Familial breast cancer: classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer

NICE guideline

Draft for consultation, January 2013

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.

Contents

Introduction

Familial breast cancer typically occurs in people with an unusually high number of family members affected by breast, ovarian or a related cancer. If more cases of breast, ovarian or a related cancer are seen in a family than would be expected by chance alone, this can be a sign that genes have caused or contributed to its development. Breast cancer in people who have a family history of breast, ovarian or a related cancer may need different management from that in people without a family history of these cancers. This is because of differences in the future risk of developing contralateral breast cancer.

The risk of developing breast cancer depends on the:

- nature of the family history
- number of relatives who have developed breast, ovarian or a related cancer
- age at which relatives developed breast cancer
- age of the person.

There is a need to update the recommendations in NICE clinical guideline 41 on genetic testing thresholds, surveillance and use of preventive therapies for people without breast cancer who are at increased risk because of a family history of breast, ovarian or a related cancer.

For people with a diagnosis of breast cancer and a family history of breast, ovarian or a related cancer recommendations are needed on the management of breast cancer at the time of diagnosis and on subsequent surveillance. These areas are not covered by current NICE guidance (NICE clinical guidelines 41 and 80).

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good

evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

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Patient-centred care

This guideline offers best practice advice on the classification and care of people at risk of familial breast cancer and the management of breast cancer and related risks in people with a family history of breast cancer.

Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If someone does not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent, the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in Patient experience in adult NHS services.

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also ‘Patient-centred care’).

Interventions that must (or must not) be used

We usually use ‘must’ or ‘must not’ only if there is a legal duty to apply the recommendation. Occasionally we use ‘must’ (or ‘must not’) if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a ‘strong’ recommendation

We use ‘offer’ (and similar words such as ‘refer’ or ‘advise’) when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, ‘Do not offer…’) when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use ‘consider’ when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient’s values

and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation wording in guideline updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations shaded in grey and ending **[2004]** (see 'Update information' box below for details about how recommendations are labelled). In particular, for recommendations labelled **[2004]**, the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Update information

This guidance is an update of NICE clinical guideline 14 (published May 2004) and NICE clinical guideline 41 (published July 2006) and will replace them.

New and updated recommendations have been included on the classification and care of people at risk of familial breast cancer and the management of breast cancer and related risks in people with a family history of breast cancer.

Where recommendations are shaded in grey and end **[2004]** the evidence has not been updated since the original guideline. Yellow shading in these recommendations indicates where wording changes have been made for the purposes of clarification only.

You are invited to comment on the new and updated recommendations in this guideline only. These are marked as **[2013]** if the evidence has been reviewed but no change has been made to the recommendation, or **[new 2013]** if the evidence has been reviewed and the recommendation has been added or updated.

Appendix A contains recommendations from the 2004 and 2006 guidelines that NICE proposes deleting in the 2013 update. This is because the evidence has been reviewed and the recommendation has been updated, or because NICE has updated other relevant guidance and has replaced the original recommendations. Where there are replacement recommendations, details are provided. Where there is no replacement recommendation, an explanation for the proposed deletion is given. You are invited to comment on the deleted recommendations as part of the consultation on the 2013 update.

The original NICE guideline and supporting documents are here.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Family history and carrier probability

- When available in secondary care use a carrier probability calculation method with demonstrated acceptable performance (calibration and discrimination) as well as family history to determine who should be offered referral to tertiary care. Examples of acceptable methods include BOADICEA and the Manchester scoring system. **[new 2013]** [1.1.19]

Information and support

- To ensure a patient–professional partnership, patients should be offered individually tailored information, including information about sources of support (including local and national organisations). **[2004]** [1.2.2]

Carrier probability at which genetic testing should be offered

- For a person with no personal history of breast cancer, offer genetic testing in tertiary care to a family member with breast or ovarian cancer if their combined *BRCA1* and *BRCA2* mutation carrier probability is 10% or more (or they have a Manchester score of 15 or more). **[new 2013]** [1.5.8]
- Offer genetic testing in tertiary care to a person with no personal history of breast or ovarian cancer if their combined *BRCA1* and *BRCA2* mutation carrier probability is 10% or more, when they have a first-degree affected relative with a carrier probability of 20% in the family but is unavailable for testing (or a Manchester score of 17 or more). **[new 2013]** [1.5.10]

Surveillance for women with no personal history of breast cancer

- Offer annual mammographic surveillance to all women:
    - aged 40–49 years at moderate risk of breast cancer
    - aged 40 years and over at high risk of breast cancer. **[new 2013]** [1.6.3]

- Offer annual MRI surveillance to all women:

- aged 20–49 years with a *TP53* mutation
- aged 20–49 years with a greater than 30% probability of being a *TP53* carrier
- aged 30–49 years with a *BRCA1* or *BRCA2* mutation
- aged 30–49 years who have not had a genetic test but are at greater than 30% probability of being a *BRCA1* carrier. **[new 2013]** [1.6.9]

Surveillance for people with a personal and family history of breast cancer

- Offer annual MRI surveillance to all women aged 30–49 years with a personal history of breast cancer who are at high risk of contralateral breast cancer or have a *BRCA1* or *BRCA2* mutation. **[new 2013]** [1.6.12]
- Offer annual mammographic surveillance to all women aged 50–69 years with a personal history of breast cancer who are at high risk of contralateral breast cancer or have a *BRCA1* or *BRCA2* mutation. **[new 2013**] [1.6.13]

Chemoprevention for women with no personal history of breast cancer

- Offer tamoxifen[1] or raloxifene[2] for 5 years to post-menopausal women at high risk of breast cancer unless they have a past history of thromboembolic disease or endometrial cancer. **[new 2013]** [1.7.22]

[1] At the time of consultation (January 2013), tamoxifen 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 Good practice in prescribing medicines – guidance for doctors for further information.

[2] At the time of consultation (January 2013), raloxifene 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 Good practice in prescribing medicines – guidance for doctors for further information.

Risk-reducing mastectomy for women with no personal history of breast cancer

- All women considering bilateral risk-reducing mastectomy should be able to discuss their breast reconstruction options (immediate and delayed) with a member of a surgical team with specialist oncoplastic or breast reconstructive skills. **[2004]** [1.7.37]

1 Recommendations

The following guidance is based on the best available evidence. The full guideline [hyperlink to be added for final publication] gives details of the methods and the evidence used to develop the guidance.

The recommendations in this guideline apply to women and men unless otherwise specified.

In this guideline breast cancer risk categories are:

Breast cancer risk category	10-year breast cancer risk aged 40	Lifetime breast cancer risk from aged 20	Likelihood of a mutation in *BRCA1*/*BRCA2* or TP 53	Care setting
Near population risk	Less than 3% between age 40 and 50 years (equivalent to less than 1 in 33)	Lifetime risk of less than 17% (equivalent to less than 1 in 6)	Very low	Primary care
Moderate risk	A risk of 3–8% between age 40 and 50 years (equivalent to between 1 in 12 to 1 in 33)	Lifetime risk of 17% or a greater but less than 30% (equivalent to greater than 1 in 4)	Less than 10%	Secondary care
High risk	A risk of greater than 8% between age 40 and 50 years (equivalent to more than 1 in 12)	A lifetime risk of 30% or greater (equivalent to greater or equal to 1 in 3)	A 10% or greater chance of a faulty *BRCA1*, *BRCA2* or *TP53* gene in the family (equivalent to greater than or equal to 1 in 10)	Tertiary care

1.1 Clinical significance of a family history of breast cancer

Accuracy of family history

Family history-taking and initial assessment in primary care

1.1.1 When a person with no personal history of breast cancer presents with breast symptoms or has concerns about relatives with breast cancer, a first- and second-degree family history should be taken in primary care to assess risk, because this allows appropriate classification and care. **[2004]**

1.1.2 Healthcare professionals should respond to a person who presents with concerns but should not, in most instances, actively seek to identify people with a family history of breast cancer. **[2004]**

1.1.3 In some circumstances, it may also be clinically relevant to take a family history, for example, for women older than age 35 years using an oral contraceptive pill or for women being considered for long-term HRT use. **[2004]**

1.1.4 A person should be given the opportunity to discuss concerns about their family history of breast cancer if it is raised during a consultation. **[2004]**

1.1.5 A second-degree family history (that is, including aunts, uncles and grandparents) should be taken in primary care before explaining risks and options. **[2004]**

1.1.6 A second-degree family history needs to include paternal as well as maternal relatives. **[2004]**

1.1.7 Asking people to discuss their family history with relatives is useful in gathering the most accurate information. **[2004]**

1.1.8 Tools such as family history questionnaires and computer packages exist that can aid accurate collection of family history information and they should be made available. **[2004]**

1.1.9 For referral decisions, attempts should be made to gather as accurate information as possible on:

- age of diagnosis of any cancer in relatives
- site of tumours
- multiple cancers (including bilateral disease)
- Jewish ancestry[3]. **[2004]**

Family history-taking in secondary care

1.1.10 A family history should be taken when a person with no personal history of breast cancer presents with breast symptoms or has concerns about relatives with breast cancer. **[2004]**

1.1.11 A third-degree family history should be taken in secondary care where possible and appropriate. **[2004]**

1.1.12 Tools such as family history questionnaires and computer packages exist that can aid accurate collection of family history information and risk assessment and they should be made available. **[2004]**

Family history-taking in tertiary care

1.1.13 A third-degree family history should be taken in tertiary care for a person with no personal history of breast cancer, if this has not been done previously. **[2004]**

1.1.14 For accurate risk estimation, the following are required:

- age of death of affected and unaffected relatives

[3] Women with Jewish ancestry are around 5–10 times more likely to carry *BRCA1* or *BRCA2* mutations than women in non-Jewish populations.

- current age of unaffected relatives. **[2004]**

1.1.15 In general, it is not necessary to validate breast cancer-only histories (via medical records/cancer registry/death certificates). **[2004]**

1.1.16 If substantial management decisions, such as risk-reducing surgery, are being considered and no mutation has been identified, clinicians should seek confirmation of breast cancer-only histories (via medical records/cancer registry/death certificates). **[2004]**

1.1.17 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk-reducing surgery. **[2004]**

1.1.18 Abdominal malignancies at young ages and possible sarcomas should be confirmed in specialist care. **[2004]**

Family history and carrier probability

1.1.19 When available in secondary care use a carrier probability calculation method with demonstrated acceptable performance (calibration and discrimination) as well as family history to determine who should be offered referral to tertiary care. Examples of acceptable methods include BOADICEA and the Manchester scoring system. **[new 2013]**

1.1.20 In tertiary care use a carrier probability calculation method with demonstrated acceptable performance (calibration and discrimination) to assess the probability of a *BRCA1* or *BRCA2* mutation. Examples of acceptable methods include BOADICEA and the Manchester scoring system. **[new 2013]**

1.1.21 If there are problems with using or interpreting carrier probability calculation methods use clinical judgement when deciding whether to offer genetic testing. **[new 2013]**

Communicating cancer risk and carrier probability

1.1.22 People should be offered a personal risk estimate but information should also be given about the uncertainties of the estimation. **[2004]**

1.1.23 When a personal risk value is requested, it should be presented in more than one way (for example, a numerical value, if calculated, and qualitative risk). **[2004]**

1.1.24 People should be sent a written summary of their consultation in a specialist genetic clinic, which includes their personal risk information. **[2004]**

1.2 Information and support

1.2.1 Effective care involves a balanced partnership between patients and healthcare professionals. Patients should have the opportunity to make informed choices about any treatment and care and to share in decision making. **[2004]**

1.2.2 To ensure a patient–professional partnership, patients should be offered individually tailored information, including information about sources of support (including local and national organisations). **[2004]**

1.2.3 Tailoring of information should take into account format (including whether written or taped) as well as the actual content and form that should be provided (see box 1). **[2004]**

1.2.4 Standard information should be evidence based wherever possible, and agreed at a national level if possible (NICE's Information for the public provides a good starting point). **[2004]**

1.2.5 Standard information should not contradict messages from other service providers, including commonly agreed information across localities. **[2004]**

Box 1 Information provision for people with concerns about familial breast cancer risk

Standard written information for all people

- Risk information about population level and family history levels of risk, including a definition of family history.
- The message that, if their family history alters, their risk may alter.
- Breast awareness information.
- Lifestyle advice regarding breast cancer risk, including information about:
    - HRT and oral contraceptives (women only)
    - lifestyle, including diet, alcohol, etc
    - breastfeeding, family size and timing (women only).
- Contact details of those providing support and information, including local and national support groups.
- People should be informed prior to appointments that they can bring a family member/friend with them to appointments.
- Details of any trials or studies that may be appropriate.

For people cared for in primary care

- Standard written information (as above).
- Advice to return to discuss any implications if there is a change in family history or breast symptoms develop.

For people being referred to secondary care

- Standard written information (as above).
- Information about the risk assessment exercise that will take place and advice about how to obtain a comprehensive family history if required.
- Information about potential outcomes, depending on the outcome of the risk assessment (including referral back to primary care, management within secondary care or referral to a specialist genetics service) and what may happen at each level.

For people being referred back to primary care

- Standard written information (as above).
- Detailed information about why secondary or a specialist genetics service are not needed.

- Advice to return to primary care to discuss any implications if there is a change in family history change or breast symptoms develop.

For people being cared for in secondary care

- Standard written information (as above).
- Details of the risk assessment outcome, including why they are not being referred to a specialist genetics service.
- Details of surveillance options including risk and benefits.

For people being referred to tertiary care

- Standard written information (as above).
- Details of the risk assessment outcome, including why they are being referred to a specialist genetics service.
- Details of surveillance options, including risk and benefits.
- Details of what should be expected in a specialist genetics service, including counselling and genetic testing.

For people being cared for in tertiary care

- Standard written information (as above).
- Information about hereditary breast cancer.
- Information about genetic testing, both predictive testing and mutation finding, including details of what the tests mean and how informative they are likely to be, and the likely timescale of being given the results.
- Information about the risks and benefits of risk-reducing surgery when it is being considered, including both physical and psychological impact.

1.3 Care of people in primary care

Care and management in primary care

1.3.1 People without a personal history of breast cancer can be cared for in primary care if the family history shows only one first-degree or second-degree relative diagnosed with breast cancer at older than

age 40 years[4], provided that none of the following are present in the family history:

- bilateral breast cancer
- male breast cancer
- ovarian cancer
- Jewish ancestry
- sarcoma in a relative younger than age 45 years
- glioma or childhood adrenal cortical carcinomas
- complicated patterns of multiple cancers at a young age
- paternal history of breast cancer (two or more relatives on the father's side of the family). **[2004]**

1.3.2 People who do not meet the criteria for referral should be cared for in primary care by giving standard written information (see box 1). **[2004]**

Referral from primary care

1.3.3 People without a personal history of breast cancer who meet the following criteria should be offered referral to secondary care:

- one first-degree female relative diagnosed with breast cancer at younger than age 40 years

  or

  one first-degree male relative diagnosed with breast cancer at any age

  or

- one first-degree relative with bilateral breast cancer where the first primary was diagnosed at younger than age 50 years

  or

[4] In most cases this will equate to less than a 3% 10-year risk of breast cancer at age 40 years.

- two first-degree relatives, or one first-degree **and** one second-degree relative, diagnosed with breast cancer at any age

or

- one first-degree or second-degree relative diagnosed with breast cancer at any age **and** one first-degree or second-degree relative diagnosed with ovarian cancer at any age (one of these should be a first-degree relative)

or

- three first-degree or second-degree relatives diagnosed with breast cancer at any age. **[2004]**

1.3.4 Advice should be sought from the designated secondary care contact if any of the following are present in the family history in addition to breast cancers in relatives not fulfilling the above criteria:

- bilateral breast cancer
- male breast cancer
- ovarian cancer
- Jewish ancestry
- sarcoma in a relative younger than age 45 years
- glioma or childhood adrenal cortical carcinomas
- complicated patterns of multiple cancers at a young age
- paternal history of breast cancer (two or more relatives on the father's side of the family). **[2004]**

1.3.5 Discussion with the designated secondary care contact should take place if the primary care health professional is uncertain about the appropriateness of referral because the family history presented is unusual or difficult to make clear decisions about, or where the person is not sufficiently reassured by the standard information provided. **[2004]**

1.3.6 Direct referral to a specialist genetics service should take place where a high-risk predisposing gene mutation has been identified (for example, *BRCA1*, *BRCA2* or *TP53*). **[2004]**

Patient education and information

Information for women who are being referred

1.3.7 Women who are being referred to secondary or tertiary care should be provided with written information about what happens at this stage (see box 1). **[2004]**

Information and ongoing support for women who are not being referred

1.3.8 Support mechanisms (for example, risk counselling, psychological counselling and risk management advice) need to be identified, and should be offered to women not eligible for referral and/or surveillance on the basis of age or risk level who have ongoing concerns. **[2004]**

Support for primary care

1.3.9 Support is needed for primary care health professionals to care for women with a family history of breast cancer. Essential requirements for support for primary care are:

- a single point and locally agreed mechanism of referral for women identified as being at increased risk
- educational materials about familial breast cancer
- decision-support systems
- standardised patient information leaflets
- a designated secondary care contact to discuss management of 'uncertain' cases. **[2004]**

1.4 Care of people in specialist (secondary and tertiary) care

Care and management approach in secondary care

1.4.1 Care of people in secondary care (such as a breast care team, family history clinic or breast clinic) should be undertaken by a multidisciplinary team. It should include the following:

- written protocols for management
- central, standardised resources
- mammographic surveillance available to standard of the national breast screening programme[5]
- access to surveillance (see section 1.6) **[new 2013]**
- access to a team offering risk-reducing surgery
- standardised written information
- designated/lead clinicians
- a designated contact for primary care
- a designated contact in tertiary care
- audit
- clinical trials access
- access to psychological assessment and counselling
- information about support groups and voluntary organisations
- administrative support. **[2004]**

1.4.2 People who meet the following criteria should be offered secondary care and do not require referral to tertiary care:

one first-degree relative diagnosed with breast cancer at younger than age 40 years

or

[5] National breast screening programmes: England – NHS Breast Screening Programme (NHSBSP); Wales – Breast Test Wales; Northern Ireland – NI Breast Screening Programme

two first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 50 years

or

three first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 60 years

or

- a formal risk assessment (usually carried out in tertiary care) or a family history pattern is likely to give risks of greater than 3–8% risk in the next 10 years for women aged 40 years, or a lifetime risk of 17% or greater but less than 30%[6]

provided that none of the following are present in the family history:

- bilateral breast cancer
- male breast cancer
- ovarian cancer
- Jewish ancestry
- sarcoma in a relative younger than 45 years of age
- glioma or childhood adrenal cortical carcinomas
- complicated patterns of multiple cancers at a young age
- very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family). **[2004]**

1.4.3 People whose risk does not meet the criteria for referral to secondary care (see recommendation 1.3.3) can be referred back to primary care:

- with appropriate information being offered (see box 1), and
- support mechanisms (for example, risk counselling, psychological counselling and risk management advice) need to be identified, and should be offered to people not eligible for

[6] For the purpose of these calculations, a women's age should be assumed to be 40 for a women in her forties. A 10-year risk should be calculated for the age range 40-49.

referral and/or surveillance on the basis of age or risk level who have ongoing concerns. **[2004]**

Referral to tertiary care

1.4.4 People who meet the following referral criteria should be offered a referral to tertiary care.

- At least the following female breast cancers only in the family:
  - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative) **[2004]**

    or
  - three first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative) **[2004]**

    or
  - four relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative). **[2004]**

  or
- Families containing one relative with ovarian cancer at any age **and**, on the same side of the family:
  - one first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years **[2004]**

    or
  - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years **[2004]**

    or
  - another ovarian cancer at any age. **[2004]**

  or
- Families affected by bilateral cancer (each breast cancer has the same count value as one relative):

  - one first-degree relative with cancer diagnosed in both breasts at younger than an average age 50 years **[2004]**

    or

  - one first-degree or second-degree relative diagnosed with bilateral cancer **and** one first or second degree relative diagnosed with breast cancer at younger than an average age of 60 years. **[2004]**

or

- Families containing male breast cancer at any age **and**, on the same side of the family, at least:
  - one first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years **[2004]**

    or

  - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years. **[2004]**

or

- A formal risk assessment has given risk estimates of:
  - a 10% or greater chance of a gene mutation being harboured in the family (see recommendations 1.5.8–1.5.14) **[new 2013]**

    or

  - a greater than 8% risk of developing breast cancer in the next 10 years **[2004]**

    or

  - a 30% or greater lifetime risk of developing breast cancer **[2004]**

    or

  - a family Manchester score of 15 or more **and**:
    - ◊ an affected first-degree relative, **or**
    - ◊ an affected second-degree paternal relative. (see recommendations 1.5.8–1.5.14) **[new 2013]**.

1.4.5 Clinicians should seek further advice from a specialist genetics service for families containing any of the following, in addition to breast cancers:

- Jewish ancestry **[2004]**
- sarcoma in a relative younger than age 45 years **[2004]**
- glioma or childhood adrenal cortical carcinomas **[2004]**
- complicated patterns of multiple cancers at a young age **[2004]**
- very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family) **[2004]**
- triple negative breast cancer under the age of 40 years **[new 2013]**.

1.4.6 The management of a high-risk people may take place in secondary care if they do not want genetic testing or risk-reducing surgery and do not wish to be referred to a specialist genetics service. **[2004]**

1.4.7 Following initial consultation in secondary care, written information should be provided to reflect the outcomes of the consultation (see box 1). **[2004]**

Care of people in tertiary care

1.4.8 Care of people referred to tertiary care should be undertaken by a multi-disciplinary team. In addition to having access to the components found in secondary care, it should also include the following:

- clinical genetic risk assessment
- verification for abdominal malignancies and possible sarcomas. **[2004]**

Genetic counselling for people with no personal history of breast cancer

1.4.9 Women with no personal history of breast cancer meeting criteria for referral to tertiary care should be offered a referral for genetic counselling regarding their risks and options. **[2004]**

1.4.10 Women attending genetic counselling should receive standardised information beforehand describing the process of genetic counselling, information to obtain prior to the counselling session, the range of topics to be covered and brief educational material about hereditary breast cancer and genetic testing. **[2004]**

1.4.11 Predictive genetic testing should not be offered without adequate genetic counselling. **[2004]**

1.5 Genetic testing

Genetic testing for people with a family history but no personal history of breast cancer

1.5.1 All eligible people should have access to information on genetic tests aimed at mutation finding. **[2004]**

1.5.2 Pre-test counselling (preferably two sessions) should be undertaken. **[2004]**

1.5.3 Discussion of genetic testing (predictive and mutation finding) should be undertaken by a healthcare professional with appropriate training. **[2004]**

1.5.4 Eligible people and their affected relatives should be informed about the likely informativeness of the test (the meaning of a positive and a negative test) and the likely timescale of being given the results. **[2004]**

Mutation tests

1.5.5 Tests aimed at mutation finding should first be carried out on an affected family member where possible. **[2004]**

1.5.6 If possible the development of a genetic test for a family should usually start with the testing of an affected individual (mutation searching/screening) to try to identify a mutation in the appropriate gene (such as *BRCA1*, *BRCA2* or *TP53*) (see recommendations 1.5.8–1.5.14). **[2004]**

1.5.7 A search/screen for a mutation in a gene (such as *BRCA1*, *BRCA2* or *TP53*) should aim for as close to 100% sensitivity as possible for detecting coding alterations and the whole gene(s) should be searched. **[2004]**

Carrier probability at which genetic testing should be offered

1.5.8 For a person with no personal history of breast cancer, offer genetic testing in tertiary care to a family member with breast or ovarian cancer if their combined *BRCA1* and *BRCA2* mutation carrier probability is 10% or more (or they have a Manchester score of 15 or more). **[new 2013]**

1.5.9 For a person with no personal history of breast cancer, consider genetic testing in tertiary care for a family member with breast cancer or ovarian cancer if their combined *BRCA1* and *BRCA2* mutation carrier probability is between 5% and 10%. **[new 2013]**

1.5.10 Offer genetic testing in tertiary care to a person with no personal history of breast or ovarian cancer if their combined *BRCA1* and *BRCA2* mutation carrier probability is 10% or more, when they have a first-degree affected relative with a carrier probability of 20% in the family but is unavailable for testing (or a Manchester score of 17 or more). **[new 2013]**

1.5.11 Consider genetic testing in tertiary care for a person with no personal history of breast or ovarian cancer if their combined *BRCA1* and *BRCA2* mutation carrier probability is between 5% and 10%, when they have a first-degree affected relative with a carrier probability of 10–20% in the family but is unavailable for testing (or a Manchester score of 14–16). **[new 2013]**

1.5.12 For a person with a personal history of breast and/or ovarian cancer, offer genetic testing in tertiary care if their combined *BRCA1* and *BRCA2* mutation carrier probability is 10% or more (or they have a Manchester score of 15 or more). **[new 2013]**

1.5.13 For a person with a personal history of breast and/or ovarian cancer, consider genetic testing in tertiary care if their combined *BRCA1* and *BRCA2* mutation carrier probability is between 5% and 10%. **[new 2013]**

1.5.14 Clinical genetics laboratories should record gene variants of uncertain significance, periodically review for evidence of causality and ensure that families are contacted as appropriate. **[new 2013]**

Genetic testing for *BRCA1 BRCA2* and *TP53* mutations within 4 weeks of diagnosis of breast cancer

1.5.15 Do not offer fast track genetic testing (within 4 weeks of a diagnosis of breast cancer) except as part of a clinical trial. **[new 2013]**

1.5.16 Offer people eligible for referral to a specialist genetics clinic a choice of accessing genetic testing during initial management or at any time thereafter. **[new 2013]**

1.5.17 Discuss the individual needs of the person with the specialist genetics team as part of the multidisciplinary approach to care. **[new 2013]**

1.5.18 Offer detailed consultation with healthcare professionals who have appropriate up-to-date genetic knowledge and training to all those who are offered genetic testing, regardless of the time frame for testing. **[new 2013]**

1.6 Surveillance and strategies for early detection of breast cancer

Breast awareness

1.6.1 Women at increased risk of breast cancer should be 'breast aware' in line with Department of Health advice for all women.[7] **[2004]**

Surveillance for women with no personal history of breast cancer

1.6.2 Do not routinely offer ultrasound surveillance to women at moderate or high risk of breast cancer but consider it:

- when MRI surveillance would normally be offered but is not suitable (for example, because of claustrophobia)
- for problem solving mammographically or MRI detected abnormalities **[new 2013]**

1.6.3 Offer annual mammographic surveillance to all women:

- aged 40–49 years at moderate risk of breast cancer
- aged 40 years and over at high risk of breast cancer. **[new 2013]**

1.6.4 Offer annual mammographic surveillance to women aged 30–39 years at moderate or high risk of breast cancer only as part of an approved research study. **[new 2013]**

1.6.5 Do not offer mammographic surveillance to women under 30 years and at moderate or high risk of breast cancer. **[new 2013]**

1.6.6 Do not offer mammographic surveillance to women under 50 years with a *TP53* mutation or a greater than 30% probability of being a *TP53* carrier. **[new 2013]**

[7] www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_062697

1.6.7 Offer mammographic surveillance as part of the population screening programme[8] to women aged 50 years and over with a *TP53* mutation or a greater than 30% probability of being a *TP53* carrier. **[new 2013]**

1.6.8 Consider annual mammographic surveillance for women aged 50 years and over at moderate risk of breast cancer. **[new 2013]**

1.6.9 Offer annual MRI surveillance to all women:

- aged 20–49 years with a *TP53* mutation
- aged 20–49 years with a greater than 30% probability of being a *TP53* carrier
- aged 30–49 years with a *BRCA1* or *BRCA2* mutation
- aged 30–49 years who have not had a genetic test but are at greater than 30% probability of being a *BRCA1* carrier. **[new 2013]**

1.6.10 Do not offer MRI surveillance to women:

- at moderate risk of breast cancer
- at high risk of breast cancer unless they have a known *BCRA1*, *BCRA2* or *TP53* mutation or a greater than 30% probability of being a *TP53* or *BCRA1* carrier. **[new 2013]**

1.6.11 Do not offer MRI surveillance to any women aged 50 years and over. **[new 2013]**

[8] National breast screening programmes: England – NHS Breast Screening Programme (NHSBSP); Wales – Breast Test Wales; Northern Ireland – NI Breast Screening Programme

Table 1 Summary of recommendations on surveillance for women with no personal history of breast cancer

Age	Group 1 Moderate risk of breast cancer[9]	Group 2 High risk of breast cancer[10] (but not fulfilling criteria for group 3, 4 or 5)	Group 3 Untested but greater than 30% *BRCA1* carrier probability[11]	Group 4 Known *BRCA1/2* carrier	Group 5 *TP53* mutation carriers[12] or greater than 30% *TP53* carrier probability
20–29	Do not offer mammography	Do not offer mammography	Do not offer mammography	Do not offer mammography	Do not offer mammography
	Do not offer MRI	Do not offer MRI	Do not offer MRI	Do not offer MRI	Annual MRI
30–39	Mammography only as part of an approved research study	Mammography only as part of an approved research study	Mammography only as part of an approved research study	Mammography only as part of an approved research study	Do not offer mammography
	Do not offer MRI	Do not offer MRI	Annual MRI	Annual MRI	Annual MRI
40–49	Annual mammography	Annual mammography	Annual mammography	Annual mammography	Do not offer mammography
	Do not offer MRI	Do not offer MRI	Annual MRI	Annual MRI	Annual MRI
50–59	Consider annual mammography	Annual mammography	Annual mammography	Annual mammography	Mammography as part of population screening programme
	Do not offer MRI	Do not offer MRI	Do not offer MRI	Do not offer MRI	Do not offer MRI
60+	Consider annual mammography	Annual mammography	Annual mammography	Annual mammography	Mammography as part of population screening programme
	Do not offer MRI	Do not offer MRI	Do not offer MRI	Do not offer MRI	Do not offer MRI

[9] Lifetime risk of developing breast cancer is at least **17% but less than 30%.**
[10] Lifetime risk of developing breast cancer is at least 30%.
[11] Women who at first assessment had a 30–50% *BRCA1* carrier probability and reach 50 years of age without developing breast cancer will now have a lower than 30% carrier probability.
[12] Women who at first assessment had a 30%or greater *TP53* carrier probability and reach 50 years of age without developing breast cancer will now have a lower than 30% carrier probability and should no longer be offered MRI surveillance.

Surveillance for women with a personal and family history of breast cancer

1.6.12 Offer annual MRI surveillance to all women aged 30–49 years with a personal history of breast cancer who are at high risk of contralateral breast cancer or have a *BRCA1* or *BRCA2* mutation. **[new 2013]**

1.6.13 Offer annual mammographic surveillance to all women aged 50–69 years with a personal history of breast cancer who are at high risk of contralateral breast cancer or have a *BRCA1* or *BRCA2* mutation. **[new 2013]**

Healthcare professionals involved in surveillance for people with a personal and family history of breast cancer should ensure that surveillance is line with 'Early and locally advanced breast cancer' (NICE clinical guideline 80) and in particular the following two recommendations:

1.6.14 Offer annual mammography to all patients with early breast cancer, including DCIS[13], until they enter the NHSBSP/BTWSP[14]. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years. [2009]

1.6.15 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. [2009]

Recommendations for all women having surveillance

1.6.16 Offer support (for example, risk counselling, psychological counselling and risk management advice) to women who have ongoing concerns but are not eligible for surveillance additional to

[13] Ductal carcinoma in situ.

[14] NHS Breast Screening Programme/Breast Test Wales Screening Programme.

that offered by the national breast screening programmes[15]. **[new 2013]**

1.6.17 Before decisions on surveillance are made, discuss and give written information on the risks and benefits of surveillance, including:

- the possible reduced sensitivity of mammography in younger women with dense breasts and the increased likelihood of further investigations
- possible over diagnosis
- the risk associated with exposure to radiation
- the possible psychological impact of a recall visit. **[new 2013]**

1.6.18 Review eligibility for surveillance if family history changes (for example, if another member of the family develops breast cancer or a mutation is identified). **[new 2013]**

1.6.19 At the start of a surveillance programme and when there is a transition or change to the surveillance plan, give women:

- information about the surveillance programme, including details of the tests, how often they will have them and the duration of the programme
- information about the risks and benefits of surveillance
- details of sources of support and further information. **[new 2013]**

1.6.20 Ensure that women know the reasons for any changes to the surveillance plan. **[new 2013]**

[15] National breast screening programmes: England – NHS Breast Screening Programme (NHSBSP); Wales – Breast Test Wales; Northern Ireland – NI Breast Screening Programme

1.6.21 For women under 50 years who are having mammography, use digital mammography at centres providing digital mammography to the national breast screening programme standards. **[new 2013]**

1.6.22 Ensure that individual strategies are developed for all women having mammographic surveillance and that surveillance is:

- to national breast screening programme standards
- audited
- only undertaken after written information is given about risks and benefits. **[new 2013]**

1.6.23 Ensure that MRI surveillance includes MRI of both breasts performed to national breast screening programme standards. **[new 2013]**

1.6.24 When women not known to have a genetic mutation are referred to a specialist genetics clinic, offer them assessment of their carrier probability using a carrier probability calculation method with acceptable performance (calibration and discrimination) to determine whether they meet or will meet the criteria for MRI surveillance. (An example of an acceptable method is BOADICEA). **[new 2013]**

1.6.25 Do not offer surveillance to women who have undergone a bilateral mastectomy. **[new 2013]**

1.7 Risk reduction and treatment strategies

Risk factors

1.7.1 People should be provided with standardised written information about risk, including age as a risk factor (see box 1). **[2004]**

1.7.2 Modifiable risk factors should be discussed on an individual basis in the relevant care setting. **[2004]**

Menstrual and reproductive factors

1.7.3 Healthcare professionals should be able to provide information on the effects of hormonal and reproductive factors on breast cancer risk. **[2004]**

Hormonal contraceptives

1.7.4 Advice to women up to age 35 years with a family history of breast cancer should be in keeping with general health advice on the use of the oral contraceptive pill. **[2004]**

1.7.5 Women aged over 35 years with a family history of breast cancer should be informed of an increased risk of breast cancer associated with taking the oral contraceptive pill, given that their absolute risk increases with age. **[2004]**

1.7.6 For women with *BRCA1* mutations, the conflicting effects of a potential increased risk of breast cancer under the age of 40 years and the lifetime protection against ovarian cancer risk from taking the oral contraceptive pill should be discussed. **[2004]**

1.7.7 Women should not be prescribed the oral contraceptive pill purely for prevention of cancer, although in some situations reduction in ovarian cancer risk may outweigh any increase in risk of breast cancer. **[2004]**

1.7.8 If a woman has a *BRCA1* mutation and is considering a risk-reducing oophorectomy before the age of 40 years, the oral contraceptive pill should not be prescribed purely for the reduction in ovarian cancer risk. **[2004]**

Breastfeeding

1.7.9 Women should be advised to breast feed if possible because this is likely to reduce their risk of breast cancer, and is in accordance with general health advice. **[2004]**

Hormone replacement therapy

1.7.10 Women with a family history of breast cancer who are considering taking, or already taking, HRT should be informed of the increase in breast cancer risk with type and duration of HRT. **[2004]**

1.7.11 Advice to individual women on the use of HRT should vary according to the individual clinical circumstances (such as asymptomatic menopausal symptoms, age, severity of menopausal symptoms, or osteoporosis). **[2004]**

1.7.12 HRT usage in a woman at familial risk should be restricted to as short a duration and as low a dose as possible. Oestrogen-only HRT should be prescribed where possible. **[2004]**

1.7.13 A woman having an early (natural or artificial) menopause should be informed of the risks and benefits of HRT, but generally HRT usage should be confined to women younger than age 50 years if at moderate or high risk (see also recommendations 1.7.52 and 1.7.53). **[2004]**

1.7.14 Alternatives to HRT should be considered for specific symptoms such as osteoporosis or menopausal symptoms (see also recommendations 1.7.52 and 1.7.53). **[2004]**

1.7.15 Consideration should be given to the type of HRT if it is being considered for use in conjunction with risk-reducing gynaecological surgery. **[2004]**

Alcohol consumption

1.7.16 Women with a family history should be informed that alcohol may increase their risk of breast cancer slightly. However, this should be considered in conjunction with any potential benefit of moderate alcohol intake on other conditions (such as heart disease) and adverse effects associated with excessive alcohol intake. **[2004]**

Smoking

1.7.17 Women should be advised not to smoke, in line with current health advice. **[2004]**

Weight and physical activity

1.7.18 Women should be advised on the probable increased postmenopausal risk of breast cancer from being overweight. **[2004]**

1.7.19 Women should be advised about the potential benefits of physical exercise on breast cancer risk. **[2004]**

Chemoprevention for women with no personal history of breast cancer

1.7.20 Healthcare professionals within a specialist genetics clinic should discuss and give written information on the absolute risks and benefits (including side effects of drugs and the extent of risk reduction) of all options for preventive treatment to women at high risk of breast cancer. **[new 2013]**

1.7.21 Offer tamoxifen[16] for 5 years to pre-menopausal women at high risk of breast cancer unless they have a past history of thromboembolic disease or endometrial cancer. **[new 2013]**

1.7.22 Offer tamoxifen[16] or raloxifene[17] for 5 years to post-menopausal women at high risk of breast cancer unless they have a past history of thromboembolic disease or endometrial cancer. **[new 2013]**

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[16] At the time of consultation (January 2013), tamoxifen 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 Good practice in prescribing medicines – guidance for doctors for further information.

[17] At the time of consultation (January 2013), raloxifene 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 Good practice in prescribing medicines – guidance for doctors for further information.

1.7.23 Do not offer tamoxifen[16] or raloxifene[17] to women who were at high risk of breast cancer but have had a bilateral mastectomy. **[new 2013]**

1.7.24 Healthcare professionals within secondary care and/or specialist genetics clinics should discuss and give written information on the absolute risk and benefits (including side effects of drugs and the extent of risk reduction) of all options for preventive treatment to women at moderate risk of breast cancer. **[new 2013]**

1.7.25 Consider prescribing tamoxifen[16] for 5 years to pre-menopausal women at moderate risk of developing breast cancer within the next 10 years. **[new 2013]**

1.7.26 Consider prescribing tamoxifen[16] or raloxifene[17] for 5 years to post-menopausal women at moderate risk of developing breast cancer within the next 10 years. **[new 2013]**

1.7.27 Do not continue treatment with tamoxifen[16] or raloxifene[17] beyond 5 years. **[new 2013]**

1.7.28 Inform women that they must stop tamoxifen[16] at least:

- 3 months before trying to conceive
- 6 weeks before surgery. **[new 2013]**

Risk-reducing mastectomy for women with no personal history of breast cancer

1.7.29 Bilateral risk-reducing mastectomy is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team. **[2004]**

1.7.30 Bilateral mastectomy should be raised as a risk-reducing strategy option with all women at high risk. **[2004]**

1.7.31 Women considering bilateral risk-reducing mastectomy should have genetic counselling in a specialist cancer genetics clinic before a decision is made. **[2004]**

1.7.32 Discussion of individual breast cancer risk and its potential reduction by surgery should take place and take into account individual risk factors, including the woman's current age (especially at extremes of age ranges). **[2004]**

1.7.33 Family history should be verified where no mutation has been identified before bilateral risk-reducing mastectomy. **[2004]**

1.7.34 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with bilateral risk-reducing mastectomy. **[2004]**

1.7.35 Pre-operative counselling about psychosocial and sexual consequences of bilateral risk-reducing mastectomy should be undertaken. **[2004]**

1.7.36 The possibility of breast cancer being diagnosed histologically following a risk-reducing mastectomy should be discussed pre-operatively. **[2004]**

1.7.37 All women considering bilateral risk-reducing mastectomy should be able to discuss their breast reconstruction options (immediate and delayed) with a member of a surgical team with specialist oncoplastic or breast reconstructive skills. **[2004]**

1.7.38 A surgical team with specialist oncoplastic/breast reconstructive skills should carry out risk-reducing mastectomy and/or reconstruction. **[2004]**

1.7.39 Women considering bilateral risk-reducing mastectomy should be offered access to support groups and/or women who have undergone the procedure. **[2004]**

Risk-reducing oophorectomy for women with no personal history of breast cancer

1.7.40 Risk-reducing bilateral oophorectomy is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team. **[2004]**

1.7.41 Information about bilateral oophorectomy as a potential risk-reducing strategy should be made available to women who are classified as high risk. **[2004]**

1.7.42 Family history should be verified where no mutation has been identified before bilateral risk-reducing oophorectomy. **[2004]**

1.7.43 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with bilateral risk-reducing oophorectomy. **[2004]**

1.7.44 Any discussion of bilateral oophorectomy as a risk-reducing strategy should take fully into account factors such as anxiety levels on the part of the woman concerned. **[2004]**

1.7.45 Healthcare professionals should be aware that women being offered risk-reducing bilateral oophorectomy may not have been aware of their risks of ovarian cancer as well as breast cancer and should be able to discuss this. **[2004]**

1.7.46 The effects of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy. **[2004]**

1.7.47 Options for management of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy, including the advantages, disadvantages and risk impact of HRT. **[2004]**

1.7.48 Women considering risk-reducing bilateral oophorectomy should have access to support groups and/or women who have undergone the procedure. **[2004]**

1.7.49 Women considering risk-reducing bilateral oophorectomy should be informed of possible psychosocial and sexual consequences of the procedure and have the opportunity to discuss these issues. **[2004]**

1.7.50 Women not at high risk who raise the possibility of risk-reducing bilateral oophorectomy should be offered appropriate information, and if seriously considering this option should be offered referral to the team that deals with women at high risk. **[2004]**

1.7.51 Women undergoing bilateral risk-reducing oophorectomy should have their fallopian tubes removed as well. **[2004]**

HRT for women with no personal history of breast cancer who have a bilateral salpingo-oophorectomy before the natural menopause

1.7.52 When women with no personal history of breast cancer have either a *BRCA1* or *BRCA2* mutation or a family history of breast cancer and they have had a bilateral salpingo-oophorectomy before their natural menopause, offer them:

- combined HRT if they have a uterus
- oestrogen only HRT if they don't have a uterus

up until the time they would have expected natural menopause. **[new 2013]**

1.7.53 Manage menopausal symptoms occurring when HRT is stopped in the same way as symptoms of natural menopause. **[new 2013]**

Risk-reducing breast or ovarian surgery for people with a personal history of breast cancer

Counselling

1.7.54 Refer women with a personal history of breast cancer who wish to consider risk-reducing surgery for appropriate genetic and psychological counselling before surgery. **[new 2013]**

Risk-reducing mastectomy

1.7.55 Discuss the risks and benefits of risk-reducing mastectomy with women with a known or suspected *BRCA1*, *BRCA2* or *TP53* mutation. **[new 2013]**

1.7.56 For a woman considering risk-reducing mastectomy include in the discussion of risks and benefits:

- the likely prognosis of their breast cancer, including their risk of developing a distal recurrence of their previous breast cancer
- a clear quantification of the risk of developing breast cancer in the other breast
- the potential negative impact of mastectomy on body image and sexuality
- the very different appearance and feel of the breasts after reconstructive surgery
- the potential benefits of reducing the risk in the other breast and relieving the anxiety about developing breast cancer. **[new 2013]**

1.7.57 Give all women considering a risk-reducing mastectomy the opportunity to discuss their options for breast reconstruction (immediate and delayed) with a member of a surgical team with specialist skills in oncoplastic surgery or breast reconstruction. **[new 2013]**

1.7.58 Ensure that risk-reducing mastectomy and breast reconstruction are carried out by a surgical team with specialist skills in oncoplastic surgery and breast reconstruction. **[new 2013]**

1.7.59 Offer women who have *BRCA1*, *BRCA2* or *TP53* mutations but who decide against risk-reducing mastectomy, surveillance according to their level of risk. **[new 2013]**

Risk-reducing bilateral salpingo-oophorectomy

1.7.60 Discuss the risks and benefits of risk-reducing bilateral salpingo-oophorectomy with women with a known or suspected *BRCA1*, *BRCA2* or *TP53* mutation. Include in the discussion the positive effects of reducing the risk of breast and ovarian cancer and the negative effects of a surgically induced menopause. **[new 2013]**

1.7.61 Defer risk-reducing bilateral salpingo-oophorectomy until women have completed their family. **[new 2013]**

Contraindications to risk-reducing surgery for people with a personal history of breast cancer

1.7.62 Do not offer risk-reducing surgery to people with comorbidities that would considerably increase the risks of surgery. **[new 2013]**

1.7.63 Do not offer risk-reducing surgery to people who have a limited life expectancy from their cancer or other conditions. **[new 2013]**

Radiotherapy for people with a personal history of breast cancer who are *TP53* mutation carriers

1.7.64 When a person has invasive breast cancer or ductal carcinoma in situ and is known to have a *TP53* mutation or a high likelihood of a *TP53* mutation:

- inform them of all the possible treatment options
- make sure they know about the uncertainties associated with these treatment options
- inform them of the risks associated with each treatment (for example, the risk of recurrence, the risk of new primary breast cancer and the risks of malignancy associated with radiotherapy and chemotherapy). **[new 2013]**

1.7.65 Offer people with invasive breast cancer or ductal carcinoma in situ and a high likelihood of a *TP53* mutation, genetic testing to help determine their treatment options. **[new 2013]**

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline.

2.1 Carrier probability calculation models

Further research is recommended into developing and validating models for calculating carrier probability, which incorporate additional data, such as the molecular pathology of tumours and the prevalence of mutations in different ethnic groups. **[new 2013]**

Why this is important

This guideline recommends offering genetic testing to people with a 10% likelihood of carrying a *BRCA1/2* mutation and considering testing at a 5% likelihood threshold. Models to assess the likelihood of a *BRCA1/2* mutation need to be improved because their estimates still have wide confidence margins. Models are sensitive to population prevalence of mutations and need adjustment for pathological subtypes of breast and ovarian cancer, which are particularly associated with *BRCA1* mutations. Improving the predictive powers of these models will provide more cost-effective testing.

2.2 Rapid genetic testing

Research is recommended to determine the benefits and harms of creating rapid access to genetic testing for people with newly diagnosed breast cancer. This research should address the optimum model for service delivery and organisation, the clinical and cost effectiveness of such a change, uptake outcomes and patients' experience. **[new 2013]**

Why this is important

There is no clear evidence base for rapid genetic testing at the time of diagnosis of primary breast cancer. Knowledge of genetic status may increase uptake of risk-reducing mastectomy and in future guide first-line chemotherapy. To be useful for such decision-making, results of genetic tests

are needed within 4 weeks of diagnosis. This creates logistic problems in providing enough information for considered decision-making and delivering results of genetic tests in a supportive environment. Some GDG members were of the opinion that people had enough to cope with shortly after diagnosis without additional worries about genetic testing. However, others thought that early knowledge of genetic status would help decisions about surgery thus avoiding the need to consider this at a future date. For example, initial treatment by wide local excision often necessitates radiotherapy, which makes an acceptable cosmetic operation more challenging. Genetic counselling to facilitate such decisions soon after diagnosis would require reorganisation of current services.

2.3 Benefits of MRI surveillance in women over 50 years

Research is recommended to establish the risk and benefits of MRI surveillance compared with mammography in women over 50 years with a personal history of breast cancer. Studies should include sub-analysis for breast density. **[new 2013]**

Why this is important

There have been at least six large trials of MRI surveillance in women at high risk of breast cancer. However, none of these contained enough women to assess the potential benefit of MRI over mammography alone in women over 50 years. After 50 years of age, mammography becomes more sensitive and the trade-off between sensitivity and specificity may make MRI less cost effective. Although breast density decreases with age, and particularly after the menopause, there is no sudden change at any particular age. For this reason breast density should be included as a confounding variable.

2.4 Chemoprevention to reduce incidence of breast cancer

A randomised controlled trial is recommended to compare the clinical and cost effectiveness of aromatase inhibitors and tamoxifen for reducing the incidence of breast cancer in women with a family history of breast or ovarian cancer. **[new 2013]**

Why this is important

This guideline recommends offering raloxifene or tamoxifen to women at high risk of developing breast cancer and considering such treatment as chemoprevention for women at moderate risk. One randomised study in North America showed an aromatase inhibitor (exemestane) to be effective for the primary prevention of breast cancer. However, there has been no randomised control trial comparing aromatase inhibitors with tamoxifen or raloxifene (selective oestrogen receptor modulators or SERMs). Such a trial could better inform women of the best available approach for the chemoprevention of breast cancer.

2.5 Impact of risk-reducing surgery

Further research is recommended to compare psychosocial and clinical outcomes in women who chose and women who do not choose to have risk-reducing surgery. **[new 2013]**

Why this is important

Many women are happy with their decision to undergo risk-reducing surgery. However, some women do subsequently regret this choice. A greater understanding of the factors that predict satisfaction or regret will help to guide women's choices in the future. Studies show that risk-reducing surgery significantly reduces risk of breast cancer, but there is insufficient evidence to decide between, for example, skin sparing mastectomy and total mastectomy. The pros and cons of risk-reducing surgery in women with a diagnosis of cancer also need further study.

3 Other information

3.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Cancer to develop this guideline. The Centre established a Guideline Development Group (see section 4), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in The guidelines manual.

3.2 Related NICE guidance

Details are correct at the time of consultation on the guideline (January 2013). Further information is available on the NICE website.

Published

General

- Patient experience in adult NHS services. NICE clinical guidance 138 (2012).
- Medicines adherence. NICE clinical guidance 76 (2009).

Condition-specific

- Breast cancer (early and locally advanced). NICE clinical guideline 80 (2009).
- Advanced breast cancer. NICE clinical guideline 81 (2009).
- Improving outcomes in breast cancer. NICE cancer service guidance CSGBC (2002).
- Ovarian cancer. NICE clinical guideline 122 (2011).

Under development

NICE is developing the following guidance (details available from the NICE website):

- Suspected cancer: recognition and management of suspected cancer in children, young people and adults (update).NICE clinical guideline. Publication date to be confirmed.
- Prostate cancer (update). NICE clinical guideline. Publication expected November 2013.

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Appendix A: Recommendations to be deleted[18]

Recommendation	Comment

• At entry to an MRI surveillance programme, and at each subsequent change in the programme, women should be provided with a documented plan which includes:
  ◦ a clear description of the method(s) and intervals, including the risks and benefits
  ◦ the reasons for any changes to the surveillance plan
  ◦ sources of support and further information. [1.4.4.10]
• MRI of both breasts should be performed to high quality standards ensuring both high temporal and spatial resolution. Dynamic sequences are recommended post contrast. They should be double-read where possible. [1.4.4.14]
• MRI and any accompanying mammography data should be collected for audit purposes to support a national database.
	Replaced by
	• Do not routinely offer ultrasound surveillance to women at moderate or high risk of breast cancer but consider it when MRI surveillance would normally be offered but is not suitable (for example, because of claustrophobia). [1.6.2]
	• Offer annual mammographic surveillance to all women:
	  ◦ aged 40–49 years at moderate risk of breast cancer
	  ◦ aged 40 years and over at high risk of breast cancer. [1.6.3]
	• Offer annual mammographic surveillance to women aged 30–39 years at moderate or high risk of breast cancer only as part of an approved research study. [1.6.4]
	• Do not offer mammographic surveillance to women under 30 years and at moderate or high risk of breast cancer. [1.6.5]
	• Do not offer mammographic surveillance to women under

[18] In the left-hand column recommendation numbers refer to numbers in CG41. In the right-hand column recommendation numbers refer to numbers in this guideline.

[1.4.4.15]
• When mammography is recommended in women under 50, digital mammography should be used in preference to conventional mammography at centres where this is available to NHS Breast Screening Programme standards. [1.4.4.9]
• Women who have been referred to a clinical genetics centre who are not known to have a genetic mutation should be offered an assessment of their 10-year breast cancer risk using a validated risk assessment tool (for example, Tyrer-Cuzick or BOADICEA) to assess whether they are or will be eligible for MRI. [1.4.4.6]
• Women who are known to have a genetic mutation should be offered annual MRI surveillance if they are:
  • *BRCA1* and *BRCA2* mutation carriers aged 30–49 years
  • *TP53* mutation carriers aged 20 years or older. [1.4.4.11]
• MRI surveillance should be offered annually when indicated:
• From 30–39 years:
to a women at a 10-year
	50 years with a *TP53* mutation or a greater than 30% probability of being a *TP53* carrier. [1.6.6]
	• Offer mammographic surveillance as part of the population screening programme to women aged 50 years and over with a *TP53* mutation or a greater than 30% probability of being a *TP53* carrier. [1.6.7]
	• Consider annual mammographic surveillance for women aged 50 years and over at moderate risk of breast cancer. [1.6.8]
	• Offer annual MRI surveillance to all women:
	  • aged 20–49 years with a *TP53* mutation
	  • aged 20–49 years with a greater than 30% probability of being a *TP53* carrier
	  • aged 30–49 years with a *BRCA1* or *BRCA2* mutation
	  • aged 30–49 years who have not had a genetic test but are at greater than 30% probability of being a *BRCA1* carrier. [1.6.9]
	• Do not offer MRI surveillance to

risk of greater than 8%[19]
 	
• From 40–49 years:
  • to a women at a 10-year risk of greater than 20%, or
  • to a women at a 10-year risk of greater than 12% where mammography has shown a dense breast pattern[20]. [1.4.4.12]
• Women who have not been tested but have a high chance of carrying a *BRCA1* or *TP53* genetic mutation should be offered annual MRI surveillance from 30–49 years if they are at:
  • a 50% risk of carrying one of these mutations in a tested family, or
  • a 50% risk of carrying a *BRCA1* or *TP53* mutation in an untested or inconclusively tested family with at least a
	women:
	  • at moderate risk of breast cancer
	  • at high risk of breast cancer unless they have a known *BCRA1*, *BCRA2* or *TP53* mutation or a greater than 30% probability of being a *TP53* or *BCRA1* carrier. [1.6.10]
	• Do not offer MRI surveillance to any women aged 50 years and over. [1.6.11]
	• Offer support (for example, risk counselling, psychological counselling and risk management advice) to women who have ongoing concerns but are not eligible for surveillance additional to that offered by the breast screening programme. [1.6.16]
	• Before decisions on surveillance are made, discuss and give written information on the risks and

[19] A 10-year risk of 8% aged 30–39 and a 10-year risk of 12% risk aged 40–49 years would be fulfilled by women with the following family histories:

- 2 close relatives diagnosed with average age under 30 years*
- 3 close relatives diagnosed with average age under 40 years*
- 4 close relatives diagnosed with average age under 50 years*

A genetic test would usually be required to determine a 10-year risk of 20% or greater in women aged 40–49 years.
*All relatives must be on the same side of the family and one must be a mother or sister of the woman

[20] As defined by the 3-point mammographic classification used by UK breast radiologists (Breast Group of the Royal College of Radiologists 1989).

60% chance of carrying a *BRCA1* or *TP53* mutation (that is, a 30% risk of carrying one of these mutations themselves). [1.4.4.13] • Mammographic surveillance should not be available for women younger than age 30 years. [1.4.4.2] • For women aged 30–39 years satisfying referral criteria for secondary or specialist care, mammographic surveillance should be carried out: • only as part of a research study (ethically approved) or nationally approved and audited service • and • individualised strategies should be developed for exceptional cases, such as: • women from families with *BRCA1*, *BRCA2* or *TP53* mutations • women with equivalent high breast cancer risk. [1.4.4.3] • Support mechanisms (for example, risk counselling, psychological	benefits of surveillance, including: • the possible reduced sensitivity of mammography in younger women with dense breasts and the increased likelihood of further investigations • possible over diagnosis • the risk associated with exposure to radiation • the possible psychological impact of a recall visit. [1.6.17] • Review eligibility for surveillance if family history changes (for example, if another member of the family develops breast cancer or a mutation is identified). [1.6.18] • At the start of a surveillance programme and when there is a transition or change to the surveillance plan, give women: • information about the surveillance programme, including details of the tests, how often they will have them and the duration of the programme • information about the risks and benefits of

counselling and risk management advice) need to be identified and should be offered to women not being offered mammographic surveillance who have ongoing concerns. [1.4.4.4]
• All women satisfying referral criteria to secondary or specialist care (at raised risk or greater) should be offered mammographic surveillance from age 40 years. [1.4.4.5]
• For women aged 40–49 years at raised risk or greater, mammographic surveillance should be:
  • annual
  • to NHS Breast Screening Programme standards
  • audited
  • part of the NHS Research and Development Health Technology Assessment programme evaluation of mammographic surveillance of women younger than 50 years with a family history wherever possible
  • only undertaken after provision of written
	surveillance
	  • details of sources of support and further information. [1.6.19]
	• Ensure that women know the reasons for any changes to the surveillance plan. [1.6.20]
	• For women under 50 years who are having mammography, use digital mammography at centres providing digital mammography to breast screening programme standards. [1.6.21]
	• Ensure that individual strategies are developed for all women having mammographic surveillance and that surveillance is:
	  • to breast screening programme standards
	  • audited
	  • only undertaken after written information is given about risks and benefits. [1.6.22]
	• Ensure that MRI surveillance includes MRI of both breasts performed to breast screening programme standards. [1.6.23]
	• When women not known to have a genetic mutation are referred to a specialist genetics clinic, offer them assessment of their carrier

information about the positive and negative aspects of surveillance. [1.4.4.7]
• For women aged 50 years and older, surveillance should be:
  • as part of the NHS Breast Screening Programme, screened every 3 years
  • more frequent mammographic surveillance should take place only as part of a research study (ethically approved) or nationally approved and audited service
  • and
  • individualised strategies should be developed for exceptional cases, such as:
  • women from families with *BRCA1*, *BRCA2* or *TP53* mutations
  • women with equivalent high breast cancer risk. [1.4.4.8]
• If ongoing assessment of surveillance efficacy for women younger than age 50 years subsequently shows it is not cost
	probability using a carrier probability calculation method with acceptable performance (calibration and discrimination) to determine whether they meet or will meet the criteria for MRI surveillance. (An example of an acceptable method is BOADICEA). [1.6.24]
	• Do not offer surveillance to women who have undergone a bilateral mastectomy. [1.6.25]

effective, surveillance should be stopped.
• Before decisions on surveillance are made, written patient information and discussion should be offered. This should:
  • reflect the possible reduced sensitivity of mammographic detection of the younger age group with dense breasts and the increased potential for further investigations
  • discuss the potential advantages and disadvantages of breast surveillance for early detection of breast cancer, including
  • radiation risks
  • the possible psychological impact of a recall visit. [1.4.4.1]
On the basis of current evidence, ultrasound should not be used in routine surveillance practice but may have a role in problem-solving mammographically or MRI-detected abnormalities. [1.4.4.16]	