Early and locally advanced breast cancer: diagnosis and management

NICE guideline

Draft for consultation, January 2018

This guideline covers diagnosing and managing early and locally advanced breast cancer. It aims to help healthcare professionals offer the right treatments to people, taking into account the person's individual preferences.

Who is it for?

- Healthcare professionals
- Commissioners and providers of breast cancer services
- People with early and locally advanced breast cancer, their families and carers

This guideline will update and replace NICE clinical guideline 80 (published 2009), and NICE technology appraisal guidance 107, 108, 109 and 112 (published 2006).

We have reviewed the evidence and updated or added new recommendations on diagnosis and treatment for people with early and locally advanced breast cancer. You are invited to comment on the new and updated recommendations. These are marked as **[2018]**.

You are also invited to comment on recommendations that NICE proposes to delete from the 2009 guideline.

We have not updated recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See update information for a full explanation of what is being updated.

This version of the guideline contains:

- the draft recommendations
- rationale and impact sections that explain why the committee made the 2018 recommendations and how they might affect practice
- the guideline context
- recommendations for research.

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

Full details of the evidence and the committee's discussion on the 2018 recommendations is in the evidence reviews. Evidence for the 2009 recommendations is in the full version of the 2009 guideline.

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Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in your care.

Breast cancer affects women and men, and can affect those who have undergone a gender reassignment or who are non-binary. We have used the term ‘women’ in this guideline for recommendations that usually only relate to women (such as breast-conserving surgery) and ‘people’ in all other cases. However, no discrimination is intended and recommendations relate to all those who have early or locally advanced breast cancer.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, for example, we use 'offer' to reflect a strong recommendation, usually where there is clear evidence of benefit and we use 'consider' to reflect a recommendation for which the evidence of benefit is less certain. There is also information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Referral, diagnosis and preoperative assessment

Preoperative assessment of the breast and axilla

1.1.1 Do not routinely use MRI of the breast in the preoperative assessment of people with biopsy-proven invasive breast cancer or ductal carcinoma in situ (DCIS). **[2009]**

1.1.2 Offer MRI of the breast to people 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. **[2009]**

Preoperative staging of the axilla

1.1.3 Perform pretreatment ultrasound evaluation of the axilla for people having investigations for early invasive breast cancer and, if abnormal lymph nodes are identified, perform ultrasound-guided needle sampling. **[2009]**

1.2 Providing information and psychological support

1.2.1 All members of the breast cancer clinical team should follow the recommendations on communication in NICE's guideline on patient experience in adult NHS services. **[2009, amended 2018]**

1.2.2 All people with breast cancer should have a named key worker who will support them throughout diagnosis, treatment and follow-up. **[2009, amended 2018]**

1.2.3 Offer all people with breast cancer prompt access to specialist psychological support and, where appropriate, psychiatric services. **[2009]**

1.2.4 Discuss opportunities for people with breast cancer to be involved in research, and support entry into clinical trials and other studies. **[2018]**

> To find out why the committee made the 2018 recommendation on involvement in research and how it might affect practice, see rationale and impact.

1.3 Surgery to the breast

1.3.1 Offer further surgery (re-excision or mastectomy, as appropriate) after breast-conserving surgery where invasive cancer and/or DCIS is present at the radial margins ('tumour on ink'; 0 mm). **[2018]**

1.3.2 For women who have had breast-conserving surgery where invasive cancer and/or DCIS is present within 2 mm of, but not at, the radial margins (greater than 0 mm and less than 2 mm):

- discuss the benefits and risks of further surgery (re-excision or mastectomy) to minimise the risk of local recurrence

- take into account the woman's preferences, comorbidities, tumour characteristics and the potential use of radiotherapy (also see radiotherapy after breast-conserving surgery). **[2018]**

To find out why the committee made the 2018 recommendations on surgery to the breast and how they might affect practice, see rationale and impact.

1.3.3 All breast units should audit their recurrence rates after treatment for DCIS. **[2009]**

Paget's disease

1.3.4 Offer breast-conserving surgery with removal of the nipple–areolar complex as an alternative to mastectomy for people with Paget's disease of the nipple that has been assessed as localised. Offer oncoplastic repair techniques to maximise cosmesis. **[2009]**

1.4 Surgery to the axilla

Invasive breast cancer

1.4.1 Perform minimal surgery, rather than lymph node clearance, to stage the axilla for people with 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. **[2009]**

1.4.2 Perform SLNB using the dual technique with isotope and blue dye. **[2009]**

1.4.3 Breast units should audit their axillary recurrence rates. **[2009]**

Ductal carcinoma in situ

1.4.4 Do not perform SLNB routinely for women with a preoperative diagnosis of DCIS who are having breast-conserving surgery, unless they are considered to be at high risk[1] of invasive disease. People at high risk of

[1] Risk can be estimated using a range of standardised tools and clinical expertise.

invasive disease include those with a palpable mass or extensive microcalcifications. **[2009]**

1.4.5 Offer SLNB to all people who are having a mastectomy for DCIS. **[2009]**

Evaluation and management of a positive axillary lymph node

1.4.6 Offer axillary node clearance to people with invasive breast cancer who have a preoperative ultrasound-guided needle biopsy with pathologically proven lymph node metastases. **[2009, amended 2018]**

1.4.7 Offer further axillary treatment (axillary node clearance or radiotherapy) after SLNB to people who have 1 or more sentinel lymph node macrometastases. **[2018]**

1.4.8 Discuss the benefits and risks of having no further axillary treatment after primary breast-conserving surgery (within clinical trials where available) with women who:

- have 1 or 2 sentinel lymph node macrometastases **and**
- have been advised to have whole breast radiotherapy with systemic therapy (which may be endocrine therapy). **[2018]**

1.4.9 Do not offer further axillary treatment after primary surgery to people with invasive breast cancer who have only micrometastases in their sentinel lymph nodes. **[2018]**

1.4.10 Do not offer further axillary treatment after primary surgery to people with invasive breast cancer who have only isolated tumour cells in their sentinel lymph nodes. Regard these people as having lymph node-negative breast cancer. **[2018]**

To find out why the committee made the 2018 recommendations on evaluation and management of a positive axillary lymph node and how they might affect practice, see rationale and impact.

1.5 Breast reconstruction

1.5.1 Offer immediate breast reconstruction to women who have been advised to have a mastectomy, including those who may need radiotherapy, unless they have significant comorbidities that rule out reconstructive surgery. **[2018]**

1.5.2 Discuss the benefits and risks of breast reconstruction with women. Topics to discuss include:

- the timing of breast reconstruction surgery (at the same time as mastectomy or later)
- different breast reconstruction surgery options and what they involve
- how the timing of breast reconstruction surgery affects the options available
- the uncertainty over long-term outcomes in women having radiotherapy. **[2018]**

1.5.3 Offer all appropriate breast reconstruction options, whether or not they are all available locally. **[2018]**

To find out why the committee made the 2018 recommendations on breast reconstruction and how they might affect practice, see rationale and impact.

1.6 Diagnostic assessment and adjuvant therapy planning

Predictive factors

1.6.1 Request the oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth receptor 2 (HER2) status of all invasive breast cancers simultaneously at the time of initial histopathological diagnosis. **[2018]**

1.6.2 Assess the ER status of all invasive breast cancers using standardised and quality assured immunohistochemical techniques, and report the results quantitatively. **[2009]**

1.6.3 Assess the PR status of all invasive breast cancers using standardised and quality assured immunohistochemical techniques, and report the results quantitatively. **[2018]**

1.6.4 Assess the HER2 status of all invasive breast cancers using standardised and quality assured techniques, and report the results quantitatively. **[2009]**

1.6.5 Ensure that the ER, PR and HER2 statuses are available and recorded at the multidisciplinary team meeting when systemic treatment is being discussed. **[2018]**

To find out why the committee made the 2018 recommendations on predictive factors and how they might affect practice, see rationale and impact.

Adjuvant therapy planning

1.6.6 Consider adjuvant therapy after surgery for people with invasive breast cancer, and ensure that recommendations are recorded at the multidisciplinary team meeting. **[2009]**

1.6.7 Base recommendations about adjuvant therapy on assessment of the prognostic and predictive factors, and the possible risks and benefits of the treatment. Make decisions with the person after discussing these factors. **[2009]**

1.6.8 Use the PREDICT tool to estimate prognosis and the absolute benefits of adjuvant therapy for women with invasive breast cancer. **[2018]**

1.6.9 When using versions 1.2 and 2.0 of the PREDICT tool[2], be aware that:

- it should be used with caution in:
  - women younger than 30 with ER-positive breast cancer
  - women aged 70 and over

[2] The potential limitations in versions of PREDICT after 2.0 may differ from those listed here.

  - women with HER2-positive breast cancer
- it has not been validated in men **and**
- the validation may have under-represented some ethnic groups. **[2018]**

To find out why the committee made the 2018 recommendations on adjuvant therapy planning and how they might affect practice, see rationale and impact.

1.6.10 Offer genetic testing for BRCA1 and BRCA2 mutations to women under 50 years with triple-negative breast cancer, but no family history of breast or ovarian cancer. (Also see genetic testing in the NICE guideline on familial breast cancer.) **[2017, amended 2018]**

1.7 Endocrine therapy

1.7.1 Treat people with invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery. **[2009]**

Adjuvant endocrine therapy for invasive breast cancer

1.7.2 Offer tamoxifen as the initial adjuvant endocrine therapy for men and premenopausal women with ER-positive invasive breast cancer. **[2009, amended 2018]**

1.7.3 Offer an aromatase inhibitor[3] as the initial adjuvant endocrine therapy for postmenopausal women with ER-positive invasive breast cancer who are at medium or high risk[4] of disease recurrence. Offer tamoxifen to women who are at low risk[4] of disease recurrence, or if aromatase inhibitors are not tolerated or are contraindicated. **[2009, amended 2018]**

[3] Please refer to the summary of product characteristics for individual aromatase inhibitors because there are differences in their licensed indications.
[4] Risk can be estimated using a range of standardised tools and clinical expertise.

Ovarian function suppression

1.7.4 Consider ovarian function suppression in addition to endocrine therapy for premenopausal women with ER-positive invasive breast cancer. **[2018]**

1.7.5 Discuss the benefits and risks of ovarian function suppression in addition to endocrine therapy with premenopausal women with ER-positive invasive breast cancer. Explain to women that ovarian function suppression may be most beneficial for those women who are at sufficient risk of disease recurrence to have been offered chemotherapy. **[2018]**

To find out why the committee made the 2018 recommendations on ovarian function suppression and how they might affect practice, see rationale and impact.

Extended endocrine therapy

1.7.6 Offer extended therapy (total duration of endocrine therapy of more than 5 years) with an aromatase inhibitor[5] for postmenopausal women with ER-positive invasive breast cancer who are at medium or high risk[6] of disease recurrence and who have been taking tamoxifen for 2 to 5 years. **[2018]**

1.7.7 Consider extended therapy (total duration of endocrine therapy of more than 5 years) with an aromatase inhibitor[5] for postmenopausal women with ER-positive invasive breast cancer who are at low risk[6] of disease recurrence and who have been taking tamoxifen for 2 to 5 years. **[2018]**

1.7.8 Consider extending the duration of tamoxifen therapy for longer than 5 years for both premenopausal and postmenopausal women with ER-positive invasive breast cancer. **[2018]**

To find out why the committee made the 2018 recommendations on extended endocrine therapy and how they might affect practice, see rationale and impact.

[5] Please refer to the summary of product characteristics for individual aromatase inhibitors because there are differences in their licensed indications.
[6] Risk can be estimated using a range of standardised tools and clinical expertise.

Endocrine therapy for ductal carcinoma in situ

1.7.9 Offer endocrine therapy after breast-conserving surgery for women with ER-positive DCIS if radiotherapy is recommended but not received. **[2018]**

1.7.10 Consider endocrine therapy after breast-conserving surgery for women with ER-positive DCIS if radiotherapy is not recommended. **[2018]**

1.7.11 Discuss the benefits and risks of endocrine therapy after breast-conserving surgery for women with ER-positive DCIS. **[2018]**

To find out why the committee made the 2018 recommendations on endocrine therapy for DCIS and how they might affect practice, see rationale and impact.

1.8 Adjuvant chemotherapy for invasive breast cancer

1.8.1 For people with breast cancer of sufficient risk that chemotherapy is indicated, offer a regimen that contains both a taxane[7] and anthracycline[8]. **[2018]**

1.8.2 Discuss with people the benefits and risks of adding a taxane[7] to anthracycline[8]-containing regimens. Topics to discuss include:

- the benefits of reduced cardiac toxicity and reduced nausea
- the risks of additional side-effects, including neuropathy, neutropenia and hypersensitivity
- the different adverse effects and dosing frequencies of different docetaxel and paclitaxel regimens, and the additional clinic visits that may be needed

[7] Please refer to the summary of product characteristics for individual taxanes because there are differences in their licensed indications.
[8] Please refer to the summary of product characteristics for individual anthracyclines because there are differences in their licensed indications.

- that absolute benefit is proportional to absolute risk of recurrence. **[2018]**

1.8.3 Weekly and fortnightly paclitaxel should be available locally because these regimens are tolerated better than 3-weekly docetaxel, particularly in people with comorbidities. **[2018]**

> To find out why the committee made the 2018 recommendations on adjuvant chemotherapy for invasive breast cancer and how they might affect practice, see rationale and impact.

Biological therapy

1.8.4 Offer adjuvant trastuzumab given at 3-week intervals for 1 year in combination with surgery, chemotherapy and radiotherapy as appropriate, for people with HER2-positive invasive breast cancer. **[2009, amended 2018]**

1.8.5 Assess cardiac function before starting treatment with trastuzumab. **[2009]**

1.8.6 Use trastuzumab with caution in people with HER2-positive invasive breast cancer who have any of the following:

- a baseline left ventricular ejection fraction (LVEF) of 55% or less
- a history of, or current, congestive heart failure
- a history of myocardial infarction
- angina pectoris needing medication
- cardiomyopathy
- cardiac arrhythmias needing medical treatment
- clinically significant valvular heart disease
- haemodynamic effective pericardial effusion
- poorly controlled hypertension. **[2009, amended 2018]**

1.8.7 Repeat cardiac function assessments every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50%, suspend trastuzumab treatment. Restart trastuzumab only after reassessing cardiac function and discussing the possible benefits and risks. Cardiac function assessments should also be repeated every 6 months following discontinuation of treatment until 24 months from the last administration of trastuzumab. **[2009, amended 2018]**

1.8.8 Consider trastuzumab as adjuvant treatment for people with T1a/T1b HER2-positive invasive breast cancer, taking into account any comorbidities, prognostic features and possible cardiac toxicity of anthracycline treatment. **[2018]**

To find out why the committee made the 2018 recommendation on biological therapy and how it might affect practice, see rationale and impact.

1.9 Bisphosphonate therapy

Adjuvant bisphosphonate therapy

1.9.1 Offer bisphosphonates (zoledronic acid or sodium clodronate)[9] as adjuvant therapy to postmenopausal women with node-positive invasive breast cancer. **[2018]**

1.9.2 Consider bisphosphonates (zoledronic acid or sodium clodronate)[9] as adjuvant therapy for postmenopausal women with invasive breast cancer and a high risk[10] of recurrence. **[2018]**

1.9.3 Discuss the benefits and risks of bisphosphonate treatment with women, particularly the risk of osteonecrosis of the jaw, atypical femoral fractures

[9] Although this use is common in UK clinical practice, at the time of consultation (January 2018), bisphosphonates did not have UK marketing authorisations for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[10] Risk can be estimated using a range of standardised tools and clinical expertise.

and osteonecrosis of the external auditory canal. Follow the Medicines and Healthcare products Regulatory Agency/Commission on Human Medicines (MHRA/CHM) advice on bisphosphonates. **[2018]**

To find out why the committee made the 2018 recommendations on adjuvant bisphosphonate therapy and how they might affect practice, see rationale and impact.

Bone health

1.9.4 Offer a baseline dual-energy X-ray absorptiometry (DEXA) scan to assess bone mineral density (BMD) in women with invasive breast cancer who are not receiving bisphosphonates as adjuvant therapy and who:

- are starting adjuvant aromatase inhibitor treatment **or**
- have treatment-induced menopause **or**
- are starting ovarian ablation/suppression therapy. **[2009, amended 2018]**

1.9.5 Do not offer a DEXA scan to women with invasive breast cancer who are receiving tamoxifen alone, regardless of their pretreatment menopausal status. **[2009]**

1.9.6 Offer bisphosphonates to women 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)[11]. **[2009]**

1.10 Radiotherapy

Radiotherapy after breast-conserving surgery

1.10.1 Offer whole breast radiotherapy to women with invasive breast cancer who have had breast-conserving surgery with clear margins. **[2018]**

[11] This guidance is not NICE accredited.

1.10.2 Consider partial breast radiotherapy (as an alternative to whole breast radiotherapy) for women who have had breast-conserving surgery for invasive cancer (excluding lobular type) with clear margins and who:

- have a low absolute risk of local recurrence (defined as women aged 50 and over with tumours that are 3 cm or less, N0, ER-positive, HER2-negative and grade 1 to 2) **and**
- have been advised to have adjuvant endocrine therapy for a minimum of 5 years. **[2018]**

1.10.3 When considering partial breast radiotherapy (see recommendation 1.10.2), discuss the benefits and risks, and explain that:

- local recurrence with partial breast radiotherapy at 5 years is equivalent to that with whole breast radiotherapy
- the risk of local recurrence beyond 5 years is not yet known
- there is a potential reduction in late adverse effects. **[2018]**

1.10.4 When delivering partial breast radiotherapy, consider:

- external beam radiotherapy to a dose of 40 Gy in 15 fractions **or**
- multicatheter interstitial brachytherapy. **[2018]**

1.10.5 Consider omitting radiotherapy for women who:

- have had breast-conserving surgery for invasive breast cancer with clear margins **and**
- have a very low absolute risk of local recurrence (defined as women aged 65 and over with tumours that are T1N0, ER-positive, HER2-negative and grade 1 to 2) **and**
- are willing to take adjuvant endocrine therapy for a minimum of 5 years. **[2018]**

1.10.6 When considering omitting radiotherapy (see recommendation 1.10.5), discuss the benefits and risks, and explain that:

- without radiotherapy, local recurrence occurs in about 10 women per 1,000 per year, and with radiotherapy, occurs in about 2 women per 1,000 per year
- overall survival at 10 years is the same with or without radiotherapy
- there is no increase in serious late effects if radiotherapy is given (for example, congestive cardiac failure, myocardial infarction or secondary cancer). **[2018]**

1.10.7 Offer adjuvant radiotherapy to women with DCIS following breast-conserving surgery with clear margins, and discuss with them the possible benefits and risks (also see surgery to the breast). **[2009, amended 2018]**

1.10.8 Use a radiotherapy technique that minimises the dose to the lung and heart. **[2018]**

1.10.9 Use a deep inspiratory breath-hold radiotherapy technique for people with left-sided breast cancer to reduce the dose to the heart. **[2018]**

To find out why the committee made the 2018 recommendations on radiotherapy after breast-conserving surgery and how they might affect practice, see rationale and impact.

Radiotherapy after mastectomy

1.10.10 Offer adjuvant postmastectomy radiotherapy to people with node-positive (macrometastases) invasive breast cancer or involved resection margins. **[2018]**

1.10.11 Consider adjuvant postmastectomy radiotherapy for people with node-negative T3 or T4 invasive breast cancer. **[2018]**

1.10.12 Do not offer radiotherapy following mastectomy to people with invasive breast cancer who are at low risk[12] of local recurrence (for example, most people who have lymph node-negative breast cancer). **[2018]**

To find out why the committee made the 2018 recommendations on radiotherapy after mastectomy and how they might affect practice, see rationale and impact.

Dose fractionation

1.10.13 Use external beam radiotherapy giving 40 Gy in 15 fractions as standard practice for women with invasive breast cancer after breast-conserving surgery or mastectomy. **[2009]**

Breast boost following breast-conserving surgery

1.10.14 Offer an external beam boost to the tumour bed for women with invasive breast cancer and a high risk[12] of local recurrence, following whole breast radiotherapy. **[2009, amended 2018]**

1.10.15 Inform women of the risk of side effects associated with an external beam boost to the tumour bed following whole breast radiotherapy. **[2009, amended 2018]**

Radiotherapy to nodal areas

1.10.16 Do not offer adjuvant radiotherapy to regional lymph nodes to people with invasive breast cancer who have been shown to have histologically lymph node-negative breast cancer. **[2009, amended 2018]**

1.10.17 Do not offer adjuvant radiotherapy to the axilla after axillary clearance for invasive breast cancer. **[2009, amended 2018]**

1.10.18 Offer adjuvant radiotherapy to the supraclavicular fossa to people with invasive breast cancer and 4 or more involved axillary lymph nodes. **[2009]**

[12] Risk can be estimated using a range of standardised tools and clinical expertise.

1.10.19 Offer adjuvant radiotherapy to the supraclavicular fossa to people with invasive breast cancer and 1 to 3 positive lymph nodes if they have other poor prognostic factors (for example, T3 and/or histological grade 3 tumours) and good performance status. **[2009]**

1.10.20 Consider including the internal mammary chain within the nodal radiotherapy target for people with node-positive (macrometastases) invasive breast cancer. **[2018]**

To find out why the committee made the 2018 recommendation on radiotherapy to nodal areas and how it might affect practice, see rationale and impact.

1.11 Primary systemic therapy

Neoadjuvant chemotherapy

1.11.1 Offer neoadjuvant chemotherapy to people with ER-negative invasive breast cancer as an option to reduce tumour size. **[2018]**

1.11.2 Offer neoadjuvant chemotherapy to people with HER2-positive invasive breast cancer in line with the NICE technology appraisal on pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer. **[2018]**

1.11.3 Consider neoadjuvant chemotherapy for people with ER-positive invasive breast cancer as an option to reduce tumour size if chemotherapy is indicated. **[2018]**

To find out why the committee made the 2018 recommendations on neoadjuvant chemotherapy and how they might affect practice, see rationale and impact.

Neoadjuvant regimens

1.11.4 Consider platinum-based[13] neoadjuvant chemotherapy regimens for people with triple-negative invasive breast cancer. **[2018]**

[13] Although this use is common in UK clinical practice, at the time of consultation (January 2018), platinums did not have UK marketing authorisations for this indication. The prescriber should follow

1.11.5 Discuss the benefits and risks of platinum-based[13] neoadjuvant chemotherapy with people who have triple-negative invasive breast cancer, particularly the risk of increased toxicity. **[2018]**

To find out why the committee made the 2018 recommendations on neoadjuvant regimens and how they might affect practice, see rationale and impact.

Neoadjuvant endocrine therapy

1.11.6 Consider neoadjuvant endocrine therapy for postmenopausal women with ER-positive invasive breast cancer as an option to reduce tumour size to facilitate breast-conserving surgery if there is no definite indication for chemotherapy. **[2018]**

1.11.7 Advise premenopausal women that neoadjuvant chemotherapy may be more likely to produce a clinical response than neoadjuvant endocrine therapy, but that some tumours do respond to neoadjuvant endocrine therapy. **[2018]**

1.11.8 Discuss with women the benefits and risks of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy. **[2018]**

To find out why the committee made the 2018 recommendations on neoadjuvant endocrine therapy and how they might affect practice, see rationale and impact.

Radiotherapy after neoadjuvant chemotherapy

1.11.9 Offer local treatment with mastectomy (or, in exceptional cases, breast-conserving surgery) followed by radiotherapy to people with locally advanced or inflammatory breast cancer that has been treated with chemotherapy. **[2009]**

relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

1.11.10 Offer postmastectomy radiotherapy after neoadjuvant chemotherapy if pretreatment investigations show node-positive (macrometastases) breast cancer. **[2018]**

1.11.11 Offer postmastectomy radiotherapy after neoadjuvant chemotherapy if post-treatment surgical investigations show node-positive (macrometastases) breast cancer or involved resection margins. **[2018]**

1.11.12 Consider postmastectomy radiotherapy after neoadjuvant chemotherapy if pretreatment investigations show node-negative T3 breast cancer. **[2018]**

1.11.13 Consider postmastectomy radiotherapy if post-treatment surgical investigations show node-negative T3 breast cancer. **[2018]**

To find out why the committee made the 2018 recommendations on radiotherapy after neoadjuvant chemotherapy and how they might affect practice, see rationale and impact.

1.12 Complications of local treatment and menopausal symptoms

Lymphoedema

1.12.1 Inform people with breast cancer about the risk of developing lymphoedema, and give them relevant written information before treatment with surgery and radiotherapy. **[2009]**

1.12.2 Give advice on how to prevent infection that may cause or exacerbate lymphoedema to people who have had treatment for breast cancer. **[2009, amended 2018]**

1.12.3 When informing people with breast cancer about the risk of developing lymphoedema, advise them that:

- they do not need to restrict their physical activity

- there is no consistent evidence of increased risk of lymphoedema associated with air travel, travel to hot countries, manicures, hot-tub use or sports injuries
- there is no consistent evidence of increased risk of lymphoedema associated with medical procedures (for example, blood tests, injections, intravenous medicines and blood pressure measurement) on the treated side, and the decision to perform medical procedures using the arm on the treated side should depend on clinical need and the possibility of alternatives. **[2018]**

1.12.4 Ensure that people with breast cancer who develop lymphoedema have rapid access to a specialist lymphoedema service. **[2009]**

To find out why the committee made the 2018 recommendation on lymphoedema and how it might affect practice, see rationale and impact.

Arm mobility

1.12.5 All breast units should have written local guidelines agreed with the physiotherapy department for postoperative physiotherapy. **[2009]**

1.12.6 Identify pre-existing shoulder conditions preoperatively in people with breast cancer, as this may inform further decisions on treatment. **[2009]**

1.12.7 Give instructions on functional exercises, which should start the day after surgery, to people with breast cancer. This should include relevant written information from a member of the breast or physiotherapy team. **[2009]**

1.12.8 Refer people to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment. **[2009]**

Menopausal symptoms

1.12.9 Stop systemic hormone replacement therapy (HRT) in women who are diagnosed with breast cancer. **[2009]**

1.12.10 Do not offer HRT (including oestrogen/progestogen combination) routinely to women with menopausal symptoms and a history of breast cancer. In exceptional circumstances, offer HRT[14] to women with severe menopausal symptoms and with whom the associated risks have been discussed. **[2009]**

1.12.11 Offer women information and counselling about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment. **[2009]**

1.12.12 Consider selective serotonin reuptake inhibitor antidepressants[15] for women with breast cancer for relieving menopausal symptoms, particularly hot flushes, but not for those taking tamoxifen. **[2009, amended 2018]**

1.12.13 Do not offer soy (isoflavone), red clover, black cohosh, vitamin E or magnetic devices to treat menopausal symptoms in women with breast cancer. **[2009]**

1.13 Follow-up

Follow-up imaging

1.13.1 Offer annual mammography to all people with breast cancer, including DCIS, until they enter the NHSBSP/BTWSP. People diagnosed with breast cancer who are already eligible for screening should have annual mammography for 5 years. **[2009]**

1.13.2 Do not offer mammography of the ipsilateral soft tissues after mastectomy. **[2009]**

[14] At the time of consultation (January 2018), HRT did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[15] At the time of consultation (January 2018), selective serotonin reuptake inhibitors did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

1.13.3 Do not offer ultrasound or MRI for routine post-treatment surveillance in people who have had treatment for invasive breast cancer or DCIS. **[2009]**

Clinical follow-up

1.13.4 People who have had treatment for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals). A copy should be sent to the GP and a copy given to the person. 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 people with lymphoedema. **[2009]**

1.14 Lifestyle

1.14.1 Advise people with breast cancer that the following are associated with a lower risk of recurrence:

- a healthy lifestyle
- achieving and maintaining a healthy weight (see the NICE guidelines on preventing excess weight gain and obesity) **and**
- regular physical activity (see the NICE guideline on physical activity for adults). **[2018]**

1.14.2 Advise people with breast cancer that alcohol intake below 5 units per week is associated with a lower risk of recurrence. **[2018]**

To find out why the committee made the 2018 recommendations on lifestyle and how they might affect practice, see rationale and impact.

Recommendations for research

The guideline committee has made the following recommendations for research. The committee's full set of research recommendations is detailed in the full guideline.

1 Surgery to the breast

What is the optimum tumour-free margin width after breast-conserving surgery for women with ductal carcinoma in situ (DCIS) and invasive breast cancer?

Why this is important

An important determinant of local recurrence is the surgical margin width (the distance from the breast cancer to the edge of the surgical excision). If the surgical margin is considered 'involved', then re-excision can take place as a further operation.

The threshold for considering if a margin is 'involved' is therefore important. If the margin is wide, then unnecessary re-excision can be avoided, whereas if the margin is narrow, local recurrence rate will be increased. From the evidence review, it was not possible to clearly define an optimum margin width between 0 mm and 2 mm to minimise local recurrence rates and minimise further surgery, and therefore it was felt this was an important topic for further research.

2 Bisphosphonates

Which groups of people with early and locally advanced breast cancer would benefit from the use of adjuvant bisphosphonates?

Why this is important

Bisphosphonates are widely used in people with advanced malignancies involving bone. Since the previous NICE guideline was published in 2009, data have been published exploring the use of bisphosphonates in preventing secondary breast cancer, with disease-related outcomes, and information on which subgroups are likely to benefit most from bisphosphonate treatment.

The evidence reviewed for this guideline identified that sodium clodronate leads to improved overall survival in mixed populations and improves disease-free survival in postmenopausal women, and that zoledronic acid improves disease-free survival in

postmenopausal women and in node-positive early breast cancer. There is, however, a lack of evidence regarding disease-free survival and overall survival, particularly for specific subgroups, such as premenopausal women on ovarian suppression, those with node-positive or node-negative disease, and those with positive or negative oestrogen or progestogen statuses. Therefore, further research is needed to determine the long-term survival benefits for bisphosphonates and to better define subgroups most likely to benefit.

3 Postmastectomy radiotherapy

What are the long-term outcomes for breast reconstruction in women having radiotherapy to the chest wall?

Why this is important

Postmastectomy breast reconstruction improves women's quality of life after mastectomy and is offered to women undergoing mastectomy. Reconstruction can be performed at the time of mastectomy (immediate breast reconstruction) or planned as a later procedure (delayed reconstruction). Some women need treatment with postmastectomy chest wall radiotherapy to reduce the risk of disease recurrence. However, it is known that radiotherapy can alter outcomes after breast reconstruction, including impairing cosmetic outcomes and increasing rates of re-operation and complications.

Research is therefore needed to understand whether immediate breast reconstruction or delayed breast reconstruction is optimal in women who may need postmastectomy radiotherapy, particularly regarding longer-term outcomes and different types of reconstruction.

4 Neoadjuvant endocrine therapy in premenopausal women

Is neoadjuvant endocrine therapy safe in premenopausal women with early breast cancer?

Why this is important

Endocrine therapy is an established part of adjuvant treatment for breast cancer in women with oestrogen receptor (ER)-positive disease. It reduces local and distant recurrence and reduces the risk of new breast cancers.

Endocrine therapy is well tolerated and safe to deliver as an outpatient treatment, does not need invasive monitoring, and needs less intensive visit schedules than neoadjuvant chemotherapy.

Endocrine therapy has been shown to achieve tumour shrinkage when used as first-line treatment (before surgery). However, in premenopausal women, this response was only identified in a proportion of women and evidence came from a single small study.

Although neoadjuvant chemotherapy is effective in achieving tumour shrinkage, not all premenopausal women need chemotherapy, and therefore neoadjuvant endocrine therapy may be an alternative.

No evidence was identified to confirm the long-term safety of neoadjuvant endocrine therapy in premenopausal women or to indicate which premenopausal women will benefit from it to achieve tumour shrinkage, and so research is needed to ascertain this.

5 Neoadjuvant endocrine therapy in postmenopausal women

Is there a benefit for neoadjuvant endocrine therapy in postmenopausal women with early breast cancer?

Why this is important

Endocrine therapy is an established part of adjuvant treatment for breast cancer in women with oestrogen receptor-positive disease. It reduces local and distant recurrence and reduces the risk of new breast cancers.

Endocrine therapy is well tolerated and safe to deliver as an outpatient treatment, does not need invasive monitoring, and needs less intensive visit schedules than neoadjuvant chemotherapy.

Endocrine therapy has been shown to achieve tumour shrinkage when used as first-line treatment (before surgery). However, in the postmenopausal women subgroup, the evidence was of low quality.

While neoadjuvant chemotherapy is an effective option to achieve tumour shrinkage, not all postmenopausal women need or may benefit from chemotherapy, and therefore neoadjuvant endocrine therapy may be an alternative. Research is needed to determine if this is the case.

6 Neoadjuvant treatment

What are the indications for postmastectomy radiotherapy after neoadjuvant chemotherapy?

Why this is important

Neoadjuvant chemotherapy is being increasingly used for selected groups of people with early breast cancer. The results of this approach have improved dramatically over recent years with up to 50–60% of people now showing a complete pathological response. Postoperative radiotherapy is generally recommended for women who have mastectomy after neoadjuvant chemotherapy because currently, available data do not permit people to be identified for whom radiotherapy could be safely omitted.

Complete pathological response has been shown to correlate with improved disease-free survival in women with ER-negative or human epidermal growth receptor 2 (HER2)-positive disease. It is therefore likely that women whose disease responds well to preoperative treatment will also derive less benefit from radiotherapy. Potentially, the toxicity of radiotherapy (cardiac damage, second malignancies) may outweigh the benefits in this subgroup. A randomised controlled trial is needed to test this hypothesis.

Rationale and impact

Referral, diagnosis and preoperative assessment

Why the committee made recommendation 1.2.4

The committee agreed, based on their clinical expertise, that continued improvement in breast cancer survival as well as post-diagnosis quality of life needs ongoing research into new or refined treatment options to allow further optimisation of care.

How the recommendation might affect practice

Recruitment into clinical trials wherever possible is already standard practice so the recommendation is unlikely to result in a change in practice.

Surgery to the breast

Why the committee made recommendations 1.3.1 and 1.3.2

There was some evidence that there was a reduced risk of ductal carcinoma in situ (DCIS) local recurrence if tissue margins were greater than 0 mm, so the committee recommended further surgery (re-excision or mastectomy) to extend the margins if needed. Although there was no consistent evidence about tissue margins for invasive breast cancer, the committee agreed that further surgery should be offered.

The committee agreed that complete excision of the tumour with clear margins was essential for the high-quality care of people with DCIS or invasive breast cancer.

Although there was evidence that aiming for wider margins reduced local recurrence, this did not improve overall survival. In addition, aiming for wider margins could lead to some people having unnecessary extra surgery. Given this uncertainty, the committee agreed the importance of personalised care and discussion to decide whether further surgery is needed.

How the recommendations might affect practice

The rates of further surgery currently vary across the country. Although the committee noted that the recommendations will reinforce current best practice, there may be some centres that will need to amend their practice in order to follow these recommendations.

Full details of the evidence and the committee's discussion are in evidence review A: surgery to the breast.

Evaluation and management of a positive axillary lymph node

Why the committee made recommendations 1.4.7–1.4.10

There was no new evidence that led the committee to change from the existing recommended practice (as recommended in the previous NICE guideline CG80) of:

- not offering axillary treatment to people with isolated tumour cells in their sentinel lymph nodes
- offering axillary clearance to people with pre-operatively pathologically proven involvement of the axillary lymph nodes.

The committee agreed that current evidence shows that further axillary treatment does not improve survival for people with micrometastases and there are risks such as lymphoedema, therefore further treatment should not be offered to this population.

There were unclear benefits and risks of further axillary treatment in people with only 1 or 2 sentinel lymph nodes who have had breast-conserving surgery and have been advised to have whole breast radiotherapy and systemic therapy, so the committee agreed that the risks and benefits of further treatment should be discussed with this group.

How the recommendations might affect practice

The committee agreed that the recommendations will result in a minor change in practice because some centres currently use mainly surgery and may not use radiotherapy. In addition, more time may need to be factored in to plan and deliver radiotherapy treatment.

Full details of the evidence and the committee's discussion are in evidence review B: management of the positive axilla.

Breast reconstruction

Why the committee made recommendations 1.5.1–1.5.3

The committee agreed that the main benefits of immediate breast reconstruction compared with delayed reconstruction are improved aesthetic satisfaction, improved health-related quality of life, lower rates of complications and a reduced need for further surgery. In addition, although radiotherapy can impact on outcomes after breast reconstruction, there was no consistent evidence of a difference in outcomes between radiotherapy delivered after immediate reconstructions compared with delayed reconstructions. Therefore, the committee agreed that the benefits

outweighed potential risks sufficiently to offer immediate reconstruction to all women, despite the lack of good evidence.

How the recommendations might affect practice

The recommendations may result in a substantial change in practice because many centres do not routinely offer immediate breast reconstruction to all women (including those who have been advised to have radiotherapy). The impact will depend on how many immediate reconstructions are already carried out. In addition, the uptake of immediate breast reconstruction will also depend on women's preferences. There may be cost savings associated with immediate reconstructions because fewer surgical procedures are needed (reconstruction is done at the same time as mastectomy and there are lower rates of additional symmetrisation surgery).

Full details of the evidence and the committee's discussion are in evidence review I: postmastectomy radiotherapy.

Predictive factors

Why the committee made recommendations 1.6.1, 1.6.3 and 1.6.5

There was not enough good evidence, so the committee agreed, using a formal consensus scoring system and their knowledge and experience, that progesterone receptor (PR) status should be assessed for all invasive breast cancers because:

- it will help when tailoring adjuvant therapy
- it will reduce delays in starting treatment
- if people are already having testing at this stage, their PR status can be assessed without them having to wait for additional test results.

The committee also agreed that oestrogen receptor (ER), PR and human epidermal growth receptor 2 (HER2) status assessments should be requested simultaneously at the time of initial diagnosis to ensure that results are available at the initial multidisciplinary team meeting. This will avoid delays and the need for additional discussions.

How the recommendations might affect practice

Most people with invasive breast cancer have PR testing in current practice, although it is not always performed at diagnosis. The recommendations should reduce variation in practice and delays in starting treatment, and the need for people to be reviewed at more than 1 multidisciplinary meeting, and so may lead to a small cost-saving.

Full details of the evidence and the committee's discussion are in evidence review C: adjuvant systemic therapy planning.

Adjuvant therapy planning

Why the committee made recommendations 1.6.8 and 1.6.9

Good evidence showed that the prognostic tool PREDICT is an accurate tool to estimate prognosis and the benefits of treatment in most people.

How the recommendations might affect practice

The committee agreed that most healthcare professionals already use the PREDICT tool, so this recommendation will not mean a big change in practice.

Full details of the evidence and the committee's discussion are in evidence review C: adjuvant systemic therapy planning.

Ovarian function suppression

Why the committee made recommendations 1.7.4 and 1.7.5

There was evidence that ovarian function suppression increased overall survival when combined with tamoxifen, and that women who have had chemotherapy benefited more. However, ovarian function suppression did not improve disease-free survival. In addition, it induces a temporary menopause and can worsen the menopausal symptoms seen with tamoxifen.

Given the limited evidence of benefits and the side effects of the treatment, the committee agreed that healthcare professionals should discuss the potential benefits and risks with women. This will help women to decide which treatment is right for them.

How the recommendations might affect practice

There is variation among centres in the use of ovarian function suppression, so the recommendations should lead to greater consistency and improve access to the treatment, even though not all women will wish to have it. There will be an increase in required resources for centres that do not currently provide ovarian function suppression, because additional appointments will be needed to administer the medication and monitor side effects. However, this was not anticipated to be a substantial cost increase due to the number of centres already offering ovarian function suppression. Further, increased costs will be at least partially offset by improvements in survival outcomes.

Full details of the evidence and the committee's discussion are in evidence review D: endocrine therapy for invasive disease.

Extended endocrine therapy

Why the committee made recommendations 1.7.6–1.7.8

Good evidence showed that switching to an aromatase inhibitor after 5 years of tamoxifen improved disease-free survival compared with postmenopausal women who had only received tamoxifen for 5 years, with the benefits being greater in those women who had a greater risk of disease recurrence.

The evidence showed no benefit in terms of disease-free survival or overall survival from continuing tamoxifen beyond 5 years. However, some of the studies on tamoxifen were conducted in the 1980s and may not be relevant to current practice. In the committee's experience, continuing tamoxifen can be beneficial for some women.

However, evidence showed that being on endocrine therapy for more than 5 years can increase the risk of problems such as endometrial cancer, osteoporosis, toxicity and phlebitis. The committee agreed that people will often prioritise survival even if this means they will have a reduced quality of life, but that people need to be informed about the possible benefits and risks so they can make a choice.

Because of the risk of problems with taking endocrine therapy for more than 5 years, the committee agreed that healthcare professionals should discuss the potential

benefits and risks with women to help them make an informed choice about treatment, based on their own risk factors.

How the recommendations might affect practice

Some centres already review treatment at 5 years, and continue endocrine therapy with tamoxifen or an aromatase inhibitor when it could benefit women. Because a large number of women will be affected by these recommendations, the resource impact will be large for centres that are not currently providing treatment after 5 years.

Full details of the evidence and the committee's discussion are in evidence review D: endocrine therapy for invasive disease.

Endocrine therapy for ductal carcinoma in situ

Why the committee made recommendations 1.7.9–1.7.11

There was good evidence that endocrine therapy after breast-conserving surgery for ER-positive DCIS improved disease-free survival and reduced rates of local recurrence in women who did not have radiotherapy. Because of their concerns about overtreatment, the committee agreed that women who were at higher risk (those who should have had radiotherapy, but who did not receive it) would benefit more.

The committee agreed that the benefits and risks of endocrine therapy should be discussed with the woman because of the potential treatment-related complications such as menopausal symptoms, and the impact on family planning.

How the recommendations might affect practice

Offering endocrine therapy after initial treatment of DCIS will be a change of practice because it is not currently routinely offered to these women. However, because of the small number of people with DCIS who will not receive radiotherapy, and the low cost of the medicines, the committee agreed that the impact will not be significant.

Full details of the evidence and the committee's discussion are in evidence review D: endocrine therapy for invasive disease.

Adjuvant chemotherapy for invasive breast cancer

Why the committee made recommendations 1.8.1–1.8.3

There was good evidence of improved survival when taxanes are added to anthracycline-based chemotherapy in people with node-positive and node-negative breast cancer. In both groups, the benefits and risks of treatment should be discussed because of the potential side effects associated with taxanes. Three-weekly docetaxel was identified as a regimen with potentially more toxicity than weekly or fortnightly paclitaxel.

How the recommendations might affect practice

These recommendations may result in a substantial change in practice because of increased taxane use, particularly for people with node-negative breast cancer and comorbidities.

In addition, there will be an increase in weekly and fortnightly chemotherapy regimens being offered (for people who cannot tolerate 3-weekly regimens). These regimens have a higher cost because they are more resource intensive, and may affect capacity in chemotherapy services.

Full details of the evidence and the committee's discussion are in evidence review E: adjuvant chemotherapy.

Biological therapy

Why the committee made recommendation 1.8.8

There was evidence that adjuvant trastuzumab can improve disease-free survival and overall survival in some people with T1a and T1b HER2-positive invasive breast cancer who were treated with adjuvant trastuzumab and chemotherapy. However, only a small number of people will benefit from this treatment and, because trastuzumab can cause heart problems, it is important to avoid offering it to people who do not need it. Because of this, the committee agreed that adjuvant trastuzumab should be an option for women with T1a and T1b tumours rather than a standard treatment.

Chemotherapy alone compared with no treatment was found to be more cost effective than chemotherapy and trastuzumab combined. However, the committee agreed that it was more appropriate to offer combined chemotherapy and trastuzumab, because it is the HER2-positivity that increases risk of recurrence for people with small (T1a and T1b) tumours sufficiently for chemotherapy to be of benefit. From a clinical perspective, it does not make sense to not treat the component that is increasing risk (that is, trastuzumab treatment for HER2-positivity). Further, the effect of chemotherapy alone in the economic model may be overestimated as the data was taken from the HERA trial, which included larger tumours, as this evidence was considered more robust than the clinical evidence in this review.

How the recommendation might affect practice

Currently, T1 tumours are not routinely treated with adjuvant trastuzumab, so this recommendation will lead to a change in practice. However, the committee agreed that the number of additional people having treatment would be small and so the impact on current practice would be minor.

Full details of the evidence and the committee's discussion are in evidence review F: adjuvant biological therapy.

Adjuvant bisphosphonate therapy

Why the committee made recommendations 1.9.1–1.9.3

There was good evidence that treatment with sodium clodronate and zoledronic acid improved disease-free and overall survival in postmenopausal women with node-positive invasive breast cancer.

There was little evidence on other bisphosphonates. The committee recommended considering zoledronic acid or sodium clodronate treatment for other high-risk populations, based on the evidence that sodium clodronate has overall survival benefits in mixed populations.

Although there is evidence that intravenous (IV) bisphosphonates have a higher risk of osteonecrosis of the jaw, oral bisphosphonates have a higher risk of gastrointestinal problems. There is also a risk of atypical femoral fractures and

osteonecrosis of the external auditory canal with bisphosphonates. Because each drug and regimen has different risks, the potential benefits and risks should be discussed with women to help them make an informed choice.

The committee did not look at the evidence relating to the use of bisphosphonates for bone health or for the use of baseline dual-energy X-ray absorptiometry (DEXA) scanning, so did not make any new recommendations.

How the recommendations might affect practice

Bisphosphonates are not consistently offered as adjuvant treatment, so this recommendation may lead to an increase in prescribing.

GPs may need to monitor people taking oral bisphosphonates, but this is likely to be an annual review so would not have a large workload impact. However, people may make more GP visits if they have side effects from bisphosphonate treatment.

The committee agreed that IV bisphosphonates would usually be administered at the same time as chemotherapy drugs for the first 6 months of treatment, so this would not result in extra hospital visits for this period. After that, extra visits for administration and monitoring may be needed.

Full details of the evidence and the committee's discussion are in evidence review G: adjuvant bisphosphonates.

Radiotherapy after breast-conserving surgery

Why the committee made recommendations 1.10.1, 1.10.5 and 1.10.6 on whole breast radiotherapy and omitting radiotherapy

There is evidence that whole breast radiotherapy after breast-conserving surgery reduces the risk of recurrence and increases overall survival. It also decreases rates of depression and anxiety.

However, because the risk of breast cancer recurring at 5 years is very low and there are harms associated with radiotherapy, the benefits of radiotherapy for women with a very low risk of recurrence are less certain. For these women, the committee

agreed that healthcare professionals should fully discuss the benefits and risks with women before a decision is made.

How the recommendations might affect practice

Most women are already offered radiotherapy after breast-conserving surgery so this reflects current practice, but more time may be needed to discuss the balance of benefits and risks with women.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Why the committee made recommendations 1.10.2–1.10.4 on partial breast radiotherapy

Good evidence showed that partial breast radiotherapy led to similar results to whole breast radiotherapy after breast-conserving surgery in women with a low risk of local recurrence. In addition, it may have fewer treatment-related adverse effects.

How the recommendations might affect practice

The committee was aware that current practice for external beam partial breast radiotherapy after breast-conserving surgery is based on the Royal College of Radiologists' 2016 consensus statement, so there would be no change to recommended practice.

However, because multicatheter interstitial brachytherapy is not widely used in the UK, the committee agreed that this would involve a change in practice if centres decided to use this technique rather than external beam radiotherapy.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Why the committee made recommendation 1.10.8 on radiotherapy techniques

There was good evidence that radiotherapy to the internal mammary nodes reduced locoregional recurrence and improved survival. However, the committee took into account the potential for lung and heart toxicity, so recommended using a radiotherapy technique that minimises this risk.

How the recommendation might affect practice

This recommendation is likely to require a change in practice for many centres. There will be some impact on resources in order to implement this recommendation because additional training will be needed and local protocols will need developing. However, the long-term impact on resources will be minimal: some additional planning time will be needed but there is no impact on the length or number of radiotherapy sessions.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Why the committee made recommendation 1.10.9 on radiotherapy techniques

There was evidence that deep inspiratory breath-hold radiotherapy techniques reduce the mean radiotherapy heart dose for adults with left-sided invasive breast cancer receiving whole breast radiotherapy. The committee did not identify any harms. There was also evidence that deep inspiration breath-hold radiotherapy techniques did not reduce the target coverage of whole breast radiotherapy.

There was no evidence about the use of deep inspiration breath-hold radiotherapy techniques for people with right-sided breast cancer, so the committee did not make separate recommendations for this subgroup.

How the recommendation might affect practice

Currently, deep inspiratory breath-hold radiotherapy techniques are not routinely offered to people with invasive breast cancer having whole breast radiotherapy. However, the committee noted that the Royal College of Radiologists has produced consensus statements that advise using this technique, and that many centres already offer it.

The recommendation will ensure consistent practice and ensure that people can access the best care.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Radiotherapy after mastectomy

Why the committee made recommendations 1.10.10–1.10.12

The committee agreed that adjuvant postmastectomy radiotherapy should be offered to people who have macroscopically node-positive invasive breast cancer or have involved resection margins. This is because the evidence showed a beneficial effect on survival and local recurrence. Although the evidence was limited and the committee acknowledged that radiotherapy is associated with lung and cardiac morbidity, they concluded that for this group of women, the benefits of radiotherapy outweigh the harms.

There was evidence of a beneficial effect of postmastectomy radiotherapy on local recurrence and overall survival for people with node-negative invasive breast cancer. However, the committee agreed that there was a risk of over-treatment if all people with node-negative invasive breast cancer received postmastectomy radiotherapy. Therefore, the committee recommended that adjuvant postmastectomy radiotherapy should be considered for people with node-negative T3 or T4 invasive breast cancer. There was no evidence for this specific subgroup but they would be considered at increased risk of recurrence and mortality relative to smaller, node-negative invasive breast cancers due to the size of the tumour.

The committee agreed that radiotherapy after mastectomy should not be offered to women with early invasive breast cancer who are at low risk of local recurrence (for example, most women who are lymph node-negative) because the evidence showed limited benefit in survival and local recurrence.

How the recommendations might affect practice

The committee agreed that the recommendations will reinforce current practice, so there would be little change in practice.

Full details of the evidence and the committee's discussion are in evidence review I: postmastectomy radiotherapy.

Radiotherapy to nodal areas

Why the committee made recommendation 1.10.20

There was good evidence that radiotherapy to the internal mammary nodes reduced locoregional recurrence and improved survival. However, the committee took into account the potential for lung and heart toxicity, and agreed the importance of using a radiotherapy technique that minimises this risk.

How the recommendation might affect practice

This recommendation is likely to require a change in practice for many centres. There will be some impact on resources in order to implement this recommendation because additional training will be needed and local protocols will need developing. However, the long-term impact on resources will be minimal: some additional planning time will be needed but there is no impact on the length or number of radiotherapy sessions.

Full details of the evidence and the committee's discussion are in evidence review H: breast radiotherapy.

Neoadjuvant chemotherapy

Why the committee made recommendations 1.11.1–1.11.3

There was good evidence to say that having chemotherapy before surgery (neoadjuvant chemotherapy) enables some women to have breast-conserving surgery who would otherwise have had total removal of their breast. The committee agreed that the response to neoadjuvant therapy could help to guide the choice of subsequent adjuvant therapy.

How the recommendations might affect practice

The committee agreed that the recommendations would not result in a major change in practice because neoadjuvant chemotherapy is already offered in many centres. These recommendations will help improve consistency in practice.

Full details of the evidence and the committee's discussion are in evidence review J: neoadjuvant treatment of early and locally advanced breast cancer

Neoadjuvant endocrine therapy

Why the committee made recommendations 1.11.6–1.11.8

For postmenopausal women, there was some evidence that breast conservation rates, changes in tumour size and overall survival are the same with neoadjuvant endocrine therapy and neoadjuvant chemotherapy. Endocrine therapy is safer and has fewer side effects than chemotherapy, but there was not enough evidence to recommend endocrine therapy over chemotherapy for every woman. The committee agreed that healthcare professionals should discuss the potential benefits and risks with women, to help them decide which treatment is right for them.

The evidence for premenopausal women showed that neoadjuvant chemotherapy was more effective than endocrine therapy, but that endocrine therapy may be effective in some women. However, some women may prefer endocrine therapy because it is safer and has fewer side effects. Because of this, the committee agreed that healthcare professionals should discuss the potential benefits and risks with women, to help them decide which treatment is right for them.

How the recommendations might affect practice

Neoadjuvant endocrine therapy is already being used, although there may be an increase in the number of people being offered it.

Full details of the evidence and the committee's discussion are in evidence review J: neoadjuvant treatment of early and locally advanced breast cancer.

Radiotherapy after neoadjuvant chemotherapy

Why the committee made recommendations 1.11.10–1.11.13

There was not enough evidence to recommend subgroups of women in whom postmastectomy radiotherapy could be safely omitted after neoadjuvant chemotherapy. Therefore, the committee agreed that the recommendations for postmastectomy radiotherapy among people who have not received neoadjuvant chemotherapy applied to this population. People with node-negative T4 cancer were not included because they are covered by recommendations for postmastectomy radiotherapy (see evidence review I: postmastectomy radiotherapy).

How the recommendations might affect practice

The committee noted that decisions about postmastectomy radiotherapy after neoadjuvant chemotherapy are currently based on pretreatment investigations, so there will be no change to practice.

Full details of the evidence and the committee's discussion are in evidence review J: neoadjuvant treatment of early and locally advanced breast cancer.

Neoadjuvant regimens

Why the committee made recommendations 1.11.4 and 1.11.5

There was evidence that platinum-based neoadjuvant chemotherapy regimens can improve pathological complete response (pCR) rate and breast-conservation rate in people with triple-negative invasive breast cancer. However, the committee took into account that platinum-based regimens can cause anaemia, thrombocytopenia, neutropenia and febrile neutropenia, and bone marrow problems and renal problems in older people. The committee agreed that healthcare professionals should have a full discussion with people about the benefits and risks of these regimens.

There was no evidence on people with the BRCA germline mutation, so the committee did not make separate recommendations for this subgroup.

How the recommendations might affect practice

Currently, platinum-based neoadjuvant chemotherapy is not routinely offered to people with triple-negative early and locally advanced breast cancer, although the committee was aware that some centres may offer it. The recommendations will therefore bring a change in practice and will make practice more consistent across the NHS. The committee estimated that approximately 30–40% of people receiving neoadjuvant chemotherapy may be affected by this recommendation.

Full details of the evidence and the committee's discussion are in evidence review J: neoadjuvant treatment of early and locally advanced breast cancer.

Lymphoedema

Why the committee made recommendation 1.12.3

Good evidence showed that there is no increased risk of lymphoedema associated with maintaining exercise levels after axillary intervention, so the committee agreed that people should not restrict or avoid physical activity.

Although the evidence was limited and mixed, the committee concluded that there is no consistent evidence of increased risk of lymphoedema associated with air travel, travel to hot countries, manicures, hot-tub use, sports injuries, or medical procedures on the treated side.

How the recommendation might affect practice

Advice about preventing lymphoedema is already being provided as part of routine care, so there is unlikely to be much change in practice. However, these recommendations will lead to greater consistency in the advice offered. They should also reduce inequality and improve the quality of standard care if people who have had axillary treatment need immunisations or elective procedures.

Full details of the evidence and the committee's discussion are in evidence review B: management of the positive axilla.

Lifestyle

Why the committee made recommendations 1.14.1 and 1.14.2

There was evidence that both dietary changes (reducing fat intake and maintaining a healthy weight) and physical activity increase survival in people with invasive breast cancer.

There was some evidence that cancer recurrence is more likely in people who drink more than 3 or 4 alcoholic drinks per week or 6 g of alcohol per day. This equates to approximately 5 units of alcohol per week.

How the recommendations might affect practice

The committee discussed that many NHS services would already be advising people with breast cancer about the importance of a healthy lifestyle, and how they can

make lifestyle changes to reduce the risk of recurrence. The committee agreed that these recommendations will help to direct conversations towards effective lifestyle changes. There will be no impact on resources because these discussions were already happening, and most of the lifestyle changes will be 'self-care' and implemented by patients themselves.

Full details of the evidence and the committee's discussion are in evidence review K: lifestyle.

Putting this guideline into practice

[This section will be completed after consultation]

NICE has produced tools and resources [link to tools and resources tab] to help you put this guideline into practice.

[Optional paragraph if issues raised] Some issues were highlighted that might need specific thought when implementing the recommendations. These were raised during the development of this guideline. They are:

- [add any issues specific to guideline here]
- [Use 'Bullet left 1 last' style for the final item in this list.]

Putting recommendations into practice can take time. How long may vary from guideline to guideline, and depends on how much change in practice or services is needed. Implementing change is most effective when aligned with local priorities.

Changes recommended for clinical practice that can be done quickly – like changes in prescribing practice – should be shared quickly. This is because healthcare professionals should use guidelines to guide their work – as is required by professional regulating bodies such as the General Medical and Nursing and Midwifery Councils.

Changes should be implemented as soon as possible, unless there is a good reason for not doing so (for example, if it would be better value for money if a package of recommendations were all implemented at once).

Different organisations may need different approaches to implementation, depending on their size and function. Sometimes individual practitioners may be able to respond to recommendations to improve their practice more quickly than large organisations.

Here are some pointers to help organisations put NICE guidelines into practice:

1. **Raise awareness** through routine communication channels, such as email or newsletters, regular meetings, internal staff briefings and other communications with all relevant partner organisations. Identify things staff can include in their own practice straight away.

2. **Identify a lead** with an interest in the topic to champion the guideline and motivate others to support its use and make service changes, and to find out any significant issues locally.

3. **Carry out a baseline assessment** against the recommendations to find out whether there are gaps in current service provision.

4. **Think about what data you need to measure improvement** and plan how you will collect it. You may want to work with other health and social care organisations and specialist groups to compare current practice with the recommendations. This may also help identify local issues that will slow or prevent implementation.

5. **Develop an action plan**, with the steps needed to put the guideline into practice, and make sure it is ready as soon as possible. Big, complex changes may take longer to implement, but some may be quick and easy to do. An action plan will help in both cases.

6. **For very big changes** include milestones and a business case, which will set out additional costs, savings and possible areas for disinvestment. A small project group could develop the action plan. The group might include the guideline champion, a senior organisational sponsor, staff involved in the associated services, finance and information professionals.

7. **Implement the action plan** with oversight from the lead and the project group. Big projects may also need project management support.

8. **Review and monitor** how well the guideline is being implemented through the project group. Share progress with those involved in making improvements, as well as relevant boards and local partners.

NICE provides a comprehensive programme of support and resources to maximise uptake and use of evidence and guidance. See our into practice pages for more information.

Also see Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley.

Context

This guideline updates and replaces the NICE guideline on early and locally advanced breast cancer (CG80). This is because new evidence was identified in surveillance that could affect recommendations, and has already changed clinical practice in some locations.

People with symptoms that could be caused by breast cancer are referred by their GP to designated breast clinics in local hospitals (see NICE's guideline on suspected cancer: recognition and referral). In addition, eligible women are invited for screening through the NHS Breast Screening Programme (NHSBSP) in England or the Breast Test Wales Screening Programme (BTWSP) in Wales. For most people, 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's cancer service guideline on improving outcomes in breast cancer).

Breast cancer is the most common cancer in the UK, with approximately 54,000 new cases of invasive disease and around 7,000 new cases of pre-invasive (in situ) disease diagnosed annually. Most of the breast cancers occur in women, but just over 300 men in the UK are also diagnosed with invasive breast cancer every year.

Most breast cancers are diagnosed at an early stage and are therefore potentially curable with modern treatments. Survival rates have improved over recent decades

with almost 90% of women diagnosed with breast cancer surviving their disease for 5 or more years after diagnosis. Survival is, however, linked to the stage of the disease at diagnosis; only 15% of women diagnosed with stage IV disease are alive at 5 years. Breast cancer remains the leading cause of death in women aged 35–49 years, and is second only to lung cancer as the leading cause of cancer death in all women.

The main risk factor for breast cancer is being female; the disease is 100 times less common in men. It is also a disease of ageing, with the risk of breast cancer increasing with increasing age. Some breast cancers are linked to lifestyle factors that include obesity, alcohol intake and use of hormone replacement therapy, whereas other lifestyle factors, including physical activity and breastfeeding, protect against breast cancer. About 5% of breast cancers are due to inherited mutations in high-risk genes such as BRCA1/2 and p53.

Groups that are covered

Adults (18 and over) with:

- newly diagnosed invasive adenocarcinoma of the breast of any size (T1–T4), with or without spread to locoregional lymph nodes (N0–N3) and with no distant metastases (M0)
- newly diagnosed ductal carcinoma in situ (DCIS)
- Paget's disease of the breast.

Groups that are not covered

Adults (18 and over) with:

- invasive adenocarcinoma of the breast and distant metastases (clinical or pathological M1)
- rare breast tumours (for example, angiosarcoma, lymphoma)
- benign breast tumours (for example, fibroadenoma)
- phyllodes tumour
- locally recurrent breast cancer or DCIS
- lobular carcinoma in situ (LCIS)
- no personal history of breast cancer and an increased risk of breast cancer due to family history.

More information

To find out what NICE has said on topics related to this guideline, see our web page on breast cancer.

Update information

July 2018

This guideline is a partial update of NICE clinical guideline CG80 (published 2009) and will replace it.

New recommendations have been added for the diagnosis and treatment of people with early and locally advanced breast cancer.

Recommendations are marked as **[2018]** if the recommendation is new or the evidence has been reviewed.

NICE proposes to delete some recommendations from the 2009 guideline, because either the evidence has been reviewed and the recommendations have been updated, or NICE has updated other relevant guidance and has replaced the original recommendations. Recommendations that have been deleted or changed sets out these recommendations and includes details of replacement recommendations. Where there is no replacement recommendation, an explanation for the proposed deletion is given.

Where recommendations are shaded in grey and end **[2009]**, the evidence has not been reviewed since the original guideline.

Where recommendations are shaded in grey and end **[2009, amended 2018]**, the evidence has not been reviewed but changes have been made to the recommendation wording that change the meaning (for example, because of equalities duties or a change in the availability of medicines, or incorporated guidance has been updated). These changes are marked with yellow shading, and explanations of the reasons for the changes are given in 'Recommendations that have been deleted or changed' for information.

See also the original NICE guideline and supporting documents.

Recommendations that have been deleted or changed

Recommendations to be deleted

Recommendation in 2009 guideline	Comment
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.	Replaced by: 1.3.1 Offer further surgery (re-excision or mastectomy, as appropriate) after breast-conserving surgery where invasive cancer and/or DCIS is present at the radial margins ('tumour on ink'; 0 mm). [2018] 1.3.2 For women who have had breast-conserving surgery where invasive cancer and/or DCIS is present within 2 mm of, but not at, the radial margins (greater than 0 mm and less than 2 mm): • discuss the benefits and risks of further surgery (re-excision or mastectomy) to minimise the risk of local recurrence • take into account the woman's preferences, comorbidities, tumour characteristics and the potential use of radiotherapy (also see Radiotherapy after breast-conserving surgery). [2018]
1.3.2 Enter patients with screen-detected DCIS into the Sloane Project (UK DCIS audit).	This recommendation has been deleted because the Sloane Project closed in 2012.
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.	This recommendation has been deleted because this programme is no longer running.
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.	Replaced by: 1.4.10 Do not offer further axillary treatment after primary surgery to people with invasive breast cancer who have only isolated tumour cells in their sentinel lymph nodes. Regard these people as having lymph node-negative breast cancer. [2018]
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	Replaced by: 1.5.1 Offer immediate breast reconstruction to women who have been advised to have a mastectomy, including those who may need radiotherapy,

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.	unless they have significant comorbidities that rule out reconstructive surgery. [2018] 1.5.2. Discuss the benefits and risks of breast reconstruction with women. Topics to discuss include: • the timing of breast reconstruction surgery (at the same time as mastectomy or later) • different breast reconstruction surgery options and what they involve • how the timing of breast reconstruction surgery affects the options available • the uncertainty over long-term outcomes in women having radiotherapy. [2018] 1.5.3 Offer all appropriate breast reconstruction options, whether or not they are all available locally.[2018]
1.6.2 Do not routinely assess progesterone receptor status of tumours in patients with invasive breast cancer.	Replaced by: 1.6.3 Assess the PR status of all invasive breast cancers using standardised and quality assured immunohistochemical techniques, and report the results quantitatively. [2018]
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.	Replaced by: 1.6.5 Ensure that the ER, PR and HER2 statuses are available and recorded at the multidisciplinary team meeting when systemic treatment is being discussed. [2018]
1.6.7 Consider using Adjuvant! Online to support estimations of individual prognosis and the absolute benefit of adjuvant treatment for patients with early invasive breast cancer.	Replaced by: 1.6.8 Use the PREDICT tool to estimate prognosis and the absolute benefits of adjuvant therapy for women with invasive breast cancer. [2018] 1.6.9 When using versions 1.2 and 2.0 of the PREDICT tool, be aware that: • it should be used with caution in: – women younger than 30 with ER-positive breast cancer – women aged 70 and over – women with HER2-positive breast cancer • it has not been validated in men **and**

	• the validation may have under-represented some ethnic groups. [2018]
1.6.8 Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery in patients with early breast cancer having these treatments.	This recommendation has been deleted because it has been replace by another Department of Health standard.
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.	Replaced by: 1.7.4 Consider ovarian function suppression in addition to endocrine therapy for premenopausal women with ER-positive invasive breast cancer. [2018]
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.	Replaced by: 1.7.5 Discuss the benefits and risks of ovarian function suppression in addition to endocrine therapy with premenopausal women with ER-positive breast cancer. Explain to women that ovarian function suppression may be most beneficial for those women who are at sufficient risk of disease recurrence to have been offered chemotherapy. [2018]
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 and who have who have been treated with tamoxifen for 2-3 years	1.7.6 Offer extended therapy (total duration of endocrine therapy of more than 5 years) with an aromatase inhibitor for postmenopausal women with ER-positive invasive breast cancer who are at medium or high risk of disease recurrence and who have been taking tamoxifen for 2 to 5 years. [2018] [5] Please refer to the summary of product characteristics for individual aromatase inhibitors because there are differences in their licensed indications. [6] Risk can be estimated using a range of standardised tools and clinical expertise.
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.	1.7.7 Consider extended therapy (total duration of endocrine therapy of more than 5 years) with an aromatase inhibitor[5] for postmenopausal women with ER-positive invasive breast cancer who are at low risk[6] of disease recurrence and who have been taking tamoxifen for 2 to 5 years. [2018] 1.7.8 Consider extending the duration of tamoxifen therapy for longer than 5 years for both premenopausal and postmenopausal women with ER-positive invasive breast cancer. [2018]

	[5] Please refer to the summary of product characteristics for individual aromatase inhibitors because there are differences in their licensed indications. [6] Risk can be estimated using a range of standardised tools and clinical expertise.
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	The recommendation has been deleted as it has been superseded by the new recommendations 1.7.6, 1.7.7 and 1.7.8 (see above).
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.	The recommendation has been deleted as it has been superseded by the new recommendations 1.7.6, 1.7.7 and 1.7.8 (see above).
1.7.8 Do not offer adjuvant tamoxifen after breast conserving surgery to patients with DCIS.	Replaced by: 1.7.9 Offer endocrine therapy after breast-conserving surgery for women with ER-positive DCIS if radiotherapy is recommended but not received. [2018] 1.7.10 Consider endocrine therapy after breast-conserving surgery for women with ER-positive DCIS if radiotherapy is not recommended. [2018] 1.7.11 Discuss the benefits and risks of endocrine therapy after breast-conserving surgery for women with ER-positive DCIS. [2018]
1.8.1 Offer docetaxel to patients with lymph node-positive breast cancer as part of an adjuvant chemotherapy regimen.	Replaced by: 1.8.1 For people with breast cancer of sufficient risk that chemotherapy is indicated, offer a regimen that contains both a taxane[7] and anthracycline[8]. [2018] 1.8.2 Discuss with people the benefits and risks of adding a taxane[7] to anthracycline[8]-containing regimens. Topics to discuss include: • the benefits of reduced cardiac toxicity and reduced nausea • the risks of additional side-effects, including neuropathy, neutropenia and hypersensitivity

	• the different adverse effects and dosing frequencies of different docetaxel and paclitaxel regimens, and the additional clinic visits that may be needed • that absolute benefit is proportional to absolute risk of recurrence. [2018] 1.8.3 Weekly and fortnightly paclitaxel should be available locally because these regimens are tolerated better than 3-weekly docetaxel, particularly in people with comorbidities. [2018] [7] Please refer to the summary of product characteristics for individual taxanes because there are differences in their licensed indications. [8] Please refer to the summary of product characteristics for individual anthracyclines because there are differences in their licensed indications.
1.8.2 Do not offer paclitaxel as an adjuvant treatment for lymph node-positive breast cancer.	Replaced by recommendations 1.8.1, 1.8.2 and 1.8.3 (see above).
1.11.1 Patients with early invasive breast cancer who have had breast conserving surgery with clear margins should have breast radiotherapy.	Replaced by: 1.10.1 Offer whole breast radiotherapy to women with invasive breast cancer who have had breast-conserving surgery with clear margins. [2018]
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.	Replaced by: 1.10.10 Offer adjuvant postmastectomy radiotherapy to people with node-positive (macrometastases) invasive breast cancer or involved resection margins. [2018]
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.	This recommendation has been replaced because the SUPREMO trial has finished recruiting. Replaced by: 1.10.11 Consider adjuvant postmastectomy radiotherapy for people with node-negative T3 or T4 invasive breast cancer. [2018]
1.11.11 If ALND is not possible following a positive axillary SLNB or four-node	Replaced by:

sample, offer adjuvant radiotherapy to the axilla to patients with early breast cancer (see recommendations in sections 1.4.1 and 1.4.7).	1.4.7 Offer further axillary treatment (axillary node clearance or radiotherapy) after SLNB to people who have 1 or more sentinel lymph node macrometastases. [2018]
1.11.14 Do not offer adjuvant radiotherapy to the internal mammary chain to patients with early breast cancer who have had breast surgery.	Replaced by: 1.10.20 Consider including the internal mammary chain within the nodal radiotherapy target for people with node-positive (macrometastases) invasive breast cancer. [2018]
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.	Replaced by: 1.11.1 Offer neoadjuvant chemotherapy to people with ER-negative invasive breast cancer as an option to reduce tumour size. [2018] 1.11.2 Offer neoadjuvant chemotherapy to people with HER2-positive invasive breast cancer in line with the NICE technology appraisal on pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer. [2018] 1.11.3 Consider neoadjuvant chemotherapy for people with ER-positive invasive breast cancer as an option to reduce tumour size if chemotherapy is indicated. [2018] 1.11.6 Consider neoadjuvant endocrine therapy for postmenopausal women with ER-positive invasive breast cancer as an option to reduce tumour size to facilitate breast-conserving surgery if there is no definite indication for chemotherapy. [2018] 1.11.7 Advise premenopausal women that neoadjuvant chemotherapy may be more likely to produce a clinical response than neoadjuvant endocrine therapy, but that some tumours do respond to neoadjuvant endocrine therapy. [2018] 1.11.8 Discuss with women the benefits and risks of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy. [2018]
1.13.11 Tibolone or progestogens are not recommended for women with menopausal symptoms who have breast cancer.	This recommendation has been deleted because tibolone is no longer considered as a treatment option, and progestogens may be used.
1.13.13 Clonidine, venlafaxine and gabapentin should only be offered to treat hot flushes in women with breast	This recommendation has been deleted because the committee advised that any discussion about medication would include a discussion of the side effects.

cancer after they have been fully informed of the significant side effects.	
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.	This recommendation has been deleted because screening is no longer stratified.
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.	This recommendation has been deleted because there is now no choice of follow-up care.

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2

1 Amended recommendation wording (change to meaning)

Recommendation in 2009 guideline	Recommendation in current guideline	Reason for change
1.2.1 All members of the breast cancer clinical team should have completed an accredited communication skills training programme.	1.2.1 All members of the breast cancer clinical team should follow the recommendations on communication in NICE's guideline on patient experience in adult NHS services. [2009, amended 2018]	Specific communications skills training programmes do not take place any more.
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.	1.2.2 All people with breast cancer should have a named key worker who will support them throughout diagnosis, treatment and follow-up. [2009, amended 2018]	The name of the professional has changed to key worker, per the breast cancer quality standard QS12.
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.	1.4.6 Offer axillary node clearance to people with invasive breast cancer who have a preoperative ultrasound-guided needle biopsy with pathologically proven lymph node metastases. [2009, amended 2018]	This has been partly updated and replaced by the evidence review for question 2.1; the remaining part on biopsy has been retained.
1.6.9 Offer genetic testing for BRCA1 and BRCA2 mutations to women under 50 years with triple-negative breast cancer, but no family history of breast or ovarian cancer. [2017]	1.6.10 Offer genetic testing for BRCA1 and BRCA2 mutations to women under 50 years with triple-negative breast cancer, but no family history of breast or ovarian cancer. (Also see genetic testing in the NICE guideline on familial breast cancer.) [2017, amended 2018]	A new clinical guideline (CG164) is now available on familial breast cancer which covers information on genetic testing.
1.7.3 Postmenopausal women with ER-positive early invasive breast cancer who are not considered to be at low risk should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy.	1.7.2 Offer tamoxifen as the initial adjuvant endocrine therapy for men and premenopausal women with ER-positive invasive breast cancer. [2009, amended 2018]	The guideline committee were aware that the original recommendations had not made clear that premenopausal women (and men)

Offer tamoxifen if an aromatase inhibitor is not tolerated or contra-indicated.	1.7.3 Offer an aromatase inhibitor[3] as the initial adjuvant endocrine therapy for postmenopausal women with ER-positive invasive breast cancer who are at medium or high risk[4] of disease recurrence. Offer tamoxifen to women who are at low risk[4] of disease recurrence, or if aromatase inhibitors are not tolerated or are contraindicated. [2009, amended 2018] [3] Please refer to the summary of product characteristics for individual aromatase inhibitors because there are differences in their licensed indications. [4] Risk can be estimated using a range of standardised tools and clinical expertise.	should receive tamoxifen first-line, and that it should be used in low risk post-menopausal women as well as if aromatase inhibitors are not tolerated or contra-indicated.
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	1.8.4 Offer adjuvant trastuzumab given at 3-week intervals for 1 year in combination with surgery, chemotherapy and radiotherapy as appropriate, for people with HER2-positive invasive breast cancer. [2009, amended 2018]	The guideline committee amended the wording in line with the current summary of product characteristics.
1.9.2 Do not offer trastuzumab treatment to women who have any of the who have any of the following: • a baseline left ventricular ejection fraction (LVEF) of 55% or less • a history of documented congestive heart failure • high risk uncontrolled arrhythmias • angina pectoris needing medication • clinically significant valvular heart disease • evidence of transmural infarction on ECG	1.8.6 Use trastuzumab with caution in people with HER2-positive invasive breast cancer who have any of the following: • a baseline left ventricular ejection fraction (LVEF) of 55% or less • a history of, or current, congestive heart failure • a history of myocardial infarction • angina pectoris needing medication • cardiomyopathy • cardiac arrhythmias needing medical treatment	The guideline committee amended the wording in line with the current summary of product characteristics.

• poorly controlled hypertension.	• clinically significant valvular heart disease • haemodynamic effective pericardial effusion • poorly controlled hypertension. [2009, amended 2018]	
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.	1.8.7 Repeat cardiac function assessments every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50%, suspend trastuzumab treatment. Restart trastuzumab only after reassessing cardiac function and discussing the possible benefits and risks. Cardiac function assessments should also be repeated every 6 months following discontinuation of treatment until 24 months from the last administration of trastuzumab. [2009, amended 2018]	The guideline committee amended the wording in line with the current summary of product characteristics.
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 (BMD) if they: • are starting adjuvant aromatase inhibitor treatment or • have treatment-induced menopause or • are starting ovarian ablation/suppression therapy.	1.9.4 Offer a baseline dual-energy X-ray absorptiometry (DEXA) scan to assess bone mineral density (BMD) in women with invasive breast cancer who are not receiving bisphosphonates as adjuvant therapy and who: • are starting adjuvant aromatase inhibitor treatment or • have treatment-induced menopause or • are starting ovarian ablation/suppression therapy. [2009, amended 2018]	The guideline committee reworded this recommendation to exclude those people who were receiving bisphosphonates as adjuvant therapy.
1.11.2 Offer adjuvant radiotherapy to patients with DCIS following adequate breast-conserving surgery and discuss with them the possible benefits and risks (also recommendation in section1.3.1)	1.10.7 Offer adjuvant radiotherapy to women with DCIS following breast-conserving surgery with clear margins, and discuss with them the possible benefits and risks (also see surgery	The word ‘adequate’ was changed to ‘with clear margins’.

	to the breast). [2009, amended 2018]	
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 and whole breast radiotherapy.	1.10.14 Offer an external beam boost to the tumour bed for women with invasive breast cancer and a high risk[12] of local recurrence, following whole breast radiotherapy. [2009, amended 2018] [12] Risk can be estimated using a range of standardised tools and clinical expertise.	The term site of local excision has been amended to tumour bed, and breast conserving surgery has been removed as this is now covered by additional recommendations.

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.	1.10.15 Inform women of the risk of side effects associated with an external beam boost to the tumour bed following whole breast radiotherapy. [2009, amended 2018]	The term site of local excision has been amended to tumour bed, and breast conserving surgery has been removed as this is now covered by additional recommendations. The wording has also been simplified.
1.11.9 Do not offer adjuvant radiotherapy to axilla or supraclavicular fossa to patients with early breast cancer who have been shown to be histologically lymph node-negative.	1.10.16 Do not offer adjuvant radiotherapy to regional lymph nodes to people with invasive breast cancer who have been shown to have histologically lymph node-negative breast cancer. [2009, amended 2018]	The term axilla and supraclavicular fossa has been changed to 'regional lymph nodes'.
1.11.10 Do not offer adjuvant radiotherapy to the axilla after ALND for invasive breast cancer. [2009, amended 2018]	1.10.17 Do not offer adjuvant radiotherapy to the axilla after axillary clearance for invasive breast cancer. [2009, amended 2018]	The term ALND has been changed to 'axillary clearance'.
1.13.12 The selective serotonin re-uptake inhibitor antidepressants paroxetine and fluoxetine may be offered to women with breast cancer for relieving menopausal symptoms, particularly hot flushes, but not to those taking tamoxifen.	1.12.12 Consider selective serotonin reuptake inhibitor antidepressants[15] for women with breast cancer for relieving menopausal symptoms, particularly hot flushes, but not for those taking tamoxifen. [2009, amended 2018] [15] At the time of consultation (January 2018), selective serotonin reuptake inhibitors did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.	The guideline committee is aware of new evidence on other SSRIs and has amended the wording accordingly, but cannot be specific as there was no new evidence review in this guideline update.

1

Changes to recommendation wording for clarification only (no change to meaning)

Recommendation numbers in current guideline	Comment
All recommendations except those labelled [2018]	Recommendations have been edited into the direct style (in line with current NICE style for recommendations in guidelines) where possible. Yellow highlighting has not been applied to these changes.