NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Familial breast cancer: The classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (update), including the management of women and men diagnosed with breast cancer who also have a history of familial breast cancer

1.1 Short title

Familial breast cancer (update)

2 The remit

The National Collaborating Centre for Cancer has been commissioned by NICE to update 'Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (partial update of NICE clinical guideline 14)', 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. 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 asked NICE to produce a short clinical guideline on the management of women and men diagnosed with breast cancer who also have a history of familial 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 women within a family where there have been an unusually high number of family members affected by breast or a related cancer. If there have been more cases of breast or related cancers than would be expected by chance alone, it may be that genes transmitted between generations are sufficient to cause or, more typically, contribute to the development of breast cancer. Environmental factors will also usually contribute to the development of breast cancer. Familial clustering may therefore be the result of chance, an increase in genetic susceptibility, a common lifestyle and/or environmental factors. For these women, the degree of risk of developing breast cancer varies according to the:

- nature of the family history
- number of relatives who have developed breast cancer
- age at which the relative(s) developed breast cancer
- age of the individual concerned

b) The lifetime risk of developing breast cancer is about 11-12.5% for the British female population. Women with relatives who have or have had breast cancer may have a higher risk. The possibility of identifying those women at increased risk has implications for the ability to prevent or reduce morbidity.

c) The care of women recently diagnosed with breast cancer who have a family history of breast or ovarian cancer may need to be managed differently from that of women without a family history because of the future risk of contralateral breast cancer or ovarian cancer.

3.2 Current practice

a) There is a need to update the guidance (CG41) on genetic testing thresholds, surveillance and use of chemoprevention for women without breast cancer who are at increased risk because of a strong family history of breast/ovarian cancer.

b) For women with a diagnosis of breast cancer and a strong family history new guidance is required to fill the gaps between CG41 and CG80 to address differences in management of breast cancer at diagnosis and subsequent surveillance.

Update of CG41

c) Implementation of CG41 has been patchy. Genetic testing for *BRCA1* and *BRCA2* mutations is still largely driven by testing of a family member affected with breast or ovarian cancer. The threshold for testing at a 20% likelihood for *BRCA1*/*BRCA2* mutation combined has drifted down to 10% in many centres. It is being offered at lower thresholds as high throughput more rapid testing has become available. This questions whether testing thresholds should be lowered and whether unaffected women at very high risk of *a BRCA1* and *BRCA 2* mutation should have access to testing even if an affected family member is unavailable for testing.

d) The use of tamoxifen and raloxifene as chemopreventive agents are increasing, especially in North America, but use in England and Wales is limited because there is no EMEA approval for preventive use.

e) Women without breast cancer who carry *BRCA1* or *BRCA2* mutations and have early oophorectomy are tending not to use HRT and may be encouraged not to do so by their clinicians. Evidence is emerging to suggest that they should take HRT until 50 years of age to protect their heart and bone as use in this situation

does not appear to abrogate the protective effect on breast cancer risk.

New short clinical guideline

f) The risks of further breast cancer primaries in women with breast cancer and a family history means that options for ongoing surveillance (MRI) and risk reducing surgery are potentially different to those outlined for women with early and locally advanced breast cancer in 'Early and locally advanced breast cancer: diagnosis and treatment', NICE clinical guideline 80 (2009).

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

h) Improvements in genetic testing now make this a possible option for women to inform decision around management decisions. In particular it may be better for women at high risk of or who carry a TP53 mutation to be offered mastectomy rather than conservative surgery and radiotherapy. Early identification of familial/genetic breast cancer cases may allow potential alteration of surgical, radiotherapy and systemic treatments to give improved outcomes.

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

Update of NICE clinical guideline 41

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 or ovarian cancer.

b) Specific consideration will be given to populations with a particularly high prevalence of *BRCA1*/*BRCA2* such as people of Ashkenazi Jewish origin.

New short clinical guideline

c) Women and men (18 years and older) with a recent diagnosis of breast cancer and a family history of breast or ovarian cancer.

d) Specific consideration will be given to populations with a particularly high prevalence of *BRCA1*/*BRCA2* such as people of Ashkenazi Jewish origin.

4.1.2 Groups that will not be covered

Update of CG41

a) Children (younger than 18).

b) Men without breast cancer aged 18 years and older who may be at increased risk of developing breast cancer because of a family history of breast or ovarian cancer.

New short clinical guideline

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

Update of CG41

a) The optimal way to assess the risk threshold for women without breast cancer but with a family history of breast/ovarian cancer.

b) The risk threshold at which genetic testing should be offered to women without breast cancer with a family history of breast/ovarian cancer, and who have no available living relatives with breast/ovarian cancer to test

c) The effectiveness of chemoprevention in women without breast cancer but with a family history of breast or ovarian cancer, to reduce their incidence of breast cancer.

d) What are the specific surveillance requirements of women with a family history of breast or ovarian cancer without a personal history of breast cancer.

e) Should women without breast cancer but with a family history of breast cancer who have had an oophorectomy prior to the natural menopause take HRT.

New short clinical guideline

f) The optimal way to assess the risk threshold for women with breast cancer and with a family history of breast/ovarian cancer.

g) The risk threshold at which genetic testing should be offered to:

- women with breast cancer to inform future care
- women and men with breast cancer in order to develop genetic tests for their relatives

h) In genetic testing (in <4 weeks) for *BRCA 1 & 2* and *TP53* at the time of diagnosis of breast cancer in women and men with a family

history of breast or ovarian cancer to inform their 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 at what time point?

i) The effectiveness of risk reducing breast and ovarian surgery in women diagnosed with breast cancer and with a family history of breast or ovarian cancer.

- What is the risk threshold for discussing the option of risk reducing surgery?
- In which circumstances is it inappropriate to offer risk reducing surgery?

j) What are the specific surveillance requirements of women with a family history of breast or ovarian cancer with a personal history of breast cancer.

k) In women with newly diagnosed breast cancer or high-grade DCIS with a *TP53* mutation or at high risk of a *TP53* mutation, is mastectomy more effective than breast conserving surgery + radiotherapy?

4.4 Main outcomes

a) Reduction in incidence of familial breast cancer.

b) Mortality from breast cancer.

c) 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 consultation draft of the scope. The consultation dates are 31 March to 28 April 2011.

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
- Familial breast cancer. NICE clinical guideline 14 (2004). Available from

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).