumour from the epithelial-stromal junction of the adjacent most superficial epithelial papilla to the deepest point of invasion. Vascular space involvement, venous or lymphatic, does not affect classification.

$b$: The presence of bullous oedema is not sufficient to classify a tumour as stage IV.
Annex 6
Staging criteria for lymphoedema

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Subclinical stage, where swelling is not evident but lymphatic damage has occurred.</td>
</tr>
<tr>
<td>1</td>
<td>Early onset of oedema that subsides with elevation.</td>
</tr>
<tr>
<td>2</td>
<td>Pitting oedema that does not subside on elevation.</td>
</tr>
<tr>
<td>3</td>
<td>Oedema with fibrotic changes.</td>
</tr>
<tr>
<td>4</td>
<td>Skin and tissue changes including thickening, skin folds, fat deposits and warty overgrowths.</td>
</tr>
</tbody>
</table>
Annex 7
Algorithm of imaging to detect relapsed disease

Cervical cancer treated with chemoradiotherapy

- asymptomatic
- PET-CT scan at nine months.

- symptomatic
- MRI or CT should be considered to assess potential clinical recurrence.

Consider for salvage therapy

- Pelvic MRI should be considered for surgical planning if pelvic exenteration appropriate.
- Whole body PET scan or PET-CT for all patients with recurrent or persistent disease demonstrated on MRI or CT.
Annex 8
Algorithm for management of renal failure in patients with cervical cancer (adapted from Ganatra et al)\textsuperscript{212}

Identify obstructive uropathy

- Investigations should be performed to exclude additional treatable causes of renal failure
- There should be a careful assessment of results of the investigations and discussion with the patient

**bladder outlet obstruction**
- urethral catheter
- suprapubic catheter
- debulking therapy

**ureteric obstruction**
- no treatment
- PCN
- retrograde stent

Unsuccessful
- PCN and attempt antegrade stent
- More frequent changes or alternative stents
- Change stent every 3-4 months

Successful
- Urinary diversion may be considered in suitable patients
Annex 9
Screening tool for measuring distress (see footnote)\(^\text{236}\)

Instructions: First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.

Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.

- Child care
- Housing
- Insurance/financial
- Transportation
- Work/school
- Dealing with children
- Dealing with partner
- Depression
- Fears
- Nervousness
- Sadness
- Worry
- Loss of interest in usual activities
- Appearance
- Bathing/dressing
- Breathing
- Changes in urination
- Constipation
- Diarrhea
- Eating
- Fatigue
- Feeling swollen
- Fevers
- Getting around
- Indigestion
- Memory/concentration
- Mouth sores
- Nausea
- Nose dry/congested
- Pain
- Sexual
- Skin dry/itchy
- Sleep
- Tingling in hands/feet

Other Problems:

Screening tools for measuring distress

Extreme distress

No distress

---


“These Guidelines are a work in progress that will be refined as often as new significant data becomes available. The NCCN Guidelines are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN guideline is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. These Guidelines are copyrighted by the National Comprehensive Cancer Network. All rights reserved. These Guidelines and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN.”
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260. Fellowes D, Wilkinson S, Moore P. Communication skills training for health care professionals working with cancer patients, their families and/or carers. Cochrane Database of Systematic Reviews 2004, Issue 2.

ALGORITHM FOR THE INVESTIGATION OF POST-COITAL BLEEDING

Women with symptoms suggestive of cervical cancer eg abnormal vaginal bleeding

Clinical suspicion of cancer

Local cause (eg polyp)

Treat or refer to gynaecology

No clinically obvious cancer

Pre-menopausal

Test for *Chlamydia trachomatis*

Chlamydia +ve

Refer to gynaecology

Chlamydia -ve no local cause

Post-menopausal

Clinical cancer of the cervix

D Refer for a gynaecological investigation

*Chlamydia trachomatis* testing should be done if appropriate

D Refer to SIGN 62:
Investigation of post-menopausal bleeding

Include visual inspection of cervix

Asymptomatic women attending for cervical screening

Refer to SIGN 42:
Management of genital *Chlamydia trachomatis*

Treat as appropriate

Asymptomatic women attending for cervical screening

Refer to SIGN 42:
Management of genital *Chlamydia trachomatis*

Treat as appropriate

Asymptomatic women attending for cervical screening

Refer to SIGN 42:
Management of genital *Chlamydia trachomatis*

Treat as appropriate