NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Guideline

Suspected cancer: recognition and referral

Ovarian cancer age and serum CA125 thresholds, and non-site-specific weight loss update

Draft for consultation, January 2026

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.

This guideline will update NICE guideline NG12 (published June 2015).

Who is it for?

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

What does it include?

- new and updated recommendations on ovarian cancer age and serum CA125 thresholds (recommendations 1.5.6 to 1.5.9, and 1.5.11)
- a new and updated recommendation on endometrial cancer (recommendation 1.5.15)
- a new and updated recommendation on non-site-specific weight loss (recommendation 1.13.2)

- a recommendation for research related to ovarian cancer age and serum CA125 thresholds
- a recommendation for research related to endometrial cancer
- the rationale and impact sections that explains why the committee made the 2026 recommendations and how they might affect services.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

New and updated recommendations

We have reviewed the evidence on ovarian cancer age and serum CA125 thresholds, endometrial cancer and non-site-specific weight loss. You are invited to comment on the new and updated recommendations. These are marked as **[2026]**

We have not reviewed the evidence for the recommendations shaded in grey, which have been provided for context, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification or to bring recommendations in line with new content.

1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity) and safeguarding.

Healthcare professionals should follow our general guidelines for people delivering care:

- Babies, children and young people's experience of healthcare
- Decision making and mental capacity
- Patient experience in adult NHS services
- Shared decision making
- Transition from children's to adults' services

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).

1.5 Gynaecological cancers

Ovarian cancer

The recommendations in this section have been incorporated from NICE's guideline on ovarian cancer and have not been updated. The recommendations for ovarian cancer apply to women, and trans men and non-binary people with female reproductive organs who are aged 18 and over.

1.5.1 Make a referral to a gynaecological cancer service using a suspected cancer pathway referral if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously uterine fibroids). **[2011]**

1.5.2 Carry out tests in primary care (see recommendations 1.5.6 to 1.5.9) if a woman, or a trans man or non-binary person with female reproductive organs (especially if they are aged 50 or over) reports having any of the following symptoms on a persistent or frequent basis – particularly more than 12 times per month:

- persistent abdominal distension (often referred to 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, or a trans man or non-binary person with female reproductive organs reports unexplained weight loss, fatigue or changes in bowel habit. **[2011]**

1.5.4 Advise any woman, or trans man or non-binary person with female reproductive organs who is not suspected of having ovarian cancer to return to their GP if their symptoms become more frequent 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, or trans man or non-binary person with female reproductive organs who is aged 50 or over and who has experienced symptoms within the last 12 months that suggest irritable bowel syndrome (IBS), because IBS rarely presents for the first time at this age. (See NICE's guideline on irritable bowel syndrome in adults). **[2011]**

1.5.6 For women, and trans men and non-binary people with female reproductive organs who are aged 39 and under, do not use serum CA125 measurement in isolation for decision making. It is not an accurate indicator of ovarian cancer risk in this age group. Although the risk of ovarian cancer is low, it remains a clinical concern and is often diagnosed late. **[2026]**

1.5.7 Consider an ultrasound scan of the abdomen and pelvis for those aged 39 and under with persistent symptoms that suggest ovarian cancer (see recommendations 1.5.1 to 1.5.5). **[2026]**

1.5.8 Measure CA125 in primary care for women, and trans men and non-binary people with female reproductive organs aged 40 and over with

symptoms that suggest ovarian cancer (see recommendations 1.5.1 to 1.5.5). **[2026]**

1.5.9 Arrange an ultrasound scan of the abdomen and pelvis depending on age and serum CA125 according to the thresholds in table 1. **[2026]**

Table 1 Age and serum CA125 thresholds

Age group (years)	CA125 threshold (IU/ml)
40 – 49	35 IU/ml or greater
50 – 59	31 IU/ml or greater
60 – 69	24 IU/ml or greater
70 – 79	25 IU/ml or greater
80+	31 IU/ml or greater

1.5.10 If the ultrasound suggests ovarian cancer, make a referral to a gynaecological cancer service using a suspected cancer pathway referral. **[2011]**

1.5.11 If the serum CA125 does not meet the threshold outlined in recommendation 1.5.9, or meets the threshold but with a normal ultrasound scan:

- identify any other potential causes of the symptoms, and investigate as appropriate, and
- if no other cause is identified, advise a return to the GP if the symptoms become more frequent and/or persistent. **[2026]**

For a short explanation of why the committee made the 2026 recommendations and how they might affect practice, see the rationale and impact section on age and serum CA125 thresholds for detecting ovarian cancer.

Full details of the evidence and the committee's discussion are in evidence review X: age and serum CA125 thresholds for detection of suspected ovarian cancer in adults.

Endometrial cancer

Age 55 and over

1.5.12 Refer women, and trans men and non-binary people with female reproductive organs using a suspected cancer pathway referral for endometrial cancer if they are aged 55 and over with unexplained post-menopausal bleeding that cannot be attributed to hormone replacement therapy (HRT). **[2015 amended 2026]**

1.5.13 Consider a direct access ultrasound scan to assess for endometrial cancer in women, and trans men and non-binary people with female reproductive organs who are 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]**

Age under 55

1.5.14 Consider a suspected cancer pathway referral for endometrial cancer in women, and trans men and non-binary people with female reproductive organs who are aged under 55 with unexplained post-menopausal bleeding that cannot be attributed HRT. **[2015 amended 2026]**

Unscheduled bleeding and HRT

1.5.15 There is limited evidence for women, and trans men and non-binary people with female reproductive organs who experience unscheduled vaginal bleeding on sequential or continuous HRT. The British Menopause Society has published guidance on unscheduled bleeding on HRT (British Menopause Society: Management of unscheduled bleeding on HRT). **[2026]**

For a short explanation of why the committee made the 2026 recommendation and related research recommendation, and how they might affect practice, see the rationale and impact section on unscheduled bleeding and HRT.

Cervical cancer

1.5.16 Consider a suspected cancer pathway referral for women, and trans men and non-binary people with female reproductive organs if, on examination, the appearance of their cervix is consistent with cervical cancer. **[2015]**

Vulval cancer

1.5.17 Consider a suspected cancer pathway referral for vulval cancer in women, and trans men and non-binary people with female reproductive organs who have an unexplained vulval lump, ulceration or bleeding. **[2015]**

Vaginal cancer

1.5.18 Consider a suspected cancer pathway referral for vaginal cancer in women, and trans men and non-binary people with female reproductive organs who have an unexplained palpable mass in or at the entrance to the vagina. **[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 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. **[2015]**

Symptoms of concern in adults

1.13.2 For people aged 60 and over with unexplained weight loss (greater than 5% mean weight loss within a 6-month period), 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 urgent investigation or a suspected cancer pathway referral. **[2026]**

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. **[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. **[2015]**

For a short explanation of why the committee made the 2026 recommendation and how it might affect practice, see the rationale and impact section on unexplained weight loss as a non-site-specific symptom in adults in primary care.

Recommendations on patient support, safety netting and the diagnostic process

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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).

1.14 Patient information and support

1.14.1 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]**

1.14.2 Give the person information on the possible diagnosis (both benign and malignant) in accordance with their wishes for information (see also NICE's guideline on patient experience in adult NHS services). **[2015]**

1.14.3 The information given to people with suspected cancer and their families and 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]**

1.14.4 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]**

1.14.5 Reassure people in the safety netting 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]**

1.14.6 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]**

1.14.7 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]**

1.14.8 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 If needed, contact a specialist (for example, by telephone or email) to discuss whether a referral is needed if there is uncertainty about the interpretation of symptoms and signs. 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 non-urgent 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 urgent 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]**

Terms used in this guideline

This section defines terms that have been used in a particular way for 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 done 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

Person to receive a diagnosis or ruling out of cancer within 28 days of being referred urgently by their GP for suspected cancer. For further details, see NHS England's webpage on faster diagnosis of cancer.

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).

Unexplained post-menopausal bleeding

Vaginal bleeding that cannot be attributed to HRT timing, expected settling-in timing, or any identified benign cause, and therefore requires further assessment to exclude underlying pathology.

Unscheduled vaginal bleeding on HRT

Vaginal bleeding that occurs after starting or changing an HRT regimen that is expected to be bleed-free (continuous combined HRT), or bleeding that occurs in addition to the planned withdrawal bleed (sequential HRT). It can occur within the first 6 months of starting HRT, or within 3 months of changing a dose or preparation.

Urgent

To happen or be done before 2 weeks.

Very urgent

To happen within 48 hours.

Young people

Aged 16 to 24 years.

Research recommendations

Dual compared with sequential CA125 and ultrasound testing for ovarian cancer

What is the diagnostic test accuracy and cost-effectiveness of dual compared with sequential CA125 and ultrasound testing for ovarian cancer in people presenting with symptoms of suspected cancer in primary care?

Unscheduled bleeding on HRT

What is the diagnostic accuracy of unscheduled vaginal bleeding for the detection of endometrial cancer in adults taking HRT to inform decision making for referral via a suspected cancer pathway?

Rationale and impact

This section briefly explains why the committee made the recommendations and how they might affect practice.

Age and serum CA125 thresholds for detecting ovarian cancer

Why the committee made the recommendations

For the utility of serum CA125 measurement and age thresholds, the committee agreed that using age-based serum CA125 thresholds in women, and trans men and non-binary people aged 40 and over can support referral decisions for ultrasound.

Moderate-certainty evidence showed that in women over 50, serum CA125 levels meet the predictive value needed to justify a strong recommendation to arrange an ultrasound scan. Based on the clinical and health economic evidence, the committee agreed age-specific thresholds in 10-year age bands for this age group.

For those aged 40 to 49 years, although the evidence was less certain and did not meet the required predictive value needed to justify a strong recommendation to arrange an ultrasound scan, the CA125 threshold of ≥35 U/ml still shows moderate-to-high sensitivity. The committee agreed that for this age group, the measurement of CA125 remains useful in guiding decisions about further investigations.

The committee acknowledged that the low prevalence of ovarian cancer in younger age groups affects serum CA125 performance, which increases the risk of false reassurance and late diagnosis, particularly in those aged 39 and under. For this age group, the committee agreed that serum CA125 is not sufficiently accurate to support decision making. Therefore, the committee recommended that serum CA125 should not be used in isolation to guide suspected ovarian cancer decisions. The committee

therefore recommended considering an ultrasound scan for those with persistent symptoms over reliance on serum CA125.

The committee agreed that the referral thresholds for serum CA125 should be reflected in the recommendations; they agreed not to label CA125 <35 U/ml as a 'normal' level and emphasised preserving clinical discretion in investigating vague or non-specific symptoms when appropriate.

The committee discussed the possible impact of the recommendations on numbers of ultrasound scans, and acknowledged that in practice, healthcare professionals frequently request a CA125 measurement and an ultrasound simultaneously. No evidence was identified comparing dual testing with the currently recommended sequential use. As a result, the committee did not make any new recommendations about simultaneous testing with serum CA125 and an ultrasound scan, did not change the existing recommendations, and made a research recommendation relating to dual use.

How the recommendations might affect practice

Implementing age-based CA125 thresholds may increase the use of ultrasound in those aged 50 and over. The economic analysis suggested that additional annual funding would be needed, mainly because of increased ultrasound and follow-up care. However, as many GPs currently request ultrasound alongside CA125 testing, the recommendations could reduce unnecessary concurrent testing. Introducing age-based CA125 thresholds may also require updates to laboratory reporting systems and clinical pathways.

In the 40 to 49 age group, the current CA125 threshold remains unchanged, so no significant change in practice is expected. For those aged 39 years and under, the recommendations promote clinical judgement and an approach, which may reduce unnecessary CA125 testing but could increase targeted ultrasound use. Given the low prevalence of ovarian cancer in these younger age groups and the high current use of ultrasound in practice, these changes are not expected to have a significant resource impact.

Unscheduled bleeding on HRT

Why the committee made the recommendations

The guideline currently recommends referral via a suspected cancer pathway for endometrial cancer for people aged 55 and over with postmenopausal bleeding, and consideration of referral for those under 55. These recommendations do not address unscheduled bleeding that may be associated with HRT.

We undertook a systematic review to assess the diagnostic accuracy of unscheduled vaginal bleeding for detecting endometrial cancer in adults taking HRT, to inform referral decisions via a suspected cancer pathway. No relevant studies were identified.

In 2024, the British Menopause Society (BMS), in partnership with other specialist organisations and Royal Colleges, published guidance on the 'Management of unscheduled bleeding on hormone replacement therapy (HRT)'. The authors acknowledge a significant lack of evidence in many areas, with recommendations based on expert opinion. The committee noted this and the absence of studies in the NICE systematic review.

The committee discussed the increasing use of HRT (data from the NHS Business Services Authority showed a 47% increase in prescriptions in England in 2022/23) and agreed that recommendations are needed despite the evidence gap.

The committee acknowledged that the BMS recommendations are widely used in practice and agreed to signpost to them, while highlighting the lack of evidence and evolving clinical practice.

Given the lack of evidence, the committee recommended research to establish when unscheduled bleeding in those taking HRT should prompt referral via a suspected cancer pathway.

How the recommendations might affect practice

Raising the awareness of the BMS guideline among healthcare professionals could help reduce unnecessary referrals for cases of unscheduled bleeding attributable to

HRT. This may reduce the stress and anxiety for people who are unnecessarily referred and ease the pressure on the healthcare system.

Unexplained weight loss as a non-site-specific symptom in adults in primary care

Why the committee made the recommendations

The evidence showed that positive predictive values of 3% or above were seen in people aged 60 and over who presented in primary care with unexplained weight loss (a mean loss of more than 5% of body weight within a 6-month period). Based on this finding, the committee recommended adding age and unexplained weight loss thresholds to the existing recommendation on unexplained weight loss as a non-site-specific symptom of cancer. Although the certainty of the evidence was low – this was a single study without data on sensitivity or specificity to assess imprecision based on the GRADE framework – the study was well-conducted, directly applicable to the UK and based on a sufficiently large sample size. The committee agreed that a potential benefit of this recommendation would be to identify those people with cancer more rapidly. Furthermore, the committee agreed that introducing age thresholds for unexplained weight loss may minimise the number of inappropriate referrals people without cancer, while maximising the number of appropriate referrals for people with cancer. The committee also agreed to retain the list of potential cancers associated with unexplained weight loss.

The committee acknowledged that the updated recommendation does not apply to adults aged 18 to 59. However, they were reassured that the guideline's recommendations on safety netting allow for reviews of people with any symptom that may be associated with an increased risk of cancer.

How the recommendations might affect practice

The committee agreed that the potential benefit of introducing age thresholds for unexplained weight loss could be to save time and resources by reducing the number of unnecessary referrals, while improving the accuracy of referrals for people most at risk of cancer.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on cancer.

For details of the guideline committee see the committee member list.

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

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