Diagnosis and treatment of early breast cancer, including locally advanced disease—summary of NICE guidance

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

Why read this summary?

Breast cancer is the commonest cancer in women, with over 40,500 new cases diagnosed each year in England and Wales. 1 2 Despite a steady decline in age standardised mortality rates owing to screening and better management, the disease still causes 10,900 deaths each year in England and Wales, 1 2 with a huge social and emotional impact. This article outlines the most important recent recommendations from the National Institute for Health and Clinical Excellence (NICE) on the diagnosis and treatment of early and locally advanced breast cancer. 3

Recommendations

NICE recommendations are based on systematic reviews of best available evidence. When minimal evidence is available, recommendations are based on the Guideline Development Group’s opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

This new guideline covers women presenting with breast cancer in whom the primary tumour may have been non-palpable and detected by screening mammography through to women with cancers over 5 cm but in whom there is no evidence of spread beyond the breast and axillary lymph nodes. The guideline includes a large spectrum of disease, ranging from ductal carcinoma in situ (DCIS) to inflammatory breast cancer, and also includes breast cancer in men, which is rare. Advanced breast cancer is the subject of another guideline. 4

Diagnosis and preoperative assessment

- Magnetic resonance imaging (MRI) of the breast is not recommended as a routine preoperative assessment of patients with invasive breast cancer or DCIS but can help when a discrepancy exists between the clinical and radiological assessment, when breast density prevents mammographic assessment, or when breast conservation surgery to assess tumour size is being considered in lobular cancer. [Based on moderate quality evidence from case-control and case series studies and on the experience of the Guideline Development Group]
- Ensure that pretreatment ultrasonography of the axilla is carried out and ultrasound guided needle biopsy also if abnormal lymph nodes are detected. [Based on moderate quality clinical evidence from case series studies that informed an economic analysis of cost effectiveness]

Psychological support

- Members of the breast cancer clinical team should have completed an approved communication skills training programme.
- Allocate patients to a named breast care nurse specialist to support them throughout their care and follow-up.
- Ensure that specialist psychological support, including psychiatric services, is readily available when necessary.

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Surgery to the breast and axilla

Surgery is the primary treatment for DCIS and early invasive breast cancer, preferably with breast conservation when possible.

- After breast conserving surgery for DCIS a minimum radial margin of excision of 2 mm is recommended, with pathological examination in line with the reporting standards of the NHS breast screening programme. If the margin is less than 2 mm consider re-excision after discussing the risks and benefits with the patient. Enter patients with screen detected DCIS into the Sloane Project (the UK prospective audit of screen detected non-invasive carcinomas of the breast). Breast units should audit their recurrence rates.

- When no evidence exists of lymph node involvement by ultrasonography or a negative ultrasound guided biopsy, the axilla should be staged by minimal surgery, preferably sentinel lymph node biopsy, rather than lymph node clearance. Perform sentinel lymph node biopsy using the dual technique with isotope and blue dye. Breast units should audit their axillary recurrence rates. [Based on an overall moderate quality of evidence from randomised controlled trials, case series, and a meta-analysis of case series studies]

- Further axillary treatment, preferably by lymph node dissection as it gives additional staging information, is required if macrometastases or micrometastases are present in the sentinel lymph node or if there is histologically proved cancer in the preoperative ultrasound guided needle biopsy. Patients with isolated tumour cells in the sentinel lymph node biopsy, rather than lymph node clearance. Perform sentinel lymph node biopsy using the dual technique with isotope and blue dye. Breast units should audit their axillary recurrence rates. [Based on an overall moderate quality of evidence from randomised controlled trials, case series, and a meta-analysis of case series studies]

- Discuss immediate breast reconstruction with all patients for whom mastectomy is advised, unless they have significant comorbidity or where adjuvant therapy may be compromised, and discuss the full choice of the different types of breast reconstruction, whether available locally or not. [Based on low quality evidence from observational studies and on the experience of the Guideline Development Group]

Planning adjuvant treatment

- Measure the oestrogen receptor status of all invasive cancers using immunohistochemistry and report this quantitatively. The routine measurement of the progesterone receptor status is not needed. Assess the human epidermal growth factor receptor 2 status by using a standardised and qualitatively assured method. Ensure these results are available and recorded at the multidisciplinary team meeting to guide adjuvant treatment decisions.

- Consider adjuvant therapy at the multidisciplinary meeting for all patients with invasive breast cancer after surgery, taking into account the prognostic and predictive factors, the potential benefits and side effects, and the outcome of discussions with the patient.

- The web based tool Adjuvant! Online is useful for estimating the absolute benefit of adjuvant treatment for an individual. [Based on the experience of the Guideline Development Group and the recommendations in the Department of Health’s cancer reform strategy]

Endocrine therapy in invasive disease

- For postmenopausal patients with oestrogen receptor positive invasive breast cancer that is not considered to be low risk, offer an aromatase inhibitor, either anastrozole or letrozole, as initial adjuvant therapy. If tamoxifen was chosen as the primary adjuvant treatment an aromatase inhibitor, either exemestane or anastrozole, can be offered after two to three years of tamoxifen, or letrozole after five years of tamoxifen in higher risk patients. When aromatase inhibitors are poorly tolerated or contraindicated as the primary adjuvant treatment, tamoxifen should be given. [Based on high quality randomised controlled trials]

Trastuzumab therapy

- After surgery, chemotherapy and radiotherapy (when applicable) in patients who have breast cancer that is positive for human epidermal growth factor receptor 2 and who have satisfactory cardiac function, offer trastuzumab every three weeks for one year or until disease progression. Trastuzumab is a humanised monoclonal antibody that targets the human epidermal growth factor receptor 2, which is overexpressed in about 15% of breast cancers. Periodic follow-up of cardiac function during the year is mandatory.

Managing bone health

- Offer baseline dual energy x ray absorptiometry to assess bone mineral density in patients starting aromatase inhibitor treatment, those who have had treatment induced menopause, or those having ovarian ablation or suppression, as all these treatments can cause considerable bone loss and consequent risk of fracture. [Based on a high quality guideline and the experience of the Guideline Development Group]

- Offer bisphosphonates to patients according to UK consensus guidance for managing breast cancer treatment induced bone loss. [Based on high quality evidence from observational studies and on the experience of the Guideline Development Group]

Adjuvant radiotherapy

- Recommend breast radiotherapy after breast conservation surgery in patients with invasive disease, and consider it after surgery for DCIS.

- After mastectomy, discuss chest wall radiotherapy in higher risk patients, mainly depending on lymph node involvement.

- A dose of 40 Gy in 15 fractions using external beam radiotherapy is recommended.

- Do not irradiate the nodal areas routinely.

Primary systemic therapy

- Endocrine therapy alone rather than primary surgery is not appropriate unless surgery is contraindicated. [Based on a Cochrane review of moderate quality randomised controlled trials]

- After preoperative chemotherapy for locally advanced or inflammatory breast cancer, offer mastectomy followed
by radiotherapy. It would be exceptional to perform breast conservation.

**Complications of local treatment and menopausal symptoms**

- Provide patients with information before surgery or radiotherapy on the risk of lymphoedema and factors such as infection that may cause or exacerbate it, including postoperative physiotherapy regimens. If lymphoedema develops ensure rapid access to a lymphoedema service.
- Discontinue hormone replacement therapy in all patients diagnosed with invasive breast cancer, and do not offer it routinely to women with menopausal symptoms who have a previous history of the disease. Offer support, written information, and counselling for those women who might develop menopausal symptoms as a result of their treatment.

**Follow-up**

- After treatment for invasive cancer and DCIS, offer annual mammography for five years to all patients. [Based on low to moderate quality evidence from observational studies and on the experience of the Guideline Development Group] The frequency of screening after this should be stratified according to risk by the NHS breast screening programme (England) and Breast Test Wales.
- Discuss clinical follow-up (which can be in primary, secondary, or shared care) with the patient. Provide an agreed written care plan including details of the designated named healthcare professionals, dates for review of any adjuvant therapy and surveillance mammography, and other contacts such as the lymphoedema service. [Based on the experience of the Guideline Development Group]

**Overcoming barriers**

The challenge for clinicians and commissioners is applying this guideline in a way that provides informed choice and equity of access to services for all patients. Resources in training and infrastructure may be needed for the wider use of ultrasound and mammographic follow-up and will be necessary for identifying and supporting centres offering specialist MRI services. All women advised to have a mastectomy need advice on the appropriateness, timeliness, and types of reconstructive procedures from oncoplastic specialists, who may have to network across sites. For those whose treatments affect bone health, access to surveillance and early intervention are essential to reduce serious complications; this will require commissioner support to acquire scan time for dual energy x ray absorptiometry.

Many of these recommendations have cost implications. A costing tool developed by NICE is available, and an implementation pack will be available soon. Most of the recommendations can be implemented and audited by the multidisciplinary breast cancer teams under the supervision of the cancer networks.

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Further information on the guidance

Current areas of inconsistency

How follow-up for patients with early and locally advanced breast cancer should be carried out has been controversial for many years. The existing NICE service guidance for “improving outcomes in breast cancer” recommends that hospital based follow-up after treatment for early breast cancer should be limited to three years. However, peer review has shown considerable variation across England and Wales in implementing this recommendation and has led to uncertainty about who should undertake follow-up and where it should be performed. There is great variation and conflicting advice on follow-up mammography. The new guideline has given clear advice on what individual breast cancer multidisciplinary teams should now do.

Immediate versus delayed breast reconstruction has been debated for several years. For patients who are concerned about loss of body image, immediate reconstruction has the advantage of a single breast procedure and fewer operations to obtain an acceptable and usually good cosmetic outcome. However, a large quantity of information about reconstruction has to be discussed with patients for them to make informed decisions, and this can be difficult when at the same time absorbing the diagnosis of breast cancer. Furthermore, all methods of reconstruction have potential complications that might delay subsequent adjuvant therapy. The guideline makes a sensible and pragmatic recommendation that will give more choice to patients with breast cancer who want reconstruction.

Methods

The development of this guideline was based on methods outlined by the NICE guidelines manual. Four different versions of the guideline have been produced: a full version containing all the evidence and the recommendations; a quick reference guide; a version known as the “NICE guideline,” which lists the recommendations; and a lay translation of the NICE guideline for patients and the public. All the versions are available on the NICE website (www.nice.org.uk/CG80).

Future updates of the guideline will be produced as part of the NICE guideline development programme.

Future research and remaining uncertainties

The Guideline Development Group also made the following research recommendations.

- What is the effectiveness of cognitive behavioural therapy compared with other psychological interventions for patients with breast cancer?
- In the absence of good data comparing clinical outcomes between axillary radiotherapy and complete axillary lymph node dissection, entry into appropriate clinical trials (such as AMAROS (after mapping of the axilla: radiotherapy or surgery), a randomised controlled trial) is recommended for patients with early breast cancer when sentinel lymph node biopsy shows metastasis in the axilla.
- How effective is trastuzumab in patients with invasive breast cancer: (a) as adjuvant therapy without chemotherapy and (b) as primary systemic treatment, in terms of quality of life, side effects, disease recurrence rates, disease-free survival, and overall survival? In patients who are also receiving or have completed chemotherapy, what is the most effective scheduling and duration of treatment with trastuzumab?
- In patients with early invasive breast cancer, how effective are (a) different hypofractionation radiotherapy regimens, (b) partial breast radiotherapy, and (c) newer radiotherapy techniques (including intensity modulated radiotherapy), in terms of long term outcomes such as quality of life, side effects, disease recurrence rates, disease-free survival, and overall survival?
- For patients who have been treated for early invasive breast cancer or DCIS, what is the optimal frequency and length of surveillance of follow-up mammography?