NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

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

1.1 Short title

Familial breast cancer

2 The remit

The National Collaborating Centre for Cancer has been commissioned by NICE to partially update 'Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care', NICE clinical guideline 41 (2006), available from www.nice.org.uk/guidance/CG41. See section 4.3.1 of this scope for details of which sections will be updated. Sections 4.3.1 a and b of the update will include men. We will also carry out an editorial review of all recommendations to ensure that they comply with NICE's duties under equalities legislation. This update is being undertaken as part of the guideline review cycle.

The Department of Health has also asked NICE to produce a short clinical guideline on the management of breast cancer in women and men who have a family history of breast cancer[1].

[1] This remit has not been finalised and is subject to ministerial agreement.

3 Clinical need for the guideline

3.1 Epidemiology

a) 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. Environmental factors also contribute to the development of breast cancer, so familial clustering may be the result of chance, increased genetic susceptibility, lifestyle or common environmental factors.

b) For people with a family history of breast, ovarian or a related 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.

c) In the UK, the lifetime risk of developing breast cancer is about 11–12.5% for a woman, and less than 0.1% for a man. People with relatives who have, or have had breast, ovarian or a related cancer might have a higher risk than the general population. Identifying people at increased risk could prevent or reduce morbidity.

d) 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 (that is, cancer in the other breast) or, in women of developing ovarian cancer.

3.2 Current practice

Classification and care of women at risk of familial breast cancer

a) Implementation of NICE clinical guideline 41 has been patchy. Genetic testing for *BRCA1* and *BRCA2* mutations is still largely driven by the finding of a *BRCA1* or *BRCA2* mutation in a family member with breast or ovarian cancer.

b) The threshold for testing has decreased from a 20% likelihood of *BRCA1* or *BRCA2* mutation to 10% in many centres. Testing is now offered at lower thresholds because high throughput and more rapid testing is available. This has led to questions about whether testing thresholds should be lowered and whether unaffected women at very high risk of *BRCA1* or *BRCA2* mutation should have access to testing even if an affected family member is unavailable for testing.

c) The use of tamoxifen and raloxifene as preventive drugs is increasing, especially in North America, but use in England and Wales is limited because there is no European marketing authorisation for preventive use at present.

d) Women without breast cancer who have *BRCA1* or *BRCA2* mutations and have early bilateral salpingo-oophorectomy (removal of both ovaries and fallopian tubes) tend not to use hormone replacement treatment (HRT) and may be encouraged not to take HRT by their clinicians. New evidence suggests that these women should take HRT until around 50 years of age to reduce their risk of cardiovascular disease and osteoporosis because use in this situation does not appear to negate the protective effect of a bilateral salpingo-oophorectomy on breast cancer risk.

Management of breast cancer and related risks in people with a family history of breast cancer

e) The risk of further primary breast tumours (that is, a second tumour in the contralateral [previously unaffected] breast that is not related

to the first one) in people with breast cancer and a family history of breast, ovarian cancer or a related cancer means that options for ongoing surveillance and risk-reducing surgery could differ from those recommended in 'Early and locally advanced breast cancer: diagnosis and treatment', NICE clinical guideline 80 (2009).

f) Current practice in the UK varies considerably as to whether the risk of second primary tumours is discussed or whether risk-reducing surgery (contralateral mastectomy, bilateral salpingo-oophorectomy or both) is presented as a realistic primary treatment option to people newly diagnosed with invasive breast cancer, or as a delayed option. Genetic testing at the time of diagnosis is used across North America and Europe, but is very rare in the UK.

g) Improvements in genetic testing now make testing at the time of diagnosis an option that people could use to inform their decisions about treatment. In particular, it may be better for women at high risk of, or who have, a *TP53* mutation to be offered mastectomy rather than conservative surgery and radiotherapy. Early identification of cases of familial breast cancer may allow surgical, radiotherapy and systemic treatments to be altered to improve outcomes.

Need for guidance

h) 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 those recommendations in NICE clinical guideline 41 that are not being updated, the GDG will be asked to carry out an editorial review to ensure that they comply with NICE's duties under equalities legislation (for example, to determine whether the recommendations made for women in the original guideline are also applicable to men).

i) For people with a diagnosis of breast cancer and a family history of breast, ovarian or a related cancer new guidance is needed to fill the gaps between NICE clinical guidelines 41 and 80 to address differences in management of breast cancer at diagnosis and in subsequent surveillance.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

Classification and care of women at risk of familial breast cancer (update)

a) Adult women (18 years and older) without breast cancer who may be at increased risk of developing breast cancer because of a family history of breast, ovarian or a related cancer.

b) Adult men (18 years and older) without breast cancer who may be at increased risk of developing breast cancer because of a family history of breast, ovarian or a related cancer, for the consideration of risk thresholds for testing only (see 4.3.1 a and b).

c) Specific consideration will be given to the needs of people from groups with a particularly high prevalence of *BRCA1* or *BRCA2* mutations, such as people of Jewish origin.

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d) Adult women and men (18 years and older) with a recent diagnosis of breast cancer and a family history of breast, ovarian or a related cancer.

e) Specific consideration will be given to the needs of people from groups with a particularly high prevalence of *BRCA1* or *BRCA2* mutations, such as people of Jewish origin.

4.1.2 Groups that will not be covered

Classification and care of women at risk of familial breast cancer (update)

a) Children (younger than 18).

b) Men, except for the consideration of risk thresholds for testing (see 4.3.1 a and b).

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c) Children (younger than 18).

4.2 Healthcare setting

a) All settings in which NHS care is received.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

Classification and care of women at risk of familial breast cancer (update)

a) Assessing the risk threshold for genetic testing (for the update this part of the topic will be extended to include the threshold for testing for men as well as women).

b) The risk threshold at which genetic testing should be offered to people who do not have living relatives who have had breast, ovarian or a related cancer available to test (for the update this part

of the topic will be extended to include the threshold for offering testing to men as well as women).

c) Chemoprevention to reduce the incidence of breast cancer in women.

d) Specific surveillance needs of women with no personal history of breast cancer.

e) HRT for women who have had a bilateral salpingo-oophorectomy before the natural menopause.

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f) Assessing risk thresholds for genetic testing.

g) The risk thresholds at which genetic testing should be offered to an affected person to:

- inform future care
- initiate genetic tests for their relatives.

h) Genetic testing for *BRCA1 BRCA2* and *TP53* within 4 weeks of diagnosis of breast cancer to inform treatment and future surveillance:

- Does a delay in genetic testing at diagnosis affect outcome?
- Who should discuss the outcomes of genetic testing with the patient and when?

i) Risk-reducing breast or ovarian surgery:

- At what level of risk of future primary breast cancer, and in what circumstances, should the option of risk-reducing surgery be discussed?
- In what circumstances is offering risk-reducing surgery not appropriate?

j) The specific surveillance needs of people with a personal history of breast cancer.

k) Mastectomy compared with breast-conserving surgery plus radiotherapy for people with newly diagnosed breast cancer or high-grade ductal carcinoma in situ with a *TP53* mutation or at high risk of a *TP53* mutation.

4.4 Main outcomes

a) Incidence of familial breast cancer.

b) Mortality from breast cancer.

c) Health related quality of life.

4.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually only be from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see ‘Further information’).

4.6 Status

4.6.1 Scope

This is the final scope.

4.6.2 Timing

The development of the guideline recommendations will begin in July 2011.

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

This guideline will update and replace the following NICE guidance.

- Familial breast cancer. NICE clinical guideline 41 (2006). Available from www.nice.org.uk/guidance/CG41

5.1.2 Other related NICE guidance

- Advanced breast cancer. NICE clinical guideline 81 (2009). Available from www.nice.org.uk/guidance/CG81
- Breast cancer (early and locally advanced). NICE clinical guideline 80 (2009). Available from www.nice.org.uk/guidance/CG80
- Improving outcomes in breast cancer. NICE cancer service guidance CSGBC (2002). Available from www.nice.org.uk/guidance/CSGBC

6 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders' the public and the NHS'
- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).