1. 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 contra-lateral breast cancer, the risk of other tumours in the body e.g. ovarian cancer and the risk to other relatives.

This guideline describes the classification and care of people at risk of familial breast cancer. It provides recommendation for genetic testing surveillance and risk reduction and treatment strategies for people without breast cancer who are at increased risk because of a family history of breast, ovarian or a related cancer. This guideline also covers people with a diagnosis of breast cancer and/or family history of breast, ovarian or a related cancer. It makes new recommendations on genetic testing thresholds, surveillance, risk reduction and treatment strategies (NICE CLINICAL GUIDELINE 164, JUNE 2013) This is an update from the 2004/6 guidelines.

2. Scope

These guidelines are intended for use by all clinical geneticists/familial breast cancer nurses and cancer genetic/ genetic counsellors involved in risk assessment and counselling of clients with breast cancer, a family history of breast and / or ovarian cancer

3. Recommendations, Standards and Procedural Statements

Family history-taking in specialist genetic clinic

A third-degree family history should be taken in a specialist genetic clinic for a person with no personal history of breast cancer, if this has not been done previously.

For accurate risk estimation, the following are required:

- Age of death of affected and unaffected relatives
- Current age of unaffected relatives.

Confirming the family history:

In general, it is not necessary to validate breast cancer-only histories (via medical records/cancer registry/death certificates). However, this is preferable to ensure the management is accurate.

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

Abdominal malignancies at young ages and possible sarcomas should be confirmed in specialist care.

In a specialist genetic clinic, 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.

If there are problems with using or interpreting carrier probability calculation methods, use clinical judgement when deciding whether to offer genetic testing. This is based on who would benefit from genetic testing in the family and how the result might be used by relatives for screening and/or preventative surgical decision making.

**Communicating cancer risk and carrier probability**

People should be offered a personal risk estimate but information should also be given about the uncertainties of the estimation.

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).

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

**Information and support**

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.

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

1. National Hereditary Breast Cancer Helpline
2. YOU TUBE channel, [www.youtube.com/user/ClinicalGenetics](http://www.youtube.com/user/ClinicalGenetics) (Optional)
3. Familial breast and ovarian cancer triage systems such as cancerPDX.com can be used as a familial cancer triage and management system.
For people being cared for in a specialist genetic clinic

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.
People who meet the following referral criteria should be offered a referral to a specialist genetic clinic.

Carrier probability at which genetic testing should be offered

- Offer genetic testing in specialist genetic clinics to a relative with a personal history of breast and/or ovarian cancer if that relative has a combined BRCA1 and BRCA2 mutation carrier probability of 10% or more.
- Offer genetic testing in specialist genetic clinics 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 and an affected relative is unavailable for testing.
- If there are problems with using or interpreting carrier probability calculation methods, use clinical judgement when deciding whether to offer genetic testing.

Care of people in a specialist genetic clinic

Care of people referred to a specialist genetic clinic 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:

- Verification for abdominal malignancies and possible sarcomas.

Genetic testing

- Offer genetic testing in specialist genetic clinics to a relative with a personal history of breast and/or ovarian cancer if that relative has a combined BRCA1 and BRCA2 mutation carrier probability of 10% or more.
- Offer genetic testing in specialist genetic clinics 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 and an affected relative is unavailable for testing.
- If there are problems with using or interpreting carrier probability calculation methods, use clinical judgement when deciding whether to offer genetic testing.
- Offer fast-track genetic testing (within 4 weeks of a diagnosis of breast cancer) only as part of a clinical trial.
• Discuss the individual needs of the person with the specialist genetics team as part of the multidisciplinary approach to care. [new 2013]
• Offer detailed consultation with a clinical geneticist or genetics counsellor to all those with breast cancer who are offered genetic testing, regardless of the timeframe for testing.

BRCA1 and BRCA2 mainstreaming testing is available through trained gynae-oncology team for patients with high grade serous ovarian cancer without a wider relevant family history of breast, prostate or ovarian cancer.

Gene panels for suspected mendelian disease is available e.g. Li-Fraumeni, Peutz Jeghers, Cowden or diffuse gastric cancer and lobular breast cancer

**Surveillance for women with no personal history of breast cancer**

**Offer annual mammographic surveillance to women:**

- aged 40–59 years at high risk of breast cancer but with a 30% or lower probability of being a BRCA or TP53 carrier
- aged 40–59 years who have not had genetic testing but have a greater than 30% probability of being a BRCA carrier
- aged 40–69 years with a known BRCA1 or BRCA2 mutation.

**Offer annual MRI surveillance to women:**

- aged 30–49 years who have not had genetic testing but have a greater than 30% Probability of being a BRCA carrier
  - aged 20–49 years with a known TP53 mutation.

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

- Offer annual mammographic surveillance to all women aged 50–69 years with a personal history of breast cancer who:
  - remain at high risk of breast cancer (including those who have a BRCA1 or BRCA2 mutation), and do not have a TP53 mutation.
  - Offer annual MRI surveillance to all women aged 30–49 years with a personal history of breast cancer who remain at high risk of breast cancer, including those who have a BRCA1 or BRCA2 mutation.

**Chemoprevention for women with no personal history of breast cancer**

Offer either tamoxifen or raloxifene for 5 years to postmenopausal women with a uterus and at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer.
Healthcare professionals within a specialist genetic clinic should discuss and give written information on the absolute risks and benefits of all options for chemoprevention to women at high risk or moderate risk of breast cancer.

Discussion and information should include the side effects of drugs, the extent of risk reduction, and the risks and benefits of alternative approaches, such risk-reducing surgery and surveillance. [new 2013]

Do not offer tamoxifen or raloxifene to women who were at high risk of breast cancer but have had a bilateral mastectomy.

Inform women that they should stop tamoxifen at least:

- 2 months before trying to conceive
- 6 weeks before elective surgery. [new 2013]

**Preventative surgery**

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

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.

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.

Ensure that risk-reducing mastectomy and breast reconstruction are carried out by a surgical team with specialist skills in oncoplastic surgery and breast reconstruction.

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

**Risk-reducing bilateral salpingo-oophorectomy**

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.
Defer risk-reducing bilateral salpingo-oophorectomy until women have completed their family. Contraindications to risk-reducing surgery for people with a personal history of breast cancer
Do not offer risk-reducing surgery to people with comorbidities that would considerably increase the risks of surgery.
Do not offer risk-reducing surgery to people who have a limited life expectancy from their cancer or other conditions.
Offer people with invasive breast cancer or ductal carcinoma in situ and a 30% probability of a TP53 mutation, genetic testing to help determine their treatment options.

**Genetic counselling for people with no personal history of breast cancer**

Women with no personal history of breast cancer meeting criteria for referral to a specialist genetic clinic should be offered a referral for genetic counselling regarding their risks and options.

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.

**Genetic testing**

Offer genetic testing in specialist genetic clinics 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 and an affected relative is unavailable for testing.

BRCA1 and BRCA2 mainstreaming testing is available through trained the gynae-oncology team for patients with high grade serous ovarian cancer without a wider relevant family history of breast, prostate or ovarian cancer. Gene panels for suspected mendelian disease is available if suspected mendelian disease is suspected e.g. Li-Fraumeni, Peutz Jeghers, Cowden or diffuse gastric cancer and lobular breast cancer

**Surveillance for women with no personal history of breast cancer**

- Offer annual mammographic surveillance to women:
  - aged 40–59 years at high risk of breast cancer but with a 30% or lower probability of being a BRCA or TP53 carrier
  - aged 40–59 years who have not had genetic testing but have a greater than 30% probability of being a BRCA carrier
  - aged 40–69 years with a known BRCA1 or BRCA2 mutation.
- Offer annual MRI surveillance to women:
  - aged 30–49 years who have not had genetic testing but have a greater than 30% probability of being a BRCA carrier
  - aged 20–49 years who have not had genetic testing but have a greater than 30% probability of being a TP53 carrier aged 20–49 years with a known TP53 mutation.
Chemoprevention for women with no personal history of breast cancer

- Discuss either tamoxifen or raloxifene for 5 years to postmenopausal women with a uterus and at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer. This would be prescribed by the patient’s GP.
- Healthcare professionals within a specialist genetic clinic should discuss and give written information on the absolute risks and benefits of all options for chemoprevention to women at high risk or moderate risk of breast cancer.

Discussion and information should include the side effects of drugs, the extent of risk reduction, and the risks and benefits of alternative approaches, such risk-reducing surgery and surveillance.

Do not offer tamoxifen or raloxifene to women who were at high risk of breast cancer but have had a bilateral mastectomy.

Inform women that they should stop tamoxifen at least:
- 2 months before trying to conceive
- 6 weeks before elective surgery.

Offering genetic testing

Offer people eligible for referral to a specialist genetic clinic a choice of accessing genetic testing during initial management or at any time thereafter.

Offer fast-track genetic testing (within 4 weeks of a diagnosis of breast cancer) only as part of a clinical trial.

Discuss the individual needs of the person with the specialist genetics team as part of the multidisciplinary approach to care.

Offer detailed consultation with a clinical geneticist or genetics counsellor to all those with breast cancer who are offered genetic testing, regardless of the timeframe for testing.

6. Legal Liability Guideline Statement

Guidelines or Procedures issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines or Procedures and always only providing that such departure is confined to the specific needs of individual circumstances. In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional it is fully appropriate and justifiable - such decision to be fully recorded in the patient’s notes.
7. Supporting Documents and Key References
- Clinical genetics referral form
- BRCA1 and BRCA2 mutation testing guidelines
- Familial breast cancer NICE guidelines
- NICE guidelines training pack, implementation plan and breast screening leaflet

8. Key Words: Breast, Familial, Ovarian, Cancer

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<tr>
<td>Guideline Lead (Name and Title)</td>
</tr>
<tr>
<td>Julian Barwell - Consultant/Honorary Professor Clinical Genetics</td>
</tr>
</tbody>
</table>

Details of Changes made during review:

Approved by:
Dr Julian Barwell - Consultant in Cancer Genetics
Vanita Jivanji - Senior Genetic Counsellor
Dr Huw Dorkins - Consultant in Cancer Genetics
Dr Pradeep Vasudevan - Head of Service
Mr Ian Scudamore - Clinical Director for Women’s CMG
Family history and other risk factors of breast cancer checked.

Also in family history:
- Sarcoma
- Jewish ancestry
- Male breast cancer in family.
- 4 diagnosed breast cancers in family.
- 3 diagnosed breast cancers in family aged under 60. (1)
- 2 diagnosed breast cancers in family aged under 50.
- 2 ovarian cancers in family.
- 1 ovarian cancer and 1 breast cancer aged under 50 in family (serous ovarian histology)

Refer the patient to genetics department.

Discuss:
- Pros and cons of genetic testing
- Survivorship
- Screening
- Cascade of information to relatives
- Preventative surgery if a mutation is discovered.

Hormonal (triple) negative breast cancer diagnosed under the age of 60.

Clinician prompted question.

Nil present.

If diagnosed under 40 moderate risks, screening for 1st degree relatives. (2)

Contact: Dr Julian Barwell
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Julian.barwell@uhl-tr.nhs.uk

Moderate risk if overall:
- 2 family members diagnosed with breast cancer over 50
- 3 family members diagnosed with breast cancer over 60 (3)

Relatives need cascading

Reassure the patient.

Yes

No

Yes

Yes
NICE guidelines for patients who are at risk of inherited breast cancer.

Appendix 1

Patient asks their primary care physician about their familial breast cancer susceptibility.

- 1 family member diagnosed with breast cancer over 40-Low.
- 2 family members diagnosed with breast cancer over 50-Moderate.
- 3 family members diagnosed with breast cancer over 60-Moderate.

Family history researched:
- Sarcoma
- Jewish ancestry
- Male breast cancer in family.
- 4 diagnosed breast cancers in family.
- 3 diagnosed breast cancers in family aged under 60.
- 2 diagnosed breast cancers in family aged under 50.
- 2 ovarian cancers in family.
- 1 ovarian cancer and 1 breast cancer aged under 50 in family.
- Known gene mutation in family.

Near Population risk
<17% Life-time risk.
<3% 40-49

Moderate risk
17-30% life-time risk.
3-8% 40-49

High Risk
>30% life-time risk.
8-12% 40-49

Very High Risk
12% ten year risk between that ages of 40-50

- Consider genetic testing of affected family member.
- Possible preventative surgery.
- Mammograms
- Chemoprevention
- Life style changes.

Reassure the patient.

- Mammograms
- Life style changes
- Consider chemoprevention

Referral to breast screening unit.

BOADICEA computer modelling or Manchester Scoring System. (4)
Supporting notes:
1. All age criteria are for average age of the affected individuals in the family, at the point of diagnosis.

2. This advice is for first degree female relatives and second degree female relatives through first degree male relatives

3. All consider BOCS study recruitment and BRCA1 and BRCA2 diagnostic testing in a research setting:

**Main Inclusion Criteria**
- Any individual with breast and ovarian cancer
- Any individual with bilateral breast cancer
- Any individual with male breast cancer
- Any individual with ovarian cancer who has at least one relative with ovarian or breast cancer
- Any individual with unilateral breast cancer who has at least two relatives with breast or ovarian cancer
- Any individual in whom a BRCA1/2 gene test has been performed.

4. Manchester Scoring table

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>BRCA1 Score</th>
<th>BRCA2 Score</th>
</tr>
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<tbody>
<tr>
<td><strong>Age at onset of female breast cancer.</strong></td>
<td></td>
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<tr>
<td>&lt;30 y</td>
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<td>5</td>
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<td>30-39 y</td>
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</tr>
<tr>
<td>≥60 y</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Age at onset male breast cancer.</strong></td>
<td></td>
<td></td>
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<tr>
<td>&lt;60 y</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>≥60 y</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>Pancreatic Cancer</strong></td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Age at onset prostate cancer.</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 y</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>≥60 y</td>
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