NICE National Institute for Health and Care Excellence

NICE Pathways

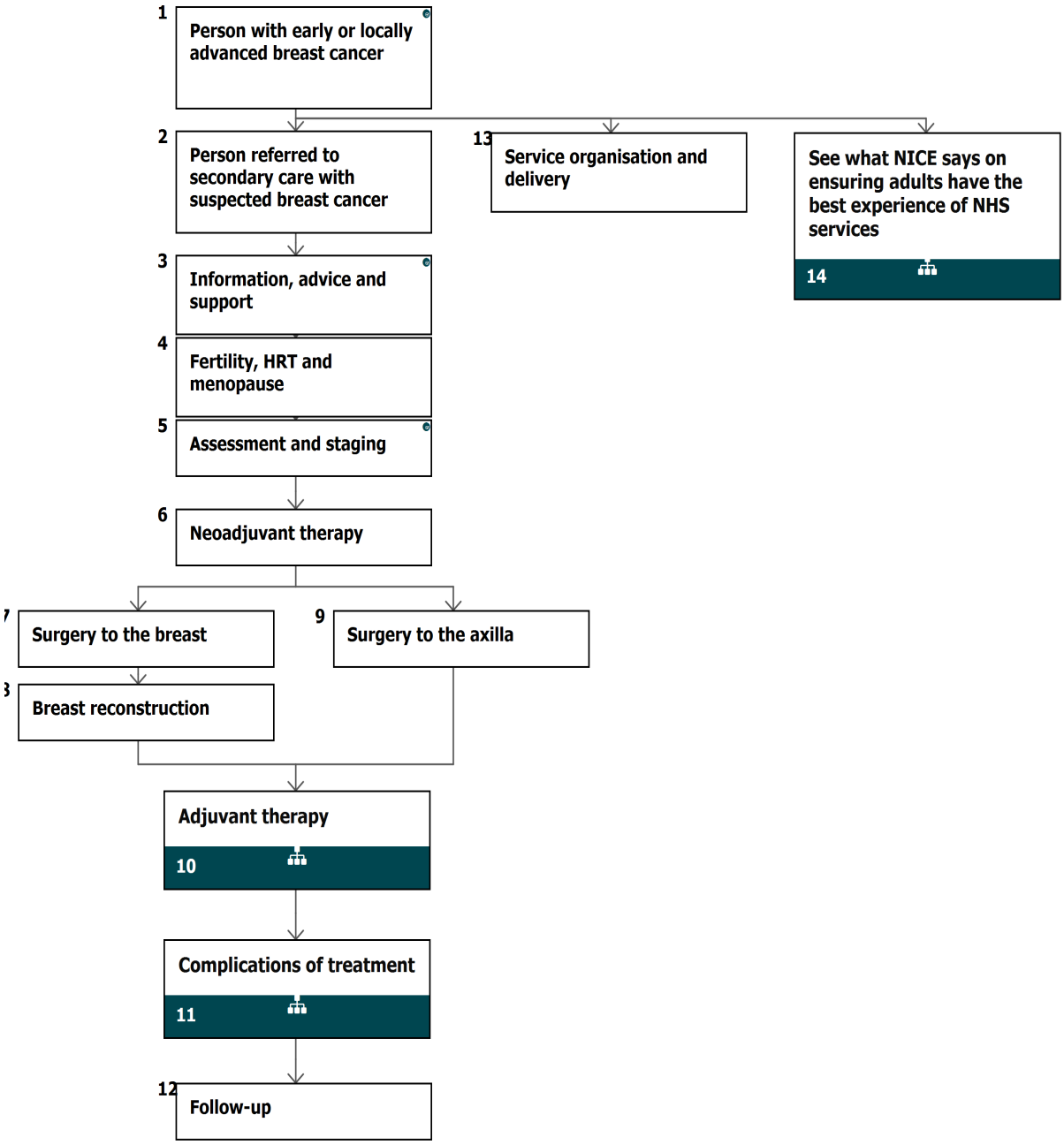
Early and locally advanced breast cancer overview

NICE Pathways bring together everything NICE says on a topic in an interactive flowchart. NICE Pathways are interactive and designed to be used online.

They are updated regularly as new NICE guidance is published. To view the latest version of this NICE Pathway see:

http://pathways.nice.org.uk/pathways/early-and-locally-advanced-breast-cancer
NICE Pathway last updated: 19 March 2019

This document contains a single flowchart and uses numbering to link the boxes to the associated recommendations.



1 Person with breast cancer

See also what NICE says on recognition and referral from primary to secondary care for suspected breast cancer.

Quality standards

The following quality statement is relevant to this part of the interactive flowchart.

1. Timely diagnosis

2 Adult referred to secondary care with suspected breast cancer

See what NICE says on recognition and referral from primary to secondary care for suspected breast cancer.

3 Information, advice and support

Providing information and psychological support

All members of the breast cancer clinical team should follow NICE's recommendations on communication to enable adult patients to actively participate in their care.

All people with breast cancer should have a named clinical nurse specialist or other specialist key worker with equivalent skills, who will support them throughout diagnosis, treatment and follow-up.

Offer all people with breast cancer prompt access to specialist psychological support and, where appropriate, psychiatric services.

NICE has written information for the public on early and locally advanced breast cancer.

Clinical trials and other studies

Discuss opportunities for people with breast cancer to be involved in research, and encourage entry into clinical trials and other studies.

See why we made the recommendation on clinical trials and other studies and how it might

affect practice [See page 16].

Risk of developing lymphoedema

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

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.

See why we made the recommendation on risk of developing lymphoedema and how it might affect practice [See page 21].

See also information on managing lymphoedema.

Lifestyle

Advise people with breast cancer that a healthy lifestyle is associated with a lower risk of recurrence, and that this should include:

- achieving and maintaining a healthy weight (see NICE's recommendations on obesity)
- limiting alcohol intake to below 5 units per week **and**
- regular physical activity (see NICE's recommendations on physical activity).

For guidance on smoking cessation, see NICE's recommendations on stop smoking interventions and services.

See why we made the recommendations on lifestyle and how they might affect practice [See page 22].

Quality standards

The following quality statement is relevant to this part of the interactive flowchart.

6. Key worker

4 Fertility, HRT and menopause

Preserving fertility

For guidance on fertility preservation, see NICE's recommendations on cryopreservation to preserve fertility in people diagnosed with cancer.

See why we made the recommendation on preserving fertility and how it might affect practice [See page 16].

Hormone replacement therapy

Stop systemic HRT in women who are diagnosed with breast cancer.

Menopause

Offer women information and counselling about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment. See also information on managing menopausal symptoms.

5 Assessment and staging

Ultrasound and needle sampling

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.

NICE has published a medtech innovation briefing on Aixplorer ShearWave Elastography for ultrasound imaging and assessing suspicious breast lesions.

MRI

Do not routinely use MRI of the breast in the preoperative assessment of people with biopsy-proven invasive breast cancer or DCIS. See also what NICE says on preoperative tests.

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.

Receptor testing for invasive breast cancer

Request the ER, PR and HER2 status of all invasive breast cancers simultaneously at the time of initial histopathological diagnosis.

Assess the ER status of all invasive breast cancers using standardised and quality-assured immunohistochemical techniques, and report the results quantitatively.

Assess the PR status of all invasive breast cancers using standardised and quality-assured immunohistochemical techniques, and report the results quantitatively.

Assess the HER2 status of all invasive breast cancers using standardised and quality-assured techniques, and report the results quantitatively.

Ensure that the ER, PR and HER2 statuses are available and recorded at the preoperative and postoperative multidisciplinary team meetings when systemic treatment is discussed.

See why we made the recommendations on receptor testing for invasive breast cancer and how they might affect practice [See page 19].

NICE has published a medtech innovation briefing on MammaTyper in vitro diagnostic test for determining breast cancer subtypes.

Gene testing for under 50s with triple-negative breast cancer

Offer genetic testing for BRCA1 and BRCA2 mutations to women under 50 years with triple-negative breast cancer, including those with no family history of breast or ovarian cancer. See also NICE's recommendations on genetic testing for familial breast cancer.

Biopsy

NICE has published interventional procedures guidance on image-guided radiofrequency excision biopsy of breast lesions with **special arrangements** for clinical governance, consent and audit or research.

NICE has published a medtech innovation briefing on ATEC system for vacuum-assisted breast biopsy.

Quality standards

The following quality statements are relevant to this part of the interactive flowchart.

2. Preoperative MRI scan

4. ER and HER2 receptor status

6 Neoadjuvant therapy

Neoadjuvant chemotherapy

Offer neoadjuvant chemotherapy to people with ER-negative invasive breast cancer as an option to reduce tumour size.

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 (see below).

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

For people with triple-negative invasive breast cancer, consider a neoadjuvant chemotherapy regimen that contains both a platinum[1] and an anthracycline.

Discuss the benefits and risks of adding a platinum to an anthracycline-containing neoadjuvant chemotherapy regimen. Topics to discuss include those in the table on the benefits and risks of adding a platinum to anthracycline-containing neoadjuvant chemotherapy for triple-negative invasive breast cancer [See page 25], and particularly the risk of increased toxicity.

See why we made the recommendations on neoadjuvant chemotherapy and how they might affect practice [See page 20].

Neoadjuvant endocrine therapy

Consider neoadjuvant endocrine therapy for postmenopausal women with ER-positive invasive

[1] Although this use is common in UK clinical practice, at the time of publication (July 2018), platinums 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 GMC's Prescribing guidance: prescribing unlicensed medicines for further information.

breast cancer as an option to reduce tumour size if there is no definite indication for chemotherapy.

Discuss with women the benefits and risks of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy. Topics to discuss include those in the table on the benefits and risks of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy [See page 26].

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.

See why we made the recommendations on neoadjuvant endocrine therapy and how they might affect practice [See page 21].

Pertuzumab

The following recommendation is from NICE technology appraisal guidance on pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer.

Pertuzumab, in combination with trastuzumab and chemotherapy, is recommended as an option within its marketing authorisation for the neoadjuvant treatment of HER2-positive breast cancer; that is, in adults with locally advanced, inflammatory or early-stage breast cancer at high risk of recurrence. It is recommended only if the company provides pertuzumab with the discount agreed in the patient access scheme.

NICE has written information for the public on pertuzumab.

7 Surgery to the breast

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.

Locally advanced or inflammatory breast cancer already treated with chemotherapy

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 neoadjuvant chemotherapy.

Further surgery after breast-conserving surgery

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).

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 (see also radiotherapy after breast-conserving surgery).

See why we made the recommendations on further surgery after breast-conserving surgery and how they might affect practice [See page 16].

Audit recurrence after treating ductal carcinoma in situ

All breast units should audit their recurrence rates after treatment.

Paget's disease of the nipple

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.

Intraoperative tests

The following recommendations are from NICE diagnostics guidance on intraoperative tests (RD-100i OSNA system and Metasin test) for detecting sentinel lymph node metastases in breast cancer.

Whole lymph node analysis using the RD-100i OSNA system is recommended as an option for detecting sentinel lymph node metastases during breast surgery in people with early invasive breast cancer who have a SLNB and in whom ALND will be considered. Details of the development of a national registry are included in section 7 of DG8.

The Metasin test is not recommended for detecting sentinel lymph node metastases in people with early invasive breast cancer in routine clinical NHS practice. The Metasin test shows promise and the development of robust evidence is recommended to demonstrate its utility in

clinical practice.

Intraoperative radiotherapy

The following recommendations are from NICE technology appraisal guidance on Intrabeam radiotherapy system for adjuvant treatment of early breast cancer.

The Intrabeam radiotherapy system is not recommended for routine commissioning for adjuvant treatment of early invasive breast cancer during breast-conserving surgical removal of the tumour.

Use of the Intrabeam radiotherapy system is recommended only using machines that are already available and in conjunction with NHS England specified clinical governance, data collection and submission arrangements.

The procedure should only be carried out by clinicians with specific training in the use of the Intrabeam radiotherapy system.

Patient selection for Intrabeam radiotherapy should be done by a multidisciplinary team experienced in the management of early invasive breast cancer, which includes both breast surgeons and clinical oncologists.

Clinicians wishing to undertake Intrabeam radiotherapy should take the following actions:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainties about the procedure and inform them about alternative treatment options.
- Provide patients with NICE's written information on the evidence of the risks and benefits of the range of treatment options available as an aid to shared decision-making.

NICE has written information for the public on Intrabeam radiotherapy system.

Medtech innovation briefing

NICE has published a medtech innovation briefing on axxent electronic brachytherapy system for early stage breast cancer.

Interventional procedures

NICE has published guidance that the following procedures should be used **only in the context of research**:

- endoscopic mastectomy and endoscopic wide local excision for breast cancer
- interstitial laser therapy for breast cancer.

Functional exercises to be started the day after surgery

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.

8 Breast reconstruction

Offer both breast reconstruction options to women (immediate reconstruction and delayed reconstruction), whether or not they are available locally.

Be aware that some women may prefer not to have breast reconstruction surgery.

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.

Discuss the benefits and risks of immediate breast reconstruction and delayed breast reconstruction with women. Topics to discuss include those in the table on breast reconstruction options for women who choose breast reconstruction [See page 23] and:

- 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.

See why we made the recommendations on breast reconstruction and how they might affect practice [See page 18].

Interventional procedures

NICE has published guidance on the use of the following procedures with **normal arrangements** for consent and for audit or research:

- breast reconstruction using lipomodelling after breast cancer treatment
- laparoscopic mobilisation of the greater omentum for breast reconstruction.

9 Surgery to the axilla

Invasive breast cancer

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.

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. SLNB is the preferred technique.

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

Breast units should audit their axillary recurrence rates.

Ductal carcinoma in situ

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 of invasive disease. People at high risk of invasive disease include those with a palpable mass or extensive microcalcifications. Risk can be estimated using a range of standardised tools and clinical expertise

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

Evaluation and management of a positive axillary lymph node

Offer axillary node clearance to people with invasive breast cancer who have a preoperative ultrasound-guided needle biopsy with pathologically proven lymph node metastases.

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

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).

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

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.

See why we made the recommendations on negative preoperative ultrasound-guided needle biopsy and how they might affect practice [See page 17].

Endoscopic axillary lymph node retrieval

NICE has published interventional procedures guidance on endoscopic axillary lymph node retrieval for breast cancer with **special arrangements** for consent and for audit or research.

Functional exercises to be started the day after surgery

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.

10 Adjuvant therapy

See Early and locally advanced breast cancer / Adjuvant therapy for early and locally advanced breast cancer

11 Complications of treatment

See Early and locally advanced breast cancer / Complications of early or locally advanced breast cancer treatment

12 Follow-up

Follow-up imaging

Offer annual mammography to all people with breast cancer, including DCIS, until they enter the NHSBSP in England or the BTWSP in Wales. People diagnosed with breast cancer who are already eligible for screening should have annual mammography for 5 years.

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

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

Clinical follow-up

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.

For people whose condition progresses to advanced breast cancer, see what NICE says on advanced breast cancer.

13 Service organisation and delivery

NICE has published cancer service guidance on:

- improving outcomes in breast cancer and
- improving supportive and palliative care for adults with cancer.

14 See what NICE says on ensuring adults have the best experience of NHS services

See Patient experience in adult NHS services

Rationale and impact: clinical trials and other studies

Rationale

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.

Impact

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

Rationale and impact: preserving fertility

Rationale

The committee agreed, based on their clinical expertise, that people having treatment for breast cancer should be advised about options for preserving their fertility, so cross-referred to the existing NICE guideline on this topic.

Impact

Discussion of fertility options is already standard practice so the recommendation is unlikely to result in a change in practice.

Rationale and impact: further surgery after breast-conserving surgery

Rationale

There was some evidence that there was a reduced risk of 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.

There was not enough evidence to clearly define an optimum margin width between 0 mm and 2 mm to minimise local recurrence rates and minimise further surgery, so the committee agreed that this was an important topic for further research.

Impact

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.

Rationale and impact: negative preoperative ultrasound-guided needle biopsy

Rationale

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:

- offering axillary clearance to people with preoperatively pathologically proven involvement of the axillary lymph nodes
- not offering axillary treatment after primary surgery to people with isolated tumour cells in their sentinel lymph nodes.

The committee agreed that current evidence shows that further axillary treatment after primary surgery 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 after primary surgery in people with only 1 or 2 sentinel lymph node macrometastases 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.

Studies of neoadjuvant therapy were excluded from the evidence review.

Impact

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.

Rationale and impact: breast reconstruction

Rationale

There was not much good evidence, but the committee agreed that the main benefits of immediate breast reconstruction compared with delayed reconstruction are improved aesthetic satisfaction, improved symmetry, improved health-related quality of life, lower overall rates of complications and a reduced need for further surgery. The committee agreed that in some circumstances, there are advantages to delayed reconstruction compared with immediate reconstruction (for example, reduced mastectomy flap loss, and capsular contracture). Therefore, delayed reconstruction should also be an option for women who wish to have a reconstruction after mastectomy. The committee also agreed that the option of no reconstruction should also be discussed, because this may be the preferred option for some women.

In addition, although radiotherapy can impact on outcomes after breast reconstruction, there was no consistent evidence for worse outcomes between radiotherapy delivered after immediate reconstructions compared with radiotherapy before delayed reconstructions. Therefore, the committee agreed that immediate reconstruction should be offered regardless of plans for chest wall radiotherapy.

There is little evidence regarding longer-term outcomes and different types of reconstruction. Because of this, the committee agreed that more research is needed to understand whether immediate breast reconstruction or delayed breast reconstruction is better in women who may need postmastectomy radiotherapy.

Impact

The recommendations may result in a substantial change in practice because many centres do

not routinely offer immediate breast reconstruction to all women (especially 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

Rationale and impact: receptor testing for invasive breast cancer

Rationale

There was not enough good evidence, so the committee agreed, using a formal consensus scoring system and their knowledge and experience, that 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 ER, PR and HER2 status assessments should be requested simultaneously at the time of initial diagnosis to ensure that results are available at the initial preoperative multidisciplinary team meeting (as well as the postoperative meeting). This will avoid delays and the need for additional discussions.

Impact

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 pathology results to be discussed 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.

Rationale and impact: neoadjuvant chemotherapy

Rationale

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.

Platinum-containing regimens

There was evidence that platinum-containing neoadjuvant chemotherapy regimens can improve pCR rate and breast conservation rate in people with triple-negative invasive breast cancer. However, the committee took into account that platinum-containing 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.

Impact

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.

Platinum-containing regimens

Currently, platinum-containing 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.

Rationale and impact: neoadjuvant endocrine therapy

Rationale

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 and that more research is needed to say whether neoadjuvant endocrine therapy is as effective as neoadjuvant chemotherapy.

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. The committee agreed that more research is needed on the long-term safety of neoadjuvant endocrine therapy, and to identify which premenopausal women will benefit from it.

Impact

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.

Rationale and impact: risk of developing lymphoedema

Rationale

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.

Impact

Advice about preventing lymphoedema is already being provided as part of routine care, so there is unlikely to be much change in practice. However, the recommendation will lead to greater consistency in the advice offered. It 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.

Rationale and impact: lifestyle

Rationale

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.

There was no evidence that smoking cessation reduces recurrence of breast cancer, although the view of the committee was that smoking cessation should always be recommended to people with breast cancer.

Impact

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.

Breast reconstruction options for women who choose breast reconstruction

<table>
<tr><th></th><th>Immediate breast reconstruction</th><th>Delayed breast reconstruction</th></tr>
<tr><td>Definition</td><td>Reconstruction is started in the same operation as the mastectomy.</td><td>After a mastectomy, reconstruction is done in a separate operation.</td></tr>
<tr><td rowspan="2">Number and timing of operations</td><td colspan="2">For both types, more than 1 operation is usually needed to complete the reconstruction. The total number of operations will vary. It may be affected by factors such as:
type of reconstruction (for example, some are planned in stages; a prosthesis may be worn until reconstruction is complete)
personal preferences (such as whether a nipple reconstruction is requested).</td></tr>
<tr><td>Fewer operations may be needed.</td><td>More operations may be needed.</td></tr>
<tr><td rowspan="2">Breast reconstruction options available</td><td colspan="2">These will vary depending on personal preferences (such as breast size desired), current body shape, other health conditions, previous operations and lifestyle factors (such as hobbies).

Not all hospitals or surgeons can offer all procedures. Travel to a different hospital may be needed for a specific option.</td></tr>
<tr><td>Options may be available that spare or preserve the breast skin (which may mean less scarring and a more natural look).

Limited time to make a decision about options (which may include not having a reconstruction) before surgery.</td><td>Certain options that spare or preserve the breast skin may not be available.

More time to make a decision (which may include not having a reconstruction) and to plan reconstruction.</td></tr>
</table>

<table>
<tr><td>Benefits</td><td>Breast shape remains, which may have psychological benefits.</td><td>Lifestyle changes (such as losing weight and taking regular exercise) may be possible, which increase the options and lower the risks of reconstruction surgery.

Procedures (and associated recovery) can be planned around other commitments.</td></tr>
<tr><td rowspan="2">Risks</td><td colspan="2">Surgical complications can occur after any breast reconstruction and will vary by type of procedure and personal risk factors.</td></tr>
<tr><td>May be lower rates of:

• tissue breakdown
• surgery for flap removal if it cannot be used because of a complication (which may lead to delayed reconstruction and flat appearance for a period of time)
• procedures to improve symmetry.

Complications from the mastectomy or axillary surgery can occur during the recovery period.</td><td>May be lower rates of:

• mastectomy site complications
• flap or implant failure (which may lead to delayed reconstruction and flat appearance for a period of time)
• capsular contracture (a scar layer around the implant that may lead to pain if severe).

May need to interrupt hormone therapies (tamoxifen) for further surgery.</td></tr>
<tr><td>Satisfaction</td><td colspan="2">No clear differences in satisfaction with completed reconstructions.</td></tr>
<tr><td>Reconstruction and adjuvant therapy (including radiotherapy and</td><td>Radiotherapy or chemotherapy can be given but may be delayed if there are complications from the mastectomy or reconstruction.</td><td>Complications can also occur after mastectomy alone, which may delay chemotherapy or radiotherapy.</td></tr>
</table>

chemotherapy)	Immediate reconstructions using implants may be more affected by radiotherapy than immediate flap reconstructions. May need adaptions to scans if a tissue expander is used. For example, may not be able to have MRI scans and may need modified radiotherapy planning.	

Benefits and risks of adding a platinum to anthracycline-containing neoadjuvant chemotherapy for triple-negative invasive breast cancer

	Effect of adding a platinum to anthracycline-containing (with or without taxane) neoadjuvant chemotherapy
Effect on breast conservation rate	Adding a platinum improves response rates compared with anthracycline-based (with or without taxane) chemotherapy. This may mean that some women who would otherwise need a mastectomy can be offered breast-conserving surgery.
Effect on pathological complete response rate (no residual cancer found at surgery)	Adding a platinum improves the chances of all signs of cancer disappearing in both the breast and lymph nodes in the armpit, compared with anthracycline-based (with or without taxane) neoadjuvant chemotherapy.
Effect on survival	No increase in overall survival with platinum-based chemotherapy.
Side effects NOTE: *Platinum-based*	Adding a platinum may mean that side effects are more severe. Anaemia, thrombocytopenia, neutropenia and febrile neutropenia are seen more frequently with platinum-based chemotherapy.

therapy is only suitable for fit patients with no significant comorbidities.	On average, if 1,000 women with triple-negative breast cancer receive platinum-containing neoadjuvant chemotherapy, about 70 additional women would experience severe or life-threatening side effects compared with non-platinum neoadjuvant chemotherapy. Bone marrow suppression and renal problems are likely in older people.
Licensed status	At the time of publication (July 2018), platinums did not have UK marketing authorisation for this indication.

Benefits and risks of neoadjuvant endocrine therapy compared with neoadjuvant chemotherapy

	Neoadjuvant endocrine therapy	Neoadjuvant chemotherapy
Definition	Tamoxifen or an aromatase inhibitor started before surgery. Only an option for women with ER-positive breast cancer.	Chemotherapy given before surgery. Only an option for people who would be recommended adjuvant (after surgery) chemotherapy.
Administration	Tablet taken once a day at home.	Intravenous administration in hospital, as an outpatient.
Effectiveness	**For postmenopausal women**: may be as effective as neoadjuvant chemotherapy in terms of breast conservation rates	**For postmenopausal women**: effective at improving breast conservation rates and shrinking the tumour. **For premenopausal women**: more effective

	and shrinking the tumour. **For premenopausal women**: less effective than neoadjuvant chemotherapy at shrinking the tumour (but some tumours may respond so may be effective in some women).	than endocrine therapy at shrinking the tumour.
Potential disadvantages	If neoadjuvant endocrine therapy is not effective then women may proceed to surgery earlier or may still need to have chemotherapy, either before or after surgery.	
Side effects	All endocrine therapies: menopausal symptoms such as hot flushes. For tamoxifen: increased risk of thrombosis and endometrial cancer. For aromatase inhibitors: joint and muscle pain, urogenital symptoms, bone density loss (may also occur with tamoxifen in premenopausal women). Side effects are usually reversible.	Side effects may include nausea and vomiting, risk of infections which may be life threatening, fatigue, neuropathy, cardiac toxicity, diarrhoea, constipation, sore mouth, skin and nail changes, risk of blood clots, risk of second malignancies, fluid retention, allergic reactions and hair loss. Side effects may persist long term.

	May allow women to avoid the additional side effects of chemotherapy (although women may still need adjuvant chemotherapy after surgery).	
Fertility and family planning	Women should not become pregnant while taking tamoxifen, or within 2 months of stopping, because it may have adverse effects on the baby.	Often causes temporary infertility. May cause permanent infertility
Length of course	May take longer than chemotherapy to shrink the tumour enough for breast-conserving surgery.	The duration of neoadjuvant chemotherapy is shorter than neoadjuvant endocrine therapy.

Glossary

ALND

axillary lymph node dissection (also known as axillary clearance)

BMD

bone mineral density

BTWSP

Breast Test Wales Screening Programme

DCIS

ductal carcinoma in situ

DEXA

dual energy X-ray absorptiometry

ER

oestrogen receptor

HER2

human epidermal growth factor 2

HRT

hormone replacement therapy

IV

intravenous

LCIS

lobular carcinoma in situ

LVEF

left ventricular ejection fraction

NHSBSP

NHS Breast Screening Programme

NPI

Nottingham Prognostic Index

pCR

pathological complete response

PR

progesterone receptor

SLNB

sentinel lymph node biopsy

Triple-negative breast cancer

ER, PR, HER2 negative breast cancer

Triple-negative invasive breast cancer

ER, PR, HER2 negative invasive breast cancer

Sources

Early and locally advanced breast cancer: diagnosis and treatment (2018) NICE guideline NG101

Intrabeam radiotherapy system for adjuvant treatment of early breast cancer (2018) NICE technology appraisal guidance 501

Pertuzumab for the neoadjuvant treatment of HER2-positive breast cancer (2016) NICE technology appraisal guidance 424

Intraoperative tests (RD-100i OSNA system and Metasin test) for detecting sentinel lymph node metastases in breast cancer (2013) NICE diagnostics guidance 8

Your responsibility

Guidelines

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Technology appraisals

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take these recommendations fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this interactive flowchart is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the recommendations to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to

have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Medical technologies guidance, diagnostics guidance and interventional procedures guidance

The recommendations in this interactive flowchart represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take these recommendations fully into account. However, the interactive flowchart does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Commissioners and/or providers have a responsibility to implement the recommendations, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this interactive flowchart should be interpreted in a way that would be inconsistent with compliance with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.