

Ref 1

a,b = p5 c,d,=p 6 f,l =p 7 e,g,i =p 10 j,k,m = p11
n,o,p,q =p12 r,s, t = p13 u,v,w,x,y = p 14
z,aa,bb,cc,dd = p15 ee,ff,gg,hh = p 16
ii,jj,kk,ll,mm,nn = p 17 oo,pp,qq,rr,ss,tt = p 18
uu,vv,ww = p19 xx = p20 zz,aaa = p 21

Early and locally advanced breast cancer: diagnosis and treatment

Clinical guideline

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[nice.org.uk/guidance/cg80](https://www.nice.org.uk/guidance/cg80)

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This guideline partially replaces TA107, TA108 and TA109.

This guideline is the basis of QS12.

Introduction

The NICE guideline on advanced breast cancer has been updated. It includes recommendations on exercise for people with or at risk of breast-cancer-related lymphoedema, and these are also relevant for people with early or locally advanced breast cancer. They can be found in the [managing complications](#) section of the guideline.

This guideline updates the following technology appraisals:

- 'Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer' (NICE technology appraisal guidance 107)
- 'Paclitaxel for the adjuvant treatment of early node-positive breast cancer' (NICE technology appraisal guidance 108)
- 'Docetaxel for the adjuvant treatment of early node-positive breast cancer' (NICE technology appraisal guidance 109)

NICE and the Department of Health are currently reviewing the future position on updating technology appraisals within clinical guidelines, with particular reference to implications for the funding direction on technology appraisals. In the meantime, the technology appraisal guidance remains available and should continue to be followed. The statutory funding direction remains in place for the recommendations contained in the technology appraisal guidance

Breast cancer is the most common cancer for women in England and Wales, with about 40,500 new cases diagnosed^{[1],[2]} and 10,900 deaths^{[1],[2]} recorded in England and Wales each year. In men breast cancer is rare, with about 260 cases diagnosed^{[1],[2]} and 68 deaths^{[1],[2]} in England and Wales each year. Of these new cases in women and men, a small proportion are diagnosed in the advanced stages, when the tumour has spread significantly within the breast or to other organs of the body. In addition, a considerable number of women who have been previously treated with curative intent subsequently develop either a local recurrence or metastases.

Early breast cancer is subdivided into two major categories, in situ disease, mainly in the form of ductal carcinoma in situ (DCIS), and invasive cancer. Both are heterogeneous processes with very variable appearances, biology and clinical behaviour.

a Over recent years there have been important developments in the investigation and management of breast cancer including new types of chemotherapy, and biological and hormonal agents. There is some evidence of practice variation across the country and of inconsistent availability of certain treatments and procedures. This clinical guideline helps to address these issues and offers guidance on best practice.

b This guideline assumes that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, as there is good evidence to support that use. Unlicensed drugs are marked with a footnote.

^[1] Office for National Statistics (2008) Cancer statistics registrations: registrations of cancer diagnosed in 2005, England. Series MB1 number 36. London: Office for National Statistics.

^[2] Welsh Cancer Intelligence and Surveillance Unit (2008) Cancer incidence in Wales. Cardiff: Welsh Cancer Intelligence and Surveillance Unit.

Patient-centred care

This guideline offers best practice advice on the care of patients with early or locally advanced breast cancer.

c **Treatment and care should take into account patients' needs and preferences.** Patients with early or locally advanced breast cancer should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the [Department of Health's advice on consent](#) and the [code of practice that accompanies the Mental Capacity Act](#). In Wales, healthcare professionals should follow [advice on consent from the Welsh Government](#).

d **Good communication between healthcare professionals and patients is essential.** It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Key priorities for implementation

Preoperative assessment of the breast

- f
- Offer magnetic resonance imaging (MRI) of the breast to patients with invasive breast cancer:
 - if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
 - if breast density precludes accurate mammographic assessment
 - to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer.

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Staging of the axilla

- Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered.

Surgery to the axilla

- Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique.

Breast reconstruction

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- Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.

Adjuvant therapy planning

- Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery^[3] in patients with early breast cancer having these treatments.

Aromatase inhibitors

- Postmenopausal women with oestrogen receptor (ER)-positive early invasive breast cancer who are not considered to be at low risk^[4] should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated.

Assessment of bone loss

- Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:
 - are starting adjuvant aromatase inhibitor treatment
 - have treatment-induced menopause
 - are starting ovarian ablation/suppression therapy.

Primary systemic therapy

- Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.

Follow-up imaging

- Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHS Breast Screening Programme/Breast Test Wales Screening Programme. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.

Clinical follow-up

- Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:
 - designated named healthcare professionals
 - dates for review of any adjuvant therapy
 - details of surveillance mammography
 - signs and symptoms to look for and seek advice on

- contact details for immediate referral to specialist care, and
- contact details for support services, for example support for patients with lymphoedema.

^[3] Department of Health (2007) Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.)

^[4] Low-risk patients are those in the EPG or GPG (excellent prognostic group or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have a similar prediction using Adjuvant! Online.

1 Guidance

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

1.1 Referral, diagnosis and preoperative assessment

Patients with symptoms that could be caused by breast cancer are referred by their GP to designated breast clinics in local hospitals (see [NICE clinical guideline 27](#), 'Referral guidelines for suspected cancer'). In addition, **women aged between 50 and 70 are invited for screening mammography every 3 years through** the NHS Breast Screening Programme (NHSBSP) in England or the Breast Test Wales Screening Programme (BTWSP) in Wales. For most patients, whether they are referred following breast screening or after presentation to a GP, **diagnosis in the breast clinic is made by triple assessment (clinical assessment, mammography and/or ultrasound imaging, and core biopsy and/or fine needle aspiration cytology). It is best practice to carry out these assessments at the same visit** (see [NICE cancer service guidance](#) 'Improving outcomes in breast cancer – Manual update').

Preoperative assessment of the breast and axilla

1.1.1 The routine use of magnetic resonance imaging (MRI) of the breast is not recommended in the preoperative assessment of patients with biopsy-proven invasive breast cancer or ductal carcinoma in situ (DCIS).

1.1.2 Offer MRI of the breast to patients with invasive breast cancer:

- if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment
- if breast density precludes accurate mammographic assessment
- to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer.

Preoperative staging of the axilla

1.1.3 Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if

morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered.

1.2 *Providing information and psychological support*

1.2.1 All members of the breast cancer clinical team should have completed an accredited communication skills training programme.

j 1.2.2 All patients with breast cancer should be assigned to a named breast care nurse specialist who will support them throughout diagnosis, treatment and follow-up.

1.2.3 All patients with breast cancer should be offered prompt access to specialist psychological support, and, where appropriate, psychiatric services.

1.3 *Surgery to the breast*

Ductal carcinoma in situ

k 1.3.1 For all patients treated with breast conserving surgery for DCIS a minimum of 2 mm radial margin of excision is recommended with pathological examination to NHSBSP reporting standards. Re-excision should be considered if the margin is less than 2 mm, after discussion of the risks and benefits with the patient.

1.3.2 Enter patients with screen-detected DCIS into the Sloane Project (UK DCIS audit)^[5].

1.3.3 All breast units should audit their recurrence rates after treatment for DCIS.

Paget's disease

m 1.3.4 Offer breast conserving surgery with removal of the nipple-areolar complex as an alternative to mastectomy for patients with Paget's disease of the nipple that has been assessed as localised. Offer oncoplastic repair techniques to maximise cosmesis.

1.4 *Surgery to the axilla*

Invasive breast cancer

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1.4.1 Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique.

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1.4.2 SLNB should only be performed by a team that is validated in the use of the technique, as identified in the New Start training programme^[6].

1.4.3 Perform SLNB using the dual technique with isotope and blue dye.

1.4.4 Breast units should audit their axillary recurrence rates.

Ductal carcinoma in situ

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1.4.5 Do not perform SLNB routinely in patients with a preoperative diagnosis of DCIS who are having breast conserving surgery, unless they are considered to be at a high risk of invasive disease^[7].

1.4.6 Offer SLNB to all patients who are having a mastectomy for DCIS.

Evaluation and management of a positive sentinel lymph node

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1.4.7 Offer further axillary treatment to patients with early invasive breast cancer who:

- have macrometastases or micrometastases shown in a sentinel lymph node
- have a preoperative ultrasound-guided needle biopsy with histologically proven metastatic cancer.

The preferred technique is axillary lymph node dissection (ALND) because it gives additional staging information.

1.4.8 Do not offer further axillary treatment to patients found to have only isolated tumour cells in their sentinel lymph nodes. These patients should be regarded as lymph node-negative.

1.5 **Breast reconstruction**

1.5.1 **Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option.** All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally.

1.6 **Postoperative assessment and adjuvant therapy planning**

Predictive factors

1.6.1 **Assess oestrogen receptor (ER) status of all invasive breast cancers,** using immunohistochemistry with a standardised and qualitatively assured methodology, and report the results quantitatively.

1.6.2 **Do not routinely assess progesterone receptor status of tumours in patients with invasive breast cancer.**

1.6.3 **Test human epidermal growth receptor 2 (HER2) status of all invasive breast cancers,** using a standardised and qualitatively assured methodology.

1.6.4 Ensure that the results of ER and HER2 assessments are available and recorded at the multidisciplinary team meeting when guidance about systemic treatment is made.

Adjuvant therapy planning

1.6.5 **Consider adjuvant therapy for all patients with early invasive breast cancer after surgery** at the multidisciplinary team meeting and ensure that decisions are recorded.

1.6.6 Decisions about adjuvant therapy should be made based on assessment of the prognostic and predictive factors, the potential benefits and side effects of the treatment. Decisions should be made following discussion of these factors with the patient.

1.6.7 Consider using Adjuvant! Online^[6] to support estimations of individual prognosis and the absolute benefit of adjuvant treatment for patients with early invasive breast cancer.

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1.6.8 Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery^[9] in patients with early breast cancer having these treatments.

1.7 Endocrine therapy

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Ovarian suppression/ablation for early invasive breast cancer

1.7.1 Do not offer adjuvant ovarian ablation/suppression to premenopausal women with ER-positive early invasive breast cancer who are being treated with tamoxifen and, if indicated, chemotherapy.

1.7.2 Offer adjuvant ovarian ablation/suppression in addition to tamoxifen to premenopausal women with ER-positive early invasive breast cancer who have been offered chemotherapy but have chosen not to have it.

Aromatase inhibitors for early invasive breast cancer

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1.7.3 Postmenopausal women with ER-positive early invasive breast cancer who are not considered to be at low risk^[10] should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated.

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1.7.4 Offer an aromatase inhibitor, either exemestane or anastrozole, instead of tamoxifen to postmenopausal women with ER-positive early invasive breast cancer who are not low risk^[10] and who have been treated with tamoxifen for 2–3 years.

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1.7.5 Offer additional treatment with the aromatase inhibitor letrozole for 2–3 years to postmenopausal women with lymph node-positive ER-positive early invasive breast cancer who have been treated with tamoxifen for 5 years.

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1.7.6 The aromatase inhibitors **anastrozole, exemestane and letrozole**, within their licensed indications, **are recommended as options for the adjuvant treatment of early ER-positive invasive breast cancer in postmenopausal women**^[11].

1.7.7 The choice of treatment should be made after discussion between the responsible clinician and the woman about the risks and benefits of each option. Factors to consider when making the choice include whether the woman has received tamoxifen before, the licensed indications and side-effect profiles of the individual drugs and, in particular, the assessed risk of recurrence^[11].

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Tamoxifen for ductal carcinoma in situ

1.7.8 **Do not offer adjuvant tamoxifen after breast conserving surgery to patients with DCIS.**

1.8 Chemotherapy

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1.8.1 **Offer docetaxel to patients with lymph node-positive breast cancer as part of an adjuvant chemotherapy regimen.**

1.8.2 Do not offer paclitaxel as an adjuvant treatment for lymph node-positive breast cancer.

1.9 Biological therapy

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1.9.1 **Offer trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), as an adjuvant treatment to women with HER2-positive early invasive breast cancer following surgery, chemotherapy, and radiotherapy when applicable.**

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1.9.2 **Assess cardiac function before starting treatment with trastuzumab. Do not offer trastuzumab treatment to women who have any of the following:**

- **a left ventricular ejection fraction (LVEF) of 55% or less**
- **a history of documented congestive heart failure**
- **high-risk uncontrolled arrhythmias**

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- angina pectoris requiring medication
- clinically significant valvular disease
- evidence of transmural infarction on electrocardiograph (ECG)
- poorly controlled hypertension.

ee

1.9.3 Repeat cardiac functional assessments every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50% then trastuzumab treatment should be suspended. Restart trastuzumab therapy only after further cardiac assessment and a fully informed discussion of the risks and benefits with the woman.

1.10 Assessment and treatment of bone loss

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1.10.1 Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if they:

- are starting adjuvant aromatase inhibitor treatment
- have treatment-induced menopause
- are starting ovarian ablation/suppression therapy.

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1.10.2 Do not offer a DEXA scan to patients with early invasive breast cancer who are receiving tamoxifen alone, regardless of pretreatment menopausal status.

1.10.3 Offer bisphosphonates to patients identified by algorithms 1 and 2 in 'Guidance for the management of breast cancer treatment-induced bone loss: a consensus position statement from a UK expert group' (2008)^[12] (see appendix 2 of the [full guideline](#)).

1.11 Radiotherapy

Radiotherapy after breast conserving surgery

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1.11.1 Patients with early invasive breast cancer who have had breast conserving surgery with clear margins should have breast radiotherapy.

- ii** 1.11.2 Offer adjuvant radiotherapy to patients with DCIS following adequate breast conserving surgery and discuss with them the potential benefits and risks (see recommendation in [section 1.3.1](#))

Radiotherapy after mastectomy

- jj** 1.11.3 Offer adjuvant chest wall radiotherapy to patients with early invasive breast cancer who have had a mastectomy and are at a high risk of local recurrence. Patients at a high risk of local recurrence include those with four or more positive axillary lymph nodes or involved resection margins.
- 1.11.4 Consider entering patients who have had a mastectomy for early invasive breast cancer and who are at an intermediate risk of local recurrence into the current UK trial (SUPREMO) assessing the value of postoperative radiotherapy. Patients at an intermediate risk of local recurrence include those with one to three lymph nodes involved, lymphovascular invasion, histological grade 3 tumours, ER-negative tumours, and those aged under 40.
- kk** 1.11.5 Do not offer radiotherapy following mastectomy to patients with early invasive breast cancer who are at low risk of local recurrence (for example, most patients who are lymph node-negative).

Dose fractionation

- ll** 1.11.6 Use external beam radiotherapy giving 40 Gy in 15 fractions as standard practice for patients with early invasive breast cancer after breast conserving surgery or mastectomy.

Breast boost

- mm** 1.11.7 Offer an external beam boost to the site of local excision to patients with early invasive breast cancer and a high risk of local recurrence, following breast conserving surgery with clear margins and whole breast radiotherapy.
- 1.11.8 If an external beam boost to the site of local excision following breast conserving surgery is being considered in patients with early invasive breast cancer, inform the patient of the side effects associated with this intervention, including poor cosmesis, particularly in women with larger breasts.
- nn**

Radiotherapy to nodal areas

oo 1.11.9 Do not offer adjuvant radiotherapy to the axilla or supraclavicular fossa to patients with early breast cancer who have been shown to be histologically lymph node-negative.

1.11.10 Do not offer adjuvant radiotherapy to the axilla after ALND for early breast cancer.

pp 1.11.11 If ALND is not possible following a positive axillary SLNB or four-node sample, offer adjuvant radiotherapy to the axilla to patients with early breast cancer (see recommendations in sections 1.4.1 and 1.4.7).

qq 1.11.12 Offer adjuvant radiotherapy to the supraclavicular fossa to patients with early breast cancer and four or more involved axillary lymph nodes.

1.11.13 Offer adjuvant radiotherapy to the supraclavicular fossa to patients with early breast cancer and one to three positive lymph nodes if they have other poor prognostic factors (for example, T3 and/or histological grade 3 tumours) and good performance status.

rr 1.11.14 Do not offer adjuvant radiotherapy to the internal mammary chain to patients with early breast cancer who have had breast surgery.

1.12 Primary systemic therapy

Early breast cancer

ss 1.12.1 Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery.

tt 1.12.2 Preoperative systemic therapy can be offered to patients with early invasive breast cancer who are considering breast conserving surgery that is not advisable at presentation. However, the increased risk of local recurrence with breast conserving surgery and radiotherapy rather than mastectomy after systemic therapy should be discussed with the patient.

Locally advanced or inflammatory breast cancer

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- 1.12.3 Offer local treatment by mastectomy (or, in exceptional cases, breast conserving surgery) followed by radiotherapy to patients with locally advanced or inflammatory breast cancer who have been treated with chemotherapy.

1.13 Complications of local treatment and menopausal symptoms

Lymphoedema

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- 1.13.1 Inform all patients with early breast cancer about the risk of developing lymphoedema and give them relevant written information before treatment with surgery and radiotherapy.
- 1.13.2 Give advice on how to prevent infection or trauma that may cause or exacerbate lymphoedema to patients treated for early breast cancer.
- 1.13.3 Ensure that all patients with early breast cancer who develop lymphoedema have rapid access to a specialist lymphoedema service.

Arm mobility

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- 1.13.4 All breast units should have written local guidelines agreed with the physiotherapy department for postoperative physiotherapy regimens.
- 1.13.5 Identify breast cancer patients with pre-existing shoulder conditions preoperatively as this may inform further decisions on treatment.
- 1.13.6 Give instructions on functional exercises, which should start the day after surgery, to all breast cancer patients undergoing axillary surgery. This should include relevant written information from a member of the breast or physiotherapy team.
- 1.13.7 Refer patients to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment.

Menopausal symptoms

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- 1.13.8 Discontinue hormone replacement therapy (HRT) in women who are diagnosed with breast cancer.
- 1.13.9 Do not offer HRT (including oestrogen/progestogen combination) routinely to women with menopausal symptoms and a history of breast cancer. HRT^[13] may, in exceptional cases, be offered to women with severe menopausal symptoms and with whom the associated risks have been discussed.
- 1.13.10 Offer information and counselling for all women about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment.
- 1.13.11 Tibolone or progestogens are not recommended for women with menopausal symptoms who have breast cancer.
- 1.13.12 The selective serotonin re-uptake inhibitor antidepressants paroxetine^[14] and fluoxetine^[14] may be offered to women with breast cancer for relieving menopausal symptoms, particularly hot flashes, but not to those taking tamoxifen.
- 1.13.13 Clonidine, venlafaxine^[14] and gabapentin^[14] should only be offered to treat hot flashes in women with breast cancer after they have been fully informed of the significant side effects.
- 1.13.14 Soy (isoflavone), red clover, black cohosh, vitamin E and magnetic devices are not recommended for the treatment of menopausal symptoms in women with breast cancer.

1.14 Follow-up

Follow-up imaging

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- 1.14.1 Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHSBSP/BTWSP. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.

1.14.2 On reaching the NHSBSP/BTWSP screening age or after 5 years of annual mammography follow-up we recommend the NHSBSP/BTWSP stratify screening frequency in line with patient risk category.

zz 1.14.3 Do not offer mammography of the ipsilateral soft tissues after mastectomy.

1.14.4 Do not offer ultrasound or MRI for routine post-treatment surveillance in patients who have been treated for early invasive breast cancer or DCIS.

Clinical follow-up

1.14.5 After completion of adjuvant treatment (including chemotherapy, and/or radiotherapy where indicated) for early breast cancer, discuss with patients where they would like follow-up to be undertaken. They may choose to receive follow-up care in primary, secondary, or shared care.

1.14.6 Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:

- designated named healthcare professionals
- dates for review of any adjuvant therapy
- details of surveillance mammography
- signs and symptoms to look for and seek advice on
- contact details for immediate referral to specialist care, and
- contact details for support services, for example support for patients with lymphoedema.

^[5] [The Sloane Project](#)

^[6] [NEW START Sentinel Lymph Node Biopsy Training Programme](#), The Royal College of Surgeons of England.

^[7] Patients considered at high risk of invasive disease include those with a palpable mass or extensive microcalcifications.

^[8] See [Adjuvant! Online](#)

^[9] Department of Health (2007) Cancer reform strategy. London: Department of Health. (At present no equivalent target has been set by the Welsh Assembly Government.)

^[10] Low-risk patients are those in the EPG or GPG (excellent prognostic group or good prognostic group) in the Nottingham Prognostic Index (NPI), who have 10-year predictive survivals of 96% and 93%, respectively. They would have a similar prediction using Adjuvant! Online.

^[11] This recommendation is from 'Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer' (NICE technology appraisal guidance 112).

^[12] Reid DM, Doughty J, Eastell R et al (2008) Guidance for the management of breast cancer treatment-induced bone loss: a consensus position statement from a UK Expert Group. *Cancer Treatment Reviews* 34: S3–S18.

^[13] The summaries of product characteristics state that HRT is contraindicated in women with known, past or suspected breast cancer. Informed consent should be obtained and documented.

^[14] These drugs are not licensed for the stated use. Informed consent should be obtained and documented.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The [scope](#) of this guideline is available.

Groups that are covered

- Women with newly diagnosed invasive adenocarcinoma of the breast of clinical stages 1 and 2. This is where the primary tumour is less than 5 cm in maximum diameter and there is no sign of spread beyond the breast and axillary lymph nodes.
- Women with invasive adenocarcinoma of the breast of clinical stage 3. This includes primary tumours which may be larger than 5 cm in diameter (and includes inflammatory carcinoma).
- Men with newly diagnosed invasive adenocarcinoma of the breast of clinical stages 1, 2 and 3.
- Women with newly diagnosed DCIS.
- Women with Paget's disease of the breast.

Groups that are not covered

- Women and men with invasive adenocarcinoma of the breast of clinical stage 4 (this is covered by 'Advanced breast cancer: diagnosis and treatment' [NICE clinical guideline 81](#) [2009]).
- Women and men with rare breast tumours (for example, angiosarcoma, lymphoma).
- Women and men with benign breast tumours (for example, fibroadenoma, phyllodes tumour).
- Women with lobular carcinoma in situ.
- Women with an increased risk of breast cancer due to family history. This population is covered by [Familial breast cancer](#) (NICE clinical guideline 41 [2006]).

How this guideline was developed

NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (see [appendix A](#)), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see [appendix B](#)).

There is more information about [how NICE clinical guidelines are developed](#) on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is [available](#).

3 Implementation

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in [Standards for better health](#). Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed [tools](#) to help organisations implement this guidance (listed below).

- Slides highlighting key messages for local discussion.
- Costing tools:
 - costing report to estimate the national savings and costs associated with implementation
 - costing template to estimate the local costs and savings involved.
- Audit support for monitoring local practice.

4 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.

4.1 *Psychological support*

What is the effectiveness of cognitive behavioural therapy compared with other psychological interventions for breast cancer patients?

Why this is important

There is currently a variation in the provision and quality of psychological approaches and services offered to patients with breast cancer. As a consequence of the diagnosis of breast cancer at least a quarter of patients report anxiety and depression and a third report sexual problems.

Cognitive behavioural therapy (CBT) is one form of psychotherapy that has been proven to treat and reduce depression in many patients, including cancer patients. It is a time-limited, structured and direct form of therapy that is well suited to patients with breast cancer. Unfortunately there are no studies that compare CBT with other forms of intervention in breast cancer patients alone. Other forms of psychotherapy include psychodynamic counselling, Gestalt therapy or any other psychological intervention. The comparison could include support from the breast care nurse specialist, telephone support or pure counselling.

4.2 *Optimum treatment of the axilla*

In the absence of good data about differences in clinical outcome between axillary radiotherapy and completion ALND, entry into appropriate clinical trials, for example, AMAROS, is recommended for early breast cancer patients when the axilla has been found by SLNB to contain metastasis.

Why this is important

Optimum treatment of the axilla in early breast cancer patients in whom SLNB has shown tumour positive nodes remains unresolved: completion ALND or axillary radiotherapy both have significant but differing morbidities. Studies, including AMAROS, are needed to determine effectiveness of local control and overall survival, side effects and quality of life, cost effectiveness, and whether the additional information on the total number of involved nodes obtained by ALND is relevant for

optimum management. These alternative management strategies would have significant impact on service delivery in the UK. The piecemeal introduction of intraoperative sentinel lymph node assessment with immediate ALND for a positive sentinel lymph node may make such research difficult in the near future.

4.3 *Trastuzumab*

How effective is trastuzumab in patients with invasive breast cancer (a) as adjuvant therapy without chemotherapy (b) in terms of scheduling and duration of treatment in patients who are also receiving or who have completed chemotherapy, and (c) as primary systemic treatment in terms of quality of life, side effects, disease recurrence rates, disease-free survival and overall survival?

Why this is important

In patients with HER2-positive invasive breast cancer trastuzumab is a routine adjuvant therapy, where appropriate, following surgery, chemotherapy and radiotherapy. The recommended scheduling at present is 3-weekly treatment for 1 year but there may be more effective and cost-effective regimens. Studies such as PERSEPHONE and the 2-year treatment duration arm of HERA have been designed to address these issues. There are few studies assessing the role of trastuzumab as a primary systemic treatment and even fewer using it in endocrine receptor-positive patients treated with endocrine therapy alone and no chemotherapy.

Studies are needed to resolve the questions of scheduling and duration, the place of trastuzumab with endocrine therapy in the absence of adjuvant chemotherapy and its role in primary systemic therapy.

4.4 *Radiotherapy*

What is the effectiveness in patients with early invasive breast cancer of (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?

Why this is important

Following breast conserving surgery for invasive breast cancer the international standard radiotherapy practice is to treat the whole breast, giving 50 Gy in 25 fractions of 2 Gy fractions

over 5 weeks. A 3-weekly schedule of 40 Gy in 15 fractions has been used in many centres in the UK for years and this has been supported by the recent publication of the UK Standardisation of Breast Radiotherapy (START) Trial. Further studies may show that it is possible to use even more hypofractionated regimens, which would be far more convenient for patients and more cost effective if they are equally clinically effective. In addition, with technical advances in radiotherapy treatment planning and delivery, it is possible to give partial breast radiotherapy or dose gradients across the breast in selected patients.

4.5 *Follow-up mammography*

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?

Why this is important

There is little evidence that routine follow-up of patients treated for early breast cancer to detect recurrence of early breast cancer, or of new primary disease, is either effective or offers any mortality benefit. However, it remains routine practice in most breast units in the UK to provide post-treatment follow-up with regular clinical examination and mammography for at least 5 years. This routine follow-up is usually provided in secondary care and requires significant resources. The consensus of those providing breast cancer treatment is that routine follow-up is beneficial for patient welfare and for monitoring effectiveness of treatment. There are few data on which to base guidelines on the most effective methods of providing follow-up, how frequently and for how long. Prospective randomised comparative studies are required to ascertain the most effective methods of detecting recurrence and new primary disease, and should include:

- by what means (clinical examination and/or imaging and/or serum tumour markers)
- different patient populations, depending on their risks and toxicities from treatment
- where (in primary and/or secondary care) and by whom (by patients, nurses or doctors)
- whether such follow-up provides any benefits (such as reduced mortality, morbidity and treatment costs).

5 Other versions of this guideline

5.1 *Full guideline*

The full guideline [Early and locally advanced breast cancer: diagnosis and treatment](#) contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Cancer.

5.2 *Information for the public*

NICE has produced '[information for the public](#)' explaining this guideline.

We encourage NHS and voluntary sector organisations to use text from this information in their own materials.

6 Related NICE guidance

Published

Advanced breast cancer: diagnosis and treatment. [NICE clinical guideline 81](#).

Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women. [NICE technology appraisal guidance 161](#) (2008).

Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women. [NICE technology appraisal guidance 160](#) (2008).

Brachytherapy as the sole method of adjuvant radiotherapy for breast cancer after local excision. [NICE interventional procedure guidance 268](#) (2008).

Hormonal therapies for the adjuvant treatment of early oestrogen-receptor-positive breast cancer. [NICE technology appraisal guidance 112](#) (2006).

Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of NICE clinical guideline 14). [NICE clinical guideline 41](#) (2006).

Endoscopic axillary lymph node retrieval for breast cancer. [NICE interventional procedure guidance 147](#) (2005).

Referral guidelines for suspected cancer. [NICE clinical guideline 27](#) (2005).

Interstitial laser therapy for breast cancer. [NICE interventional procedure guidance 89](#) (2004).

Improving supportive and palliative care for adults with cancer. [Cancer service guidance](#) (2004).

Improving outcomes in breast cancer – manual update. [Cancer service guidance](#) (2002).

Under development

NICE is developing the following guidance (details available from our [website](#)):

- Osteoporosis: assessment of fracture risk and the prevention of osteoporotic fractures in individuals at high risk. NICE clinical guideline. (Publication date to be confirmed.)

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

Appendix A: The Guideline Development Group

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^[15] From March 2006 to February 2008.

^[16] From March 2006 to April 2008.

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Dr John Hyslop (Chair)

Consultant Radiologist, Royal Cornwall Hospital NHS Trust

Dr Ash Paul

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Professor Liam Smeeth

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About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

The guideline was developed by the National Collaborating Centre for Cancer. The Collaborating Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

This guideline updates the following technology appraisals:

- 'Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer' (NICE technology appraisal guidance 107)
- 'Paclitaxel for the adjuvant treatment of early node-positive breast cancer' (NICE technology appraisal guidance 108)
- 'Docetaxel for the adjuvant treatment of early node-positive breast cancer' (NICE technology appraisal guidance 109)

The recommendations from this guideline have been incorporated into a [NICE Pathway](#). We have produced [information for the public](#) explaining this guideline. Tools to help you put the guideline into practice and information about the evidence it is based on are also [available](#).

Changes after publication

January 2012: minor maintenance

August 2013: minor maintenance

July 2014: added link to new recommendations in updated advanced breast cancer guideline.

April 2015: minor maintenance

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summary of product characteristics of any drugs they are considering.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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