



Suspected cancer: recognition and referral

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

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Update information

This guideline replaces CG27.

This guideline partially replaces CG122.

This guideline is the basis of QS96, QS124 and QS130.

This guideline should be read in conjunction with QS155.

Overview

This guideline covers identifying children, young people and adults with symptoms that could be caused by cancer. It outlines appropriate investigations in primary care, and selection of people to refer for a specialist opinion. It aims to help people understand what to expect if they have symptoms that may suggest cancer.

Who is it for?

- Healthcare professionals
- People involved in clinical governance in both primary and secondary care
- People with suspected cancer and their families and/or carers.

Introduction

This guideline updates and replaces NICE guideline CG27. The recommendations are labelled according to when the evidence was last reviewed (see <u>update information</u> for details).

Cancer has an enormous impact, both in terms of the number of people affected by it and the individual impact it has on people with cancer and those close to them. More than 300,000 new cancers (excluding skin cancers) are diagnosed annually in the UK, across over 200 different cancer types. Each of these cancer types has different presenting features, though they sometimes overlap. Approximately one-third of the population will develop a cancer in their lifetime. There is considerable variation in referral and testing for possible cancer, which cannot be fully explained by variation in the population.

The identification of people with possible cancer usually happens in primary care, because the large majority of people first present to a primary care clinician. Therefore, evidence from primary care should inform the identification process and was used as the basis for this guideline.

The recommendations were developed using a 'risk threshold', whereby if the risk of symptoms being caused by cancer is above a certain level then action (investigation or referral) is warranted. The positive predictive value (PPV) was used to determine the threshold. In the previous guideline, a disparate range of percentage risks of cancer was used to form the recommendations. Few corresponded with a PPV of lower than 5%. The guideline development group (GDG) felt that, in order to improve diagnosis of cancer, a PPV threshold lower than 5% was preferable. Taking into account the financial and clinical costs of broadening the recommendations, the GDG agreed to use a 3% PPV threshold value to underpin the recommendations for suspected cancer pathway <u>referrals</u> and urgent <u>direct access</u> investigations, such as brain scanning or endoscopy. Certain exceptions to a 3% PPV threshold were agreed. Recommendations were made for children and young people at below the 3% PPV threshold, although no explicit threshold value was set. The threshold was not applied to recommendations relating to tests routinely available in primary care (including blood tests such as prostate-specific antigen and imaging such as chest X-ray), primary care tests that could be used in place of specialist referral, non-urgent direct access tests and routine referrals for specialist opinion. Further information about the methods used to underpin the recommendations can be found in the full guideline.

It is well recognised that some risk factors increase the chance of a person developing cancer in the

future, for example, increasing age and a family history of cancer. However, risk factors do not affect the way in which cancer presents. Of the risk factors that were reported in the evidence, only smoking (in lung cancer) and age were found to significantly influence the chance of symptoms being predictive of cancer. Therefore, these are included in the recommendations where relevant. For all other risk factors, the recommendations would be the same for people with possible symptoms of cancer, irrespective of whether they had a risk factor. However, an exception was made to include asbestos exposure in the recommendations because of the high relative risk of mesothelioma in people who have been exposed to asbestos.

This guideline covers the recognition and selection for referral or investigation in primary care of people of all ages, including <u>children and young people</u>, who may have cancer. Although we have used the terms 'men' and 'women' for recommendations on gender-related cancers, these recommendations also extend to people who have changed or are in the process of changing gender, and who retain the relevant organs.

The guideline aims to help people understand what to expect if they have symptoms that may suggest cancer. It should also help those in secondary care to understand which services should be provided for people with suspected cancer. Finally, these recommendations are recommendations, not requirements, and they are not intended to override clinical judgement.

The recommendations in this guideline have been organised into 3 separate sections to help clinicians find the relevant information easily. In the first, the recommendations are organised by cancer site. There is a section covering patient support, safety netting and the diagnostic process. Then, for those wanting to find recommendations on specific symptoms and primary care investigations, the recommendations are in a section organised by symptoms and investigation findings.

Safeguarding children

Remember that child maltreatment:

- is common
- can present anywhere
- may co-exist with other health problems, including suspected cancer.

See <u>NICE's guideline on child maltreatment</u> for clinical features that may be associated with maltreatment.

People have the right to be involved in discussions and make informed decisions about their care, as described in <u>making decisions about your care</u>.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations (although this may not apply to recommendations made before 2009, see the section on recommendation wording in guideline updates below). It also has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

How the guideline is organised

The recommendations in this guideline have been organised into 3 separate sections to help healthcare professionals find the relevant information easily. The <u>recommendations for investigation and referral organised by site of suspected cancer</u> are also presented in <u>tables of recommendations organised by symptoms and investigation findings</u>. Either section should be used in conjunction with the <u>recommendations on patient support</u>, <u>safety netting and the diagnostic process</u>.

Recommendation wording in guideline updates

NICE began using standard wording to denote the strength of recommendations in guidelines that started development after January 2009. It does not apply to any recommendations ending [2005] (see <u>update information</u> for details about how recommendations are labelled). In particular, for recommendations labelled [2005] the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Terms used in this guideline

Children

From birth to 15 years.

Children and young people

From birth to 24 years.

Consistent with

The finding has characteristics that could be caused by many things, including cancer.

Direct access

When a test is performed and primary care retain clinical responsibility throughout, including acting on the result.

Immediate

An acute admission or referral occurring within a few hours, or even more quickly if necessary.

Non-urgent

The timescale generally used for a referral or investigation that is not considered very urgent or urgent.

Persistent

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 health professional.

Raises the suspicion of

A mass or lesion that has an appearance or a feel that makes the healthcare professional believe cancer is a significant possibility.

Safety netting

The active monitoring in primary care of people who have presented with symptoms. It has 2 separate aspects:

- timely review and action after investigations
- active monitoring of symptoms in people at low risk (but not no risk) of having cancer to see if their risk of cancer changes.

Suspected cancer pathway referral

The patient is seen within the national target for cancer referrals (2 weeks at the time of publication of this guideline).

Unexplained

Symptoms or signs that have not led to a diagnosis being made by the healthcare professional in primary care after initial assessment (including history, examination and any primary care investigations).

Urgent

To happen/be performed before 2 weeks. An urgent referral means that the woman is referred to a gynaecological cancer service within the national target in England and Wales for referral for suspected cancer, which is currently 2 weeks.

Very urgent

To happen within 48 hours.

Young people

Aged 16 to 24 years.

1 Recommendations organised by site of cancer

Use this guideline to guide referrals. If still uncertain about whether a referral is needed, consider contacting a specialist (see the recommendations on the diagnostic process). Consider a review for people with any symptom associated with increased cancer risk who do not meet the criteria for referral or investigative action (see the recommendations on safety netting).

1.1 Lung and pleural cancers

Lung cancer

- 1.1.1 Refer people using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for lung cancer if they:
 - have chest X-ray findings that suggest lung cancer or
 - are aged 40 and over with <u>unexplained</u> haemoptysis. [2015]
- 1.1.2 Offer an urgent chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over if they have 2 or more of the following unexplained symptoms, or if they have ever smoked and have 1 or more of the following unexplained symptoms:
 - cough
 - fatigue
 - shortness of breath
 - chest pain
 - weight loss
 - appetite loss. [2015]

- 1.1.3 Consider an <u>urgent</u> chest X-ray (to be performed within 2 weeks) to assess for lung cancer in people aged 40 and over with any of the following:
 - persistent or recurrent chest infection
 - finger clubbing
 - supraclavicular lymphadenopathy or persistent cervical lymphadenopathy
 - chest signs consistent with lung cancer
 - thrombocytosis. [2015]

Mesothelioma

- 1.1.4 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for mesothelioma if they have chest X-ray findings that suggest mesothelioma. [2015]
- 1.1.5 Offer an urgent chest X-ray (to be performed within 2 weeks) to assess for mesothelioma in people aged 40 and over, if:
 - they have 2 or more of the following unexplained symptoms, or
 - they have 1 or more of the following unexplained symptoms and have ever smoked, or
 - they have 1 or more of the following unexplained symptoms and have been exposed to asbestos:
 - cough
 - fatigue
 - shortness of breath
 - chest pain
 - weight loss
 - appetite loss. [2015]
- 1.1.6 Consider an urgent chest X-ray (to be performed within 2 weeks) to assess for mesothelioma in people aged 40 and over with either:

- finger clubbing or
- chest signs compatible with pleural disease. [2015]

1.2 Upper gastrointestinal tract cancers

Oesophageal cancer

- 1.2.1 Offer <u>urgent</u>, <u>direct access</u> upper gastrointestinal endoscopy (to be performed within 2 weeks) to assess for oesophageal cancer in people:
 - with dysphagia or
 - aged 55 and over with weight loss and any of the following:
 - upper abdominal pain
 - reflux
 - dyspepsia. [2015]
- 1.2.2 Consider <u>non-urgent</u> direct access upper gastrointestinal endoscopy to assess for oesophageal cancer in people with haematemesis. [2015]
- 1.2.3 Consider non-urgent direct access upper gastrointestinal endoscopy to assess for oesophageal cancer in people aged 55 or over with:
 - treatment-resistant dyspepsia or
 - upper abdominal pain with low haemoglobin levels or

nausea

vomiting

weight loss

raised platelet count with any of the following:

reflux dyspepsia upper abdominal pain, or • nausea or vomiting with any of the following: weight loss reflux dyspepsia upper abdominal pain. [2015] Pancreatic cancer 1.2.4 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for pancreatic cancer if they are aged 40 and over and have jaundice. [2015] 1.2.5 Consider an urgent direct access CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available, to assess for pancreatic cancer in people aged 60 and over with weight loss and any of the following: diarrhoea back pain abdominal pain nausea vomiting

- constipation
- new-onset diabetes. [2015]

Stomach cancer

- 1.2.6 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with an upper abdominal mass <u>consistent with</u> stomach cancer. [2015]
- 1.2.7 Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) to assess for stomach cancer in people:
 - with dysphagia or
 - aged 55 and over with weight loss and any of the following:
 - upper abdominal pain
 - reflux
 - dyspepsia. [2015]
- 1.2.8 Consider non-urgent direct access upper gastrointestinal endoscopy to assess for stomach cancer in people with haematemesis. [2015]
- 1.2.9 Consider non-urgent direct access upper gastrointestinal endoscopy to assess for stomach cancer in people aged 55 or over with:
 - treatment-resistant dyspepsia or
 - upper abdominal pain with low haemoglobin levels or

- raised platelet count with any of the following:
 - nausea
 - vomiting
 - weight loss
 - reflux
 - dyspepsia
 - upper abdominal pain, or
- nausea or vomiting with any of the following:
 - weight loss
 - reflux
 - dyspepsia
 - upper abdominal pain. [2015]

Gall bladder cancer

1.2.10 Consider an urgent direct access ultrasound scan (to be performed within 2 weeks) to assess for gall bladder cancer in people with an upper abdominal mass consistent with an enlarged gall bladder. [2015]

Liver cancer

1.2.11 Consider an urgent direct access ultrasound scan (to be performed within 2 weeks) to assess for liver cancer in people with an upper abdominal mass consistent with an enlarged liver. [2015]

1.3 Lower gastrointestinal tract cancers

Colorectal cancer

1.3.1 Refer adults using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for colorectal cancer if:

- they are aged 40 and over with <u>unexplained</u> weight loss and abdominal pain or
- they are aged 50 and over with unexplained rectal bleeding or
- they are aged 60 and over with:
 - iron-deficiency anaemia or
 - changes in their bowel habit, or
- tests show occult blood in their faeces. [2015]
- 1.3.2 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults with a rectal or abdominal mass. [2015]
- 1.3.3 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for colorectal cancer in adults aged under 50 with rectal bleeding and any of the following unexplained symptoms or findings:
 - abdominal pain
 - change in bowel habit
 - weight loss
 - iron-deficiency anaemia. [2015]
- 1.3.4 Offer testing with quantitative faecal immunochemical tests (see the <u>NICE</u> diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) to assess for colorectal cancer in adults without rectal bleeding who:
 - are aged 50 and over with unexplained:
 - abdominal pain or
 - weight loss, or
 - are aged under 60 with:
 - changes in their bowel habit, or
 - iron-deficiency anaemia, or

• are aged 60 and over and have anaemia even in the absence of iron deficiency. [2021]

Anal cancer

1.3.5 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for anal cancer in people with an unexplained anal mass or unexplained anal ulceration. [2015]

1.4 Breast cancer

- 1.4.1 Refer people using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for breast cancer if they are:
 - aged 30 and over and have an <u>unexplained</u> breast lump with or without pain or
 - aged 50 and over with any of the following symptoms in one nipple only:
 - discharge
 - retraction
 - other changes of concern. [2015]
- 1.4.2 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for breast cancer in people:
 - with skin changes that suggest breast cancer or
 - aged 30 and over with an unexplained lump in the axilla. [2015]
- 1.4.3 Consider <u>non-urgent</u> referral in people aged under 30 with an unexplained breast lump with or without pain. See also recommendations 1.16.2 and 1.16.3 for information about seeking specialist advice. [2015]

1.5 Gynaecological cancers

Ovarian cancer

The recommendations in this section have been incorporated from <u>NICE's guideline on ovarian</u> <u>cancer</u> and have not been updated. The recommendations for ovarian cancer apply to women aged 18 and over.

- 1.5.1 Make an <u>urgent</u> referral to a gynaecological cancer service if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously uterine fibroids). [2011, amended 2020]
- 1.5.2 Carry out tests in primary care (see recommendations 1.5.6 to 1.5.9) if a woman (especially if 50 or over) reports having any of the following symptoms on a <u>persistent</u> or frequent basis particularly more than 12 times per month:
 - persistent abdominal distension (women often refer to this as 'bloating')
 - feeling full (early satiety) and/or loss of appetite
 - pelvic or abdominal pain
 - increased urinary urgency and/or frequency. [2011]
- 1.5.3 Consider carrying out tests in primary care (see recommendations 1.5.6 to 1.5.9) if a woman reports <u>unexplained</u> weight loss, fatigue or changes in bowel habit. [2011]
- 1.5.4 Advise any woman who is not suspected of having ovarian cancer to return to her GP if her symptoms become more frequent and/or persistent. [2011]
- 1.5.5 Carry out appropriate tests for ovarian cancer (see recommendations 1.5.6 to 1.5.9) in any woman of 50 or over who has experienced symptoms within the last 12 months that suggest irritable bowel syndrome (IBS), because IBS rarely presents for the first time in women of this age. (See NICE's guideline on irritable bowel syndrome in adults). [2011]
- 1.5.6 Measure serum CA125 in primary care in women with symptoms that suggest ovarian cancer (see recommendations 1.5.1 to 1.5.5). [2011]
- 1.5.7 If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis. [2011]
- 1.5.8 If the ultrasound suggests ovarian cancer, make an <u>urgent</u> referral to a gynaecological cancer service. [2011, amended 2020]
- 1.5.9 For any woman who has normal serum CA125 (less than 35 IU/ml), or CA125 of 35 IU/ml or greater but a normal ultrasound:

- assess her carefully for other clinical causes of her symptoms and investigate if appropriate
- if no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent. [2011]

Endometrial cancer

- 1.5.10 Refer women using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for endometrial cancer if they are aged 55 and over with post-menopausal bleeding (unexplained vaginal bleeding more than 12 months after menstruation has stopped because of the menopause). [2015]
- 1.5.11 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for endometrial cancer in women aged under 55 with post-menopausal bleeding. [2015]
- 1.5.12 Consider a <u>direct access</u> ultrasound scan to assess for endometrial cancer in women aged 55 and over with:
 - unexplained symptoms of vaginal discharge who:
 - are presenting with these symptoms for the first time or
 - have thrombocytosis or
 - report haematuria, or
 - visible haematuria and:
 - low haemoglobin levels or
 - thrombocytosis or
 - high blood glucose levels. [2015]

Cervical cancer

1.5.13 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for women if, on examination, the appearance of their cervix is consistent with cervical cancer. [2015]

Vulval cancer

1.5.14 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for vulval cancer in women with an unexplained vulval lump, ulceration or bleeding. [2015]

Vaginal cancer

1.5.15 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for vaginal cancer in women with an unexplained palpable mass in or at the entrance to the vagina. [2015]

1.6 Urological cancers

Prostate cancer

- 1.6.1 Refer men using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for prostate cancer if their prostate feels malignant on digital rectal examination. [2015]
- 1.6.2 Consider a prostate-specific antigen (PSA) test and digital rectal examination to assess for prostate cancer in men with:
 - any lower urinary tract symptoms, such as nocturia, urinary frequency, hesitancy, urgency or retention or
 - erectile dysfunction or
 - visible haematuria. [2015]
- 1.6.3 Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) for prostate cancer if their PSA levels are above the age-specific reference range. [2015]

Bladder cancer

1.6.4 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for bladder cancer if they are:

- aged 45 and over and have:
 - unexplained visible haematuria without urinary tract infection or
 - visible haematuria that persists or recurs after successful treatment of urinary tract infection, or
- aged 60 and over and have unexplained non-visible haematuria and either dysuria or a raised white cell count on a blood test. [2015]
- 1.6.5 Consider <u>non-urgent</u> referral for bladder cancer in people aged 60 and over with recurrent or <u>persistent</u> unexplained urinary tract infection. [2015]

Renal cancer

- 1.6.6 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) for renal cancer if they are aged 45 and over and have:
 - unexplained visible haematuria without urinary tract infection or
 - visible haematuria that persists or recurs after successful treatment of urinary tract infection. [2015]

Testicular cancer

- 1.6.7 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for testicular cancer in men if they have a non-painful enlargement or change in shape or texture of the testis. [2015]
- 1.6.8 Consider a <u>direct access</u> ultrasound scan for testicular cancer in men with unexplained or persistent testicular symptoms. [2015]

Penile cancer

- 1.6.9 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for penile cancer in men if they have either:
 - a penile mass **or** ulcerated lesion, where a sexually transmitted infection has been excluded as a cause, **or**

- a persistent penile lesion after treatment for a sexually transmitted infection has been completed. [2015]
- 1.6.10 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for penile cancer in men with unexplained or persistent symptoms affecting the foreskin or glans. [2015]

1.7 Skin cancers

Malignant melanoma of the skin

1.7.1 Refer people using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for melanoma if they have a suspicious pigmented skin lesion with a weighted 7-point checklist score of 3 or more. [2015]

Weighted 7-point checklist

Major features of the lesions (scoring 2 points each):

- change in size
- irregular shape
- irregular colour.

Minor features of the lesions (scoring 1 point each):

- largest diameter 7 mm or more
- inflammation
- oozing
- change in sensation.
- 1.7.2 Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) if dermoscopy suggests melanoma of the skin. [2015]
- 1.7.3 Consider a suspected cancer pathway referral (for an appointment within

2 weeks) for melanoma in people with a pigmented or non-pigmented skin lesion that suggests nodular melanoma. [2015]

Squamous cell carcinoma

1.7.4 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion <u>that raises the suspicion of</u> squamous cell carcinoma. [2015]

Basal cell carcinoma

- 1.7.5 Consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma. (Typical features of basal cell carcinoma include: an ulcer with a raised rolled edge; prominent fine blood vessels around a lesion; or a nodule on the skin (particularly pearly or waxy nodules).) [2015]
- 1.7.6 Only consider a suspected cancer pathway referral (for an appointment within 2 weeks) for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is particular concern that a delay may have a significant impact, because of factors such as lesion site or size. [2015]
- 1.7.7 Follow NICE's guidance on improving outcomes for people with skin tumours including melanoma for advice on who should excise suspected basal cell carcinomas. [2015]

1.8 Head and neck cancers

Laryngeal cancer

- 1.8.1 Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for laryngeal cancer in people aged 45 and over with:
 - persistent unexplained hoarseness or
 - an unexplained lump in the neck. [2015]

Oral cancer

1.8.2 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for oral cancer in people with either:

- unexplained ulceration in the oral cavity lasting for more than 3 weeks or
- a persistent and unexplained lump in the neck. [2015]
- 1.8.3 Consider an <u>urgent</u> referral (for an appointment within 2 weeks) for assessment for possible oral cancer by a dentist in people who have either:
 - a lump on the lip or in the oral cavity or
 - a red or red and white patch in the oral cavity <u>consistent with</u> erythroplakia or erythroleukoplakia. [2015]
- 1.8.4 Consider a suspected cancer pathway referral by the dentist (for an appointment within 2 weeks) for oral cancer in people when assessed by a dentist as having either:
 - a lump on the lip or in the oral cavity consistent with oral cancer or
 - a red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia. [2015]

Thyroid cancer

1.8.5 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for thyroid cancer in people with an unexplained thyroid lump. [2015]

1.9 Brain and central nervous system cancers

Adults

1.9.1 Consider an <u>urgent direct access</u> MRI scan of the brain (or CT scan if MRI is contraindicated) (to be performed within 2 weeks) to assess for brain or central nervous system cancer in adults with progressive, sub-acute loss of central neurological function. [2015]

Children and young people

1.9.2 Consider a <u>very urgent</u> referral (for an appointment within 48 hours) for suspected brain or central nervous system cancer in <u>children and young people</u> with newly abnormal cerebellar or other central neurological function. [2015]

1.10 Haematological cancers

Leukaemia in adults

- 1.10.1 Consider a <u>very urgent</u> full blood count (within 48 hours) to assess for leukaemia in adults with any of the following:
 - pallor
 - persistent fatigue
 - unexplained fever
 - unexplained persistent or recurrent infection
 - generalised lymphadenopathy
 - unexplained bruising
 - · unexplained bleeding
 - unexplained petechiae
 - hepatosplenomegaly. [2015]

Leukaemia in children and young people

- 1.10.2 Refer <u>children and young people</u> for <u>immediate</u> specialist assessment for leukaemia if they have unexplained petechiae or hepatosplenomegaly. [2015]
- 1.10.3 Offer a very urgent full blood count (within 48 hours) to assess for leukaemia in children and young people with any of the following:
 - pallor
 - persistent fatigue
 - unexplained fever
 - unexplained persistent infection
 - generalised lymphadenopathy

- persistent or unexplained bone pain
- unexplained bruising
- unexplained bleeding. [2015]

Myeloma

- 1.10.4 Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate to assess for myeloma in people aged 60 and over with persistent bone pain, particularly back pain, or unexplained fracture. [2015]
- 1.10.5 Offer very urgent protein electrophoresis and a Bence-Jones protein urine test (within 48 hours) to assess for myeloma in people aged 60 and over with hypercalcaemia or leukopenia and a presentation that is <u>consistent with</u> possible myeloma. [2015]
- 1.10.6 Consider very urgent protein electrophoresis and a Bence-Jones protein urine test (within 48 hours) to assess for myeloma if the plasma viscosity or erythrocyte sedimentation rate and presentation are consistent with possible myeloma. [2015]
- 1.10.7 Refer people using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) if the results of protein electrophoresis or a Bence-Jones protein urine test suggest myeloma. [2015]

Non-Hodgkin's lymphoma

Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.

Adults

1.10.8 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for non-Hodgkin's lymphoma in adults presenting with unexplained lymphadenopathy or splenomegaly. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [2015]

Children and young people

1.10.9 Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment for non-Hodgkin's lymphoma in children and young people presenting with unexplained lymphadenopathy or splenomegaly. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [2015]

Hodgkin's lymphoma

Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.

Adults

1.10.10 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for Hodgkin's lymphoma in adults presenting with unexplained lymphadenopathy. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus, weight loss or alcohol-induced lymph node pain. [2015]

Children and young people

1.10.11 Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment for Hodgkin's lymphoma in children and young people presenting with unexplained lymphadenopathy. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [2015]

1.11 Sarcomas

Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.

Bone sarcoma in adults

1.11.1 Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) for adults if an X-ray suggests the possibility of bone sarcoma. [2015]

Bone sarcoma in children and young people

- 1.11.2 Consider a <u>very urgent</u> referral (for an appointment within 48 hours) for specialist assessment for <u>children and young people</u> if an X-ray suggests the possibility of bone sarcoma. [2015]
- 1.11.3 Consider a very urgent <u>direct access</u> X-ray (to be performed within 48 hours) to assess for bone sarcoma in children and young people with <u>unexplained</u> bone swelling or pain. [2015]

Soft tissue sarcoma in adults

- 1.11.4 Consider an <u>urgent</u> direct access ultrasound scan (to be performed within 2 weeks) to assess for soft tissue sarcoma in adults with an unexplained lump that is increasing in size. [2015]
- 1.11.5 Consider a suspected cancer pathway referral (for an appointment within 2 weeks) for adults if they have ultrasound scan findings that are suggestive of soft tissue sarcoma or if ultrasound findings are uncertain and clinical concern persists. [2015]

Soft tissue sarcoma in children and young people

- 1.11.6 Consider a very urgent direct access ultrasound scan (to be performed within 48 hours) to assess for soft tissue sarcoma in children and young people with an unexplained lump that is increasing in size. [2015]
- 1.11.7 Consider a very urgent referral (for an appointment within 48 hours) for children and young people if they have ultrasound scan findings that are suggestive of soft tissue sarcoma or if ultrasound findings are uncertain and clinical concern persists. [2015]

1.12 Childhood cancers

Neuroblastoma

1.12.1 Consider <u>very urgent</u> referral (for an appointment within 48 hours) for specialist assessment for neuroblastoma in <u>children</u> with a palpable abdominal mass or <u>unexplained</u> enlarged abdominal organ. [2015]

Retinoblastoma

1.12.2 Consider <u>urgent</u> referral (for an appointment within 2 weeks) for ophthalmological assessment for retinoblastoma in children with an absent red reflex. [2015]

Wilms' tumour

- 1.12.3 Consider very urgent referral (for an appointment within 48 hours) for specialist assessment for Wilms' tumour in children with any of the following:
 - a palpable abdominal mass
 - an unexplained enlarged abdominal organ
 - unexplained visible haematuria. [2015]

1.13 Non-site-specific symptoms

Some symptoms or symptom combinations may be features of several different cancers. For some of these symptoms, the risk for each individual cancer may be low but the total risk of cancer of any type may be higher. This section includes recommendations for these symptoms.

Symptoms of concern in children and young people

1.13.1 Take into account the insight and knowledge of parents and carers when considering making a referral for suspected cancer in a child or young person. Consider referral for <u>children</u> if their parent or carer has <u>persistent</u> concern or anxiety about the child's symptoms, even if the symptoms are most likely to have a benign cause. [2015]

Symptoms of concern in adults

- 1.13.2 For people with <u>unexplained</u> weight loss, which is a symptom of several cancers including colorectal, gastro-oesophageal, lung, prostate, pancreatic and urological cancer:
 - carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and

- offer <u>urgent</u> investigation or a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks). [2015]
- 1.13.3 For people with unexplained appetite loss, which is a symptom of several cancers including lung, oesophageal, stomach, colorectal, pancreatic, bladder and renal cancer:
 - carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and
 - offer urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks). [2015]
- 1.13.4 For people with deep vein thrombosis, which is associated with several cancers including urogenital, breast, colorectal and lung cancer:
 - carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely and
 - consider urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks). [2015]

Recommendations on patient support, safety netting and the diagnostic process

Use this guideline to guide referrals. If still uncertain about whether a referral is needed, consider contacting a specialist (see the recommendations on <u>the diagnostic process</u>). Consider a review for people with any symptom associated with increased cancer risk who do not meet the criteria for referral or investigative action (see the recommendations on <u>safety netting</u>).

1.14 Patient information and support

- 1.14.1 Discuss with people with suspected cancer (and their 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. [2015]
- 1.14.2 When cancer is suspected in a child, discuss the referral decision and information to be given to the child with the parents or carers (and the child if appropriate). [2015]
- 1.14.3 Explain to people who are being referred with suspected cancer that they are being referred to a cancer service. Reassure them, as appropriate, that most people referred will not have a diagnosis of cancer, and discuss alternative diagnoses with them. [2015]
- 1.14.4 Give the person information on the possible diagnosis (both benign and malignant) in accordance with their wishes for information (see also <u>NICE's guideline on patient experience in adult NHS services</u>). [2015]
- 1.14.5 The information given to people with suspected cancer and their families and/or carers should cover, among other issues:
 - where the person is 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 before the specialist appointment
- what to expect from the service the person will be attending
- what type of tests may 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
- who to contact if they do not receive confirmation of an appointment
- other sources of support. [2015]
- 1.14.6 Provide information that is appropriate for the person in terms of language, ability and culture, recognising the potential for different cultural meanings associated with the possibility of cancer. [2015]
- 1.14.7 Have information available in a variety of formats on both local and national sources of information and support for people who are being referred with suspected cancer. For more information on information sharing, see the <u>section on enabling patients to actively participate in their care in NICE's guideline on patient experience in adult NHS services</u>. [2015]
- 1.14.8 Reassure people in the <u>safety netting</u> group (see recommendation 1.15.2) who are concerned that they may have cancer that with their current symptoms their risk of having cancer is low. [2015]
- 1.14.9 Explain to people who are being offered safety netting (see recommendation 1.15.2) which symptoms to look out for and when they should return for re-evaluation. It may be appropriate to provide written information. [2015]
- 1.14.10 When referring a person with suspected cancer to a specialist service, assess their need for continuing support while waiting for their referral appointment. This should include inviting the person to contact their healthcare professional again if they have more concerns or questions before they see a specialist. [2005]
- 1.14.11 If the person has additional support needs because of their personal

circumstances, inform the specialist (with the person's agreement). [2005]

1.15 Safety netting

- 1.15.1 Ensure that the results of investigations are reviewed and acted upon appropriately, with the healthcare professional who ordered the investigation taking or explicitly passing on responsibility for this. Be aware of the possibility of false-negative results for chest X-rays and tests for occult blood in faeces.

 [2015]
- 1.15.2 Consider a review for people with any symptom that is associated with an increased risk of cancer, but who do not meet the criteria for referral or other investigative action. The review may be:
 - planned within a time frame agreed with the person or
 - patient-initiated if new symptoms develop, the person continues to be concerned, or their symptoms recur, persist or worsen. [2015]

1.16 The diagnostic process

- 1.16.1 Take part in continuing education, peer review and other activities to improve and maintain clinical consulting, reasoning and diagnostic skills, in order to identify at an early stage people who may have cancer, and to communicate the possibility of cancer to the person. [2005]
- 1.16.2 Discussion with a specialist (for example, by telephone or email) 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. [2005]
- 1.16.3 Put in place local arrangements to ensure that letters about <u>non-urgent</u> referrals are assessed by the specialist, so that the person can be seen more urgently if necessary. [2005]
- 1.16.4 Put in place local arrangements to ensure that there is a maximum waiting period for non-urgent referrals, in accordance with national targets and local arrangements. [2005]

- 1.16.5 Ensure local arrangements are in place to identify people who miss their appointments so that they can be followed up. [2005]
- 1.16.6 Include all appropriate information in referral correspondence, including whether the referral is <u>urgent</u> or non-urgent. [2005]
- 1.16.7 Use local referral proformas if these are in use. [2005]
- 1.16.8 Once the decision to refer has been made, make sure that the referral is made within 1 working day. [2005]

Recommendations organised by symptom and findings of primary care investigations

The recommendations in this section are displayed alphabetically by symptom then in order of urgency of the action needed, to make sure that most urgent actions are not missed. Where there are several recommendations relating to the same cancer these have been grouped for ease of reference. Occasionally the same symptom may suggest more than one cancer site. In such instances the recommendations are displayed together and the GP should use their clinical judgement to decide on the most appropriate action.

Use this guideline to guide referrals. If still uncertain about whether a referral is needed, consider contacting a specialist (see the recommendations on <u>the diagnostic process</u>). Consider a review for people with any symptom associated with increased cancer risk who do not meet the criteria for referral or investigative action (see the recommendations on <u>safety netting</u>).

Abdominal symptoms

See also the <u>section on bleeding</u> for recommendations on rectal bleeding.

Abdominal distension

Symptom and specific features	Possible cancer	Recommendation
Abdominal distension (persistent or frequent – particularly more than 12 times per month) in women, especially if 50 and over.	Ovarian	Carry out tests in primary care [1.5.2] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for more information
		on tests for ovarian cancer These recommendations apply to women aged 18 and over.

Abdominal examination findings

Symptoms and signs	Possible cancer	Recommendation
Ascites and/or a pelvic or abdominal mass identified by physical examination (which is not obviously uterine fibroids) in women	Ovarian	Urgent referral [1.5.1] These recommendations apply to women aged 18 and over.

Abdominal, pelvic or rectal mass or enlarged abdominal organ

Symptom and specific features	Possible cancer	Recommendation
Abdominal or pelvic mass identified by physical examination (which is not obviously uterine fibroids) in women	Ovarian	Urgent referral [1.5.1] These recommendations apply to women aged 18 and over
Abdominal or rectal mass	Colorectal	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.3.2]
Splenomegaly (unexplained) in adults	Non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss. [1.10.8] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.
Upper abdominal massconsistent with stomach cancer	Stomach	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.2.6]

Symptom and specific features	Possible cancer	Recommendation
Upper abdominal mass consistent with an enlarged gall bladder	Gall bladder	Consider an urgent <u>direct access</u> ultrasound scan (to be performed within 2 weeks) [1.2.10]
Upper abdominal mass consistent with an enlarged liver	Liver	Consider an urgent direct access ultrasound scan (to be performed within 2 weeks) [1.2.11]
Hepatosplenomegaly	Leukaemia	Consider a <u>very urgent</u> full blood count (within 48 hours) [1.10.1]

Abdominal or pelvic pain

Symptom and specific features	Possible cancer	Recommendation
Abdominal pain with weight loss (unexplained), 40 and over	Colorectal	Refer adults using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.1]
Abdominal pain (unexplained) with rectal bleeding in adults under 50	Colorectal	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.3.3]
Abdominal pain (unexplained) without rectal bleeding, 50 and over	Colorectal	Offer testing with quantitative faecal immunochemical tests (see the NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) [1.3.4]
Upper abdominal pain with weight loss, 55 and over	Oesophageal or stomach	Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) [1.2.1] [1.2.7]

Symptom and specific features	Possible cancer	Recommendation
Upper abdominal pain with low haemoglobin levels or raised platelet count or nausea or vomiting, 55 and over	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]
Abdominal or pelvic pain (persistent or frequent – particularly more than 12 times per month) in women, especially if 50 and over	Ovarian	Carry out tests in primary care [1.5.2] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for more information on tests for ovarian cancer These recommendations apply to women aged 18 and over
Abdominal pain with weight loss, 60 and over	Pancreatic	Consider an urgent direct access CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available [1.2.5]
Irritable bowel syndrome symptoms ² within the last 12 months in women 50 and over	Ovarian	Carry out appropriate tests for ovarian cancer, because irritable bowel syndrome rarely presents for the first time in women of this age [1.5.5] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for more information on tests for ovarian cancer These recommendations apply to women aged 18 and over Also see the NICE guideline on irritable bowel
		Also see the <u>NICE guideline on irritable bowel</u> syndrome in adults.

Change in bowel habit

Symptom and specific features	Possible cancer	Recommendation	
Change in bowel habit (unexplained), 60 and over	Colorectal	Refer adults using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.1]	
Change in bowel habit (unexplained) with rectal bleeding, in adults under 50	Colorectal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.3]	
Change in bowel habit without rectal bleeding, adults under 60	Colorectal	Offer testing with quantitative faecal immunochemical tests (see the NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) [1.3.4]	
Change in bowel habit. (unexplained) in women	Ovarian	Consider carrying out tests in primary care [1.5.3] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for information on tests for ovarian cancer These recommendations apply to women aged 18 and over	
Diarrhoea or constipation with weight loss, 60 and over	Pancreatic	Consider an urgent direct access CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available [1.2.5]	

Symptom and specific features	Possible cancer	Recommendation
Irritable bowel syndrome symptoms within the last 12 months, in women 50 and over	Ovarian	Carry out appropriate tests for ovarian cancer), because irritable bowel syndrome rarely presents for the first time in women of this age [1.5.5] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for more information about tests for ovarian cancer These recommendations apply to women aged 18 and over Also see the NICE guideline on irritable bowel syndrome in adults

Dyspepsia

Symptom and specific features	Possible cancer	Recommendation
Dyspepsia (treatment-resistant), 55 and over	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]
Dyspepsia Dyspepsia with weight loss, 55 and over	Oesophageal or stomach	Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) [1.2.1] [1.2.7]
Dyspepsia with raised platelet count or nausea or vomiting, 55 and over	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]

Dysphagia

Symptom and specific features	Possible cancer	Recommendation
Dysphagia		Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) [1.2.1, 1.2.7]

Nausea or vomiting

Symptom and specific features	Possible cancer	Recommendation
Nausea or vomiting with weight loss, 60 and over	Pancreatic	Consider an urgent direct access CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available [1.2.5]
Nausea or vomiting with raised platelet count or weight loss or reflux or dyspepsia or upper abdominal pain, 55 and over	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.3][1.2.9]

Rectal examination findings

Symptom and signs	Possible cancer	Recommendation
Prostate feels malignanton digital rectal examination, in men	Prostate	Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.1]
Anal mass or anal ulceration (unexplained)	Anal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.5]
Rectal mass	Colorectal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.2]

Reflux

Symptom and specific features	Possible cancer	Recommendation
Reflux with weight loss, 55 and over	Oesophageal or stomach	Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) [1.2.1] [1.2.7]
Reflux with raised platelet count or nausea or vomiting, 55 and over	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]

Bleeding

See also:

- the section on urological symptoms for haematuria
- the section on primary care investigations for faecal occult blood.

Bleeding, bruising or petechiae

Symptom and specific features	Possible cancer	Recommendation
Bleeding, bruising or petechiae (unexplained)	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]

Haematemesis

Symptom and specific features	Possible cancer	Recommendation
Haematemesis	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.2] [1.2.8]

Haemoptysis

Symptom and specific features	Possible cancer	Recommendation
Haemoptysis (unexplained), 40 and over	Lung	Refer people using a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.1.1]

Post-menopausal bleeding

Symptom and specific features	Possible cancer	Recommendation
Post-menopausal bleeding ¹ in women 55 and over	Endometrial	Refer women using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.10]

Symptom and specific features	Possible cancer	Recommendation
Post-menopausal bleeding ¹ in women under 55	Endometrial	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.11]

¹ Unexplained vaginal bleeding more than 12 months after menstruation has stopped because of the menopause.

Rectal bleeding

Symptom and specific features	Possible cancer	Recommendation
Rectal bleeding (unexplained), 50 and over	Colorectal	Refer adults using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.1]
Rectal bleeding with abdominal pain or change in bowel habit or weight loss or iron-deficiency anaemia in adults under 50	Colorectal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.3]

Vulval bleeding

Symptom and specific features	Possible cancer	Recommendation
Vulval bleeding (unexplained) in women	Vulval	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.14]

Gynaecological symptoms

See also the section on bleeding for post-menopausal (vaginal) bleeding

Gynaecological examination findings

Symptom and signs	Possible cancer	Recommendation
Appearance of cervix consistent with cervical cancer	Cervical	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.5.13]

Vaginal symptoms

Symptom and specific features	Possible cancer	Recommendation
Vaginal discharge (unexplained) either at first presentation or with thrombocytosis or with haematuria, in women 55 and over	Endometrial	Consider a <u>direct access</u> ultrasound scan [1.5.12]
Vaginal mass (unexplained and palpable) in or at the entrance to the vagina	Vaginal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.15]

Vulval symptoms

Symptom and specific features	Possible cancer	Recommendation
Vulval bleeding (unexplained)	Vulval	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.14]
Vulval lump or ulceration (unexplained)	Vulval	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.14]

Lumps or masses

Lumps and masses

Symptom and specific features	Possible cancer	Recommendation
Anal mass (unexplained)	Anal	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.3.5]

Symptom and specific features	Possible cancer	Recommendation	
Axillary lump (unexplained), 30 and over	Breast	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.4.2]	
Breast lump (unexplained) with or without pain, 30 and over	Breast	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.4.1]	
Breast lump (unexplained) with or without pain, under 30	Breast	Consider non-urgent referral See also recommendations 1.16.2 and 1.16.3 for information about seeking specialist advice [1.4.3]	
Lip or oral cavity lump	Oral	Consider an urgent referral (for an appointment within 2 weeks) for assessment by a dentist [1.8.3] Consider a suspected cancer pathway referral by the dentist (for an appointment within 2 weeks) in people when assessed by a dentist as having a lump on the lip or in the oral cavity consistent with oral cancer [1.8.4]	
Lump (unexplained) that is increasing in size in adults	Soft tissue sarcoma	Consider an urgent <u>direct access</u> ultrasound scan (to be performed within 2 weeks) [1.11.4] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) made be referred using either pathway depending on their age and local arrangements	
Neck lump (unexplained), 45 and over	Laryngeal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.8.1]	
Neck lump (persistent and unexplained)	Oral	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.8.2]	

Symptom and specific features	Possible cancer	Recommendation	
Penile mass (and sexually transmitted infection has been excluded as a cause) in men	Penile	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.9]	
Thyroid lump (unexplained)	Thyroid	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.8.5]	
Vaginal mass (unexplained and palpable) in or at the entrance to the vagina in women	Vaginal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.15]	
Vulval lump (unexplained) in women	Vulval	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.14]	

See also the $\underline{\text{section on abdominal symptoms}}$ for abdominal, anal, pelvic and rectal lumps or masses.

Lymphadenopathy

Symptom and specific features	Possible cancer	Recommendation	
Lymphadenopathy (unexplained) in adults	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks)	
		When considering referral for Hodgkin's lymphoma, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus, weight loss or alcohol-induced lymph node pain [1.10.10]	
		When considering referral for non-Hodgkin's lymphoma, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss [1.10.8]	
		Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements	
Lymphadenopathy (supraclavicular or persistent cervical), 40 and over	Lung	Consider an urgent chest X-ray (to be performed within 2 weeks) [1.1.3]	
Lymphadenopathy (generalised) in adults	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]	

Oral lesions

Symptom and specific features	Possible cancer	Recommendation
Ulceration in the oral cavity (unexplained and lasting for more than 3 weeks)	Oral	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.8.2]

Symptom and specific features	Possible cancer	Recommendation
Lip or oral cavity lump	Oral	Consider an urgent referral (for an appointment within 2 weeks) for assessment by a dentist [1.8.3] Consider a suspected cancer pathway referral by the dentist (for an appointment within 2 weeks) in people when assessed by a dentist as having a lump on the lip or in the oral cavity consistent with oral cancer [1.8.4]

Neurological symptoms in adults

Neurological symptoms in adults

Symptom and specific features	Possible cancer	Recommendation
Loss of central neurological function (progressive, sub-acute) in adults	Brain or central nervous system	Consider an urgent <u>direct access</u> MRI scan of the brain (or CT scan if MRI is contraindicated) (to be performed within 2 weeks) [1.9.1]

Pain

See also the section on abdominal symptoms for abdominal or pelvic pain.

Pain

Symptom and specific features	Possible cancer	Recommendation
Alcohol-induced lymph		Consider <u>a suspected cancer pathway referral</u> (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.10]
node pain with unexplained lymphadenopathy in adults	Hodgkin's lymphoma	Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Back pain with weight loss, 60 and over	Pancreatic	Consider an urgent <u>direct access</u> CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available [1.2.5]
Back pain (persistent), 60 and over	Myeloma	Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate [1.10.4] See the section on primary care investigations for more information on tests for myeloma
Bone pain (persistent), 60 and over	Myeloma	Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate to assess for myeloma [1.10.4] See the section on primary care investigations for more information on tests for myeloma
Chest pain (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Chest pain (unexplained), 40 and over, exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]

Symptom and specific features	Possible cancer	Recommendation
Chest pain (unexplained) with cough or fatigue or shortness of breath or weight loss or appetite loss (unexplained), 40 and over	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]

Respiratory symptoms

Chest infection

Symptom and specific features	Possible cancer	Recommendation
Chest infection (persistent or recurrent), 40 and over	Lung	Consider an urgent chest X-ray (to be performed within 2 weeks) [1.1.3]

Chest pain

Symptom and specific features	Possible cancer	Recommendation
Chest pain (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Chest pain (unexplained), 40 and over, exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]
Chest pain (unexplained) with cough or fatigue or shortness of breath or weight loss or appetite loss (unexplained), 40 and over	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]

Cough

Symptom and specific features	Possible cancer	Recommendation
Cough (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Cough (unexplained), 40 and over, exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]
Cough (unexplained) with fatigue or shortness of breath or chest pain or weight loss or appetite loss (unexplained), 40 and over	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]

Hoarseness

Symptom and specific features	Possible cancer	Recommendation
Hoarseness (persistent and unexplained), 45 and over	Laryngeal	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.8.1]

Respiratory examination findings

Symptom and signs	Possible cancer	Recommendation
Chest signs consistent with lung cancer, 40 and over	Lung	Consider an urgent chest X-ray (to be performed within 2 weeks) [1.1.3]
Chest signs compatible with pleural disease, 40 and over	Mesothelioma	Consider an urgent chest X-ray (to be performed within 2 weeks) [1.1.6]
Finger clubbing, 40 and over	Lung or mesothelioma	Consider an urgent chest X-ray (to be performed within 2 weeks) [1.1.3] [1.1.6]

Shortness of breath

Symptom and specific features	Possible cancer	Recommendation
Shortness of breath (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Shortness of breath (unexplained), 40 and over, and exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]
Shortness of breath with cough or fatigue or chest pain or weight loss or appetite loss (unexplained), 40 and over	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Shortness of breath with unexplained lymphadenopathy in adults	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.8] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Symptom and specific features	Possible cancer	Recommendation
Shortness of breath with unexplained splenomegaly in adults	Non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.8] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Skeletal symptoms

Back pain

Symptom and specific features	Possible cancer	Recommendation
Back pain with weight loss, 60 and over	Pancreatic	Consider an urgent <u>direct access</u> CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available[1.2.5]
Back pain (persistent), 60 and over	Myeloma	Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate [1.10.4] See the section on primary care investigations for more information on tests for myeloma

Bone pain

Symptom and specific features	Possible cancer	Recommendation
Bone pain (persistent), 60 and over	Myeloma	Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate to assess for myeloma [1.10.4] See the section on primary care investigations for more information on tests for myeloma

Fracture

Symptom and specific features	Possible cancer	Recommendation
Fracture (unexplained), 60 and over	Myeloma	Offer a full blood count, blood tests for calcium and plasma viscosity or erythrocyte sedimentation rate [1.10.4] See the section on primary care investigations for more information on tests for myeloma

Skin or surface symptoms

See also the <u>section on lumps or masses</u> for oral lesions.

Skin or surface symptoms

Symptoms and signs	Possible cancer	Recommendation
Anal ulceration (unexplained)	Anal	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.3.5]
Bruising (unexplained) in adults	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]
Nipple changes of concern (in one nipple only) including discharge and retraction, 50 and over	Breast	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.4.1]
Oral cavity red or red and white patch erythroplakia or erythroleukoplakia consistent with	Oral	Consider urgent referral (for an appointment within 2 weeks) for assessment by a dentist [1.8.3] Consider a suspected cancer pathway referral by the dentist (for an appointment within 2 weeks) for people when assessed by a dentist as having a red or red and white patch in the oral cavity consistent with erythroplakia or erythroleukoplakia. [1.8.4]
Pallor	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]

Symptoms and signs	Possible cancer	Recommendation
Penile lesion (ulcerated and sexually transmitted infection has been excluded or persistent after treatment for a sexually transmitted infection has been completed) in men	Penile	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.9]
Penile mass (and sexually transmitted infection has been excluded as a cause) in men	Penile	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.9]
Penile symptoms affecting the foreskin or glans (unexplained or persistent) in men	Penile	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.10]
Petechiae (unexplained) in adults	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]
		Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.8]
Pruritus with unexplained splenomegaly in adults	Non-Hodgkin's lymphoma	Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Symptoms and signs	Possible cancer	Recommendation
Pruritus with unexplained lymphadenopathy in adults	Hodgkin's lymphoma or non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.10] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway
Skin changes that suggest breast cancer	Breast	depending on their age and local arrangements Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.4.2]
Skin lesion (pigmented and suspicious) with a weighted 7-point checklist score of 3 or more	Melanoma	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.7.1]
Skin lesion (pigmented or non-pigmented) that suggests nodular melanoma	Melanoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.7.3]
Skin lesion that <u>raises the</u> <u>suspicion of</u> a squamous cell carcinoma	Squamous cell carcinoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.7.4]

Symptoms and signs	Possible cancer	Recommendation
Skin lesion that raises the suspicion of a basal cell carcinoma	Basal cell carcinoma	Consider routine referral [1.7.5] Only consider a suspected cancer pathway referral (for an appointment within 2 weeks) if there is particular concern that a delay may have a significant impact, because of factors such as lesion site or size [1.7.6] Typical features of basal cell carcinoma include: an ulcer with a raised rolled edge; prominent fine blood vessels around a lesion; or a nodule on the skin (particularly pearly or waxy nodules)
Vulval lump or ulceration (unexplained) in women	Vulval	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.5.14]

Urological symptoms

Dysuria

Symptom and specific features	Possible cancer	Recommendation
Dysuria with <u>unexplained</u> non-visible haematuria, 60 and over	Bladder	Refer people using a <u>suspected cancer pathway</u> referral (for an appointment within 2 weeks) [1.6.4]

Erectile dysfunction

Symptom and specific features	Possible cancer	Recommendation
Erectile dysfunction in men	Prostate	Consider a prostate-specific antigen (PSA) test and digital rectal examination [1.6.2] See the <u>section on primary care investigations</u> for more information on PSA tests and digital rectal examination

Haematuria

Symptom and specific features	Possible cancer	Recommendation
Haematuria (visible and unexplained) either without urinary tract infection or that persists or recurs after successful treatment of urinary tract infection, 45 and over	Bladder or renal	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.4][1.6.6]
Haematuria (non-visible and unexplained) with dysuria or raised white cell count on a blood test, 60 and over	Bladder	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.4]
Haematuria (visible) with low haemoglobin levels or thrombocytosis or high blood glucose levels or unexplained vaginal discharge in women 55 and over	Endometrial	Consider a <u>direct access</u> ultrasound scan [1.5.12]
Haematuria (visible) in men	Prostate	Consider a prostate-specific antigen (PSA) test and digital rectal examination [1.6.2] See the section on primary care investigations for more information on PSA tests and digital rectal examination

Testicular symptoms

Symptom and specific features	Possible cancer	Recommendation
Testis enlargement or change in shape or texture (non-painful) in men	Testicular	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.7]
Testicular symptoms (unexplained or persistent), men	Testicular	Consider a direct access ultrasound scan [1.6.8]

Other urinary tract symptoms

Symptom and specific features	Possible cancer	Recommendation
Urinary tract infection (unexplained and recurrent or persistent), 60 and over	Bladder	Consider non-urgent referral for bladder cancer in people aged 60 and over with recurrent or persistent unexplained urinary tract infection [1.6.5]
Lower urinary tract symptoms, such as nocturia, urinary frequency, hesitancy, urgency or retention in men	Prostate	Consider a prostate-specific antigen (PSA) test and digital rectal examination [1.6.2] See the section on primary care investigations for more information on PSA tests and digital rectal examination
Urinary urgency and/or frequency (increased and persistent or frequent – particularly more than 12 times per month) in women, especially if 50 and over	Ovarian	Carry out tests in primary care [1.5.2] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for information on tests for ovarian cancer These recommendations apply to women aged 18 and over

Non-specific features of cancer

Appetite loss or early satiety

Symptom and specific features	Possible cancer	Recommendation
Appetite loss (unexplained)	Several, including lung, oesophageal, stomach, colorectal, pancreatic, bladder or renal	Carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely Offer urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks) [1.13.3]

Symptom and specific features	Possible cancer	Recommendation
Appetite loss (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Appetite loss (unexplained), 40 and over, exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]
Appetite loss (unexplained) with cough or fatigue or shortness of breath or chest pain or weight loss (unexplained), 40 and over	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Appetite loss or early satiety (persistent or frequent – particularly more than 12 times per month) in women, especially if 50 and over	Ovarian	Carry out tests in primary care [1.5.2] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for information on tests for ovarian cancer These recommendations apply to women aged 18 and over

Deep vein thrombosis

Symptom and specific features	Possible cancer	Recommendation
Deep vein thrombosis	Several, including urogenital, breast, colorectal or lung	Carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely Consider urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks) [1.13.4]

Diabetes

Symptom and specific features	Possible cancer	Recommendation
Diabetes (new onset) with weight loss, 60 and over	Pancreatic	Consider an urgent <u>direct access</u> CT scan (to be performed within 2 weeks), or urgent ultrasound scan if CT is not available[1.2.5]

Fatigue

Symptom and specific features	Possible cancer	Recommendation
Fatigue (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Fatigue (unexplained), 40 and over, exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]
Fatigue with cough or shortness of breath or chest pain or weight loss or appetite loss (unexplained), 40 and over	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Fatigue (persistent) in adults	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]
Fatigue (unexplained) in women	Ovarian	Carry out tests in primary care [1.5.2] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for information on tests for ovarian cancer These recommendations apply to women aged 18 and over

Fever

Symptom and specific features	Possible cancer	Recommendation
Fever (unexplained)	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]
Fever with unexplained splenomegaly in adults	Non-Hodgkin's lymphoma	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.8] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.
Fever with unexplained lymphadenopathy in adults	Hodgkin's lymphoma or non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.10] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.

See also the <u>section on respiratory symptoms</u> for chest infection.

Infection

Symptom and specific features	Possible cancer	Recommendation
Infection (unexplained and persistent or recurrent) in adults	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]

Night sweats

Symptom and specific features	Possible cancer	Recommendation
Night sweats with unexplained splenomegaly in	Non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms[1.10.8] Separate recommendations have been made for adults and for children and young people to reflect that there are
adults lymphoma	for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.	
Night sweats with	Hodgkin's	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.10]
unexplained lymphoma or lymphadenopathy in adults lymphoma	Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.	

Pallor

Symptom and specific features	Possible cancer	Recommendation
Pallor	Leukaemia	Consider a very urgent full blood count (within 48 hours) [1.10.1]

Pruritus

Symptom and specific features	Possible cancer	Recommendation
Pruritus with unexplained splenomegaly in adults	Non-Hodgkin's lymphoma	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms[1.10.8] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.
Pruritus with unexplained lymphadenopathy in adults	Hodgkin's lymphoma or non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.10] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.

Weight loss

Symptom and specific features	Possible cancer	Recommendation
Weight loss (unexplained)	Several, including colorectal, gastro-oesophageal, lung, prostate, pancreatic or urological cancer	Carry out an assessment for additional symptoms, signs or findings that may help to clarify which cancer is most likely Offer urgent investigation or a suspected cancer pathway referral (for an appointment within 2 weeks) [1.13.2]
Weight loss (unexplained) with abdominal pain, 40 and over	Colorectal	Refer adults using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.1]

Symptom and specific features	Possible cancer	Recommendation
Weight loss (unexplained) with rectal bleeding in adults under 50	Colorectal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.3]
Weight loss (unexplained) without rectal bleeding, 50 and over	Colorectal	Offer testing with quantitative faecal immunochemical tests (see the NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) [1.3.4]
Weight loss (unexplained), 40 and over, ever smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Weight loss (unexplained), 40 and over, exposed to asbestos	Mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.5]
Weight loss with cough or fatigue or shortness of breath or chest pain or appetite loss (unexplained), 40 and over, never smoked	Lung or mesothelioma	Offer an urgent chest X-ray (to be performed within 2 weeks) [1.1.2] [1.1.5]
Maight less with		Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.8]
Weight loss with unexplained splenomegaly in adults	Non-Hodgkin's lymphoma	Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.

Symptom and specific features	Possible cancer	Recommendation
Weight loss with unexplained lymphadenopathy in adults	Hodgkin's lymphoma or non-Hodgkin's lymphoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks). When considering referral, take into account any associated symptoms [1.10.8] [1.10.10] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements.
Weight loss with upper abdominal pain or reflux or dyspepsia, 55 and over	Oesophageal or stomach	Offer urgent direct access upper gastrointestinal endoscopy (to be performed within 2 weeks) [1.2.1] [1.2.7]
Weight loss (unexplained) in women	Ovarian	Consider carrying out tests in primary care [1.5.3] Measure serum CA125 in primary care [1.5.6] See the section on primary care investigations for information on tests for ovarian cancer These recommendations apply to women aged 18 and over
Weight loss with diarrhoea or back pain or abdominal pain or nausea or vomiting or constipation or new-onset diabetes, 60 and over	Pancreatic	Consider an urgent direct access CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available[1.2.5]
Weight loss with raised platelet count or nausea or vomiting, 55 and over	Oesophageal or stomach	Consider <u>non-urgent</u> direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]

Primary care investigations

Blood test findings

Investigation findings and specific features	Possible cancer	Recommendation
Anaemia (iron-deficiency), 60 and over		Refer adults using a <u>suspected cancer pathway</u> <u>referral</u> (for an appointment within 2 weeks) [1.3.1]
Anaemia (iron-deficiency, unexplained) with rectal bleeding in adults under 50	Colorectal	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.3]
Anaemia (iron deficiency) without rectal bleeding, adults under 60	Colorectal	Offer testing with quantitative faecal immunochemical tests (see the NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) [1.3.4]
Anaemia (non-iron-deficiency), without rectal bleeding, 60 and over	Colorectal	Offer testing with quantitative faecal immunochemical tests (see the NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care) [1.3.4]
Blood glucose levels high with visible haematuria in women 55 and over	Endometrial	Consider a <u>direct access</u> ultrasound scan [1.5.12]
Diabetes (new-onset) with weight loss, 60 and over		Consider an urgent direct access CT scan (to be performed within 2 weeks), or an urgent ultrasound scan if CT is not available [1.2.5]
Haemoglobin levels low with visible haematuria in women 55 and over	Endometrial	Consider a direct access ultrasound scan [1.5.12]
Haemoglobin levels low with upper abdominal pain, 55 and over		Consider <u>non-urgent</u> direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]

Investigation findings and specific features	Possible cancer	Recommendation
Hypercalcaemia or leukopenia and presentation consistent with possible myeloma, 60 and over	Myeloma	Offer very urgent protein electrophoresis and a Bence-Jones protein urine test (within 48 hours) [1.10.5]
Plasma viscosity or erythrocyte sedimentation rate and presentation consistent with possible myeloma	Myeloma	Consider very urgent protein electrophoresis and a Bence-Jones protein urine test (within 48 hours) [1.10.6]
Platelet count raised with nausea or vomiting or weight loss or reflux or dyspepsia or upper abdominal pain, 55 and over	Oesophageal or stomach	Consider non-urgent direct access upper gastrointestinal endoscopy [1.2.3] [1.2.9]
Prostate-specific antigen levels above the age-specific reference range	Prostate	Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.3]
Protein electrophoresis suggests myeloma	Myeloma	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.10.7]

Investigation findings and specific features	Possible cancer	Recommendation
Serum CA125results	Ovarian	If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis [1.5.7] Normal serum CA125 (less than 35 IU/ml), or CA125 of 35 IU/ml or greater but a normal ultrasound: • assess her carefully for other clinical causes of her symptoms and investigate if appropriate • if no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent. [1.5.9] These recommendations apply to women aged 18 and over
Thrombocytosis, 40 and over	Lung	Consider an urgent chest X-ray (to be performed within 2 weeks) [1.1.3]
Thrombocytosis with visible haematuria or vaginal discharge (unexplained) in women 55 and over	Endometrial	Consider a direct access ultrasound scan [1.5.12]
White cell count raised on a blood test with unexplained non-visible haematuria, 60 and over	Bladder	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.4]

Dermoscopy findings

Investigation findings and specific features	Possible cancer	Recommendation
Dermoscopy suggests melanoma of the skin	Melanoma	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.7.2]

Digital rectal examination findings

Examination findings and specific features	Possible cancer	Recommendation
Prostate feels malignant on digital rectal examination	Prostate	Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.6.1]

Faecal tests

Investigation findings and specific features	Possible cancer	Recommendation
Occult blood in faeces	Colorectal	Refer adults using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.3.1]

Imaging tests

Investigation findings and specific features	Possible cancer	Recommendation
Chest X-ray suggests lung cancer	Lung	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.1.1]
Chest X-ray suggests mesothelioma	Mesothelioma	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.1.4]
Ultrasound suggests ovarian cancer	Ovarian	Urgent referral for further investigation [1.5.8] These recommendations apply to women aged 18 and over
Ultrasoundnormal with CA125 of 35 IU/ml or greater	Ovarian	Assess carefully for other clinical causes of her symptoms and investigate if appropriate If no other clinical cause is apparent, advise her to return to her GP if her symptoms become more frequent and/or persistent [1.5.9] These recommendations apply to women aged 18 and over

Investigation findings and specific features	Possible cancer	Recommendation
Ultrasound suggests soft tissue sarcoma or is uncertain and clinical concern persists in adults	Soft tissue sarcoma	Consider a <u>suspected cancer pathway referral</u> (for an appointment within 2 weeks) [1.11.5] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
X-ray suggests the possibility of bone sarcoma in adults	Bone sarcoma	Consider a suspected cancer pathway referral (for an appointment within 2 weeks) [1.11.1] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Jaundice

Investigation findings and specific features	Possible cancer	Recommendation
Jaundice, 40 and over	Pancreatic	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.2.4]

Urine test findings

Investigation findings and specific features	Possible cancer	Recommendation
Bence-Jones protein urine results suggest myeloma	I Myoloma	Refer people using a suspected cancer pathway referral (for an appointment within 2 weeks) [1.10.7]

Symptoms in children and young people

Abdominal symptoms

Symptom and specific features	Possible cancer	Recommendation
Hepatosplenomegaly (unexplained) in children and young people	Leukaemia	Refer for immediate specialist assessment [1.10.2]
Abdominal mass (palpable) or enlarged abdominal organ (unexplained) in children	Neuroblastoma or Wilms' tumour	Consider very urgent referral (for an appointment within 48 hours) for specialist assessment [1.12.1] [1.12.3]
Splenomegaly (unexplained) in children and young people	Non-Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss [1.10.9] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Bleeding, bruising or rashes

Symptom and specific features	Possible cancer	Recommendation
Petechiae (unexplained) in children and young people	Leukaemia	Refer for immediate specialist assessment [1.10.2]
Bleeding or bruising (unexplained) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]

Lumps or masses

See also the <u>section on abdominal symptoms</u> for abdominal mass or unexplained enlarged abdominal organ, splenomegaly and hepatosplenomegaly.

Symptom and specific features	Possible cancer	Recommendation
Lymphadenopathy (unexplained) in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss [1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Lymphadenopathy (generalised) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]
		Consider a very urgent <u>direct access</u> ultrasound scan (to be performed within 48 hours) [1.11.6]
Lump (unexplained) that is increasing in size in children and young people Soft tissue sarcoma	Soft tissue	See the <u>section on primary care investigations</u> for more information on ultrasound scans
	Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements	

Neurological symptoms

Symptom and specific features	Possible cancer	Recommendation
Newly abnormal cerebellar or other central neurological function in children and young people	nervous system	Consider a very urgent referral (for an appointment within 48 hours) [1.9.2]

Respiratory symptoms

Symptom and specific features	Possible cancer	Recommendation
Shortness of breath with lymphadenopathy in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Shortness of breath with splenomegaly (unexplained) in children and young people	Non-Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Skeletal symptoms

Symptom and specific features	Possible cancer	Recommendation
Bone pain (persistent or unexplained) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]
Bone pain (unexplained) in children and young people	Bone sarcoma	Consider a very urgent direct access X-ray (to be performed within 48 hours) [1.11.3] See the section on primary care investigations for more information on X-rays

Symptom and specific features	Possible cancer	Recommendation
Bone swelling (unexplained) in children and young people	Bone sarcoma	Consider a very urgent direct access X-ray (to be performed within 48 hours) [1.11.3] See the <u>section on primary care</u> investigations for more information on X-rays

Skin or surface symptoms

Symptom and specific features	Possible cancer	Recommendation
Petechiae (unexplained) in children and young people	Leukaemia	Refer for immediate specialist assessment [1.10.2]
Bruising (unexplained) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]
Pallor in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]

Urological symptoms

Symptom and specific features	Possible cancer	Recommendation
Haematuria (visible and unexplained) in children		Consider very urgent referral (for an appointment within 48 hours) for specialist assessment [1.12.3]

Non-specific features of cancer

Symptom and specific features	Possible cancer	Recommendation
Fatigue (persistent) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]

Symptom and specific features	Possible cancer	Recommendation
Fever with lymphadenopathy (unexplained) in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Fever with splenomegaly (unexplained) in children and young people	Non-Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Fever (unexplained) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]
Infection (unexplained and persistent) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]

Symptom and specific features	Possible cancer	Recommendation
Lymphadenopathy (unexplained) in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms, particularly fever, night sweats, shortness of breath, pruritus or weight loss[1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Lymphadenopathy (generalised) in children and young people	Leukaemia	Offer a very urgent full blood count (within 48 hours) [1.10.3]
Night sweats with lymphadenopathy (unexplained) in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Symptom and specific features	Possible cancer	Recommendation
Night sweats with splenomegaly (unexplained) in children and young people	Non-Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Pruritus with lymphadenopathy (unexplained) in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms [1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Pruritus with splenomegaly(unexplained) in children and young people	Non-Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms[1.10.9] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Symptom and specific features	Possible cancer	Recommendation
Weight loss with lymphadenopathy (unexplained) in children and young people	Non-Hodgkin's lymphoma or Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment in children and young people. When considering referral, take into account any associated symptoms [1.10.9] [1.10.11] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
Weight loss with splenomegaly (unexplained) in children and young people	Non-Hodgkin's lymphoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment. When considering referral, take into account any associated symptoms[1.10.9] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

Ocular examination

Examination findings and specific features	Possible cancer	Recommendation
Absent red reflex in children	l Retinoblastoma	Consider urgent referral (for an appointment within 2 weeks) for ophthalmological assessment [1.12.2]

Parental concern

Symptom and specific features	Possible cancer	Recommendation
Parental or carer insight, concern or anxiety about the child's or young person's symptoms (persistent)	Childhood cancer	Take into account the insight and knowledge of parents and carers when considering making a referral for suspected cancer in a child or young person Consider referral for children if their parent or carer has persistent concern or anxiety about the child's symptoms, even if the symptoms are most likely to have a benign cause [1.13.1]

Primary care investigations

Symptom and specific features	Possible cancer	Recommendation
Ultrasound scan suggests soft tissue sarcoma or is uncertain and clinical concern persists in children and young people	Soft tissue sarcoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment [1.11.7] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements
X-ray suggests the possibility of bone sarcoma in children and young people	Bone sarcoma	Consider a very urgent referral (for an appointment within 48 hours) for specialist assessment [1.11.2] Separate recommendations have been made for adults and for children and young people to reflect that there are different referral pathways. In practice young people (aged 16 to 24) may be referred using either pathway depending on their age and local arrangements

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

2.1 Age thresholds in cancer

Longitudinal studies should be carried out to identify and quantify factors in adults that are associated with development of specific cancers at a younger age than the norm. They should be designed to inform age thresholds in clinical guidance. The primary outcome should be likelihood ratios and positive predictive values for cancer occurring in younger age groups.

Why this is important

It is recognised that several factors, such as deprivation and comorbidity, may lead to development of cancer at a younger age. People with these factors could be disadvantaged by the use of age thresholds for referral for suspected cancer.

2.2 Primary care testing

Diagnostic accuracy studies of tests accessible to primary care should be carried out for a given cancer in symptomatic people. Priority areas for research should include tests for people with cough, non-visible haematuria, suspected prostate cancer, suspected pancreatic cancer, suspected cancer in childhood and young people and other suspected rare cancers. Outcomes of interest are the performance characteristics of the test, particularly sensitivity, specificity and positive and negative predictive values.

Why this is important

There is very little information currently available on the diagnostic accuracy of tests available in primary care for people with suspected cancer. These studies will inform clinicians on the choice of investigation for symptomatic patients.

2.3 Cancers insufficiently researched in primary care

Observational studies of symptomatic primary care patients should be used to estimate the positive predictive value of different symptoms for specific cancers. Priority areas for research are

those where the evidence base is currently insufficient and should include prostate cancer, pancreatic cancer, cancer in childhood and young people and other rare cancers. Outcomes of interest are positive predictive values and likelihood ratios for cancer.

Why this is important

For several cancer sites, the primary care evidence base on the predictive value of symptoms is thin or non-existent. Filling this gap should improve future clinical guidance.

2.4 Patient experience

Qualitative studies are needed to assess the key issues in patient experience and patient information needs in the cancer diagnostic pathway, particularly in the interval between first presentation to primary care and first appointment in secondary care. Outcomes of interest are patient satisfaction, quality of life and patient perception of the quality of care and information.

Why this is important

There was very little information on both patient information needs and patient experience throughout the cancer diagnostic pathway. Filling this gap should improve future patient experience.

Finding more information and committee details

You can see everything NICE says on this topic in the <u>NICE Pathways on suspected cancer</u> recognition and referral and <u>lung cancer</u>.

To find NICE guidance on related topics, including guidance in development, see our <u>topic page on cancer</u>.

For full details of the evidence and the guideline committee's discussions, see the <u>full guideline</u>. You can also find information about <u>how the guideline was developed</u>, including <u>details of the</u> committee.

NICE has produced <u>tools and resources</u> to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see <u>resources</u> to help you put guidance into <u>practice</u>.

Update information

January 2021: We amended recommendation 1.3.4 to include the full list of criteria for faecal testing. Faecal testing should also be offered to people without rectal bleeding aged 50 or over with unexplained abdominal pain or weight loss, or to adults under 60 with changes in bowel habit or iron-deficiency anaemia. The tables of symptoms and findings have been updated to match these changes.

September 2020: Recommendation 1.3.4 was amended to clarify when to offer faecal testing for colorectal cancer to adults without rectal bleeding. The tables on abdominal and pelvic pain, change in bowel habit and primary care investigations were updated in line with this. The wording in some recommendations was edited to incorporate text previously in footnotes.

July 2017: Recommendation 1.3.4 was replaced by <u>NICE diagnostics guidance on quantitative faecal immunochemical tests to guide referral for colorectal cancer in primary care.</u>
Recommendation 1.3.1 was amended to remove a link to recommendation 1.3.4. In December 2017, the wording of 1.3.4 was clarified, and the tables on abdominal and pelvic pain, change in bowel habit and primary care investigations updated in line with this.

June 2016: Recommendations 1.3.1 and 1.3.2 have been changed to say 'adults' instead of 'people' to more accurately reflect the populations they cover.

June 2015: This guideline updates and replaces NICE guideline CG27 (published June 2005).

Recommendations are marked as [2020], [2015], [2011], [2011, amended 2020] or [2005]:

- [2020] indicates that the evidence has been reviewed and the recommendation has been added or updated in 2020.
- [2011, amended 2020] indicates that the wording has been changed but the evidence has not been reviewed since 2020.
- [2015], [2005] or [2011] indicates the date that the evidence was last reviewed.

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