



May 2024 exceptional surveillance of suspected cancer: recognition and referral (NICE guideline NG12)

Surveillance report

Published: 29 May 2024

www.nice.org.uk

Contents

Surveillance proposal 3

 Methods 3

 Information considered in this exceptional surveillance review 4

 Equalities 7

 Overall decision 7

Surveillance proposal

We will update the [section on ovarian cancer in the NICE guideline on suspected cancer](#).

The NICE guideline on suspected cancer was developed in 2015 and covers identifying children, young people and adults with symptoms that could be caused by cancer. It includes recommendations on the symptoms and signs that warrant investigation and referral for suspected cancer. The guideline updated recommendations on suspected cancer pathway referrals in line with [NHS England's standard on faster diagnosis of cancer](#) in 2023. It underwent exceptional reviews in 2021, 2022 and 2024 and a surveillance review in 2020 (see [supporting evidence](#)). The original guideline used a greater than or equal to 3% positive predictive value (PPV) as a symptom threshold for referral or investigation. However, there are exceptions to this threshold for children, young people, and certain tests.

The NHS England (NHSE) National Cancer Programme (NCP) has conducted a series of tumour site reviews for various cancers including ovarian cancer to identify opportunities for improving earlier diagnosis. These tumour site reviews include an examination of the NICE guideline and other relevant guidance, a search of scientific literature, as well as input from clinical experts and stakeholders. Each tumour site review concludes with a summary of findings and suggestions.

The purpose of this exceptional review is to examine the impact on the ovarian cancer recommendations in the NICE guideline through the assessment of NHSE NCP tumour site review for ovarian cancer and other relevant intelligence.

Methods

The exceptional surveillance process consisted of:

- Reviewing findings from NHSE NCP tumour site review against NICE's guideline on suspected cancer.
- Considering relevant information from previous surveillance reviews of the guideline.
- Considering the evidence used to develop the guideline in 2015.

- Examining related NICE guidance and quality standards.
- Examining the NICE event tracker for relevant ongoing and published events.
- Assessing the new evidence and information, including intelligence collated from NICE enquires, against current recommendations to determine whether or not to update sections of the guideline.

For further details about the process and the possible update decisions that are available, see [ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual](#).

Information considered in this exceptional surveillance review

Ovarian cancer

The ovarian cancer recommendations in NICE's guideline on suspected cancer were derived from [NICE's guideline on ovarian cancer](#). The related recommendations have not been updated since 2011. NICE's guideline on ovarian cancer underwent an [exceptional surveillance review in 2017](#), after considering all the evidence and views of topic experts, a decision was made that no update was necessary. In October 2023, [recommendation 1.1.1.1](#) and [recommendation 1.1.2.3](#) were updated in line with [NHS England's standard on faster diagnosis of cancer](#) (see the [guideline's update information](#)). NICE also has a [clinical knowledge summary \(CKS\) on managing a woman with suspected ovarian cancer](#), last revised in May and August 2023 (see the [changes for the CKS](#)). The summary in this CKS is largely based on the NICE guidelines on suspected cancer and ovarian cancer. We identified an ongoing study, [ROCKeTS](#), a UK-based phase 3 prospective study aiming to identify and validate diagnostic tests for estimating ovarian cancer probability in symptomatic women.

Impact assessment of the NHSE NCP tumour site review against recommendations in NICE's guideline on suspected cancer

NHSE NCP	NICE	Impact
<p>The NHSE NCP tumour site review suggests that current evidence shows that CA125 has a significantly higher PPV (10.1% versus 0.81%) than initially estimated in the NICE guideline. Additionally, the test's PPV varies considerably depending on the patient's age (Funston et al. 2020 and Funston et al. 2021).</p> <p>The retrospective cohort study in the UK (Funston et al. 2020), analysed data from electronic health records and included 50,870 women who underwent the CA125 test. The study indicated that the included population was assumed to be symptomatic because CA125 testing in UK primary care is usually carried out for individuals with symptoms.</p> <p>Among the 50,780 women tested, 456 (0.9%) had ovarian cancer, and 1,321 (2.6%) had non-ovarian cancer. For women with CA125 levels ≥ 35 U/ml: 3.4% of those aged <50 years had ovarian cancer, while 15.2% of those aged ≥ 50 years had ovarian cancer. Additionally, 20.4% of those aged ≥ 50 years with CA125 levels ≥ 35 U/ml had</p>	<p>Recommendations 1.5.1 to 1.5.9 state that 'If serum CA125 is 35 IU/ml or greater, arrange an ultrasound scan of the abdomen and pelvis'.</p> <p>Concerns were raised in the 2020 surveillance review about limiting ultrasound scans to women with elevated CA125, potentially leading to missed early tumour detections. However, no new relevant evidence supporting that concern was found at the time.</p> <p>During the guideline development, the guideline development group (GDG) reviewed the combination of raised serum CA125 levels and sequential ultrasound of the abdomen. There was no direct evidence comparing serum CA125, morphological ultrasound and pelvic examination in women with symptoms in primary care. Indirect evidence came from systematic reviews of these tests in secondary care or in screening studies. Due to the differences in case mix between these settings, it is likely that the tests performed differently in each setting.</p> <p>The GDG indicated that serum CA125 and sequential ultrasound reduce the number of women who would be referred, although a greater proportion of symptomatic women would be directed to the right pathway more promptly. While adopting a sequential</p>	<p>We propose to update relevant sections on CA125 threshold and age specific PPVs in NICE's guidelines on suspected cancer and ovarian cancer based on the examination of the new evidence.</p> <p>We also propose the update to further explore the accuracy and utility of dual and concurrent screening with CA125 and ultrasound, whether it</p>

NHSE NCP	NICE	Impact
<p>non-ovarian cancer. A CA125 value of 53 U/ml corresponded to a 3% probability of ovarian cancer and overall, this varied by age. Age specific values of CA125 were 104 U/ml in 40 year old women and 32 U/ml in 70 year old women. The limitation of the study includes not considering potential confounding factors influencing CA125 levels, such as race and smoking.</p> <p>The further retrospective cohort study (Funston et al. 2021) using cancer registry data (n=456) aimed to examine the CA125 test to diagnosis interval, and the stage of ovarian cancer at diagnosis, in women with normal (<35 U/ml) and abnormal (≥35 U/ml) CA125 levels. Those with abnormal CA125 levels had a median test to diagnosis interval of 35 days, while it was 64 days for those with normal CA125 levels. Women with normal CA125 levels tended to have indolent tumours and were more frequently diagnosed at an early stage of the disease. The study concluded that, despite the longer intervals between testing and diagnosis in women with normal CA125 levels, it remains uncertain whether</p>	<p>strategy as recommended means that some women with ovarian cancer would be missed in the first instance, the view of the GDG was that this was a sensible and pragmatic decision as those women whose symptoms persist would subsequently reattend and be referred. The health economic modelling identified that serum CA125 was the most cost-effective first test as opposed to ultrasound or ultrasound and serum CA125 in combination. It was recognised that there would be an impact on health service resources and women tested due to the low prevalence of ovarian cancer in the symptomatic patient group. Equally, it was felt that to ensure symptomatic women were placed along the correct pathway as soon as possible, it could only be achieved using such a sequential testing strategy.</p>	<p>improves diagnosis or reduces mortality rates associated with ovarian cancer.</p> <p>We will continue to monitor the ROCKeTS study and will assess its impact when it is published.</p>

NHSE NCP	NICE	Impact
<p>employing more sensitive testing approaches that could expedite diagnosis would lead to earlier stage diagnosis of ovarian cancer.</p> <p>The NHSE NCP tumour site review suggests that NICE update the recommendations on ovarian cancer by adopting dual testing (CA125 and ultrasound concurrently) and introducing age specific CA125 thresholds in primary care. The NHSE NCP tumour site review did not provide evidence supporting the concurrent use of CA125 and ultrasound in symptomatic women.</p>		

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

We propose to update the CA125 threshold and age specific PPVs for ovarian cancer in NICE's guidelines on suspected cancer and ovarian cancer. We will also continue to monitor the ROCKeTS study and will assess its impact when it is published.

ISBN: 978-1-4731-6156-6