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Referral guidelines for suspected cancer

Clinical Guideline 27
Developed by the National Collaborating Centre for Primary Care

Clinical Guideline 27
Referral guidelines for suspected cancer

Ordering information
You can download the following documents from www.nice.org.uk/CG027

- The NICE guideline (this document) – all the recommendations.
- Information for people being referred for cancer, their families and carers, and the public.
- The full guideline – all the recommendations, details of how they were developed, and summaries of the evidence on which they were based.

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Contents

Background

This guideline is an update of the guideline entitled ‘Referral guidelines for suspected cancer’ published by the Department of Health in 2000. The new guideline takes account of new research evidence and the findings of audits undertaken since the publication of the previous guideline. The recommendations made here supersede those in the earlier guideline.

Patient-centred care

This guideline offers best practice advice on referral for suspected cancer in adults and children.

Treatment and care should take into account patients’ individual needs and preferences. People being referred for suspected cancer should have the opportunity to make informed decisions about their care and treatment. Where patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – *Reference guide to consent for examination or treatment* (2001)

Good communication between healthcare professionals and patients is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.

Unless specifically excluded by the patient, carers and relatives should have the opportunity to be involved in decisions about the patient’s care and treatment.

Carers and relatives should also be provided with the information and support they need.

Referral timelines

The referral timelines used in this guideline are as follows:

- **immediate**: an acute admission or referral occurring within a few hours, or even more quickly if necessary
- **urgent**: the patient is seen within the national target for urgent referrals (currently 2 weeks)
- **non-urgent**: all other referrals.

Definitions

Unexplained

When used in a recommendation, 'unexplained' refers to a symptom(s) and/or sign(s) that has not led to a diagnosis being made by the primary care professional after initial assessment of the history, examination and primary care investigations (if any).

Persistent

'Persistent' as used in the recommendations in this guideline refers to the continuation of specified symptoms and/or signs beyond a period that would normally be associated with self-limiting problems. The precise period will vary depending on the severity of symptoms and associated features, as assessed by the healthcare professional. In many cases, the upper limit the professional will permit symptoms and/or signs to persist before initiating referral will be 4–6 weeks.

Key priorities for implementation

Making a diagnosis

- Diagnosis of any cancer on clinical grounds alone can be difficult. Primary healthcare professionals should be familiar with the typical presenting features of cancers, and be able to readily identify these features when patients consult with them.

- Primary healthcare professionals must be alert to the possibility of cancer when confronted by unusual symptom patterns or when patients who are thought not to have cancer fail to recover as expected. In such circumstances, the primary healthcare professional should systematically review the patient's history and examination, and refer urgently if cancer is a possibility.

- Discussion with a specialist should be considered if there is uncertainty about the interpretation of symptoms and signs, and whether a referral is needed. This may also enable the primary healthcare professional to communicate their concerns and a sense of urgency to secondary healthcare professionals when symptoms are not classical.

- Cancer is uncommon in children, and its detection can present particular difficulties. Primary healthcare professionals should recognise that parents are usually the best observers of their children, and should listen carefully to their concerns. Primary healthcare professionals should also be willing to reassess the initial diagnosis or to seek a second opinion from a colleague if a child fails to recover as expected.

Investigations

- In patients with features typical of cancer, investigations in primary care should not be allowed to delay referral. In patients with less typical symptoms and signs that might, nevertheless, be due to cancer,

investigations may be necessary but should be undertaken urgently to avoid delay. If specific investigations are not readily available locally, an urgent specialist referral should be made.

The need for support and information

- When referring a patient with suspected cancer to a specialist service, primary healthcare professionals should assess the patient's need for continuing support while waiting for their referral appointment. The information given to patients, family and/or carers as considered appropriate by the primary healthcare professional should cover, among other issues:

    - where patients are being referred to
    - how long they will have to wait for the appointment
    - how to obtain further information about the type of cancer suspected or help prior to the specialist appointment
    - who they will be seen by
    - what to expect from the service the patient will be attending
    - what type of tests will be carried out, and what will happen during diagnostic procedures
    - how long it will take to get a diagnosis or test results
    - whether they can take someone with them to the appointment
    - other sources of support, including those for minority groups.

- The primary healthcare professional should be aware that some patients find being referred for suspected cancer particularly difficult because of their personal circumstances, such as age, family or work responsibilities, isolation, or other health or social issues.

- Primary healthcare professionals should provide culturally appropriate care, recognising the potential for different cultural meanings associated with the possibility of cancer, the relative importance of family decision-making and possible unfamiliarity with the concept of support outside the family.

Continuing education for healthcare professionals

- Primary healthcare professionals should take part in education, peer review and other activities to improve or maintain their clinical consulting, reasoning and diagnostic skills, in order to identify, at an early stage, patients who may have cancer, and to communicate the possibility of cancer to the patient. Current advice on communicating with patients and/or their carers and breaking bad news[1] should be followed.

The following guidance is based on the best available evidence and expert opinion. Appendix A shows the grading scheme used for the recommendations: A, B, C, D. Recommendations on diagnostic tests are graded A(DS), B(DS), C(DS) or D(DS). A summary of the evidence on which the guidance is based is provided in the full guideline (see Section 5).

[1] *Improving communication between doctors and patients*. A report of the working party of the Royal College of Physicians (1997) www.rcplondon.ac.uk/pubs/brochures/pub_print_icbdp

1 Guidance

1.1 Support and information needs of people with suspected cancer

1.1.1 Patients should be able to consult a primary healthcare professional of the same sex if preferred. **D**

1.1.2 Primary healthcare professionals should discuss with patients (and carers as appropriate, taking account of the need for confidentiality) their preferences for being involved in decision-making about referral options and further investigations (including their potential risks and benefits), and ensure they have the time for this. **D**

1.1.3 When cancer is suspected in a child, the referral decision and information to be given to the child should be discussed with the parents or carers (and the patient if appropriate). **D**

1.1.4 Adult patients who are being referred with suspected cancer should normally be told by the primary healthcare professional that they are being referred to a cancer service, but if appropriate they should be reassured that most people referred will not have a diagnosis of cancer, and alternative diagnoses should be discussed. **D**

1.1.5 Primary healthcare professionals should be willing and able to give the patient information on the possible diagnosis (both benign and malignant) in accordance with the patient's wishes for information. Current advice on communicating with patients and/or their carers and breaking bad news[2] should be followed. **D**

1.1.6 The information given to patients, family and/or carers as appropriate by the primary healthcare professional should cover, among other issues: **D**

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[2] *Improving communication between doctors and patients*. A report of the working party of the Royal College of Physicians (1997) www.rcplondon.ac.uk/pubs/brochures/pub_print_icbdp

- where patients are being referred to
- how long they will have to wait for the appointment
- how to obtain further information about the type of cancer suspected or help prior to the specialist appointment
- who they will be seen by
- what to expect from the service the patient will be attending
- what type of tests will be carried out, and what will happen during diagnostic procedures
- how long it will take to get a diagnosis or test results
- whether they can take someone with them to the appointment
- other sources of support, including those for minority groups.

1.1.7 When referring a patient with suspected cancer to a specialist service, primary healthcare professionals should assess the patient's need for continuing support while waiting for their referral appointment. This should include inviting the patient to contact the primary healthcare professional again if they have more concerns or questions before they see a specialist. **D**

1.1.8 Consideration should be given by the primary healthcare professional to meeting the information and support needs of parents and carers. Consideration should also be given to meeting these particular needs for the people for whom they care, such as children and young people, and people with special needs (for instance, people with learning disabilities or sensory impairment). **D**

1.1.9 The primary healthcare professional should be aware that some patients find being referred for suspected cancer particularly difficult because of their personal circumstances, such as age, family or work responsibilities, isolation, or other health or social issues. **D**

1.1.10 Primary healthcare professionals should provide culturally appropriate care, recognising the potential for different cultural meanings associated with the possibility of cancer, the relative importance of family decision-making and possible unfamiliarity with the concept of support outside the family. **D**

1.1.11 The primary healthcare professional should be aware that men may have similar support needs to women but may be more reticent about using support services. **D**

1.1.12 If the patient has additional support needs because of their personal circumstances, the specialist should be informed (with the patient's agreement). **D**

1.1.13 All members of the primary healthcare team should have available to them information in a variety of formats on both local and national sources of additional support for patients who are being referred with suspected cancer. **D**

1.1.14 In situations where diagnosis or referral has been delayed, or there is significant compromise of the doctor/patient relationship, the primary healthcare professional should take care to assess the information and support needs of the patient, parents and carers, and make sure these needs are met. The patient should be given the opportunity to consult another primary healthcare professional if they wish. **D**

1.1.15 Primary healthcare professionals should promote awareness of key presenting features of cancer when appropriate. **D**

1.2 The diagnostic process

1.2.1 Diagnosis of any cancer on clinical grounds alone can be difficult. Primary healthcare professionals should be familiar with the typical presenting features of cancers, and be able to readily identify these features when patients consult with them. **D**

1.2.2 Cancers usually present with symptoms commonly associated with benign conditions. The primary healthcare professional should be ready to review the initial diagnosis in patients in whom common symptoms do not resolve as expected. **D**

1.2.3 Primary healthcare professionals must be alert to the possibility of cancer when confronted by unusual symptom patterns or when patients thought not to have cancer fail to recover as expected. In

such circumstances, the primary healthcare professional should systematically review the patient's history and examination, and refer urgently if cancer is a possibility. **D**

1.2.4 Cancer is uncommon in children, and its detection can present particular difficulties. Primary healthcare professionals should recognise that parents are usually the best observers of their children, and should listen carefully to their concerns. Primary healthcare professionals should also be willing to reassess the initial diagnosis or to seek a second opinion from a colleague if a child fails to recover as expected. **D**

1.2.5 Primary healthcare professionals should take part in continuing education, peer review and other activities to improve and maintain their clinical consulting, reasoning and diagnostic skills, in order to identify at an early stage patients who may have cancer, and to communicate the possibility of cancer to the patient. **C**

1.2.6 Discussion with a specialist should be considered if there is uncertainty about the interpretation of symptoms and signs, and whether a referral is needed. This may also enable the primary healthcare professional to communicate their concerns and a sense of urgency to secondary healthcare professionals when symptoms are not classical (for example, by telephone or email). **D**

1.2.7 There should be local arrangements in place to ensure that letters about non-urgent referrals are assessed by the specialist, the patient being seen more urgently if necessary. **D**

1.2.8 There should be local arrangements in place to ensure a maximum waiting period for non-urgent referrals, in accordance with national targets and local arrangements. **D**

1.2.9 There should be local arrangements in place to identify those patients who miss their appointments so that they can be followed up. **D**

1.2.10 The primary healthcare professional should include all appropriate information in referral correspondence, including whether the referral is urgent or non-urgent. **D**

1.2.11 The primary healthcare professional should use local referral proformas if these are in use. **D**

1.2.12 Once the decision to refer has been made, the primary healthcare professional should make sure that the referral is made within 1 working day. **D**

1.2.13 A patient who presents with symptoms suggestive of cancer should be referred by the primary healthcare professional to a team specialising in the management of the particular type of cancer, depending on local arrangements. **D**

1.2.14 In patients with features typical of cancer, investigations in primary care should not be allowed to delay referral. In patients with less typical symptoms and signs that might, nevertheless, be due to cancer, investigations may be necessary, but should be undertaken urgently to avoid delay. If specific investigations are not readily available locally, an urgent specialist referral should be made. **D**

1.3 Lung cancer

General recommendations

1.3.1 A patient who presents with symptoms suggestive of lung cancer should be referred to a team specialising in the management of lung cancer, depending on local arrangements. **D**

Specific recommendations

1.3.2 An urgent referral for a chest X-ray should be made when a patient presents with:

- haemoptysis, or
- any of the following unexplained persistent (that is, lasting more than 3 weeks) symptoms and signs:
  - chest and/or shoulder pain
  - dyspnoea
  - weight loss
  - chest signs
  - hoarseness
  - finger clubbing
  - cervical and/or supraclavicular lymphadenopathy
  - cough with or without any of the above
  - features suggestive of metastasis from a lung cancer (for example, in brain, bone, liver or skin).

A report should be made back to the referring primary healthcare professional within 5 days of referral. **D**

1.3.3 An urgent referral should be made for either of the following: **D**

- persistent haemoptysis in smokers or ex-smokers who are aged 40 years and older
- a chest X-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation).

1.3.4 Immediate referral should be considered for the following: **D**

- signs of superior vena caval obstruction (swelling of the face and/or neck with fixed elevation of jugular venous pressure)
- stridor.

Risk factors

1.3.5 Patients in the following categories have a higher risk of developing lung cancer:

- are current or ex-smokers
- have smoking-related chronic obstructive pulmonary disease (COPD)
- have been exposed to asbestos
- have had a previous history of cancer (especially head and neck).

An urgent referral for a chest X-ray or to a team specialising in the management of lung cancer should be made as for other patients (see 1.3.1 above) but may be considered sooner, for example if symptoms or signs have lasted for less than 3 weeks. **C**

Investigations

1.3.6 Unexplained changes in existing symptoms in patients with underlying chronic respiratory problems should prompt an urgent referral for chest X-ray. **D**

1.3.7 If the chest X-ray is normal, but there is a high suspicion of lung cancer, patients should be offered an urgent referral. **D**

1.3.8 In individuals with a history of asbestos exposure and recent onset of chest pain, shortness of breath or unexplained systemic symptoms, lung cancer should be considered and a chest X-ray arranged. If this indicates a pleural effusion, pleural mass or any suspicious lung pathology, an urgent referral should be made. **C**

1.4 Upper gastrointestinal cancer

General recommendations

1.4.1 A patient who presents with symptoms suggestive of upper gastrointestinal cancer should be referred to a team specialising in the management of upper gastrointestinal cancer, depending on local arrangements. **D**

Specific recommendations

1.4.2 An urgent referral for endoscopy or to a specialist with expertise in upper gastrointestinal cancer should be made for patients of any age with dyspepsia[3] who present with any of the following: **C**

- chronic gastrointestinal bleeding
- dysphagia
- progressive unintentional weight loss
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal result.

1.4.3 In patients aged 55 years and older with unexplained[4] and persistent recent-onset dyspepsia alone, an urgent referral for endoscopy should be made. **D**

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[3] The definition of dyspepsia is taken from the NICE guideline on *Dyspepsia: management of dyspepsia in adults in primary care* (www.nice.org.uk/CG017). Dyspepsia in unselected patients in primary care is defined broadly to include patients with recurrent epigastric pain, heartburn or acid regurgitation, with or without bloating, nausea or vomiting.

[4] In this guideline, unexplained is defined as 'a symptom(s) and/or sign(s) that has not led to a diagnosis being made by the primary care professional after initial assessment of the history, examination and primary care investigations (if any)'. In the context of this recommendation, the primary care professional should confirm that the dyspepsia is new rather than a recurrent episode and exclude common precipitants of dyspepsia such as ingestion of NSAIDs.

1.4.4 In patients aged less than 55 years, endoscopic investigation of dyspepsia is not necessary in the absence of alarm symptoms. **D**

1.4.5 In patients presenting with dysphagia (interference with the swallowing mechanism that occurs within 5 seconds of having commenced the swallowing process), an urgent referral should be made. **C**

1.4.6 *Helicobacter pylori* status should not affect the decision to refer for suspected cancer. **C**

1.4.7 In patients without dyspepsia, but with unexplained weight loss or iron deficiency anaemia, the possibility of upper gastrointestinal cancer should be recognised and an urgent referral for further investigation considered. **C**

1.4.8 In patients with persistent vomiting and weight loss in the absence of dyspepsia, upper gastro-oesophageal cancer should be considered and, if appropriate, an urgent referral should be made. **C**

1.4.9 An urgent referral should be made for patients presenting with either: **C**

- unexplained upper abdominal pain and weight loss, with or without back pain, or
- an upper abdominal mass without dyspepsia.

1.4.10 In patients with obstructive jaundice an urgent referral should be made, depending on the patient's clinical state. An urgent ultrasound investigation may be considered if available. **C**

Risk factors

1.4.11 In patients with unexplained worsening of their dyspepsia, an urgent referral should be considered if they have any of the following known risk factors: **C**

- Barrett's oesophagus
- known dysplasia, atrophic gastritis or intestinal metaplasia

- peptic ulcer surgery more than 20 years ago.

Investigations

1.4.12 Patients being referred urgently for endoscopy should ideally be free from acid suppression medication, including proton pump inhibitors or H_2 receptor antagonists, for a minimum of 2 weeks. **C**

1.4.13 In patients where the decision to refer has been made, a full blood count may assist specialist assessment in the outpatient clinic. This should be carried out in accordance with local arrangements. **D**

1.4.14 All patients with new-onset dyspepsia should be considered for a full blood count in order to detect iron deficiency anaemia. **D**

1.5 Lower gastrointestinal cancer

General recommendations

1.5.1 A patient who presents with symptoms suggestive of colorectal or anal cancer should be referred to a team specialising in the management of lower gastrointestinal cancer, depending on local arrangements. **D**

1.5.2 In patients with equivocal symptoms who are not unduly anxious, it is reasonable to use a period of 'treat, watch and wait' as a method of management. **D**

1.5.3 In patients with unexplained symptoms related to the lower gastrointestinal tract, a digital rectal examination should always be carried out, provided this is acceptable to the patient. **C**

Specific recommendations

1.5.4 In patients aged 40 years and older, reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more, an urgent referral should be made. **C**

1.5.5 In patients aged 60 years and older, with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms, an urgent referral should be made. **C**

1.5.6 In patients aged 60 years and older, with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding, an urgent referral should be made. **C**

1.5.7 In patients presenting with a right lower abdominal mass consistent with involvement of the large bowel, an urgent referral should be made, irrespective of age. **C**

1.5.8 In patients presenting with a palpable rectal mass (intraluminal and not pelvic), an urgent referral should be made, irrespective of age.

(A pelvic mass outside the bowel would warrant an urgent referral to a urologist or gynaecologist.) **C**

1.5.9 In men of any age with unexplained iron deficiency anaemia and a haemoglobin of 11 g/100 ml or below, an urgent referral should be made.[5] **C**

1.5.10 In non-menstruating women with unexplained iron deficiency anaemia and a haemoglobin of 10 g/100 ml or below, an urgent referral should be made.[4] **C**

Risk factors

1.5.11 In patients with ulcerative colitis or a history of ulcerative colitis, a plan for follow-up should be agreed with a specialist and offered to the patient as a normal procedure in an effort to detect colorectal cancer in this high-risk group. **C**

1.5.12 There is insufficient evidence to suggest that a positive family history of colorectal cancer can be used as a criterion to assist in the decision about referral of a symptomatic patient. **C**

Investigations

1.5.13 In patients with equivocal symptoms, a full blood count may help in identifying the possibility of colorectal cancer by demonstrating iron deficiency anaemia, which should then determine if a referral should be made and its urgency. **C (DS)**

1.5.14 In patients for whom the decision to refer has been made, a full blood count may assist specialist assessment in the outpatient clinic. This should be in accordance with local arrangements. **D**

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[5] In this guideline, unexplained is defined as 'a symptom(s) and/or sign(s) that has not led to a diagnosis being made by the primary care professional after initial assessment of the history, examination and primary care investigations (if any)'. In the context of this recommendation, unexplained means a patient whose anaemia is considered on the basis of a history and examination in primary care not to be related to other sources of blood loss (for example, ingestion of NSAIDs) or blood dyscrasia.

1.5.15 In patients for whom the decision to refer has been made, no examinations or investigations other than those referred to earlier (abdominal and rectal examination, full blood count) are recommended as this may delay referral. **D**

1.6 Breast cancer

General recommendations

1.6.1 A patient who presents with symptoms suggestive of breast cancer should be referred to a team specialising in the management of breast cancer. **D**

1.6.2 In most cases, the definitive diagnosis will not be known at the time of referral, and many patients who are referred will be found not to have cancer. However, primary healthcare professionals should convey optimism about the effectiveness of treatment and survival because a patient being referred with a breast lump will be naturally concerned. **C**

1.6.3 People of all ages who suspect they have breast cancer may have particular information and support needs. The primary healthcare professional should discuss these needs with the patient and respond sensitively to them. **D**

1.6.4 Primary healthcare professionals should encourage all patients, including women over 50 years old, to be breast aware[6] in order to minimise delay in the presentation of symptoms. **D**

Specific recommendations

1.6.5 A woman's first suspicion that she may have breast cancer is often when she finds a lump in her breast. The primary healthcare professional should examine the lump with the patient's consent. The features of a lump that should make the primary healthcare professional strongly suspect cancer are a discrete, hard lump with

[6] Breast awareness means the woman knows what her breasts look and feel like normally. Evidence suggests that there is no need to follow a specific or detailed routine such as breast self examination, but women should be aware of any changes in their breasts (see http://cancerscreening.org.uk/breastscreen/breastawareness for further information).

fixation, with or without skin tethering. In patients presenting in this way an urgent referral should be made, irrespective of age. **C**

1.6.6 In a woman aged 30 years and older with a discrete lump that persists after her next period, or presents after menopause, an urgent referral should be made. **C**

1.6.7 Breast cancer in women aged younger than 30 years is rare, but does occur. Benign lumps (for example, fibroadenoma) are common, however, and a policy of referring these women urgently would not be appropriate; instead, non-urgent referral should be considered. However, in women aged younger than 30 years:

- with a lump that enlarges, **C** or
- with a lump that has other features associated with cancer (fixed and hard), **C** or
- in whom there are other reasons for concern such as family history[7] **D**

an urgent referral should be made.

1.6.8 The patient's history should always be taken into account. For example, it may be appropriate, in discussion with a specialist, to agree referral within a few days in patients reporting a lump or other symptom that has been present for several months. **D**

1.6.9 In a patient who has previously had histologically confirmed breast cancer, who presents with a further lump or suspicious symptoms, an urgent referral should be made, irrespective of age. **C**

1.6.10 In patients presenting with unilateral eczematous skin or nipple change that does not respond to topical treatment, or with nipple distortion of recent onset, an urgent referral should be made. **C**

1.6.11 In patients presenting with spontaneous unilateral bloody nipple discharge, an urgent referral should be made. **C**

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[7] National Institute for Clinical Excellence (2004) Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. *NICE Clinical Guideline* No. 14. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk/CG014

1.6.12 Breast cancer in men is rare and is particularly rare in men under 50 years of age. However, in a man aged 50 years and older with a unilateral, firm subareolar mass with or without nipple distortion or associated skin changes, an urgent referral should be made. **C**

Investigations

1.6.13 In patients presenting with symptoms and/or signs suggestive of breast cancer, investigation prior to referral is not recommended. **D**

1.6.14 In patients presenting solely with breast pain, with no palpable abnormality, there is no evidence to support the use of mammography as a discriminatory investigation for breast cancer. Therefore, its use in this group of patients is not recommended. Non-urgent referral may be considered in the event of failure of initial treatment and/or unexplained persistent symptoms. **B (DS)**

1.7 Gynaecological cancer

General recommendations

1.7.1 A patient who presents with symptoms suggesting gynaecological cancer should be referred to a team specialising in the management of gynaecological cancer, depending on local arrangements. **D**

Specific recommendations

1.7.2 The first symptoms of gynaecological cancer may be alterations in the menstrual cycle, intermenstrual bleeding, postcoital bleeding, postmenopausal bleeding or vaginal discharge. When a patient presents with any of these symptoms, the primary healthcare professional should undertake a full pelvic examination, including speculum examination of the cervix. **C**

1.7.3 In patients found on examination of the cervix to have clinical features that raise the suspicion of cervical cancer, an urgent referral should be made. A cervical smear test is not required before referral, and a previous negative cervical smear result is not a reason to delay referral. **C**

1.7.4 Ovarian cancer is particularly difficult to diagnose on clinical grounds as the presentation may be with vague, non-specific abdominal symptoms alone (bloating, constipation, abdominal or back pain, urinary symptoms). In a woman presenting with any unexplained abdominal or urinary symptoms, abdominal palpation should be carried out. If there is significant concern, a pelvic examination should be considered if appropriate and acceptable to the patient. **D**

1.7.5 Any woman with a palpable abdominal or pelvic mass on examination that is not obviously uterine fibroids or not of gastrointestinal or urological origin should have an urgent

ultrasound scan. If the scan is suggestive of cancer, or if ultrasound is not available, an urgent referral should be made. **C**

1.7.6 When a woman who is not on hormone replacement therapy presents with postmenopausal bleeding, an urgent referral should be made. **C**

1.7.7 When a woman on hormone replacement therapy presents with persistent or unexplained postmenopausal bleeding after cessation of hormone replacement therapy for 6 weeks, an urgent referral should be made. **C**

1.7.8 Tamoxifen can increase the risk of endometrial cancer. When a woman taking tamoxifen presents with postmenopausal bleeding, an urgent referral should be made. **C**

1.7.9 An urgent referral should be considered in a patient with persistent intermenstrual bleeding and a negative pelvic examination. **D**

Vulval cancer

1.7.10 When a woman presents with vulval symptoms, a vulval examination should be offered. If an unexplained vulval lump is found, an urgent referral should be made. **C**

1.7.11 Vulval cancer can also present with vulval bleeding due to ulceration. A patient with these features should be referred urgently. **D**

1.7.12 Vulval cancer may also present with pruritus or pain. For a patient who presents with these symptoms, it is reasonable to use a period of 'treat, watch and wait' as a method of management. But this should include active follow-up until symptoms resolve or a diagnosis is confirmed. If symptoms persist, the referral may be urgent or non-urgent, depending on the symptoms and the degree of concern about cancer. **C**

1.8 Urological cancer

General recommendations

1.8.1 A patient who presents with symptoms or signs suggestive of urological cancer should be referred to a team specialising in the management of urological cancer, depending on local arrangements. **D**

Specific recommendations

Prostate cancer

1.8.2 Patients presenting with symptoms suggesting prostate cancer should have a digital rectal examination (DRE) and prostate-specific antigen (PSA) test after counselling. Symptoms will be related to the lower urinary tract and may be inflammatory or obstructive. **C**

1.8.3 Prostate cancer is also a possibility in male patients with any of the following unexplained symptoms:

- erectile dysfunction
- haematuria
- lower back pain
- bone pain
- weight loss, especially in the elderly.

These patients should also be offered a DRE and a PSA test. **C**

1.8.4 Urinary infection should be excluded before PSA testing, especially in men presenting with lower tract symptoms. The PSA test should be postponed for at least 1 month after treatment of a proven urinary infection. **C**

1.8.5 If a hard, irregular prostate typical of a prostate carcinoma is felt on rectal examination, then the patient should be referred urgently. The PSA should be measured and the result should accompany the

referral. Patients do not need urgent referral if the prostate is simply enlarged and the PSA is in the age-specific reference range.[8] **C**

1.8.6 In a male patient with or without lower urinary tract symptoms and in whom the prostate is normal on DRE but the age-specific PSA is raised or rising, an urgent referral should be made. In those patients whose clinical state is compromised by other comorbidities, a discussion with the patient or carers and/or a specialist in urological cancer may be more appropriate. **C**

1.8.7 Symptomatic patients with high PSA levels should be referred urgently. **C**

1.8.8 If there is doubt about whether to refer an asymptomatic male with a borderline level of PSA, the PSA test should be repeated after an interval of 1 to 3 months. If the second test indicates that the PSA level is rising, the patient should be referred urgently. **D**

Bladder and renal cancer

1.8.9 Male or female adult patients of any age who present with painless macroscopic haematuria should be referred urgently. **C**

1.8.10 In male or female patients with symptoms suggestive of a urinary infection who also present with macroscopic haematuria, investigations should be undertaken to diagnose and treat the infection before consideration of referral. If infection is not confirmed the patient should be referred urgently. **D**

1.8.11 In all adult patients aged 40 years and older who present with recurrent or persistent urinary tract infection associated with haematuria, an urgent referral should be made. **C**

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[8] The age-specific cut-off PSA measurements recommended by the Prostate Cancer Risk Management Programme are as follows: aged 50−59 years ≥ 3.0 ng/ml; aged 60−69 years ≥ 4.0 ng/ml; aged 70 years and older ≥ 5.0 ng/ml. (Note that there are no age-specific reference ranges for men aged over 80 years. Nearly all men of this age have at least a focus of cancer in the prostate. Prostate cancer only needs to be diagnosed in this age group if it is likely to need palliative treatment.)

1.8.12 In patients under 50 years of age with microscopic haematuria, the urine should be tested for proteinuria and serum creatinine levels measured. Those with proteinurea or raised serum creatinine should be referred to a renal physician. If there is no proteinuria and serum creatinine is normal, a non-urgent referral to a urologist should be made. **C**

1.8.13 In patients aged 50 years and older who are found to have unexplained microscopic haematuria, an urgent referral should be made. **C**

1.8.14 Any patient with an abdominal mass identified clinically or on imaging that is thought to be arising from the urinary tract should be referred urgently. **C**

Testicular cancer

1.8.15 Any patient with a swelling or mass in the body of the testis should be referred urgently. **C**

1.8.16 An urgent ultrasound should be considered in men with a scrotal mass that does not transilluminate and/or when the body of the testis cannot be distinguished. **D**

Penile cancer

1.8.17 An urgent referral should be made for any patient presenting with symptoms or signs of penile cancer. These include progressive ulceration or a mass in the glans or prepuce particularly, but can involve the skin of the penile shaft. Lumps within the corpora cavernosa not involving penile skin are usually not cancer but indicate Peyronie's disease, which does not require urgent referral. **D**

1.9 Haematological cancer

General recommendations

1.9.1 A patient who presents with symptoms suggesting haematological cancer should be referred to a team specialising in the management of haematological cancer, depending on local arrangements. **D**

1.9.2 Primary healthcare professionals should be aware that haematological cancer can present with a variety of symptoms that may have a number of different clinical explanations. **D**

1.9.3 Combinations of the following symptoms and signs may suggest haematological cancer and warrant full examination, further investigation (including a blood count and film) and possible referral:

- fatigue
- drenching night sweats
- fever
- weight loss
- generalised itching
- breathlessness
- bruising
- bleeding
- recurrent infections
- bone pain
- alcohol-induced pain
- abdominal pain
- lymphadenopathy
- splenomegaly.

The urgency of referral depends on the severity of the symptoms and signs, and findings of investigations. **C**

Specific recommendations

1.9.4 In patients with a blood count or blood film reported as acute leukaemia, an immediate referral should be made. **D**

1.9.5 In patients with persistent unexplained splenomegaly, an urgent referral should be made. **C**

Investigations

1.9.6 Investigation of patients with persistent unexplained fatigue should include a full blood count, blood film and erythrocyte sedimentation rate, plasma viscosity or C-reactive protein (according to local policy), and be repeated at least once if the patient's condition remains unexplained and does not improve. **B (DS)**

1.9.7 Investigation of patients with unexplained lymphadenopathy should include a full blood count, blood film and erythrocyte sedimentation rate, plasma viscosity or C-reactive protein (according to local policy). **B (DS)**

1.9.8 Any of the following additional features of lymphadenopathy should trigger further investigation and/or referral: **C (DS)**

- persistence for 6 weeks or more
- lymph nodes increasing in size
- lymph nodes greater than 2 cm in size
- widespread nature
- associated splenomegaly, night sweats or weight loss.

1.9.9 Investigation of a patient with unexplained bruising, bleeding, and purpura or symptoms suggesting anaemia should include a full blood count, blood film, clotting screen and erythrocyte sedimentation rate, plasma viscosity or C-reactive protein (according to local policy). **B (DS)**

1.9.10 A patient with bone pain that is persistent and unexplained should be investigated with full blood count and X-ray, urea and electrolytes, liver and bone profile, PSA test (in males) and

erythrocyte sedimentation rate, plasma viscosity or C-reactive protein (according to local policy). **C (DS)**

1.9.11 In patients with spinal cord compression or renal failure suspected of being caused by myeloma, an immediate referral should be made. **C**

1.10 Skin cancer

General recommendations

1.10.1 A patient presenting with skin lesions suggestive of skin cancer or in whom a biopsy has been confirmed should be referred to a team specialising in skin cancer. **D**

1.10.2 All primary healthcare professionals should be aware of the 7-point weighted checklist (see recommendation 1.10.8) for assessment of pigmented skin lesions. **C**

1.10.3 All primary healthcare professionals who perform minor surgery should have received appropriate accredited training in relevant aspects of skin surgery including cryotherapy, curettage, and incisional and excisional biopsy techniques, and should undertake appropriate continuing professional development. **D**

1.10.4 Patients with persistent or slowly evolving unresponsive skin conditions in which the diagnosis is uncertain and cancer is a possibility should be referred to a dermatologist. **D**

1.10.5 All excised skin specimens should be sent for pathological examination. **C (DS)**

1.10.6 On making a referral of a patient in whom an excised lesion has been diagnosed as malignant, a copy of the pathology report should be sent with the referral correspondence, as there may be details (such as tumour thickness, excision margin) that will specifically influence future management. **D**

Specific recommendations

Melanoma

1.10.7 Change is a key element in diagnosing malignant melanoma. For low-suspicion lesions, careful monitoring for change should be undertaken using the 7-point checklist (see recommendation

1.10.8) for 8 weeks. Measurement should be made with photographs and a marker scale and/or ruler. **D**

1.10.8 All primary healthcare professionals should use the weighted 7-point checklist in the assessment of pigmented lesions to determine referral:

Major features of the lesions:

- change in size
- irregular shape
- irregular colour.

Minor features of the lesions:

- largest diameter 7 mm or more
- inflammation
- oozing
- change in sensation.

Suspicion is greater for lesions scoring 3 points or more (based on major features scoring 2 points each and minor features scoring 1 point each). However, if there are strong concerns about cancer, any one feature is adequate to prompt urgent referral. **C**

1.10.9 In patients with a lesion suspected to be melanoma (see recommendation 1.10.8), an urgent referral to a dermatologist or other suitable specialist with experience of melanoma diagnosis should be made, and excision in primary care should be avoided. **C**

Squamous cell carcinomas

1.10.10 Squamous cell carcinomas present as keratinizing or crusted tumours that may ulcerate. Non-healing lesions larger than 1 cm with significant induration on palpation, commonly on face, scalp or back of hand with a documented expansion over 8 weeks, may be squamous cell carcinomas and an urgent referral should be made. **C**

1.10.11 Squamous cell carcinomas are common in patients on immunosuppressive treatment, but may be atypical and aggressive. In patients who have had an organ transplant who develop new or growing cutaneous lesions, an urgent referral should be made. **C**

1.10.12 In any patient with histological diagnosis of a squamous cell carcinoma made in primary care, an urgent referral should be made. **C**

Basal cell carcinomas

1.10.13 Basal cell carcinomas are slow growing, usually without significant expansion over 2 months, and usually occur on the face. Where there is a suspicion that the patient has a basal cell carcinoma, a non-urgent referral should be made. **C**

Investigations

1.10.14 All pigmented lesions that are not viewed as suspicious of melanoma but are excised should have a lateral excision margin of 2 mm of clinically normal skin and cut to include subcutaneous fat in depth. **B (DS)**

1.11 Head and neck cancer including thyroid cancer

General recommendations

1.11.1 A patient who presents with symptoms suggestive of head and neck or thyroid cancer should be referred to an appropriate specialist or the neck lump clinic, depending on local arrangements. **D**

1.11.2 Any patient with persistent symptoms or signs related to the oral cavity in whom a definitive diagnosis of a benign lesion cannot be made should be referred or followed up until the symptoms and signs disappear. If the symptoms and signs have not disappeared after 6 weeks, an urgent referral should be made. **D**

1.11.3 Primary healthcare professionals should advise all patients, including those with dentures, to have regular dental checkups. **D**

Specific recommendations

1.11.4 In a patient who presents with unexplained red and white patches (including suspected lichen planus) of the oral mucosa that are:

- painful, or
- swollen, or
- bleeding

an urgent referral should be made.

A non-urgent referral should be made in the absence of these features. If oral lichen planus is confirmed, the patient should be monitored for oral cancer as part of routine dental examination.[9] **C**

1.11.5 In patients with unexplained ulceration of the oral mucosa or mass persisting for more than 3 weeks, an urgent referral should be made. **C**

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[9] See: National Institute for Clinical Excellence (2004) Dental recall: recall interval between routine dental examinations. *NICE Clinical Guideline* No. 19. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk/CG019

1.11.6 In adult patients with unexplained tooth mobility persisting for more than 3 weeks, an urgent referral to a dentist should be made. **C**

1.11.7 In any patient with hoarseness persisting for more than 3 weeks, particularly smokers aged 50 years and older and heavy drinkers, an urgent referral for a chest X-ray should be made. Patients with positive findings should be referred urgently to a team specialising in the management of lung cancer. Patients with a negative finding should be urgently referred to a team specialising in head and neck cancer. **C**

1.11.8 In patients with an unexplained lump in the neck which has recently appeared or a lump which has not been diagnosed before that has changed over a period of 3 to 6 weeks, an urgent referral should be made. **C**

1.11.9 In patients with an unexplained persistent swelling in the parotid or submandibular gland, an urgent referral should be made. **D**

1.11.10 In patients with unexplained persistent sore or painful throat, an urgent referral should be made. **D**

1.11.11 In patients with unilateral unexplained pain in the head and neck area for more than 4 weeks, associated with otalgia (ear ache) but with normal otoscopy, an urgent referral should be made. **D**

Investigations

1.11.12 With the exception of persistent hoarseness (see recommendation 1.11.7), investigations for head and neck cancer in primary care are not recommended as they can delay referral. **D**

Thyroid cancer

1.11.13 In patients presenting with symptoms of tracheal compression including stridor due to thyroid swelling, immediate referral should be made. **D**

1.11.14 In patients presenting with a thyroid swelling associated with any of the following, an urgent referral should be made: **D**

- a solitary nodule increasing in size
- a history of neck irradiation
- a family history of an endocrine tumour
- unexplained hoarseness or voice changes
- cervical lymphadenopathy
- very young (pre-pubertal) patients
- patients aged 65 years and older.

1.11.15 In patients with a thyroid swelling without stridor or any of the features indicated in recommendation 1.11.14, the primary healthcare professional should request thyroid function tests. Patients with hyper- or hypothyroidism and an associated goitre are very unlikely to have thyroid cancer and could be referred, non-urgently, to an endocrinologist. Those with goitre and normal thyroid function tests who do not have any of the features indicated in recommendation 1.11.14 should be referred non-urgently. **D**

1.11.16 Initiation of other investigations by the primary healthcare professional, such as ultrasonography or isotope scanning, is likely to result in unnecessary delay and is not recommended. **D**

1.12 Brain and CNS cancer

General recommendations

1.12.1 A patient who presents with symptoms suggestive of brain or CNS cancer should be referred to an appropriate specialist, depending on local arrangements. **D**

1.12.2 If a primary healthcare professional has concerns about the interpretation of a patient's symptoms and/or signs, a discussion with a local specialist should be considered. If rapid access to scanning is available, this investigation should also be considered as an alternative. **D**

Specific recommendations

1.12.3 In patients with new, unexplained headaches or neurological symptoms, the primary healthcare professional should undertake a neurological examination guided by the symptoms, but including examination for papilloedema. The absence of papilloedema does not exclude the possibility of a brain tumour. **D**

1.12.4 In any patient with symptoms related to the CNS (including progressive neurological deficit, new-onset seizures, headaches, mental changes, cranial nerve palsy, unilateral sensorineural deafness) in whom a brain tumour is suspected, an urgent referral should be made. The development of new signs related to the CNS should be considered as potential indications for referral. **C**

Headaches

1.12.5 In patients with headaches of recent onset accompanied by either features suggestive of raised intracranial pressure (for example, vomiting, drowsiness, posture-related headache, headache with pulse-synchronous tinnitus) or other focal or non-focal neurological symptoms (for example, blackout, change in personality or memory), an urgent referral should be made. **C**

1.12.6 In patients with unexplained headaches of recent onset, present for at least 1 month but not accompanied by features suggestive of raised intracranial pressure (see recommendation 1.12.5), discussion with a local specialist or referral (usually non-urgent) should be considered. **D**

1.12.7 In patients with a new, qualitatively different unexplained headache that becomes progressively severe, an urgent referral should be made. **C**

1.12.8 Re-assessment and re-examination is required if the patient does not progress according to expectations. **D**

Seizures

1.12.9 A detailed history should be taken from the patient and an eyewitness to the event if possible, to determine whether or not a seizure is likely to have occurred.[10] **C**

1.12.10 In patients presenting with a seizure, a physical examination (including cardiac, neurological, mental state) and developmental assessment, where appropriate, should be carried out. **C**

1.12.11 In any patient with suspected recent-onset seizures, an urgent referral to a neurologist should be made. **C**

Other neurological features

1.12.12 In patients with rapid progression of:

- subacute focal neurological deficit **B**
- unexplained cognitive impairment, behavioural disturbance, or slowness or a combination of these **C**
- personality changes confirmed by a witness (for example, a carer, friend or a family member) and for which there is no

[10] National Institute for Clinical Excellence (2004) The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. *NICE Clinical Guideline* No. 20. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk/CG020

reasonable explanation even in the absence of the other symptoms and signs of a brain tumour **D**

an urgent referral to an appropriate specialist should be considered.

Risk factors

1.12.13 In patients previously diagnosed with any cancer an urgent referral should be made if the patient develops any of the following symptoms: **C**

- recent-onset seizure
- progressive neurological deficit
- persistent headaches
- new mental or cognitive changes
- new neurological signs.

1.13 Bone cancer and sarcoma

General recommendations

1.13.1 A patient who presents with symptoms suggesting bone cancer or sarcoma should be referred to a team specialising in the management of bone cancer and sarcoma, or to a recognised bone cancer centre, depending on local arrangements. **D**

1.13.2 If a primary healthcare professional has concerns about the interpretation of a patient's symptoms and/or signs, a discussion with the local specialist should be considered. **D**

1.13.3 Patients with increasing, unexplained or persistent bone pain or tenderness, particularly pain at rest (and especially if not in the joint), or an unexplained limp should be investigated by the primary healthcare professional urgently. The nature of the investigations will vary according to the patient's age and clinical features. **C (DS)**

- In older people metastases, myeloma or lymphoma, as well as sarcoma, should be considered.

Specific recommendations

Bone tumours

1.13.4 A patient with a suspected spontaneous fracture should be referred for an immediate X-ray. **B (DS)**

1.13.5 If an X-ray indicates that bone cancer is a possibility, an urgent referral should be made. **C (DS)**

1.13.6 If the X-ray is normal but symptoms persist, the patient should be followed up and/or a repeat X-ray or bone function tests or a referral requested. **C (DS)**

Soft tissue sarcomas

1.13.7 In patients presenting with a palpable lump, an urgent referral for suspicion of soft tissue sarcoma should be made if the lump is:

- greater than about 5 cm in diameter
- deep to fascia, fixed or immobile
- painful
- increasing in size
- a recurrence after previous excision.

If there is any doubt about the need for referral, discussion with a local specialist should be undertaken. **C**

1.13.8 If a patient has HIV disease, Kaposi's sarcoma should be considered and a referral made if this is suspected. **C**

1.14 Cancer in children and young people

General recommendations

1.14.1 Children and young people who present with symptoms and signs of cancer should be referred to a paediatrician or a specialist children's cancer service, if appropriate. **D**

1.14.2 Childhood cancer is rare and may present initially with symptoms and signs associated with common conditions. Therefore, in the case of a child or young person presenting several times (for example, three or more times) with the same problem, but with no clear diagnosis, urgent referral should be made. **D**

1.14.3 The parent is usually the best observer of the child's or young person's symptoms. The primary healthcare professional should take note of parental insight and knowledge when considering urgent referral. **D**

1.14.4 Persistent parental anxiety should be a sufficient reason for referral of a child or young person, even when the primary healthcare professional considers that the symptoms are most likely to have a benign cause. **D**

1.14.5 Persistent back pain in a child or young person can be a symptom of cancer and is indication for an examination, investigation with a full blood count and blood film, and consideration of referral. **C**

1.14.6 There are associations between Down's syndrome and leukaemia, between neurofibromatosis and CNS tumours, and between other rare syndromes and some cancers. The primary healthcare professional should be alert to the potential significance of unexplained symptoms in children or young people with such syndromes. **D**

1.14.7 The primary healthcare professional should convey information to the parents and child/young person about the reason for referral

and which service the child/young person is being referred to so that they know what to do and what will happen next. **D**

1.14.8 The primary healthcare professional should establish good communication with the parents and child/young person in order to develop the supportive relationship that will be required during the further management if the child/young person is found to have cancer. **D**

Specific recommendations

Leukaemia (children of all ages)

1.14.9 Leukaemia usually presents with a relatively short history of weeks rather than months. The presence of one or more of the following symptoms and signs requires investigation with full blood count and blood film:

- pallor
- fatigue
- unexplained irritability
- unexplained fever
- persistent or recurrent upper respiratory tract infections
- generalised lymphadenopathy
- persistent or unexplained bone pain
- unexplained bruising.

If the blood film or full blood count indicates leukaemia then an urgent referral should be made. **C (DS)**

1.14.10 The presence of either of the following signs in a child or young person requires immediate referral: **C**

- unexplained petechiae
- hepatosplenomegaly.

Lymphomas

Hodgkin's lymphoma presents typically with non-tender cervical and/or supraclavicular lymphadenopathy. Lymphadenopathy can also present at other sites. The natural history is long (months). Only a minority of patients have systemic symptoms (itching, night sweats, fever). Non-Hodgkin's lymphoma typically shows a more rapid progression of symptoms, and may present with lymphadenopathy, breathlessness, superior vena-caval obstruction or abdominal distension.

1.14.11 Lymphadenopathy is more frequently benign in younger children but urgent referral is advised if one or more of the following characteristics are present, particularly if there is no evidence of local infection: **C**

- lymph nodes are non-tender, firm or hard
- lymph nodes are greater than 2 cm in size
- lymph nodes are progressively enlarging
- other features of general ill-health, fever or weight loss
- the axillary nodes are involved (in the absence of local infection or dermatitis)
- the supraclavicular nodes are involved.

1.14.12 The presence of hepatosplenomegaly requires immediate referral. **C**

1.14.13 Shortness of breath is a symptom that can indicate chest involvement but may be confused with other conditions such as asthma. Shortness of breath in association with the above signs (recommendation 1.14.11), particularly if not responding to bronchodilators, is an indication for urgent referral. **C**

1.14.14 A child or young person with a mediastinal or hilar mass on chest X-ray should be referred immediately. **C**

Brain and CNS tumours

Children aged 2 years and older and young people

1.14.15 Persistent headache in a child or young person requires a neurological examination by the primary healthcare professional. An urgent referral should be made if the primary healthcare professional is unable to undertake an adequate examination. **D**

1.14.16 Headache and vomiting that cause early morning waking or occur on waking are classical signs of raised intracranial pressure, and an immediate referral should be made. **C**

1.14.17 The presence of any of the following neurological symptoms and signs should prompt urgent or immediate referral: **D**

- new-onset seizures
- cranial nerve abnormalities
- visual disturbances
- gait abnormalities
- motor or sensory signs
- unexplained deteriorating school performance or developmental milestones
- unexplained behavioural and/or mood changes.

1.14.18 A child or young person with a reduced level of consciousness requires emergency admission. **C**

Children < 2 years

1.14.19 In children aged younger than 2 years, any of the following symptoms may suggest a CNS tumour, and referral (as indicated below) is required. **C**

- Immediate referral:
  - new-onset seizures
  - bulging fontanelle
  - extensor attacks

- persistent vomiting.

- Urgent referral:
  - abnormal increase in head size
  - arrest or regression of motor development
  - altered behaviour
  - abnormal eye movements
  - lack of visual following
  - poor feeding/failure to thrive.
- Urgency contingent on other factors:
  - squint.

Neuroblastoma (all ages)

1.14.20 Most children and young people with neuroblastoma have symptoms of metastatic disease which may be general in nature (malaise, pallor, bone pain, irritability, fever or respiratory symptoms), and may resemble those of acute leukaemia. The presence of any of the following symptoms and signs requires investigation with a full blood count: **C (DS)**

- persistent or unexplained bone pain (and X-ray)
- pallor
- fatigue
- unexplained irritability
- unexplained fever
- persistent or recurrent upper respiratory tract infections
- generalised lymphadenopathy
- unexplained bruising.

1.14.21 Other symptoms which should raise concern about neuroblastoma and prompt urgent referral include: **C**

- proptosis
- unexplained back pain
- leg weakness
- unexplained urinary retention.

1.14.22 In children or young people with symptoms that could be explained by neuroblastoma, an abdominal examination (and/or urgent abdominal ultrasound) should be undertaken, and a chest X-ray and full blood count considered. If any mass is identified, an urgent referral should be made. **C (DS)**

1.14.23 Infants aged younger than 1 year may have localised abdominal or thoracic masses, and in infants younger than 6 months of age, there may also be rapidly progressive intra-abdominal disease. Some babies may present with skin nodules. If any such mass is identified, an immediate referral should be made. **C**

Wilms' tumour (all ages)

1.14.24 Wilms' tumour most commonly presents with a painless abdominal mass. Persistent or progressive abdominal distension should prompt abdominal examination, and if a mass is found an immediate referral be made. If the child or young person is uncooperative and abdominal examination is not possible, referral for an urgent abdominal ultrasound should be considered. **C**

1.14.25 Haematuria in a child or young person, although a rarer presentation of a Wilms' tumour, merits urgent referral. **C**

Soft tissue sarcoma (all ages)

1.14.26 A soft tissue sarcoma should be suspected and an urgent referral should be made for a child or young person with an unexplained mass at almost any site that has one or more of the following features. The mass is: **C**

- deep to the fascia
- non-tender
- progressively enlarging
- associated with a regional lymph node that is enlarging
- greater than 2 cm in diameter.

1.14.27 A soft tissue mass in an unusual location may give rise to misleading local and persistent unexplained symptoms and signs, and the possibility of sarcoma should be considered. These symptoms and signs include: **C**

- head and neck sarcomas:
  - proptosis
  - persistent unexplained unilateral nasal obstruction with or without discharge and/or bleeding
  - aural polyps/discharge
- genitourinary tract:
  - urinary retention
  - scrotal swelling
  - bloodstained vaginal discharge.

Bone sarcomas (osteosarcoma and Ewing's sarcoma) (all ages)

1.14.28 Limbs are the most common site for bone tumours, especially around the knee in the case of osteosarcoma. Persistent localised bone pain and/or swelling requires an X-ray. If a bone tumour is suspected, an urgent referral should be made. **C**

1.14.29 History of an injury should not be assumed to exclude the possibility of a bone sarcoma. **C**

1.14.30 Rest pain, back pain and unexplained limp may all point to a bone tumour and require discussion with a paediatrician, referral or X-ray. **C**

Retinoblastoma (mostly children aged under 2 years)

1.14.31 In a child with a white pupillary reflex (leukocoria) noted by the parents, identified in photographs or found on examination, an urgent referral should be made. The primary healthcare professional should pay careful attention to the report by a parent of noticing an odd appearance in their child's eye. **C**

1.14.32 A child with a new squint or change in visual acuity should be referred. If cancer is suspected, referral should be urgent, but otherwise referral should be non-urgent. **C**

1.14.33 A family history of retinoblastoma should alert the primary healthcare professional to the possibility of retinoblastoma in a child who presents with visual problems. Offspring of a parent who has had retinoblastoma, or siblings of an affected child, should undergo screening soon after birth. **C**

Investigations

1.14.34 When cancer is suspected in children and young people, imaging is often required. This may be best performed by a paediatrician, following urgent or immediate referral by the primary healthcare professional. **D**

1.14.35 The presence of any of the following symptoms and signs requires investigation with full blood count: **C (DS)**

- pallor
- fatigue
- irritability
- unexplained fever
- persistent or recurrent upper respiratory tract infections
- generalised lymphadenopathy
- persistent or unexplained bone pain (and X-ray)
- unexplained bruising.

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from www.nice.org.uk/CG027.

3 Implementation in the NHS

This guideline is an update of the guideline entitled 'Referral guidelines for suspected cancer' published by the Department of Health in 2000. The new guideline takes account of new research evidence and the findings of audits undertaken since the publication of the previous guideline. The recommendations made here supersede those in the earlier guideline.

3.1 Resource implications

Local health communities should review their existing practice for referral for suspected cancer against this guideline. The review should consider the resources required to implement the recommendations set out in Section 1, the people and processes involved, and the timeline over which full implementation is envisaged. It is in the interests of patients with suspected cancer that the implementation timeline be as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly.

Information on the cost impact of this guideline in England will be available on the NICE website from September 2005. This includes a template that local communities can use (www.nice.org.uk/CG027costtemplate).

3.2 General

The implementation of this guideline will build on the National Service Frameworks for NHS Cancer Plan 2000 and Older People in England and

Wales and should form part of the service development plans for each local health community in England and Wales. Other key health strategies include the service improvement guides produced by the Cancer Services Collaboratives.

This guideline should be used in conjunction with published cancer service guidance and published clinical guidelines.

3.3 Audit

Suggested audit criteria based on the key priorities for implementation are listed in Appendix D, and can be used to audit practice locally.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, on the basis of its review of the evidence. The Group regards these recommendations as the most important research areas to improve NICE guidance and patient care in the future. More details on the research recommendations can be found in the full guideline produced by the National Collaborating Centre for Primary Care (see Section 5).

When making these recommendations for research, the guideline developers have considered the potential importance of factors relating to gender, ethnicity and people with special needs.

1. A randomised controlled trial of an educational intervention to improve primary healthcare professionals' ability to detect cancer.

2. The presenting features of cancer in a large primary care population.

3. The support and information needs of patients when cancer is suspected and referral instigated.

5 Other versions of this guideline

The National Institute for Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Primary Care. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in Appendix B. Information about the independent Guideline Review Panel is given in Appendix C.

The booklet *The guideline development process – an overview for stakeholders, the public and the NHS* has more information about the Institute's guideline development process. It is available from the Institute's website.

5.1 Full guideline

The full guideline, *Referral guidelines for suspected cancer in adults and children*, is published by the National Collaborating Centre for Primary Care; it is available from the NICE website (www.nice.org.uk/CG027/fullguideline) and the website of the National Library for Health (www.nlh.nhs.uk).

5.2 Information for the public

A version of this guideline for people with suspected cancer and their carers, and for the public, is available from the NICE website (www.publications.nice.org.uk/IFP27).

6 Related NICE guidance

Clinical guidelines

National Institute for Clinical Excellence (2004) Familial breast cancer: The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. *NICE Clinical Guideline* No. 14. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2004) Dyspepsia: Managing dyspepsia in adults in primary care. *NICE Clinical Guideline* No. 17. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2005) Lung cancer: The diagnosis and treatment of lung cancer. *NICE Clinical Guideline* No. 24. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence. Breast cancer: diagnosis and treatment. *NICE Clinical Guideline*. (Publication date to be confirmed.)

National Institute for Clinical Excellence. Prostate cancer: diagnosis and treatment. *NICE Clinical Guideline*. (Publication date to be confirmed.)

Cancer service guidance

National Institute for Clinical Excellence (2002) Improving outcomes in breast cancer. *NICE Inherited Cancer Service Guidance*. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2002) Improving outcomes in urological cancers. *NICE Inherited Cancer Service Guidance*. London:

National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2003) Improving outcomes in haemato-oncology cancer. *NICE Inherited Cancer Service Guidance*. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2004) Improving outcomes in colorectal cancer. *NICE Inherited Cancer Service Guidance*. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. Guidance on cancer services. *NICE Inherited Cancer Service Guidance*. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

National Institute for Clinical Excellence (2004) Improving outcomes in head and neck cancers. *NICE Inherited Cancer Service Guidance*. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

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7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin earlier than 4 years if significant evidence that affects the guideline recommendations is identified sooner. The updated guideline will be available within 2 years of the start of the review process.

Appendix A: Grading scheme

The grading schemes and hierarchy of evidences used in this guideline (see Tables) are adapted from Eccles and Mason (2001) for non-diagnostic studies, and for diagnostic studies, from The Oxford Centre for Evidence-based Medicine Levels of Evidence (2001) and the Centre for Reviews and Dissemination (2001).

Recommendation grade	Evidence
A	Directly based on category I evidence
B	Directly based on: • category II evidence, or • extrapolated recommendation from category I evidence
C	Directly based on: • category III evidence, or • extrapolated recommendation from category I or II evidence
D	Directly based on: • category IV evidence, or • extrapolated recommendation from category I, II, or III evidence
Evidence category	**Source**
Ia	Evidence from systematic review or meta-analysis of randomised controlled trials
Ib	Evidence from at least one randomised controlled trial
IIa	Evidence from at least one well-designed controlled study without randomisation
IIb	Evidence from at least one well-designed quasi-experimental study, such as a cohort study
III	Evidence from well-designed non-experimental descriptive studies, case-control studies, or case series
IV	Evidence from expert committee reports, opinions and/or clinical experience of respected authorities

Adapted from Eccles M, Mason J (2001) How to develop cost-conscious guidelines. *Health Technology Assessmen*t 5: 8

Recommendation grade	Evidence
A (DS)*	Directly based on category I evidence
B (DS)	Directly based on category II evidence
C (DS)	Directly based on category III evidence
D (DS)	Directly based on category IV evidence
Evidence category	**Source**
Ia	Evidence from systematic review (with homogeneity)† of level-1 studies‡
Ib	Evidence from level 1 studies‡
II	Evidence from: • level 2 studies§, **or** • systematic review of level 2 studies
III	Evidence from: • level 2 studies§, **or** • systematic review of level 2 studies
IV	Evidence from expert committee reports or opinions and/or clinical experience without explicit critical experience, based on physiology, bench research or 'first principles'

* DS – diagnostic studies

[†]Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

[‡]Level-1 studies are studies:

- that use a blind comparison of the test with a validation reference standard (gold standard)
- in a sample of patients that reflects the population to whom the test would apply

[§]Level-2 studies are studies that have only one of the following:

- narrow population (the sample does not reflect the population to whom the test would apply)
- use a poor reference standard (defined as that where a 'test' is included in the 'reference', or where the 'testing' affects the 'reference')
- the comparison between the test and reference standard is not blind
- are case-control studies

[§§]Level-3 studies are studies that have at least two or three of the features listed above[§]

Adapted from *The Oxford Centre for Evidence-based Medicine Levels of Evidence* (2001) and the Centre for Reviews and Dissemination *Report Number 4* (2001).

Appendix B: The Guideline Development Group

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Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

Professor Mike Drummond (Chair)

Director, Centre for Health Economics, University of York

Mr Barry Stables

Patient/Lay Representative

Dr Imogen Stephens

Joint Director of Public Health, Western Sussex Primary Care Trust

Dr Kevork Hopayian

General Practitioner, Suffolk

Dr Robert Walker

Clinical Director, West Cumbria Primary Care Trust

Dr John Harley

Clinical Governance and Prescribing Lead, North Tees PCT

Appendix D: Technical detail on the criteria for audit

Primary healthcare professionals do not refer many patients with suspected cancer in any one year. The findings of an audit limited to patients referred by one professional in one year will be at risk of misinterpretation because of the small numbers of patients involved. Therefore, the findings of the audit suggested here should be used to generate discussion and learning.

The organisation of significant event audit meetings by a primary healthcare team would be an appropriate way to consider the findings, or delay in diagnosis in individual cases. Significant event audit across the interface with secondary care could be used to investigate the appropriateness of referrals and encourage more efficient referral practice.

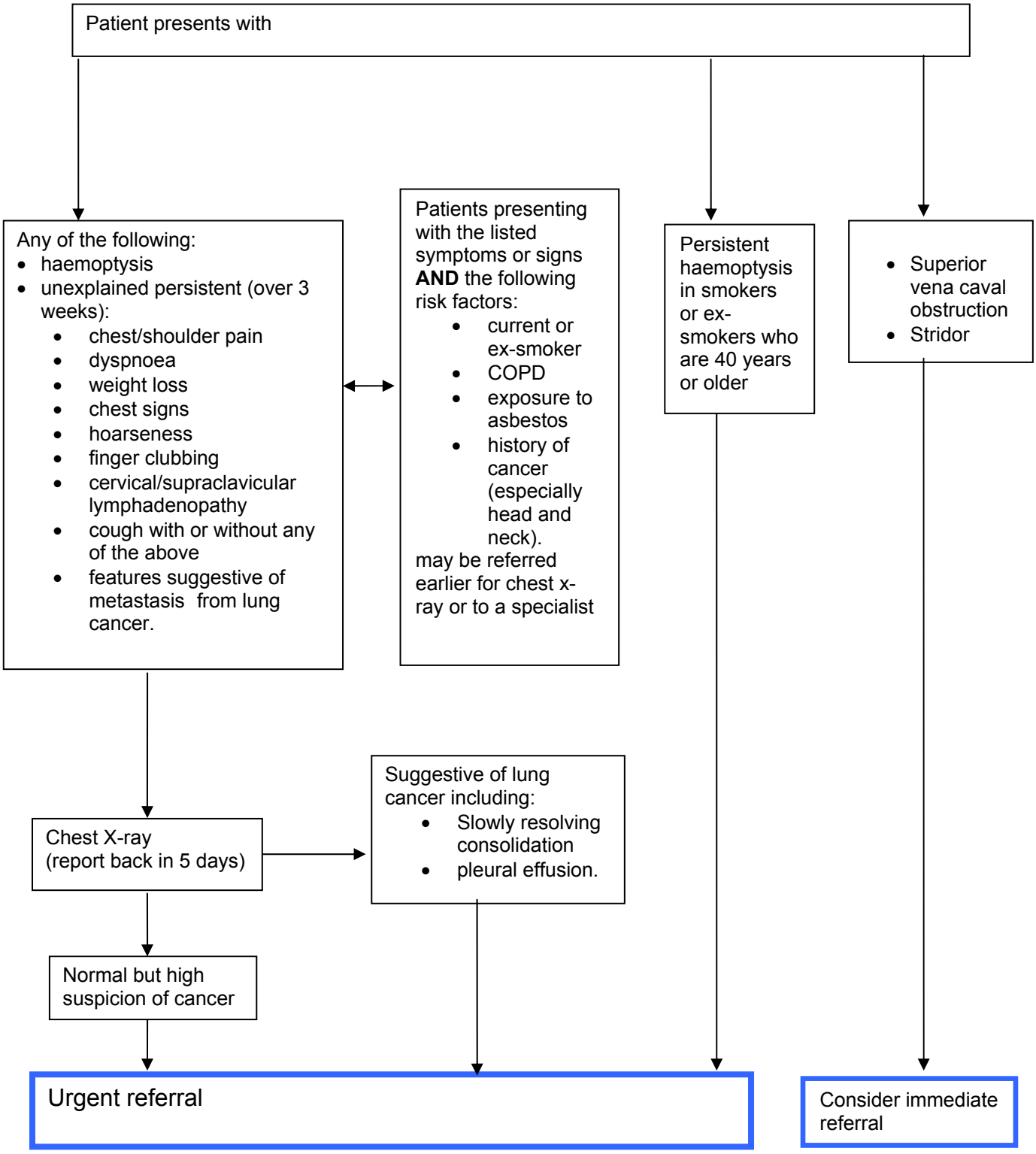
Many audits of cancer referrals have been undertaken in the past 4 years, but most have been based in secondary care and have not led to a dialogue between primary and secondary care on improving referral practice. The detection of cancer in a child would be an appropriate topic for significant event audit. In addition, primary care teams should consider the prospective collection of audit information over several years. Consideration should be given to involving patients and carers in audits. Many of the recommendations relate to information given to patients, their support and their involvement in decisions, and it would therefore be appropriate to involve them when possible in audits.

Criterion	Exception
1. Patients being referred with suspected cancer are offered a) information about the likely diagnosis, b) what to expect from the specialist service, and c) advice about seeking further help whilst awaiting the specialist consultation.	1 a) Patients who do not want information 1 b) nil 1 c) nil.
2. Patients presenting with classical features of the cancers are a) suspected of having cancer and b) initial investigation or referral is arranged at the first consultation. c) to be set locally; d) to be set locally.	2 a) nil 2 b) patients who refuse referral or investigation 2 c) none 2 d) none.
3. Patients referred for suspected cancer have had preliminary investigations undertaken in primary care as recommended in the guideline.	3) Patients who refuse investigations.

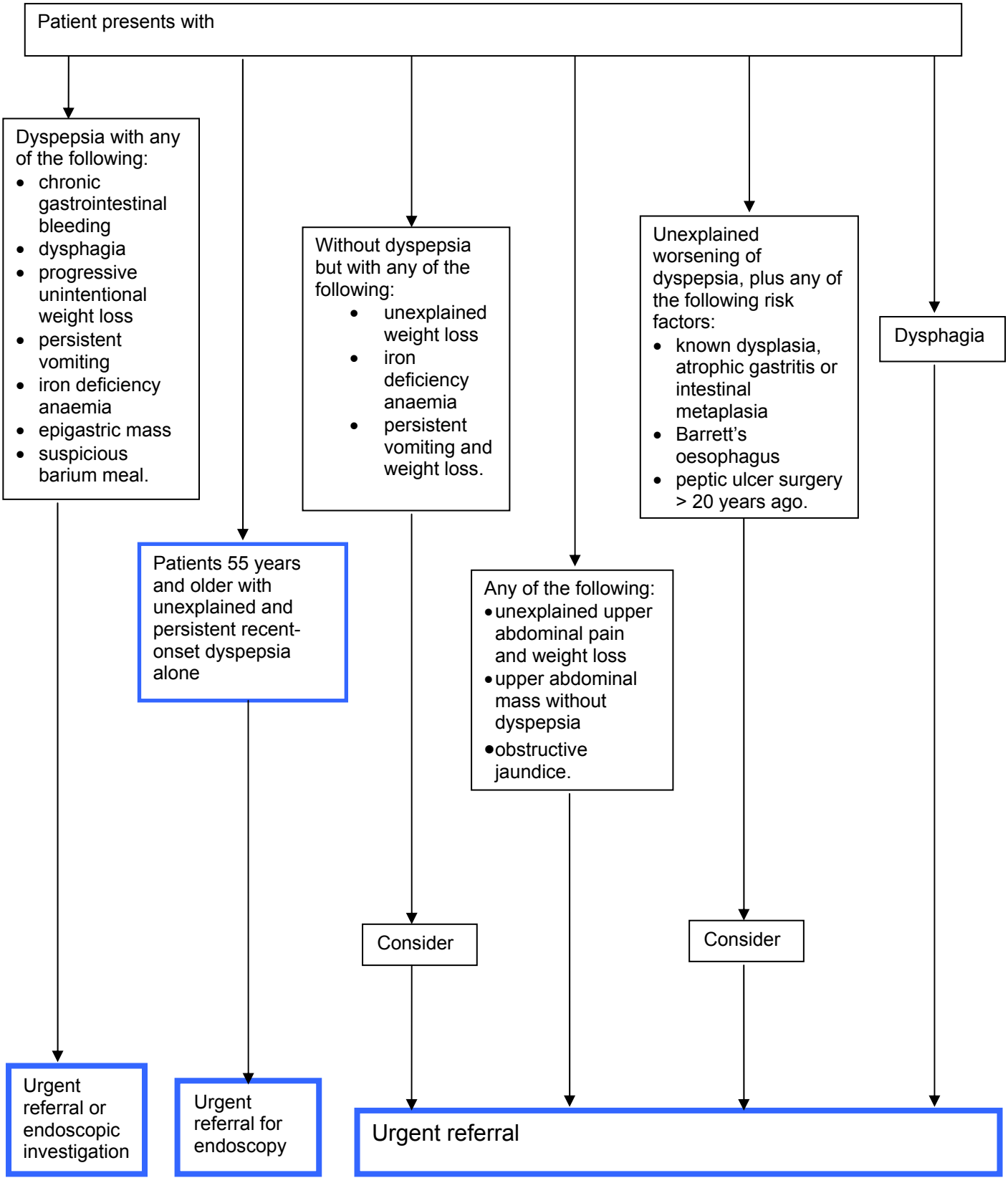
Appendix E: The algorithms

A series of algorithms now follows summarising the principal recommendations for each cancer site. These give guidance on how to proceed when a patient presents with symptoms suggestive of a cancer. They are intended to be used alongside the text version of the recommendations, which should be consulted for full, detailed guidance.

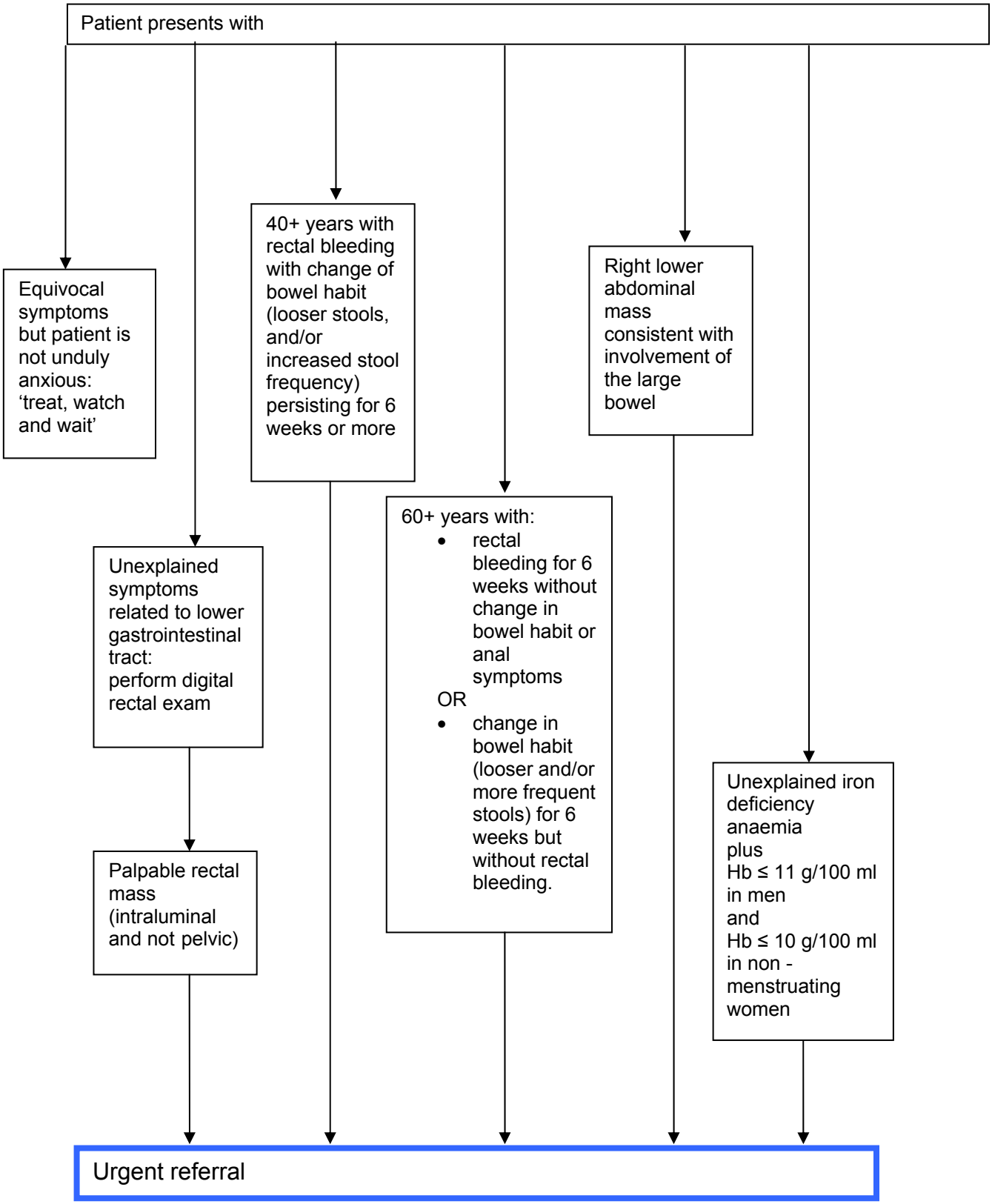
Lung cancer


Patient presents with
Any of the following:
• haemoptysis
• unexplained persistent (over 3 weeks):
• chest/shoulder pain
• dyspnoea
• weight loss
• chest signs
• hoarseness
• finger clubbing
• cervical/supraclavicular lymphadenopathy
• cough with or without any of the above
• features suggestive of metastasis from lung cancer.
Patients presenting with the listed symptoms or signs AND the following risk factors:
• current or ex-smoker
• COPD
• exposure to asbestos
• history of cancer (especially head and neck).
may be referred earlier for chest x-ray or to a specialist
Persistent haemoptysis in smokers or ex-smokers who are 40 years or older
• Superior vena caval obstruction
• Stridor
Chest X-ray (report back in 5 days)
Suggestive of lung cancer including:
• Slowly resolving consolidation
• pleural effusion.
Normal but high suspicion of cancer
Urgent referral
Consider immediate referral

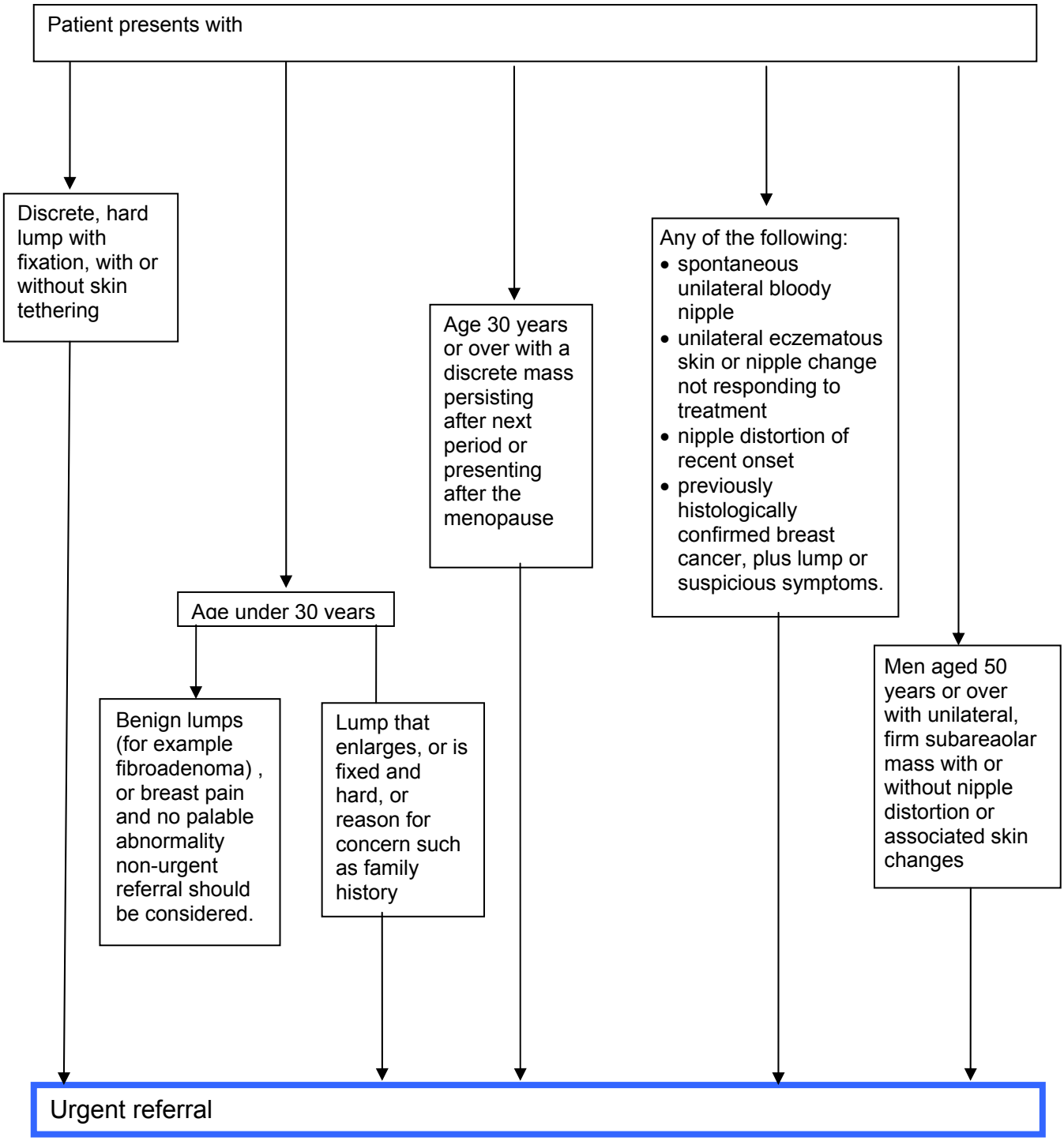
Upper gastrointestinal cancer



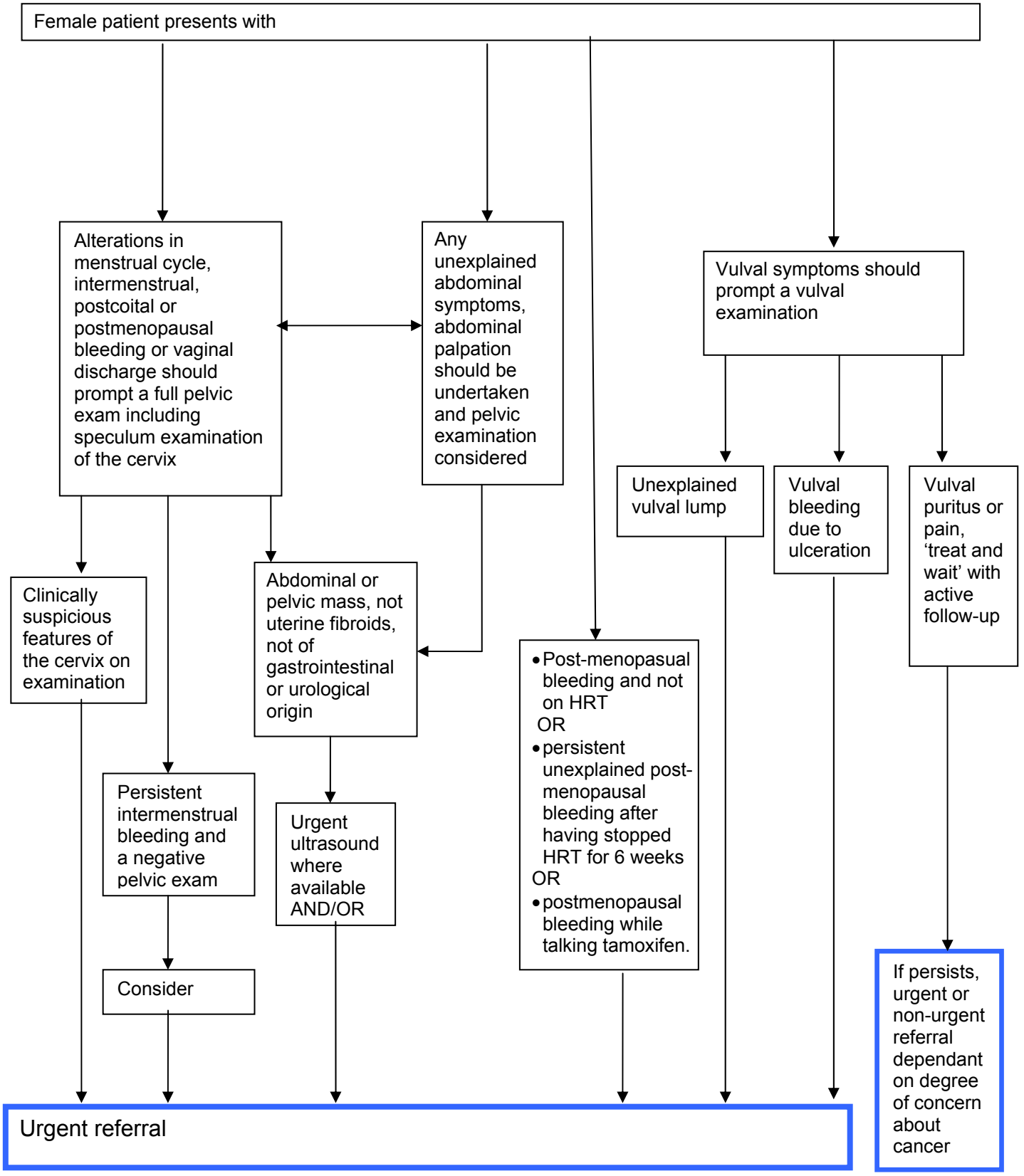
Lower gastrointestinal cancer



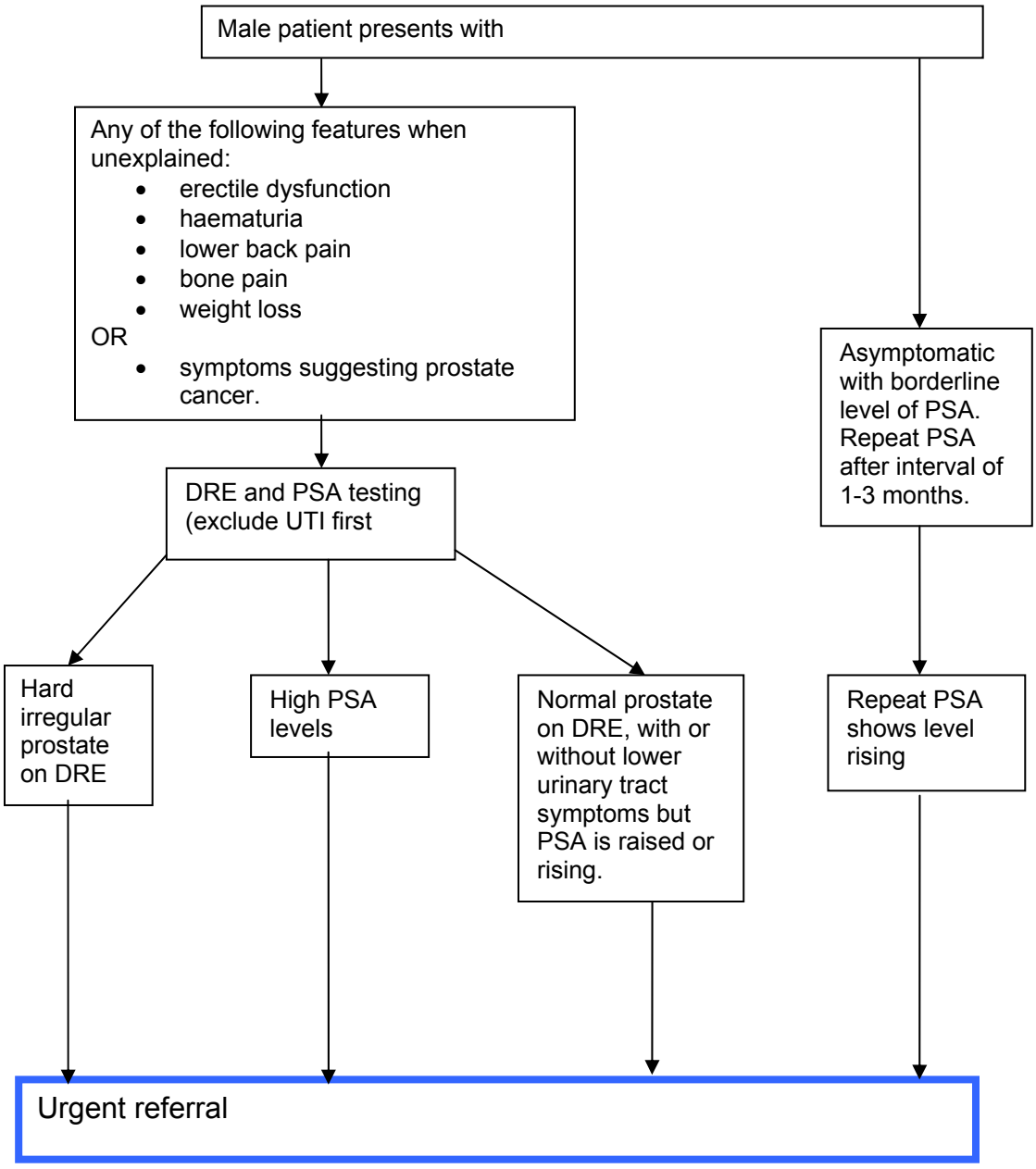
Breast cancer

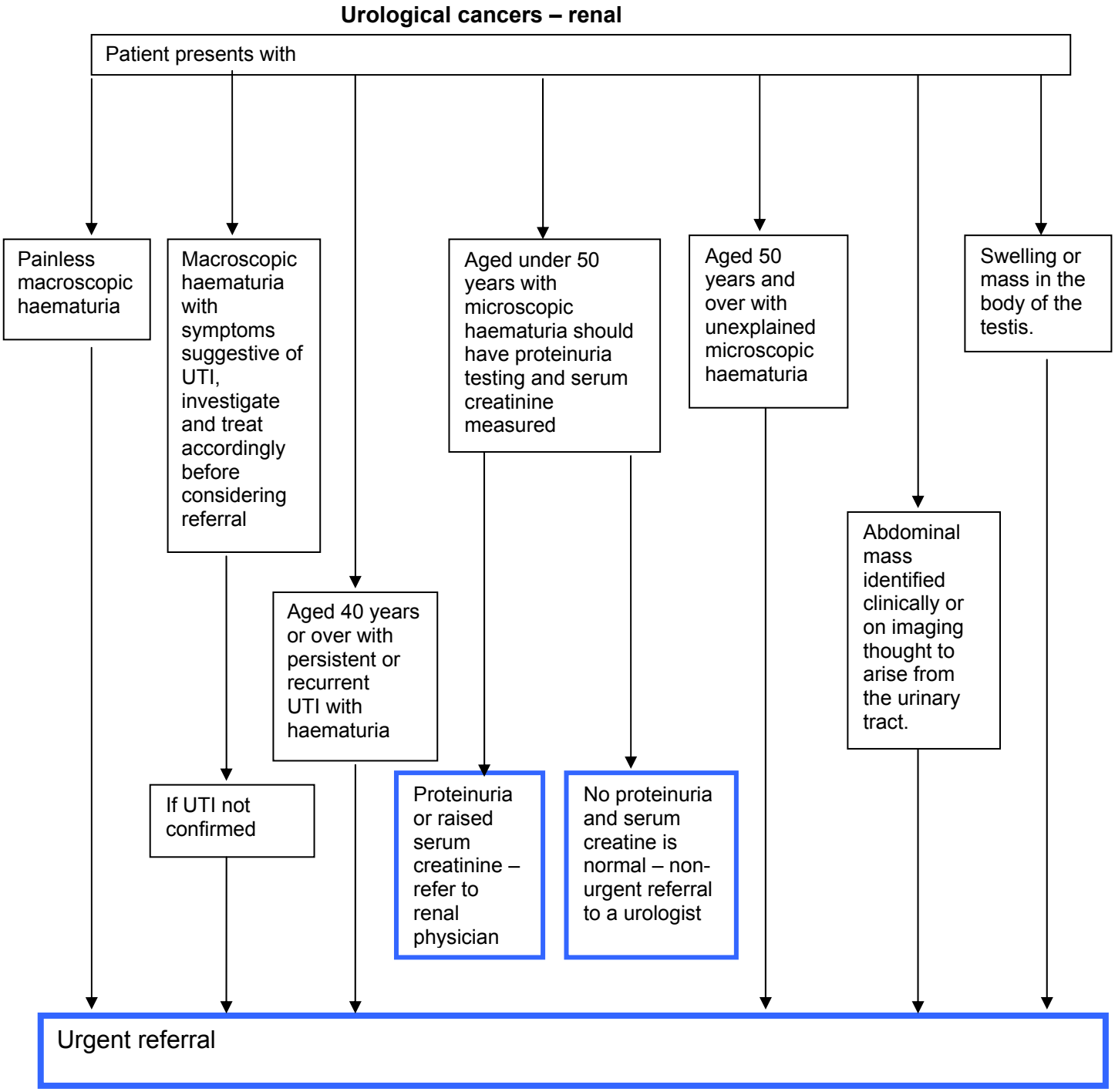


Gynaecological cancers

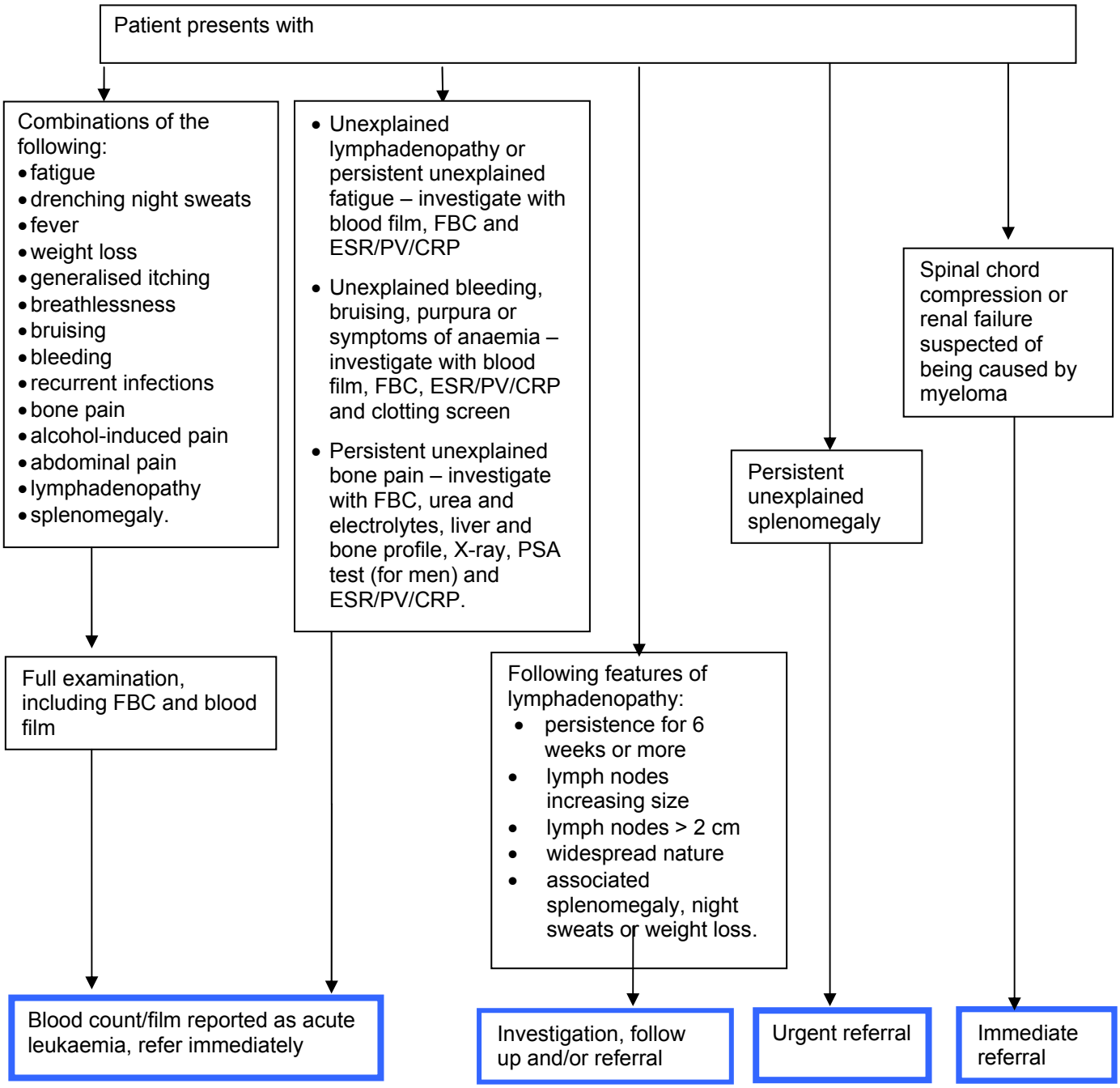


Urological cancers – prostate

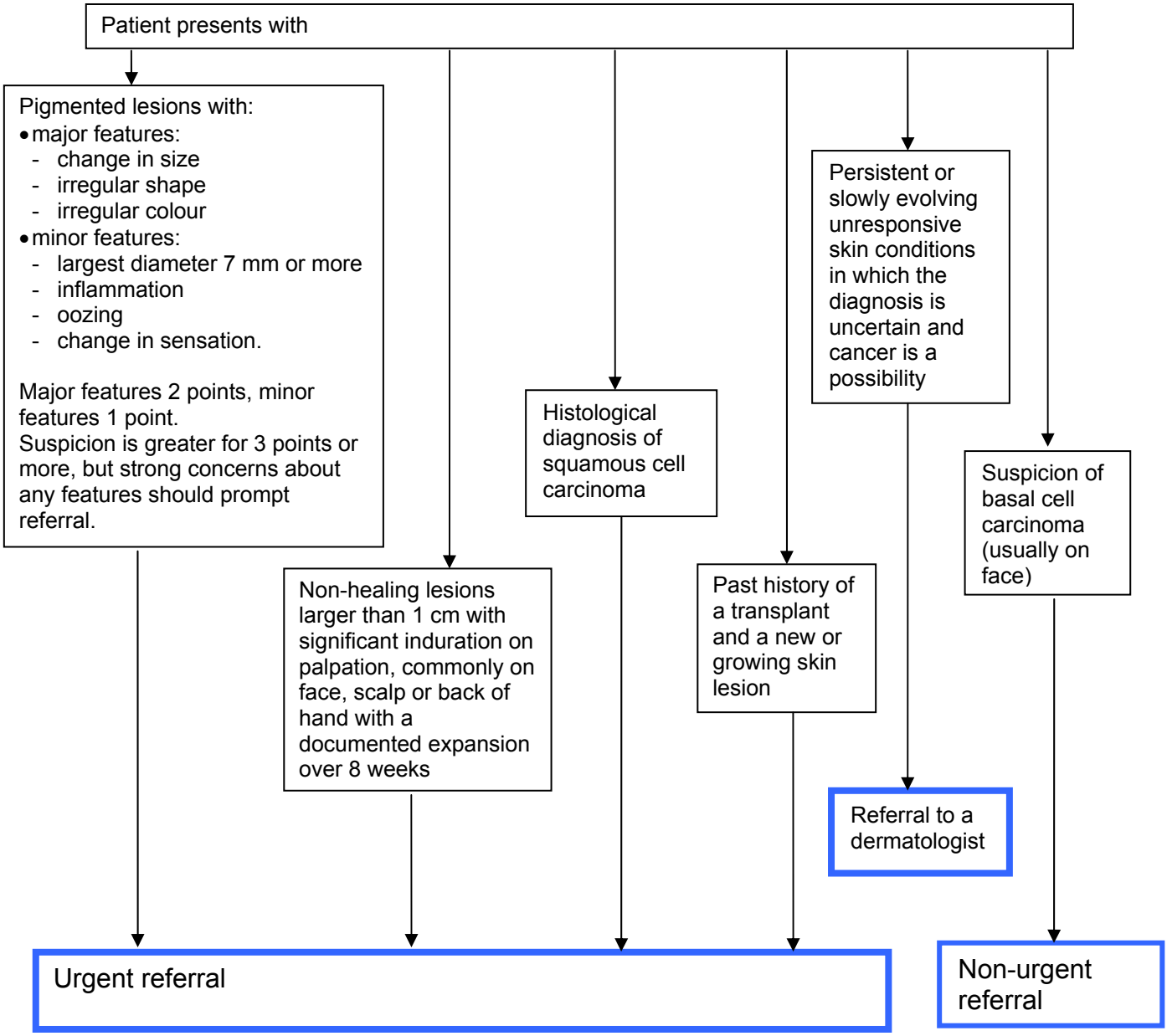



Urological cancers – renal
Patient presents with
Painless macroscopic haematuria
Macroscopic haematuria with symptoms suggestive of UTI, investigate and treat accordingly before considering referral
Aged 40 years or over with persistent or recurrent UTI with haematuria
Aged under 50 years with microscopic haematuria should have proteinuria testing and serum creatinine measured
Aged 50 years and over with unexplained microscopic haematuria
Abdominal mass identified clinically or on imaging thought to arise from the urinary tract.
Swelling or mass in the body of the testis.
If UTI not confirmed
Proteinuria or raised serum creatinine – refer to renal physician
No proteinuria and serum creatine is normal – non-urgent referral to a urologist
Urgent referral

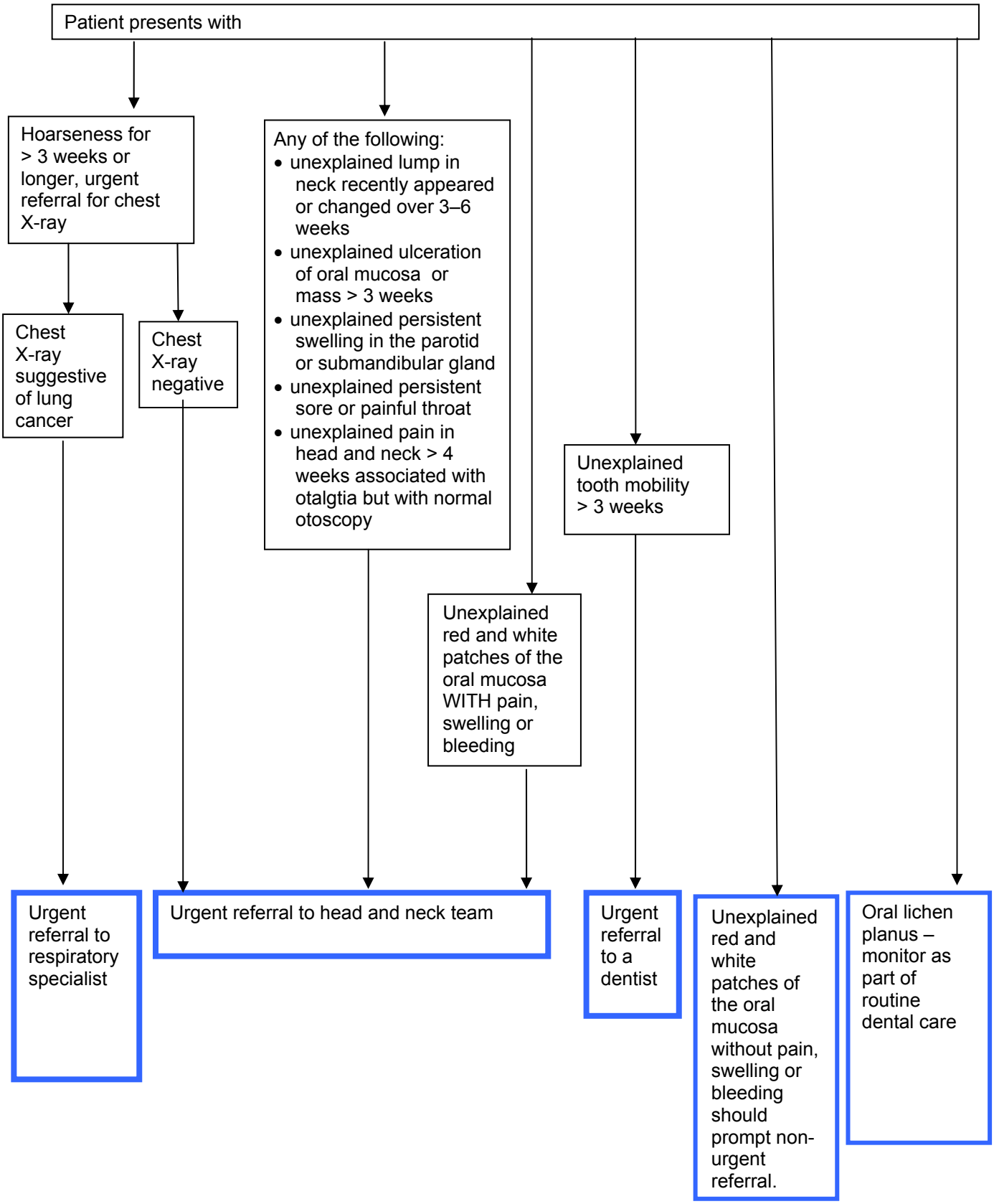
Haematological cancers



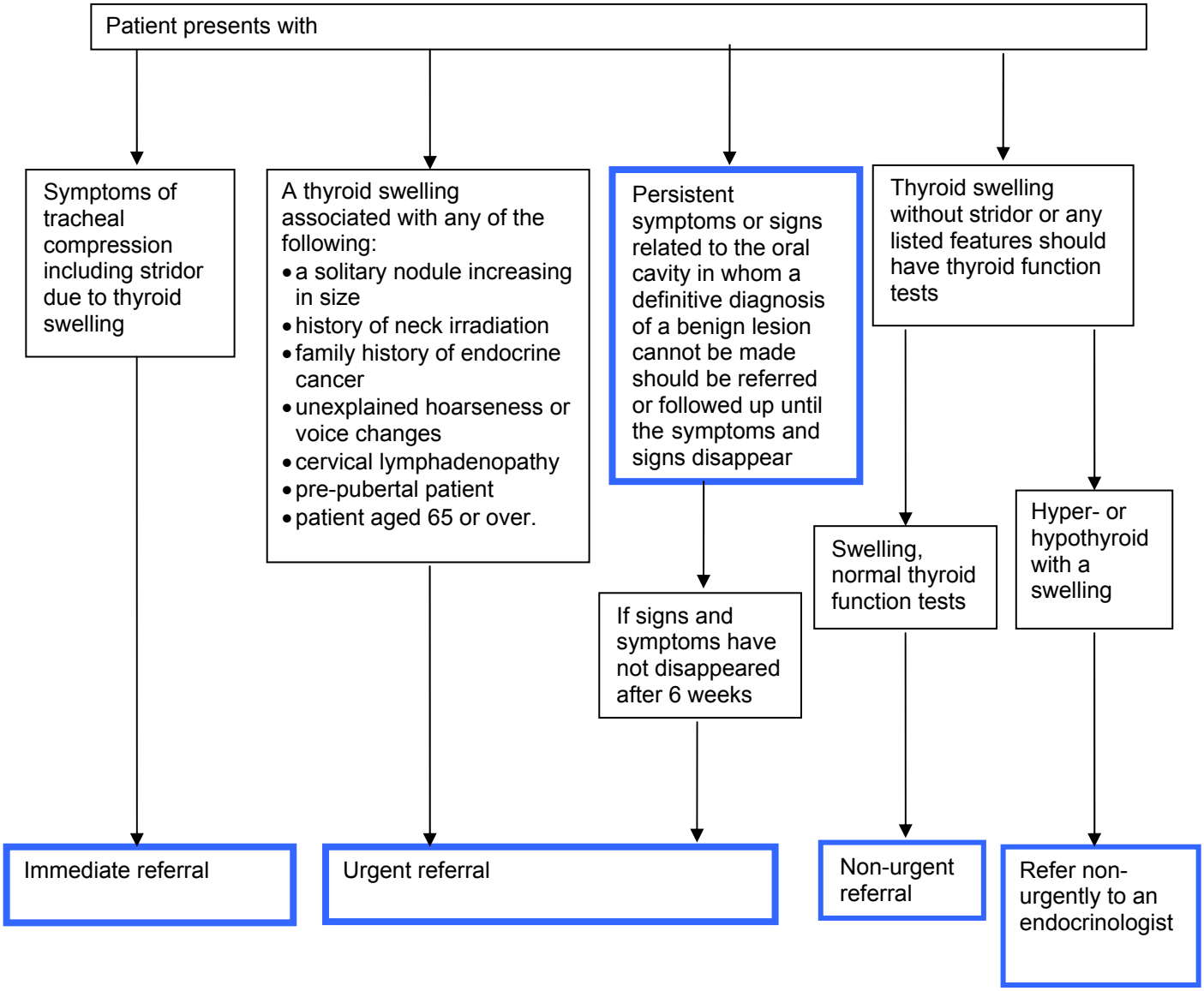
Skin cancers



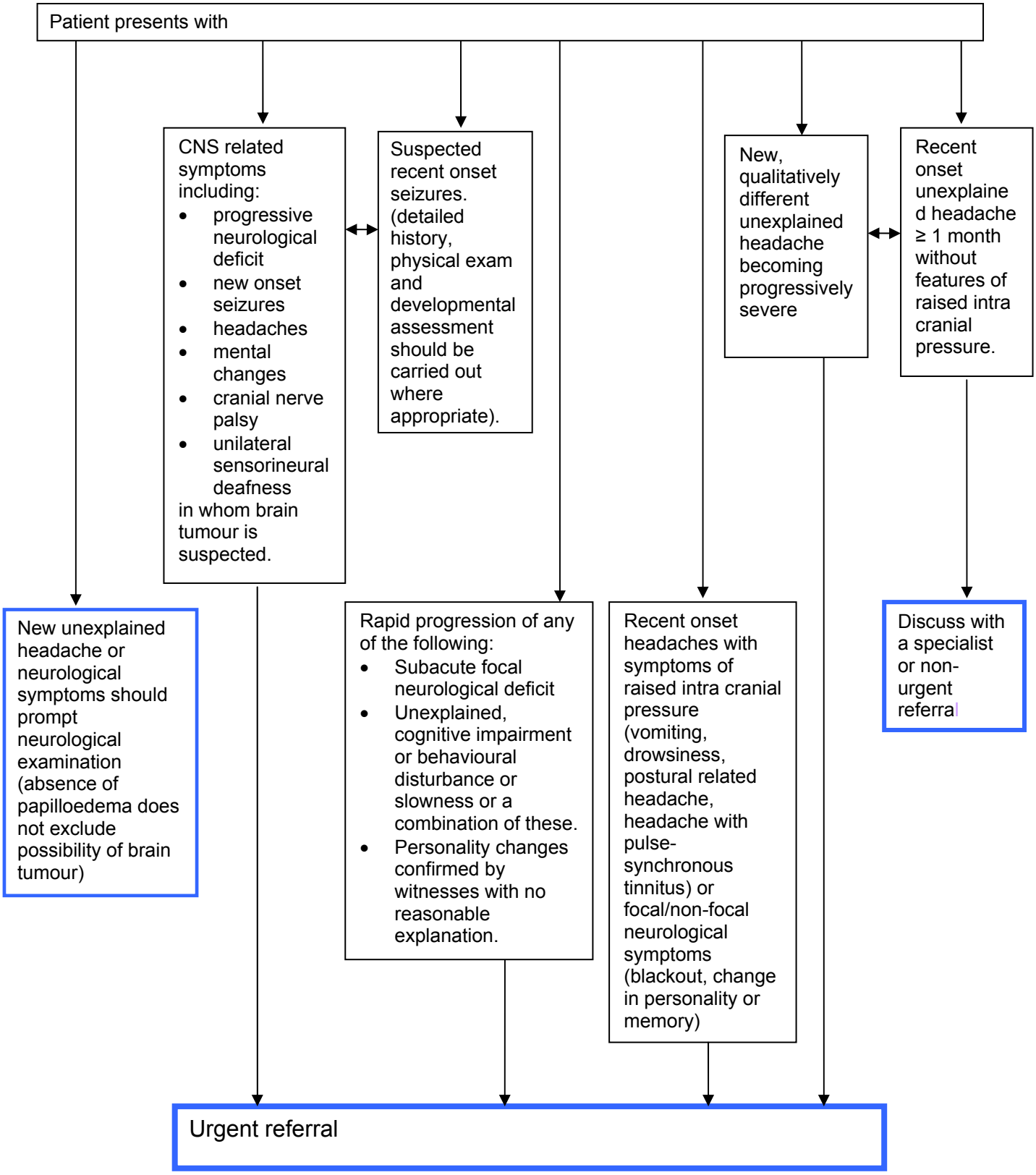
Head and neck cancers



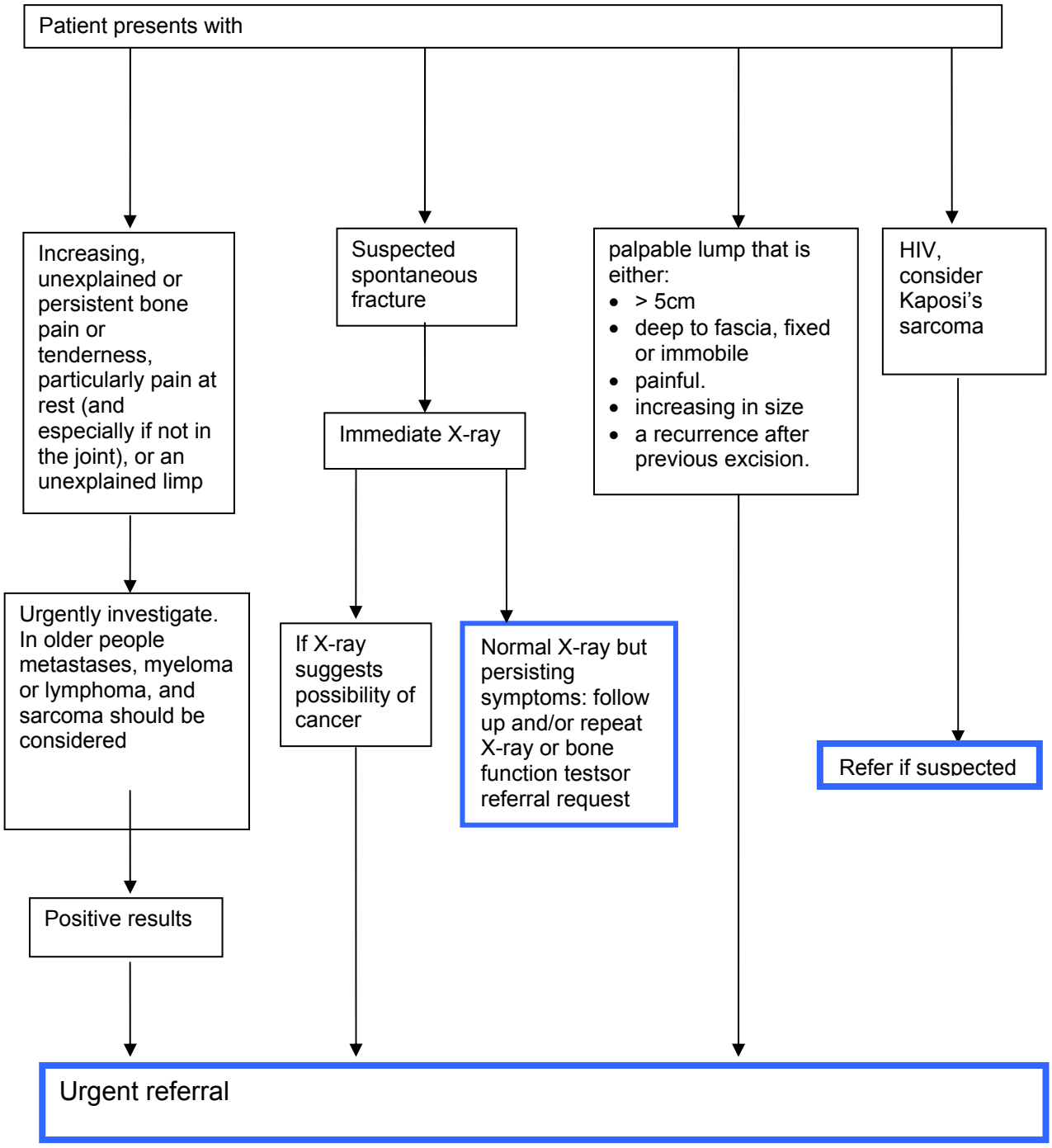
Head and neck cancers – thyroid



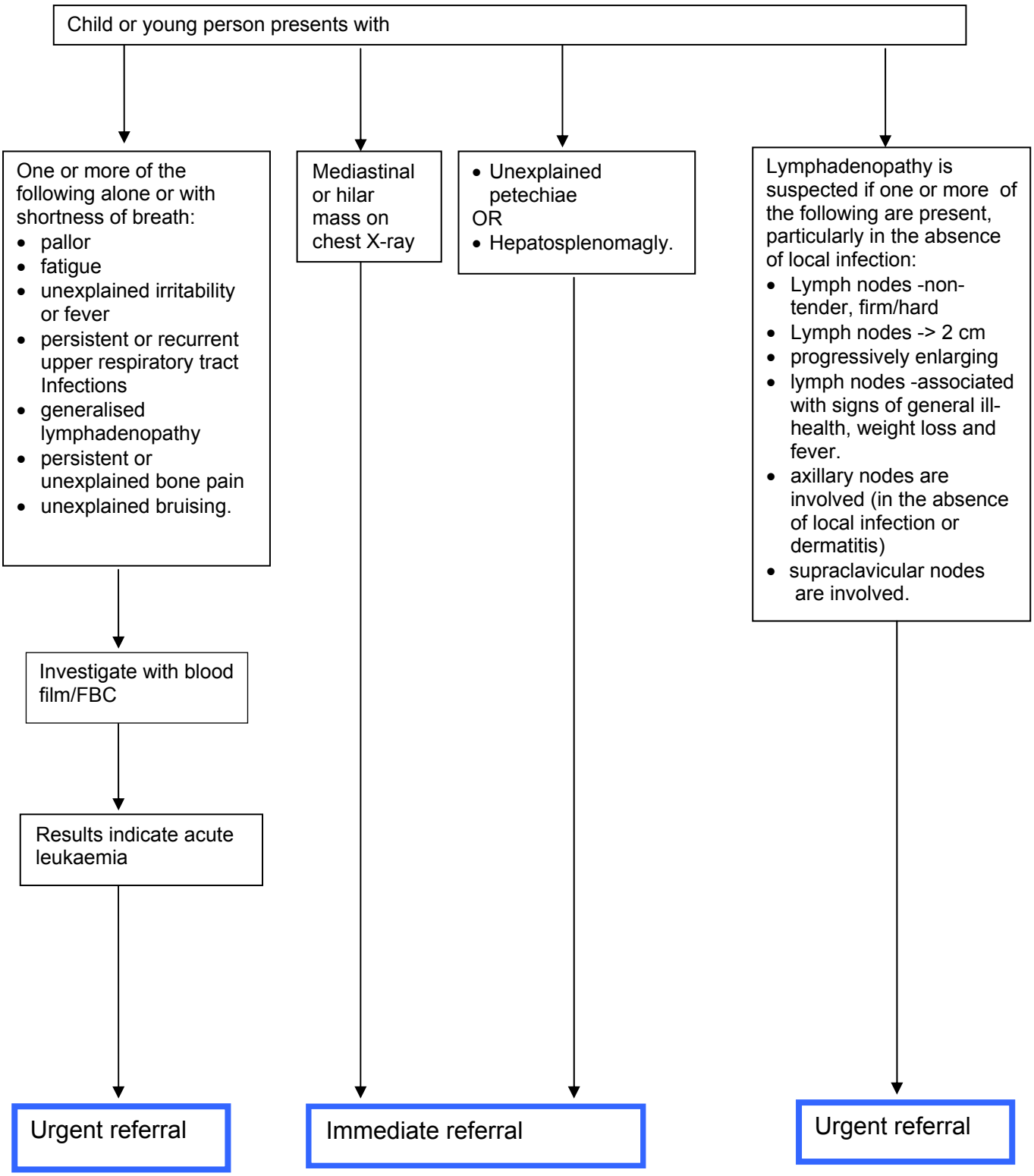
Brain and CNS cancers



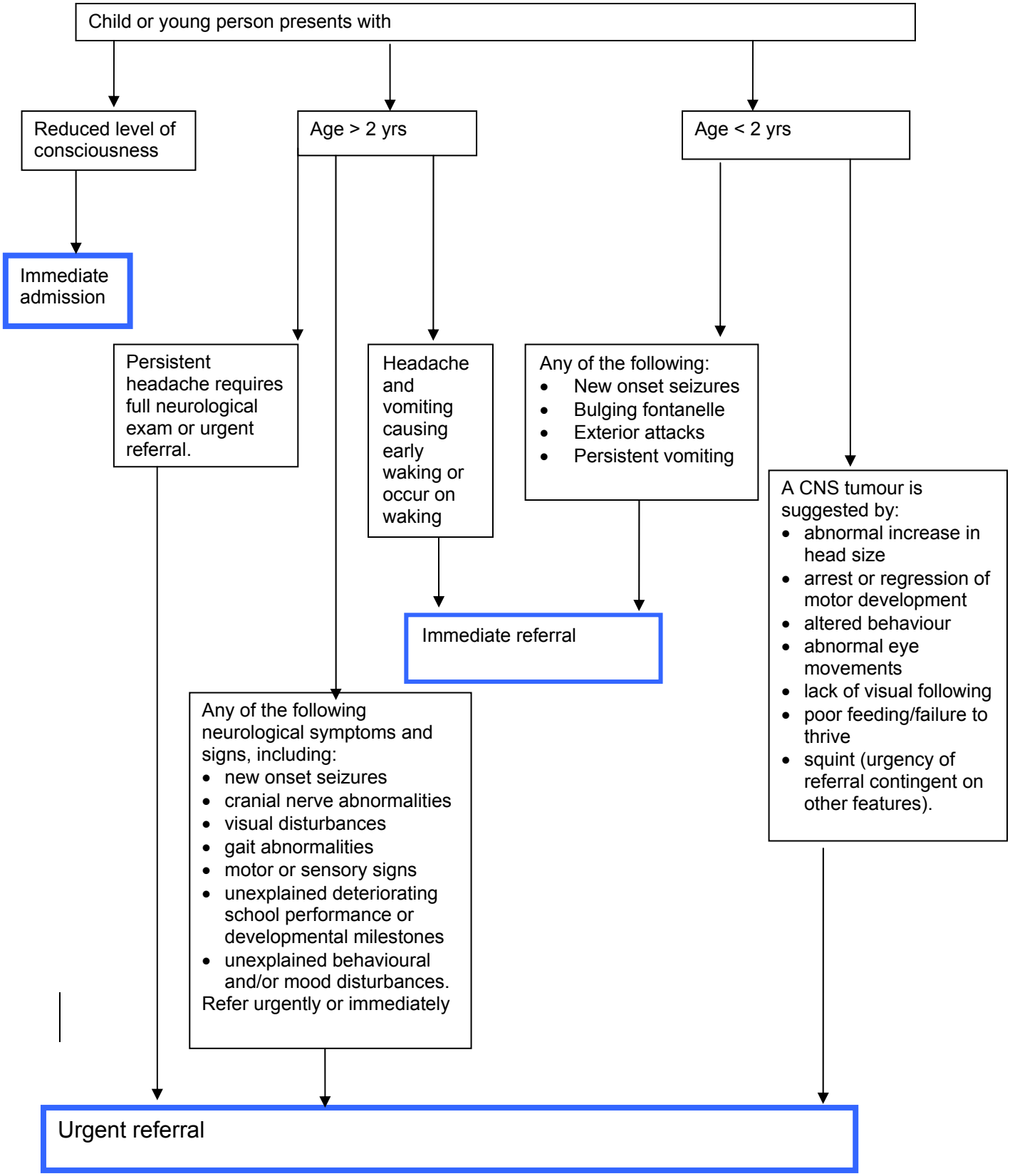
Bone cancers and soft-tissue sarcomas



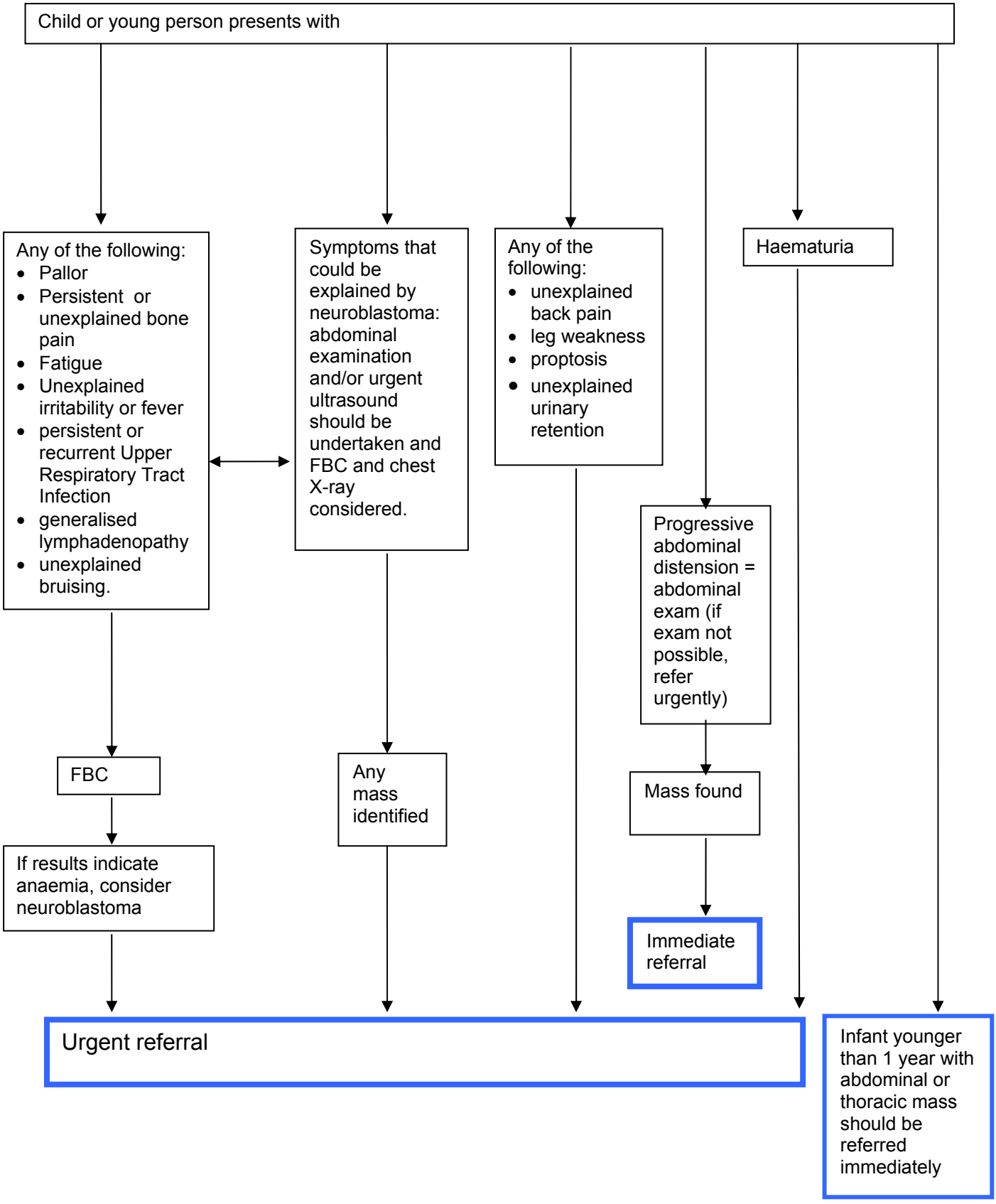
Children's cancers – leukaemia and lymphoma



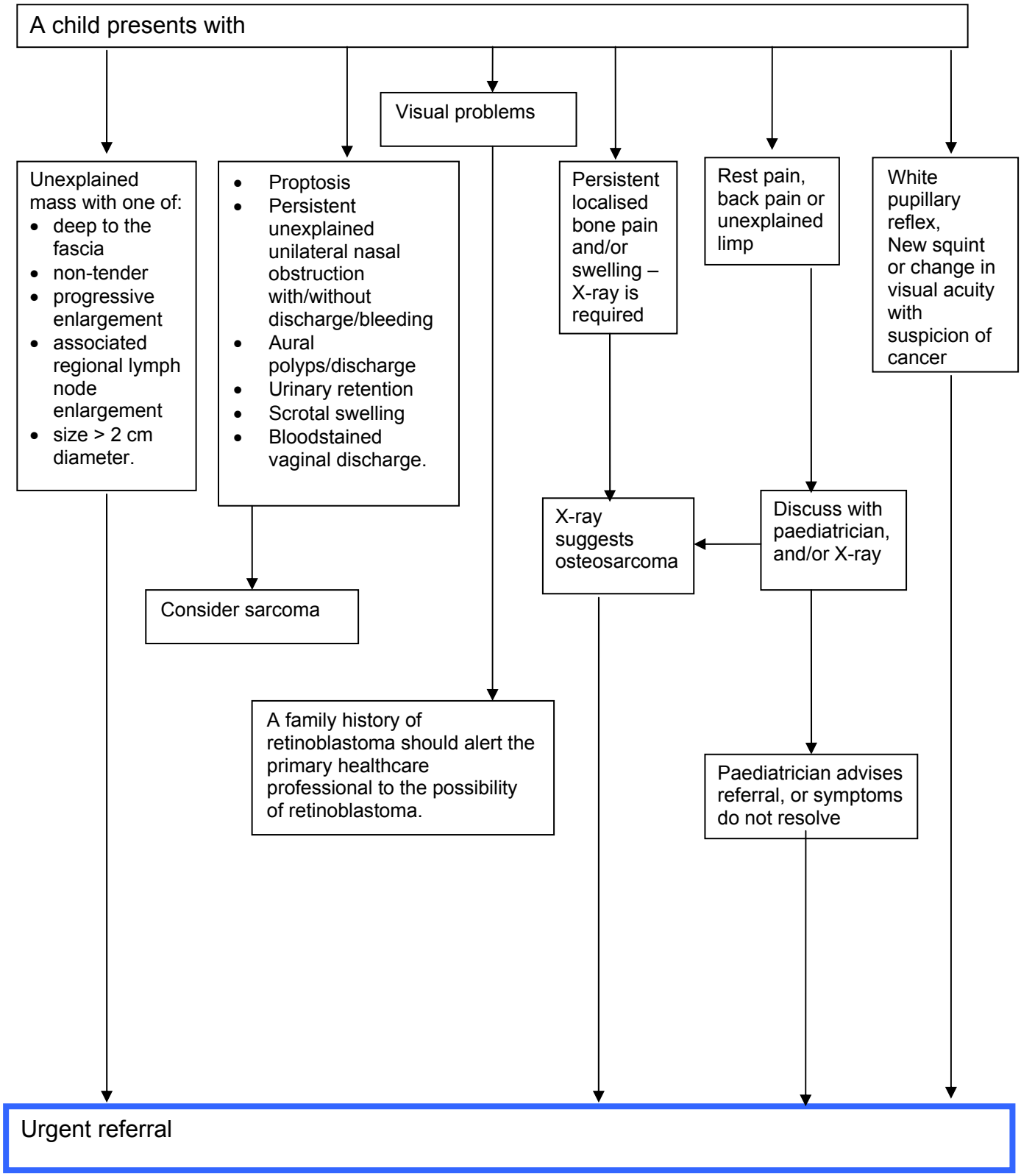
Children's cancers – brain tumours



Children's cancers – neuroblastoma and Wilm's tumour



Children's cancers – bone tumours, sarcoma and retinoblastoma



Appendix F: Differences between the Department of Health (2000) guidelines and the NICE guidelines (2005)

This paper summarises some of the differences between the NICE guidelines and the Department of Health guidelines that they replace. The differences have come about because of new evidence that has emerged since the Department of Health guidelines were published in 2000, and the fact that NICE employs a more systematic method of guideline development than does the Department of Health.

Format

The two guidelines have different formats. The NICE guideline follows the usual NICE approach of recommendations with associated evidence gradings.

Additional sections

The NICE guideline has several additional sections. These include key priorities, a section on the support and information needs of patients who are being referred because of suspected cancer, and a section dealing with the diagnostic process in primary health care. The key priorities highlight issues that should be given particular attention in implementation.

Patients being referred because of suspected cancer will have concerns and anxieties. They will also need information about what may be wrong with them and what to expect from specialist services. The guideline provides detailed recommendations on these issues.

It can be extremely difficult to recognise that it is cancer that may be causing the presenting symptoms and signs in some patients. The guideline therefore includes recommendations about the process of diagnosis and referral.

Who to refer to

The NICE guideline includes a recommendation relating to each group of cancers on who patients should be referred to. Service guidance has been taken into account, but the guideline also recognises that in some cancers the configuration of local services will vary from place to place.

The cancer sites

Lung cancer

The NICE guideline now deals with asbestos exposure and risk factors that may indicate the need for earlier referral in patients with selected symptoms.

Upper gastrointestinal cancer

The NICE guideline concludes that *Helicobacter pylori* status should not be taken into account when considering referral for suspected upper gastrointestinal cancer. It recommends that patients should avoid acid suppression medication for 2 weeks before endoscopy, and that upper gastrointestinal cancer should be considered in patients without dyspepsia who have weight loss and iron deficiency anaemia, or who have persistent vomiting and weight loss. Investigation by means of ultrasound in patients presenting with jaundice is also considered.

Lower gastrointestinal cancer

The NICE guideline includes a ‘treat, watch and wait’ period as an option in patients with equivocal symptoms. The need for digital rectal examination (DRE) in patients with unexplained gastrointestinal tract symptoms is emphasised. The risk factors of ulcerative colitis and family history of colorectal cancer are considered.

Breast cancer

The NICE guideline encourages healthcare professionals to promote breast awareness in women aged over 50 years. The NICE guideline also addresses breast cancer in men.

Gynaecological cancer

The NICE guideline includes recommendations on examination in primary care. The role of ultrasound is considered. The recommendations relating to endometrial cancer take account of cases that can occur before the menopause, and tamoxifen as a risk factor for endometrial cancer is considered.

Urological cancer

The NICE guideline includes the indications for DRE and prostate specific antigen (PSA) testing in symptomatic men, and recommends the exclusion of urinary tract infection (UTI) before taking blood for PSA testing. Haematuria with UTI is dealt with, including testing for proteinuria and creatinine in cases of microscopic haematuria. The role of ultrasound in investigation of scrotal masses is considered.

Haematological cancer

The NICE guideline lists the symptoms and signs that indicate the need for primary care haematological investigations (full blood count, erythrocyte sedimentation rate and others), and considers relevant investigation of unexplained fatigue, and the investigation of bone pain.

Skin cancer

The NICE guideline recommends use of the 7-point checklist for monitoring low-suspicion lesions and this should involve measurement with photographs and a marker scale/ruler. Primary care professionals undertaking minor surgery should have received accredited training for skin surgery.

Head and neck cancer

The NICE guideline includes advice on regular dental check-ups. Symptom time for chest X-ray due to hoarseness is lowered to 3 weeks or longer (6 weeks in the Department of Health guidelines). Referral for parotid or submandibular masses, and for sore throat, is addressed. The guideline now includes specific recommendations on referral for suspected thyroid cancer.

Brain and CNS cancer

The NICE guideline includes indications for examination and recommends discussion with a specialist if in doubt. The need to reassess if expectations of recovery are not met is stated, and the possibility of cerebral metastases in patients with a past history of cancer is considered. Scanning should be considered among the appropriate investigations if rapid access is available.

Bone cancer and sarcoma

The NICE guideline recommends urgent investigation of patients with increasing, unexplained or persistent bone pain or tenderness, particularly pain at rest (and especially if not in the joint), or an unexplained limp. The nature of the investigations will depend on patient age and clinical features, and in older people the possibility of myeloma or metastases should be considered. Discussion with a specialist is recommended if the practitioner has concerns over the interpretation of symptoms or signs.

Cancer in children and young people

Children presenting with the same problem at several consultations, and persisting symptoms as triggers for referral are addressed in the NICE guideline. The guideline also recommends that the healthcare professional should take note of parental knowledge and insight in deciding on the need for referral. Down's and other syndromes are highlighted as risk factors. The support and information needs of parents and children are considered. The guideline includes indications for full blood count and referral for lymph nodes > 2 cm in size (Department of Health guideline, 3 cm), and the significance of

unexplained shortness of breath. The features of brain cancer above and below the age of 2 years are specified, along with the features of neuroblastoma and unusual features to indicate sarcoma (for example, proptosis). Referral for soft tissue masses has been changed to size > 2 cm (3 cm in the Department of Health guideline).