Familial breast cancer

The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care

NICE guideline

Second draft for consultation, October 2003

If you wish to comment on the recommendations, please make your comments on the full version of the draft guideline.
Key messages

1. Effective care involves a balanced partnership between patients and health care professionals with shared decision making. The importance of good communication should not be underestimated.

2. To ensure a patient professional partnership, patients should be offered individually tailored information throughout their care. This should include details of local and national support organisations as well as other sources of information.

3. Most women do not develop breast cancer, and of those who do most will not have a known family history of the disease.

4. The great majority of women with a family history of breast cancer do not fall into a high-risk category and do not develop breast cancer.

5. The great majority of women with a relative with breast cancer are not at substantially increased risk of breast cancer themselves.

6. Healthcare professionals should respond to women who present with concerns, but should not, in most instances, actively seek to identify women with a family history of breast cancer.

7. Taking a family history that includes first- and second-degree relatives on both sides of the family is the first key step to caring for a woman concerned about her family history of breast cancer.

8. Risk assessment allows appropriate risk classification and care.

9. Local protocols for the care of women at risk of familial breast cancer should be developed with clear referral mechanisms between primary, secondary and tertiary care.

10. Standard written information regarding familial risk and breast cancer risk factors should be developed for use in primary, secondary and tertiary care, to provide consistent advice to women.

11. Access to psychological support and assessment is a key part of the package of care needed for many women covered by the guideline.

12. Mammographic surveillance should only be undertaken after provision of information about its potential advantages and disadvantages for the early detection of cancer, and where offered this should be of high quality (NHSBSP standard) and audited.

13. Genetic testing is appropriate for a small proportion of women with a family history of breast cancer who are from high-risk families.

14. Risk-reducing surgery (mastectomy, oophorectomy) is appropriate for a small proportion of women from high-risk families and should be managed by a multidisciplinary team.

15. This entire area suffers from a paucity of good research evidence and efforts to improve the knowledge base are to be encouraged.
The following guidance is evidence based. The grading scheme used for the recommendations (A, B, C, D) is described in Appendix A; a summary of the evidence on which the guidance is based is provided in the full guideline (see Section 5).

1 Guidance

This guidance makes recommendations on the classification of risk of familial breast cancer in women and for the care of women at risk.

1.1 Approaches to care for all women

1.1.1 Effective care involves a partnership between patients and healthcare professionals and all decision making should be shared. [D]

1.1.2 To ensure a patient–professional partnership patients need individually tailored information, including information about sources of support. Tailoring should take into account format (including whether written or taped) as well as the actual content and form (see Box 1). [D]

1.1.3 Standard information should be evidence based wherever possible, and agreed at a national level if possible (the patient version of this guideline provides a good starting point, see Section 7). [D]

1.1.4 Standard information should not contradict messages from other service providers, including commonly agreed information across localities. [D]
Box 1 Information provision

**Standard written information for all women**

- risk information about population level and family history levels of risk, should include a definition of family history
- breast awareness information
- lifestyle advice regarding breast cancer risk, including information about:
  - HRT, oral contraceptives
  - lifestyle including diet, alcohol, etc
  - breastfeeding, family size and timing
- contact details of those providing support and information, including local and national support groups

**For women cared for in primary care:**

- standard written information (as above)
- advice to return to discuss any implications if family history changes

**For women being referred to secondary care:**

- standard written information
- information about the detailed 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 with secondary care or referral to specialist genetic services – and what may happen at each level

**For women being referred back to primary care**

- standard written information
- detailed information about why they do not need care in either secondary or specialist genetic services
- advice to return to primary care to discuss any implications if family history changes

**For women being cared for in secondary care:**

- standard written information
- details of risk assessment outcome, including why they are not being referred to specialist genetic services
- details of surveillance options including risk and benefits

**For women being referred to tertiary care:**

- standard written information
- details of risk assessment outcome including why they are being referred to specialist genetic services
- details of surveillance options including risk and benefits
- details of what should be expected in specialist genetic services, including counselling and genetic testing
Box 1 Information provision – continued

For women being cared for in tertiary care:

- standard written information
- 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 findings
- information about the risks and benefits of risk-reducing surgery when it is being considered, including both physical and psychological impact

1.2 Breast self examination

1.2.1.1 Women at increased risk of breast cancer should be ‘breast aware’ in line with Department of Health advice for all women. [D]

1.3 Care of women in primary care

1.3.1 Family history taking and initial assessment

1.3.1.1 A first- and second-degree family history should be taken when a woman presents with breast symptoms or has concerns about relatives with breast cancer. [D]

1.3.1.2 Healthcare professionals should respond to women who present with concerns but should not, in most instances, actively seek to identify women with a family history of breast cancer. [D]

1.3.1.3 It may also be clinically relevant in some circumstances, such as oral contraceptive pill use in women older than age 35 or in women being considered for long term HRT use, to take a family history. [D]

1.3.1.4 Women should be given the opportunity to discuss concerns about their family history of breast cancer if it is raised during a consultation. [D]
1.3.1.5 Women who have concerns about their family history of breast cancer should have their risk assessed initially in primary care by taking a first- and second-degree family history. [D]

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

1.3.1.7 A second-degree family history needs to include paternal as well as maternal relatives. [D]

1.3.1.8 Asking women to discuss their family history with relatives is useful in gathering the most accurate information. [D]

1.3.1.9 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. [C]

1.3.1.10 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. [D]

1.3.2 Primary care management

1.3.2.1 Women can be cared for in primary care: [D]

- where there has been only one family member diagnosed with breast cancer when older than 40 years of age
- where there have been only two family members diagnosed with breast cancer when older than 60 years of age

provided that there has been none of the following

- bilateral breast cancer
- male breast cancer
• ovarian cancer
• Jewish ancestry
• sarcoma in a relative less than 45 years of age
• glioma or childhood adrenal cortical carcinomas
• complicated patterns of multiple cancers at a young age
• very strong paternal history.

1.3.2.2 Women who do not meet the criteria for referral should be cared for in primary care by giving standard written information (see Box 1).

1.3.3 Support for primary care

1.3.3.1 Support is needed for primary care health professionals to manage women with a family history of breast cancer. Essential requirements for support for primary care are: [D]
• 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
• locally agreed secondary care contact to discuss management of ‘uncertain’ cases.

1.3.4 Referral from primary care

1.3.4.1 Offer referral to secondary care if any of the following apply: [D]
• one first degree female relative diagnosed with breast cancer before age 40
• one first degree male relative diagnosed with breast cancer before age 60
• one first degree relative with bilateral breast cancer where the first primary was diagnosed before age 50

or
• two first- or second-degree relatives on the same side of the family diagnosed with breast cancer with the average age younger than 60 (one of the relatives should be a first-degree relative)

• two first- or second-degree relatives on the same side of the family diagnosed with breast cancer one being male at any age and the other aged younger than 60 (one of these should be a first-degree relative)

• two second-degree relatives on the same side of the family with diagnosis of breast cancer at an age younger than 50 years

• one first- or second-degree relative diagnosed with breast cancer before the age of 60 and a first- or second-degree relative diagnosis of ovarian cancer at any age (one of these should be a first-degree relative)

or

• three first- or second-degree relatives on the same side of the family diagnosed with breast cancer at any age

or

• 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 45 years of age
  – glioma or childhood adrenal cortical carcinomas
  – complicated patterns of multiple cancers at a young age
  – very strong paternal history.

Advice should be sought from the secondary care contact.

1.3.4.2 If there is doubt about appropriateness of referral in women younger than 30 and older than 60 years of age this should be discussed with the local contact in secondary care. [D]

1.3.4.3 Discussion with a trained designated individual in the secondary care unit should take place where there is uncertainty on the part of
the clinician because the family history presented is unusual or
difficult to make clear decisions about, or where standard
reassurance is not sufficient to reassure the women concerned. [D]

1.3.4.4 Discussion with a trained designated individual in the secondary
care unit should take place where there are unusual patterns of
uncommon cancers, especially if early onset. [D]

1.3.4.5 Direct referral to clinical genetics services should take place where
gene mutation BRCA1/2 or TP53 has already been identified. [D]

1.3.5 Information for women who are being referred

1.3.5.1 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). [C]

1.3.5.2 Women not eligible for referral and/or surveillance on the basis of
age or risk level may remain anxious about breast cancer and need
information about breast awareness and appropriate psychological
support. [D]

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

Service configurations will vary by locality. However, we have presented
recommendations for settings that are likely to be found in most localities.

1.4.1 Care of women in secondary care (such as family history
clinic or breast clinic)

1.4.1.1 Care of women referred to secondary care should be undertaken by
a multidisciplinary team. It should include the following: [D]

• written protocols for management
• central, standardised resources
• mammographic surveillance available to standard of NHS Breast
  Screening programme
• access to a team offering risk-reducing surgery
• standardised written information
• designated/lead clinicians
• designated contact for primary care
• audit
• clinical trials access
• access to psychological assessment and counselling
• information about support groups and voluntary organisations
• administrative support.

1.4.2 Family history taking

1.4.2.1 A family history should be taken when a woman presents with breast symptoms or has concerns about relatives with breast cancer. [D]

1.4.2.2 A third-degree family history should be taken in secondary care where possible. [D]

1.4.2.3 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. [C]

1.4.3 Management in secondary care

1.4.3.1 Women whose care can be provided in a secondary care setting and who do not need referral to tertiary care are women with: [D]
• only one first-degree relative who had a diagnosis of breast cancer before the age of 40 or
• only two first- or second-degree relatives who had a diagnosis of breast cancer with an average age of between 50 and 60 years or
• only three relatives who had a diagnosis of breast cancer with an average age of over 60 or
• a formal risk assessment (usually carried out in tertiary care) or a family history pattern is likely to give risks of greater than 2.7% but less than 8% risk in next 10 years (if aged 40 years and over) or lifetime risk greater than 17% but less than 25%

provided that there has been none of the following:
• bilateral breast cancer
• male breast cancer
• ovarian cancer
• Jewish ancestry
• sarcoma in a relative less than 45 years of age
• glioma or childhood adrenal cortical carcinomas
• complicated patterns of multiple cancers at a young age
• very strong paternal history.

1.4.3.2 Women whose risk is less than that in the cases listed above can be referred back to primary care, with appropriate information being offered (see Box 1 and recommendation 1.3.5.2). [D]

1.4.4 Surveillance

1.4.4.1 Mammographic surveillance should not be available for women younger than 30 years of age. [D]

1.4.4.2 For women aged 30–40 years of age satisfying referral criteria for secondary or specialist care, mammographic surveillance should be only as part of a research study or nationally approved service (audited and ethically approved). [D]

1.4.4.3 All women satisfying referral criteria to secondary or specialist care should be offered mammographic surveillance from the age of 40 years. [C]

1.4.4.4 For those aged 40–49, mammographic surveillance should be: [D]
• annual
• to NHS Breast Screening Programme standards
audited
part of the NHS R&D HTA evaluation of mammographic surveillance of women under 50 with a family history wherever possible
only undertaken after provision of written information about the positive and negative aspects of surveillance.

1.4.4.5 For those aged 50 and older, surveillance should be: [D]
• as part of the NHS Breast Screening Programme, screened every 3 years
• more frequent mammographic surveillance should take place only as part of a study or nationally approved service (audited and ethically approved).

1.4.4.6 Individualised strategies will need to be developed for exceptional cases, such as:
• women from families with BRCA1, BRCA2 or TP53 mutations [C]
• women with equivalent breast cancer risk. [D]

1.4.4.7 If ongoing assessment of efficacy of surveillance in those aged younger than 50 subsequently shows that it is not cost effective then it should be stopped. [D]

1.4.4.8 Before decisions 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 [C]
• discuss the potential advantages and disadvantages of breast surveillance for early detection of cancer, including
  – radiation risks [C]
  – the possible psychological impact of a recall visit. [D]

1.4.4.9 On the basis of current evidence, MRI and ultrasound should not be used in routine screening practice in those younger than 50 years of age.
1.4.5 Referral to tertiary care

1.4.5.1 Criteria for referral to tertiary care:

Women who meet the following referral criteria should be offered a referral:*

- At least the following female breast cancers only in the family
  - two first- or second-degree relatives diagnosed with breast cancer before the age of 50 (at least one must be a first-degree relative of the consultee) or
  - three first- or second-degree relatives diagnosed with breast cancer before the age of 60 (at least one must be a first-degree relative of the consultee) or
  - four relatives of any age (at least one must be a first-degree relative of the consultee) or

- Families containing one ovarian cancer at any age with, on the same side of the family:
  - one first- (including the relative with ovarian cancer) or second-degree relative who had a diagnosis of breast cancer before the age of 50 or
  - two first- or second-degree relatives who had a diagnosis of breast cancer before the age of 60 or
  - another ovarian cancer at any age or

- Families containing bilateral cancer (where each breast has the same count value as one relative)
  - cancer diagnosed in both breasts before the age of 50 or
  - one case of bilateral cancer plus one other relative diagnosed with breast cancer before the age of 60 or

- Families containing male breast cancer at any age with, on the same side of the family, at least:
  - one first- or second-degree relative who had a diagnosis of breast cancer before the age of 50 or
  - two first- or second-degree relatives who had a diagnosis of breast cancer before the age of 60 or

* The family will qualify if all affected relatives are on the same side of the family and usually be connected by first degree in a lineage.
(for instance mother, maternal grandmother, maternal great grandmother). For the individual to be high risk, one of the affected relatives needs to be a first-degree relative unless the paternal history is clearly inherited, for instance four relatives diagnosed at less than 60 years of age.

- A formal risk assessment (likely to have been undertaken in tertiary care) has given risk estimates of
  - a 20% or greater chance of gene mutation being harboured in the family
  - 8% or higher risk in next 10 years
  - 25% or higher lifetime risk.

1.4.5.2 Seek further advice from specialist genetics services in families containing any of the following:
- Jewish ancestry
- sarcoma in a relative less than 45 years of age
- glioma or childhood adrenal cortical carcinomas
- complicated patterns of multiple cancers at a young age
- very strong paternal history. [D]

1.4.5.3 Following initial consultation in secondary care, written information should be provided to reflect the outcomes of the consultation (see Box 1). [D]

1.4.6 Care of women in tertiary care

1.4.6.1 Care of women referred to tertiary care by a multidisciplinary team. In addition to having access to the components found in secondary care it should also include the following: [D]
- clinical genetic risk assessment
- verification for abdominal malignancies and possible sarcomas.

1.4.7 Family history taking

1.4.7.1 A third-degree family history should be taken in tertiary care, if not done so already. [D]
1.4.7.2 For accurate risk estimation the following are required: [D]

- age of death of affected and unaffected relatives
- current age of unaffected relatives.

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

1.4.7.4 If substantial management decisions, such as risk-reducing surgery are being considered, then breast cancer only histories will need confirmation (via medical records/cancer registry/death certificates). [D]

1.4.7.5 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding. [D]

1.4.7.6 Abdominal malignancies at young ages and possible sarcomas will need confirmation in specialist care. [D]

Risk assessment tools

1.4.7.7 Computerised risk-assessment models can be helpful aids to risk assessment, but can be misleading and should not yet totally replace careful clinical assessment of family trees with a manual approach. [D]

1.4.8 Genetic counselling

1.4.8.1 Women reaching threshold for referral (to tertiary care) should be offered a referral for genetic counselling regarding their risks and options. [C]

1.4.8.2 Women attending genetic counselling should receive standardised information beforehand describing the process of genetic counselling, information to obtain prior to counselling session, the range of topics to be covered and brief educational material about hereditary breast cancer and genetic testing. [D]
1.4.8.3 Predictive genetic testing should not be offered without adequate genetic counselling. [C]

1.4.9 Risk communication

1.4.9.1 Women should be offered a personal risk estimate but information should also be given about the uncertainties of the estimation. [D]

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

1.4.9.3 Women should be sent a written summary of their consultation in specialist genetic clinics, which includes their personal risk information. [D]

1.4.10 Genetic testing

1.4.10.1 All high-risk women should have access to information on genetic tests aimed at mutation finding. [D]

1.4.10.2 Testing should be offered to high-risk women, when affected family members are available, to aid informed decision making. [C]

1.4.10.3 Pre-test counselling (preferably two sessions) should be undertaken. [D]

1.4.10.4 Discussion of genetic testing (predictive and mutation finding) should be undertaken by someone with appropriate training. [D]

1.4.10.5 High-risk women 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 findings. [D]
Mutation tests

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

1.4.10.7 Women from families with a 20% chance of carrying a BRCA1 or BRCA2 mutation should have access to testing. [D]

1.4.10.8 The development of a genetic test for a family will 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 and TP53). [D]

1.4.10.9 This search/screen should aim for as close to 100% sensitivity as possible for detecting coding alterations and the whole gene(s) should be searched. [D]

1.4.11 Risk-reducing surgery

1.4.11.1 In services offering risk reducing surgery the following should be available: [D]
- facilities to verify family history and clinical genetic risk assessment
- mammography before surgery
- psychological assessment and counselling
- information about support groups
- oncoplastic skills.

1.4.12 Risk-reducing mastectomy

1.4.12.1 Information on bilateral mastectomy should be raised as a risk-reducing strategy option with all women at high risk. [D]

1.4.12.2 Women considering bilateral risk-reducing mastectomy should attend a specialist cancer genetics clinic. [D]

1.4.12.3 Discussion of individual risk factors, such as age (in particular, extremes of age ranges) should take place. [D]
1.4.12.4 Family history should be verified in any woman before bilateral risk-reducing mastectomy. [D]

1.4.12.5 Pre-operative counselling about psychosocial/sexual consequences should be undertaken. [D]

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

1.4.12.7 All women considering bilateral risk-reducing mastectomy should be able to discuss their breast reconstruction options (immediate and delayed) with a member of the specialist oncoplastic/breast reconstructive surgical team. [D]

1.4.12.8 A specialist oncoplastic surgical team should carry out the procedure. [D]

1.4.12.9 Women considering bilateral risk reducing mastectomy should have access to support groups/women who have undergone the procedure. [D]

1.4.13 Risk-reducing oophorectomy

1.4.13.1 Information about bilateral oophorectomy as a potential risk-reducing strategy should be made available to women who are classified as high risk in this guideline. [D]

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

1.4.13.3 Any discussion of oophorectomy will raise the issue of ovarian cancer risk, which may be something that has not been considered by the woman. The healthcare professional should be prepared for this and be able to deal with its implications in the discussion. [D]
1.4.13.4 Always discuss the effects of early menopause with any woman considering oophorectomy. [D]

1.4.13.5 Discuss the options for management of early menopause with any woman considering oophorectomy, including the advantages, disadvantages and risk impact of HRT. [D]

1.4.13.6 Women considering risk-reducing oophorectomy should have access to support groups/women who have undergone the procedure. [D]

1.4.13.7 Women considering risk-reducing oophorectomy should be informed of possible psychosocial/sexual sequelae of the procedure and have the opportunity to discuss these issues. [D]

1.4.13.8 Women not at high risk who raise the possibility of risk-reducing 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. [D]

1.4.14 Tamoxifen

Tamoxifen is not licensed in the UK for use as chemoprophylaxis in women who do not have a diagnosis of breast cancer.

1.5 Risk factors

Overall, the risk factors for women with a family history are the same as for women in the general population. Evidence was sought that might show whether the risks for this group of women were different from women in the general population. Where this evidence was available it was used to derive recommendations. Where specific information about risks in women with a family history was not available then extrapolation of findings from general populations was undertaken.
1.5.1 All risk factors

1.5.1.1 Women should be provided with standardised written information about risk, including age as a risk factor. [D]

1.5.1.2 Modifiable risk factors should be discussed on an individual basis with each woman in the relevant care setting. [D]

1.5.2 HRT

1.5.2.1 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. [C]

1.5.2.2 Advice to individual women will vary according to the individual clinical circumstances (such as asymptomatic, age, severity of menopausal symptoms, osteoporosis). [D]

1.5.2.3 HRT usage in a woman at familial risk should be restricted to as short a duration and as low a dose as possible and preferably oestrogen only if possible. [D]

1.5.2.4 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 50 years of age if at moderate or high risk. [D]

1.5.2.5 Alternatives to HRT should be considered for specific symptoms such as osteoporosis or menopausal symptoms. [D]

1.5.2.6 Consideration needs to be given to the type of HRT if it is being considered for use in conjunction with risk-reducing gynaecological surgery. [D]
1.5.3 Hormonal contraceptives

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

1.5.3.2 Over the age of 35, women with a family history of breast cancer should be informed of increased risk of breast cancer from taking the oral contraceptive pill given that their absolute risk increases with age. [C]

1.5.3.3 In women who are BRCA1 carriers, the conflicting effects of a potential increased risk of breast cancer under the age of 40 and the lifetime protection against ovarian cancer risk from taking the oral contraceptive pill should be discussed. [C]

1.5.3.4 Women should not take 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. [D]

1.5.3.5 If a woman is a BRCA1 carrier and is considering a risk-reducing oophorectomy before the age of 40, the oral contraceptive pill should not be taken purely for the reduction in ovarian cancer risk. [D]

1.5.4 Breastfeeding

1.5.4.1 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. [C]

1.5.5 Alcohol consumption

1.5.5.1 Women with a family history may 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. [C]

1.5.6 Smoking

1.5.6.1 Women should be advised not to smoke, in line with current health advice. [D]

1.5.7 Weight and physical activity

1.5.7.1 Women should be advised on the probable increased postmenopausal risk of breast cancer from being overweight. [C]

1.5.7.2 Women should be advised about the potential benefits of physical exercise on breast cancer risk. [C]

1.5.8 Menstrual/reproductive factors

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

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established at the start of the development of this guideline, following a period of consultation; it is available from www.nice.org.uk/cat.asp?c=20111

The guideline is aimed at all healthcare professionals providing care to women who present with concerns about the risk of developing breast cancer because of a family history. The guideline aims to provide recommendations to help healthcare professionals in primary, secondary and tertiary care.

The scope of this guideline was care and classification of women at risk of breast cancer because of family history. It does not cover women who have
breast cancer. The guideline covers women aged 18 years and older, and men who have a family history. The guideline does not cover in detail some aspects of some interventions that may be relevant, for example it does not address methods of screening in detail because these are outside the scope

3 Implementation in the NHS

3.1 In general

The implementation of this guideline will build on the National Cancer Plan (Department of Health, 2000).

Local health communities should review their existing practice for the care of women at risk of familial breast cancer against this guideline as they develop their Local Delivery Plans. The review should consider the resources required to implement the recommendations set out in Section 1, the people and processes involved and the timeline over which full implementation is envisaged. It is in the interests of patients that the implementation timeline is as rapid as possible.

Relevant local clinical guidelines and protocols should be reviewed in the light of this guidance and revised accordingly.

This guideline should be used in conjunction with the NICE guidance detailed in Section 6.

3.2 Audit

Suggested audit criteria are listed in Appendix D. These can be used as the basis for local clinical audit, at the discretion of those in practice.

4 Research recommendations

The following research recommendations have been identified for this NICE guideline, not as the most important research recommendations, but as those that are most representative of the full range of recommendations. The
Guideline Development Group’s full set of research recommendations is detailed in the full guideline produced by the National Collaborating Centre for Primary Care (see Section 5).

- Validation of risk assessment models is urgently needed.
- Different risk communication strategies should be evaluated.
- Prospective studies are needed of the short- and long-term psychosocial and sexual impact of risk reducing surgery in women with a family history of breast cancer.
- Costs and benefits of surveillance in the 30–40 years age groups and more frequent surveillance than the NHSBSP in the over 50 age group should be assessed by national pooling of all UK data.

5 Full guideline

The National Institute for Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Primary Care. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The full guideline, *The Classification and Care of Women At Risk of Familial Breast Cancer*, is published by the National Collaborating Centre for Primary Care; it is available on its website (TBA), the NICE website (www.nice.org.uk) and on the website of the National Electronic Library for Health (www.nelh.nhs.uk). [Note: these details will apply to the published full guideline.]

The members of the Guideline Development Group are listed in Appendix B. Information about the independent Guideline Review Panel is given in Appendix C.

The booklet *The Guideline Development Process – Information for the Public and the NHS* has more information about the Institute’s guideline development process. It is available from the Institute’s website and copies can also be ordered by telephoning 0870 1555 455 (quote reference N0038).
6 Related NICE guidance


**Guideline and service guidance in progress**

Supportive and palliative care for people with cancer – service guidance.

Referral guidelines for suspected cancer.

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin earlier than 4 years if significant evidence that affects the guideline recommendations is identified sooner. The updated guideline will be available within 2 years of the start of the review process.
Versions of this document written for women at risk of familial breast cancer, their families and the public are available from the NICE website (www.nice.org.uk) and from the NHS Response Line (telephone 0870 1555 455 and quote reference number N0xxx for a version in English only and reference number N0xxx for a version in English and Welsh.)
Appendix A: Grading scheme

The grading scheme and hierarchy of evidence used in this guideline (see Table) is adapted from Eccles and Mason (2001).
<table>
<thead>
<tr>
<th>Recommendation grade</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Directly based on category I evidence</td>
</tr>
<tr>
<td>B</td>
<td>Directly based on:</td>
</tr>
<tr>
<td></td>
<td>• category II evidence, or</td>
</tr>
<tr>
<td></td>
<td>• extrapolated recommendation from category I evidence</td>
</tr>
<tr>
<td>C</td>
<td>Directly based on:</td>
</tr>
<tr>
<td></td>
<td>• category III evidence, or</td>
</tr>
<tr>
<td></td>
<td>• extrapolated recommendation from category I or II evidence</td>
</tr>
<tr>
<td>D</td>
<td>Directly based on:</td>
</tr>
<tr>
<td></td>
<td>• category IV evidence, or</td>
</tr>
<tr>
<td></td>
<td>• extrapolated recommendation from category I, II, or III evidence</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Evidence category</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>I:</td>
<td>Evidence from:</td>
</tr>
<tr>
<td></td>
<td>• meta-analysis of randomised controlled trials, or</td>
</tr>
<tr>
<td></td>
<td>• at least one randomised controlled trial</td>
</tr>
<tr>
<td>II:</td>
<td>Evidence from:</td>
</tr>
<tr>
<td></td>
<td>• at least one controlled study without randomisation, or</td>
</tr>
<tr>
<td></td>
<td>• at least one other type of quasi-experimental study</td>
</tr>
<tr>
<td>III:</td>
<td>Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case–control studies</td>
</tr>
<tr>
<td>IV:</td>
<td>Evidence from expert committee reports or opinions and/or clinical experience of respected authorities</td>
</tr>
</tbody>
</table>

Appendix B: The Guideline Development Group

Professor Gareth Evans (Chair)
Consultant Clinical Geneticist, St Mary’s Hospital, Manchester

Nasim Bahar
Patient Representative

Michelle Barclay
Patient Representative; Policy and Information Officer, Breakthrough Breast Cancer

Professor Valerie Beral
Director, Department of Health Breast Screening Advisory Committee, also Cancer Research UK Epidemiology Unit, University of Oxford (resigned February 2003)

Dr Doug Easton
Reader in Genetic Epidemiology, Strangeways Research Laboratory, Cambridge

Dr Jon Emery
General Practitioner, Cambridge

Dr Jonathan Gray
Consultant in Medical Genetics & Clinical Director, Medical Genetics Service in Wales

Dr Jane Halpin
Public Health, Watford & Three Rivers PCT, St. Albans

Dr Penny Hopwood
Consultant Psychiatrist and Psycho-Oncologist, Christie Hospital NHS Trust, Manchester
Aileen McIntosh
Deputy Director, Sheffield Evidence Based Guidelines Programme, Public Health, ScHARR, University of Sheffield

Dr James McKay
Consultant Genetic Oncologist, The Genetics Unit, Institute of Child Health, London

Clare Shaw
Research Associate, Public Health, ScHARR, University of Sheffield (until May 2003)

Carmel Sheppard
Consultant Nurse Breast Care, Portsmouth Hospitals NHS Trust/University of Southampton

Mr Mark Sibbering
Consultant Breast Surgeon, Derby City General Hospital, Derby

Wendy Watson
Patient representative,

Dr Allan Wailoo
Health economist, Sheffield Health Economics Group, ScHARR, University of Sheffield

Co-optees

Dr Sue Barter
Radiologist, Department of Diagnostic Radiology, Bedford Hospital, Bedford

Dr Sally Cottrell
Clinical scientist, Medical Genetics Unit, St George’s Hospital Medical School, London
In attendance

Nancy Turnbull
Chief Executive, National Co-ordinating Centre for Primary Care

Karen Beck
Public Health, ScHARR, University of Sheffield

Catherine Beverley
Information Officer, ScHARR, University of Sheffield

Observers

Colette Marshall
Guidelines Commissioning Manager, National Institute for Clinical Excellence

Professor Neva Haites
Scottish Inter-collegiate Guidelines Network (SIGN)
Appendix C: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

**Professor Mike Drummond**  
Director  
Centre for Health Economics (CHE)  
University of York

**Dr Marcia Kelson**  
Director  
Patient Involvement (PIU) for NICE

**Mr Barry Stables**  
Patient representative

**Dr Imogen Stephens**  
Joint Director of Public Health  
West Sussex PCT

**Kev Hopayian**  
General Practitioner  
Leiston

**Dr Robert Walker**  
Clinical Director  
West Cumbria PCT
Appendix D: Technical detail on the criteria for audit

Measures that could be used as the basis for an audit

Primary care
- The percentage of women who had a second-degree family history taken.
- The percentage of women who were given standardised written information.
- The percentage of women with a family history who met referral criteria.
- The percentage of women with a family history who were referred.

Specialist care
- The percentage of women who had a third-degree family history taken.
- The percentage of women who were classified as moderate risk.
- The percentage of women who were classified as high risk.
- The percentage of women who were given standardised written information.
- The percentage of women aged 30–39 years who underwent surveillance.
- The percentage of women aged 40–49 years who underwent surveillance.
- The percentage of women aged 50 years and older who underwent surveillance.
- The percentage of women who received genetic counselling.
- The percentage of women who underwent genetic testing.
- Waiting time for genetic test results.
- The percentage of women who had gene mutations identified.
DRAFT FOR SECOND CONSULTATION

- The percentage of women who underwent risk-reducing mastectomy.
- The percentage of women who underwent risk-reducing oophorectomy.
- The percentage of women suffering complications from risk-reducing surgery.
Appendix E: The algorithms
Are there AT LEAST*
• 1 First degree relative diagnosed with breast cancer under 40
or
• 2 relatives diagnosed with breast cancer with an average age less than 60
or
• 3 relatives diagnosed with breast cancer at any age?
*All relatives have to be on same side of family and be blood relatives of the consultee and of each other.

NO

Are there AT LEAST*
One 1st degree female relative diagnosed with breast cancer before the age of 40
or
One 1st degree male relative diagnosed with breast cancer before the age of 60.
or
One 1st or 2nd degree relative diagnosed with breast cancer before the age of 60. AND one 1st or 2nd degree relative diagnosis of ovarian cancer at any age (Note: one of these should be a 1st degree).
or
One 1st degree relative with bilateral breast cancer where the first primary was diagnosed before the age of 50.
or
Two 1st or 2nd degree relatives on the same side of the family diagnosed with breast cancer before the average age of 60 (Note: one of these should be a 1st degree).
or
Two 1st or 2nd degree relatives on the same side of the family diagnosed with breast cancer one being male at any age and the other less than 60 (Note: one of these should be a 1st degree).
or
Two 2nd degree relatives on the same side of the family before the age of 50 at diagnosis with breast cancer or
Three 1st or 2nd degree relatives on the same side of the family diagnosed with breast cancer any age
*All relatives have to be on same side of family and be blood relatives of the consultee and of each other.

YES

Has a faulty breast cancer gene already been identified in the family?

NO

Refer to secondary care

YES

Refer directly to specialist genetic services

Seek further advice from secondary care

Fig. 1 Management in Primary Care
FAMILIAL BREAST CANCER ONLY IN THE FAMILY?
Are there AT LEAST
Two 1st or 2nd degree relative* diagnosed with breast cancer before the age of 50 or
Three 1st or 2nd degree relatives* diagnosed with breast cancer before the age of 60 or
Four relatives* of any age
* At least one must be a first degree relative of the consultee

OVARIAN CANCER IN THE FAMILY?
Are there AT LEAST
One 1st or 2nd degree relative diagnosed with ovarian cancer at any age AND on the same side of the family there is
• One 1st or 2nd degree relative with a diagnosis of breast cancer before the age of 50 or
• Two 1st or 2nd degree relatives diagnosed with breast cancer before the age of 60 Or
• One other 1st or 2nd degree relative diagnosed with ovarian cancer at any age?

BILATERAL BREAST CANCER IN THE FAMILY**?
Are there AT LEAST
• One 1st or 2nd degree relative with a diagnosis of bilateral breast cancer before the age of 50 or
• One 1st or 2nd degree relative with a diagnosis of bilateral breast cancer AND one 1st or 2nd degree relative diagnosed with breast cancer before the age of 60.
* In cases of bilateral breast cancer each breast can count as one relative.

MALE BREAST CANCERS IN THE FAMILY?
Are there AT LEAST
One male breast cancer AND on the same side of the family there is
• One 1st or 2nd degree relative with a diagnosis of breast cancer before the age of 50 or
• Two 1st or 2nd degree relatives diagnosed with breast cancer before the age of 60?

A formal risk assessment (usually done in tertiary care) shows a family history patterns that equates to
8% risk in next 10 years
or 25% lifetime risk
or 20% chance of gene mutation being harboured in the family

Is there:
Jewish Ancestry
or sarcoma in a relative less than 45 years
or glioma or childhood adrenal cortical carcinomas
or very strong paternal history
or complicated patterns of multiple cancers at a young age?

Does the referred individual fulfill the criteria for referral from primary care? (see Fig 1)
Or if formal risk assessment shows a family history patterns that equates to AT LEAST 2.6% risk in next 10 years or 17% lifetime risk?

** The family will qualify if all affected relatives are on the same side of the family and usually be connected by first degree in a lineage (for instance mother, maternal grandmother, maternal great grandmother). For the individual to be high risk one of the affected relatives needs to be a first degree relative, unless the paternal history is clearly inherited for instance four relatives diagnosed at less than 60 years of age.

*** The management of a high-risk woman may take place in secondary care if she does not want genetic testing or risk reducing surgery and does not wish to be referred to a genetics service.