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GUIDELINES

Familial breast cancer: summary of updated NICE guidance

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This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

Further information about the guidance, a list of members of the guideline development group, and the supporting evidence statements are in the full version on bmj.com.

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- Rehabilitation after stroke: summary of NICE guidance (*BMJ* 2013;346:f3615)
- Assessment and initial management of feverish illness in children younger than 5 years: summary of updated NICE guidance (*BMJ* 2013;346:f2866)
- Recognition, assessment and treatment of social anxiety disorder: summary of NICE guidance (*BMJ* 2013;346:f2541)
- Long term follow-up of survivors of childhood cancer: summary of updated SIGN guidance (*BMJ* 2013;346:f1190)
- Recognition, intervention, and management of antisocial behaviour and conduct disorders in children and young people: summary of NICE-SCIE guidance (*BMJ* 2013;346:f1298)

Familial breast cancer occurs in people with one or more family members affected by breast, ovarian, or a related cancer such as primary peritoneal cancer. About 5% of all breast cancers can be attributed to inherited mutations in specific high risk genes such as BRCA1, BRCA2, and TP53.

This article summarises the most recent recommendations from the National Institute for Health and Care Excellence (NICE) on the classification and care of people at risk of familial breast cancer.[1] The guideline updates previous NICE guidance on familial breast cancer, published in 2004 and 2006.[2 3] It also provides new guidance on men and women with a newly or previously diagnosed breast cancer who have a family history of breast and ovarian cancer, as they were excluded from previous guidance.[4]

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are in the full version of this article on bmj.com.

Information and support for patients

- Offer patients individually tailored information, including information about sources of support (including local and national organisations).

Initial assessment in primary care for people without a personal history of breast cancer

- When a person with no personal history of breast cancer presents with breast symptoms or has concerns about relatives with breast cancer, take a first and second degree family history to assess risk, as this allows appropriate classification and care.
- Attempt to gather information that is as accurate as possible on age of diagnosis of any cancer in relatives, site of tumours, multiple cancers (including bilateral disease), or Jewish ancestry.
- Offer referral to secondary care for breast cancer risk estimation if the person meets any of the following criteria:
  - One first degree female relative with breast cancer at <40 years of age
  - One first degree male relative with breast cancer at any age
  - One first degree relative with bilateral breast cancer where the first primary was diagnosed at <50 years of age
  - Two first degree relatives, or one first degree plus one second degree relative, with breast cancer at any age
  - One first degree or second degree relative with breast cancer at any age plus one first degree or second degree relative with ovarian cancer at any age (one of these should be a first degree relative)
  - Three first degree or second degree relatives on the same side of the family with breast cancer at any age
  - If more than one relative is involved, they should be on the same side of the family.
- Women who do not meet these criteria can be reassured that they are at near population risk of getting breast cancer and do not require referral for specific breast cancer risk estimation.

Identification of gene carriers for people with or without a personal history of breast cancer

- When available in secondary care, use a carrier probability calculation method with demonstrated acceptable performance (in calibration and discrimination), as well as family history, to determine who should be offered referral to a specialist genetic clinic. Examples of acceptable methods include BOADICEA and the Manchester scoring system.[5 6] (New recommendation.)
- Offer genetic testing in specialist genetic clinics to anyone who has a combined BRCA1/BRCA2 mutation carrier probability of 10% or more. (New recommendation.)

Ideally offer genetic testing to a family member with a personal history of breast or ovarian cancer. However, unaffected individuals can be offered testing if an affected relative is unavailable. The treatment of people with newly diagnosed breast cancer might be different if they have familial breast cancer, but there was no clinical trial evidence to support rapid testing within four weeks of a diagnosis of breast cancer.

- Offer people eligible for referral to a specialist genetics clinic a choice of accessing genetic testing during initial management of their cancer or at any time thereafter. (New recommendation.)
- Offer fast track genetic testing (within four weeks of a diagnosis of breast cancer) only as part of a clinical trial. (New recommendation.)
- Discuss the potential risks and benefits of genetic testing. Include in the discussion the probability of finding a mutation, the implications for the individual and the family, and the implications of finding either a variant of uncertain significance or no mutation. (New recommendation.)
- As future knowledge will undoubtedly improve the identification of hereditary breast cancer, inform families with no clear genetic diagnosis that they can request review in the specialist genetic clinic at a future date. (New recommendation.)

Breast cancer risk categories. Risk estimation in secondary and tertiary care can be enhanced by use of existing risk assessment tools such as BOADICEA[5] and Tyrer-Cuzick[7]

	Breast cancer risk category		
	Near population risk	Moderate risk	High risk*
Lifetime risk from age 20	<17%	>17%–<30%	≥30%
Risk between ages 40 and 50 years	<3%	3–8%	>8%

*This group includes known BRCA1, BRCA2, and TP53 gene mutations and rare conditions that carry an increased risk of breast cancer such as Peutz-Jeghers syndrome (STK11 gene), Cowden syndrome (PTEN), and familial diffuse gastric cancer (E-cadherin).

Breast cancer surveillance

Women with a family history of breast cancer, with or without a personal history of breast cancer, who have a moderate to high risk of breast cancer on specialist risk estimation (see table) and who choose not to have risk reducing mastectomy may benefit from radiological surveillance of their breasts.

- Ensure digital mammography and breast magnetic resonance imaging (MRI) are performed to national breast screening programme standards. (New recommendation.)

MRI screening was shown to be more cost effective than mammography for high risk women with a known BRCA or TP53 mutation or >30% probability of being a mutation carrier.

- Offer annual MRI to women aged 30-49, with or without a personal history of breast cancer, if they have a BRCA1 or BRCA2 mutation or have a >30% risk of being a BRCA carrier. (New and updated recommendation.)
- Offer annual mammographic surveillance to women:
  - Aged 40-49 years at moderate risk of breast cancer
  - Aged 40-59 years at high risk of breast cancer but with a ≤30% probability of a BRCA or TP53 mutation
  - Aged 40-59 years with a >30% probability of being a BRCA carrier
  - Aged 40-69 years with a known BRCA1 or BRCA2 mutation.
  - (Updated recommendation.)
- Do not offer mammography to women aged <30 years or to women of any age with a known TP53 mutation. (New recommendation.)
- Do not routinely offer ultrasound surveillance to women at moderate or high risk of breast cancer but consider it when MRI surveillance would normally be offered but is not suitable (for example, because of claustrophobia) or when results of mammography or MRI are difficult to interpret. (New recommendation.)

Risk reduction strategies for women with no personal history of breast cancer

Hormone replacement therapy and the oral contraceptives can increase the risk of developing breast cancer.

- Inform women aged >35 years with a family history of breast cancer of the increased risk of breast cancer associated with taking oral contraceptives, given that their absolute risk increases with age.
- For women with BRCA mutations, discuss the conflicting effects of a potential increased risk of breast cancer at ages <40 years and the lifetime protection against ovarian cancer risk from taking oral contraceptives.
- For women with a family history of breast cancer who are considering taking or already taking hormone replacement therapy, inform them of the increase in breast cancer risk with type and duration of hormone replacement therapy.

Recent trial results have shown a significant reduction in the risk of breast cancer for the drugs tamoxifen and raloxifene. Both drugs can cause thromboembolic disease, and tamoxifen can cause endometrial cancer. However both drugs are cost effective.

After specialist risk assessment, for women who have no history of breast cancer and are not at increased risk of thromboembolic disease or endometrial cancer:

- Offer tamoxifen for five years if they are premenopausal and at high risk of breast cancer. (New recommendation.)
- Offer tamoxifen for five years if they are postmenopausal, at high risk of breast cancer, and do not have a uterus. (New recommendation.)
- Offer either tamoxifen or raloxifene for five years if they are postmenopausal, at high risk of breast cancer, and have a uterus. (New recommendation.)
- Consider prescribing tamoxifen for five years if they are premenopausal and at moderate risk of developing breast cancer within the next 10 years. (New recommendation.)
- Consider prescribing tamoxifen for five years if they are postmenopausal, at moderate risk of developing breast cancer within the next 10 years, and do not have a uterus. (New recommendation.)
- Consider prescribing either tamoxifen or raloxifene for five years if they are postmenopausal, at moderate risk of developing breast cancer within the next 10 years, and have a uterus. (New recommendation.)

Risk reduction strategies for all women with a family history of breast or ovarian cancer

Women at increased risk of developing breast or ovarian cancer due to their family history may consider surgery as an option to reduce this risk. For women with newly diagnosed breast cancer this may result in different surgical options than for women with no family history.

- Discuss the risks and benefits of risk reducing mastectomy with women with a known or suspected BRCA1, BRCA2, or TP53 mutation. (New and updated recommendation.)
- Ensure that risk reducing mastectomy and breast reconstruction are carried out by a surgical team with specialist skills in oncoplastic surgery and breast reconstruction. (New recommendation.)
- Discuss the risks and benefits of risk reducing bilateral salpingo-oophorectomy with women with a known or suspected BRCA1, BRCA2, or TP53 mutation. Include in the discussion the positive effects of reducing the risk of breast and ovarian cancer and the negative effects of a surgically induced menopause. (New and updated recommendation.)
- Discuss the benefit and risks of hormone replacement therapy after oophorectomy for women aged ≤50 years without breast cancer. (New recommendation.)

Overcoming barriers

The lower thresholds for genetic testing recommended in the guideline will increase the number of referrals to specialist genetic clinics, but, in the view of the Guideline Development Group, the current infrastructure should be able to deal with this. In England the NHS Breast Screening Programme has recently updated its recommendations for surveillance of women with a family history of breast cancer,[8] and these are in alignment with most of the guideline recommendations.

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3 National Institute for Health and Care Excellence. Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care. (Clinical guideline 41.) 2006. http://guidance.nice.org.uk/CG41.

4 National Institute for Health and Care Excellence. Early and locally advanced breast cancer: diagnosis and treatment. (Clinical guideline 80.) 2009. http://guidance.nice.org.uk/CG80.

5 Public Health and Primary Care, University of Cambridge. BOADICEA: BOADICEA is a computer program that is used to estimate BRCA1/BRCA2 mutation carrier probabilities and breast/ovarian cancer risks on the basis of family history. http://ccge.medschl.cam.ac.uk/boadicea/.

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EASILY MISSED?

Spontaneous oesophageal rupture

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This is one of a series of occasional articles highlighting conditions that may be more common than many doctors realise or may be missed at first presentation. The series advisers are Anthony Harnden, university lecturer in general practice, Department of Primary Health Care, University of Oxford, and Richard Lehman, general practitioner, Banbury. To suggest a topic for this series, please email us at easilymissed@bmj.com.

A 50 year old man presented to his local emergency department complaining of central chest pain and breathlessness that had begun after an episode of vomiting. Physical examination revealed diminished breath sounds at the left lung base and a temperature of 38°C. An erect chest radiograph showed a small, left sided pleural effusion. An initial diagnosis of pneumonia was made, and the patient was started on intravenous antibiotics. The next morning he had deteriorated, and a repeat chest radiograph showed an increase in the pleural effusion and pneumomediastinum. Computed tomography with oral and intravenous contrast revealed contrast in the left pleural cavity, suggesting a diagnosis of oesophageal rupture. The patient was stabilised and subsequently underwent thoracotomy and wash-out, placement of an oesophageal stent, and insertion of a feeding jejunostomy.

What is spontaneous oesophageal rupture?

Spontaneous rupture of the oesophagus (Boerhaave's syndrome) is a complete disruption of the oesophageal wall in the absence of pre-existing pathology and occurs with a sudden rise in intraoesophageal pressure, typically during vomiting. The left posterolateral lower oesophagus is most often affected, about 2-3 cm from the gastro-oesophageal junction.

Why is spontaneous oesophageal rupture missed?

Symptoms of oesophageal rupture are often non-specific, closely mimicking more common pathologies. In a retrospective review of patients with spontaneous oesophageal perforation treated at a tertiary referral centre, the initial diagnosis was correct in only 17 of 51 patients (33.3%), with symptoms most commonly attributed to pneumonia, spontaneous pneumothorax, myocardial infarction, pulmonary embolism, or other gastrointestinal tract pathologies.[4] Historically it was difficult to diagnose (with <70% of cases displaying physical signs of surgical emphysema and chest radiographs often being inconclusive), but now access to computed tomography with oral and intravenous contrast allows earlier and more precise diagnosis.

HOW COMMON IS SPONTANEOUS OESOPHAGEAL RUPTURE?

- Evidence is limited, but a study from Iceland showed an age standardised incidence of 3.1/1 000 000 per study year[1]
- According to hospital episode statistics, there were 340 admissions for oesophageal rupture during 2005-06 in England,[2] but information regarding aetiology was not captured
- Previous studies have suggested that a third of oesophageal ruptures are spontaneous, meaning that in England about 110 patients may be admitted with this condition each year[3]

Why does this matter?

Spontaneous rupture of the oesophagus results in immediate contamination of the pleural and mediastinal cavities with gastric contents. Subsequent chemical and bacterial mediastinitis and tissue necrosis lead to major sepsis and organ failure. The time between the event, diagnosis, and treatment is critical to minimise the inflammatory response and death from sepsis.[5] A systematic review of 726 patients showed that treatment delays of more than 24 hours were associated with a doubling of mortality.[6] Left untreated, mortality approaches 100%.[7] Crucially, misdiagnosis as a more common condition (such as pulmonary embolism) with initiation of treatment (such as anticoagulation) can result in delays to receiving appropriate treatment.

KEY POINTS

- Oesophageal rupture should be considered in patients presenting with severe chest pain without a cardiac diagnosis and with signs suggestive of pneumonia without a convincing history of this condition, especially if there is a history of vomiting or subcutaneous emphysema has been detected on examination
- Where possible, perform an erect chest radiograph in the emergency department, as this shows an infiltrate or effusion in up to 90% of patients, although these findings are not exclusive to oesophageal rupture
- Computed tomography of the chest and abdomen with oral contrast is usually required to make the diagnosis and confirm the site of perforation
- Prompt referral to a specialist oesophago-gastric centre is imperative, as a delay between onset of symptoms and treatment increases mortality

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Previous articles in this series

- Pelvic inflammatory disease (*BMJ* 2013;346:f3189)
- Colorectal cancer (*BMJ* 2013;346:f3172)
- Acute leg ischaemia (*BMJ* 2013;346:f2681)
- Delirium in older adults (*BMJ* 2013;346:f2031)
- Cushing's syndrome (*BMJ* 2013;346:f945)

How is spontaneous oesophageal rupture diagnosed?

Clinical

The classic history of oesophageal rupture is one of retching and vomiting after overindulgence in food or alcohol followed by severe retrosternal chest pain. However, this occurs in only about half of cases, and the pain can be unilateral, radiate to the left shoulder or arm, or be pleuritic in nature.[8] A history of vomiting, however, cannot be relied on for accurate diagnosis, as this symptom was found to be absent in 23% of cases in a review of 47 patients with spontaneous oesophageal rupture.[9] Physical examination findings include tachycardia, tachypnoea, fever, and shock. Signs of "surgical" subcutaneous emphysema are present in two thirds of cases and should therefore alert clinicians to the possibility of this condition.[10]

Investigations

An erect chest radiograph can show an infiltrate or effusion in up to 90% of patients, most commonly seen in the left side of the chest because of the predominance of perforations occurring in the left posterolateral oesophageal wall.[11] However, these signs are not exclusive to the diagnosis of oesophageal rupture, and computed tomography of the chest and abdomen, with water soluble oral contrast, is also recommended.[12] Diagnostic endoscopy may also be considered in experienced hands, especially if the location of the perforation is unclear from imaging alone. Evidence regarding the diagnosis of this condition is limited to small retrospective reviews, and predictive values for these investigations are therefore lacking.

How is spontaneous oesophageal rupture managed?

Initial management includes fluid resuscitation, administration of intravenous antibiotics and antifungals, consideration of the need for organ support (which may require intensive care), and prompt referral to a specialist oesophago-gastric centre. Conservative treatment alone is not generally advocated because of the high mortality associated with this approach.[7] There are several surgical treatment options, but the fundamental principles are to drain the site of contamination and prevent further leakage. Some centres advocate thoracotomy and drainage,[13] although oesophageal stenting has recently been explored as an alternative.[14] If the oesophagus is not viable, oesophagectomy may be required, although this is rare. Whatever treatment is chosen, nutrition must always be addressed, and a feeding jejunostomy is therefore often sited at the time of surgery.

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Patient consent not required (patient anonymised, dead, or hypothetical).

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A MEMORABLE PATIENT

No, you are not sorry

During an early house officer rotation, I was on the ward, working my way down a long list of jobs. On my morning ward round, which I planned to make quick because I knew all the patients, I saw an elderly woman who wanted to talk for "probably five minutes more."

In my attempt to cut the conversation short, I started saying sorry when she stopped me. "No you are not," she said, and then stopped talking.

It didn't just change my practice; in some way it changed my life. I realised that I wasn't really sorry, I cared only about getting my list of jobs for the day done. I had forgotten that, as a doctor, my most important priority was to look after my patients This patient couldn't have cared less whether her haemoglobin level was 10 or 13 g/dL, but she would have felt a lot better if she had found someone to listen to her.

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