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Familial breast cancer

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

This is a partial update of NICE clinical guideline 14

NICE clinical guideline 41

Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care

Ordering information

You can download the following documents from www.nice.org.uk/CG041

- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- ‘Understanding NICE guidance’ – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and summaries of the evidence they were based on.

For printed copies of the quick reference guide or ‘Understanding NICE guidance’, phone the NHS Response Line on 0870 1555 455 and quote:

- N1130 (quick reference guide)
- N1131 (‘Understanding NICE guidance’).

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

National Institute for Health and Clinical Excellence

MidCity Place
71 High Holborn
London
WC1V 6NA

www.nice.org.uk

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This is a partial update of NICE clinical guideline 14 (published May 2004).

The update has been developed by the National Collaborating Centre for Primary Care. The original guideline was also developed by the National Collaborating Centre for Primary Care. In this update, only the recommendations on magnetic resonance imaging (MRI) for breast cancer surveillance (section 1.4.4) have changed; minor amendments have been made elsewhere in this document, where necessary, to reflect these changes. These are highlighted in the document as '**New**'. The original NICE guideline and supporting documents are available from www.nice.org.uk/CG041

Introduction

This NICE guideline provides recommendations for the classification and care of women who are at a raised or high risk of developing hereditary breast cancer.

Breast cancer is the most common cancer in women. Most women with breast cancer do not have a family history of the disease, but it can be hereditary. Three genes have been identified that predispose women to breast cancer – *BRCA1*, *BRCA2* and *TP53*.

The objective of this guideline is to decrease breast cancer morbidity and mortality by assessing hereditary risk in people before breast cancer develops and providing regular surveillance to identify breast cancer at an early stage.

This guideline makes recommendations on primary, secondary and tertiary care management of women at risk of hereditary or familial breast cancer.

This guideline does not address treatments for breast cancer once the disease has been diagnosed. It also does not address screening men for breast cancer, although this may be appropriate if the risk is sufficiently high. Patients who do not have a raised or high risk of familial breast cancer should be managed in line with current national breast screening guidance after the age of 50.

Patient-centred care

This guideline offers best practice advice on the classification and care of women at risk of familial breast cancer.

Treatment and care should take into account patients' needs and preferences. People at raised or high risk of breast cancer should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001) (available from www.dh.gov.uk). From April 2007 healthcare professionals will need to follow a code of practice accompanying the Mental Capacity Act (summary available from www.dca.gov.uk/menincap/bill-summary.htm).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

Carers and relatives should have the opportunity to be involved in decisions about the patient's care and treatment, unless the patient specifically excludes them.

Carers and relatives should also be given the information and support they need.

Key priorities for implementation

Family history and referral

- When a woman presents with breast symptoms or has concerns about relatives with breast cancer, a first- and second-degree family history should be taken in primary care to assess risk, because this allows appropriate classification and care.
- 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.
- 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, and with appropriate facilities.

Care

- Access to psychological support and assessment is a key part of the package of care needed for many women covered by this guideline.
- All women aged 40–49 years satisfying referral criteria to secondary or specialist care (at raised risk or greater) should be offered annual mammographic surveillance.
- Surveillance should only be undertaken after provision of information about its potential advantages and disadvantages for the early detection of breast cancer, and where offered, this should be of high quality (equivalent to NHS Breast Screening Programme standard) and audited.
- **New** Women who are known to have a genetic mutation should be offered annual MRI surveillance if they are:
 - *BRCA1* and *BRCA2* mutation carriers aged 30–49 years
 - *TP53* mutation carriers aged 20 years or older.
- **New** MRI surveillance should be offered annually when indicated.

From 30–39 years:

- to women at a 10-year risk of greater than 8%.

From 40–49 years:

- to women at a 10-year risk of greater than 20%, or
- to women at a 10-year risk of greater than 12% where mammography has shown a dense breast pattern.
- Genetic testing is appropriate only for a small proportion of women who are from high-risk families.
- Risk-reducing surgery (mastectomy and/or oophorectomy) is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team.

1 Guidance

The following guidance is based on the best available evidence. The full guideline ('Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care') gives details of the methods and the evidence used to develop the guidance (see section 5 for details). The original full guideline is available from www.nice.org.uk/CG041

Risk levels and estimates presented in this guideline

For risk classifications, data from both Claus and coworkers (1994)¹ and the Collaborative Group on Hormonal Factors in Breast Cancer (2001)² have been used to guide the levels that are presented in the guideline.

- Women at or near population risk of developing breast cancer (that is, a 10-year risk of less than 3% for women aged 40–49 years and a lifetime risk of less than 17%) are cared for in primary care.
- Women at raised risk³ of developing breast cancer (that is, a 10-year risk of 3–8% for women aged 40–49 years or a lifetime risk of 17% or greater but less than 30%) are generally cared for in secondary care.
- Women at high risk of developing breast cancer (that is, a 10-year risk of greater than 8% for women aged 40–49 years or a lifetime risk of 30% or greater) are cared for in tertiary care. High risk also includes a 20% or greater chance of a faulty *BRCA1*, *BRCA2* or *TP53* gene in the family.

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

¹ Claus EB, Risch N, Thompson WD (1994) Autosomal dominant inheritance of early onset breast cancer. *Cancer* 73: 643–51.

² Collaborative Group of Hormonal Factors in Breast Cancer (2001) Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet* 358: 1389–99.

³ In the original guideline (CG014), raised risk was referred to as moderate risk. The definition of raised and moderate risk is the same in both guidelines.

The referral criteria given in this guideline are examples of family histories that may equate to the levels of risk described above, in order that women are referred and assessed appropriately. However, other family histories may also lead to a suspicion of an increased risk, due to the numbers of breast or other cancers in the family or in cases of bilateral cancer where each breast has the same count value as one relative. If in doubt, clinicians should seek advice from a designated contact.

In the context of this guideline:

All affected relatives must be on the same side of the family and be blood relatives of the woman and each other.

In cases of bilateral breast cancer, each breast cancer has the same count value as one relative.

First-degree relatives: mother, father, daughter, son, sister, brother.

Second-degree relatives: grandparent, grandchild, aunt, uncle, niece and nephew; half sister and half brother.

Third-degree relatives: great grandparent, great grandchild, great aunt, great uncle, first cousin, grand nephew and grand niece.

1.1 *Approaches to care for all women*

The provision of information is a very important aspect of helping women understand their risk level for breast cancer, and also how this compares with other health risks.

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

- 1.1.2 To ensure a patient–professional partnership, patients should be offered individually tailored information, including information about sources of support (including local and national organisations).
- 1.1.3 Tailoring of information should take into account format (including whether written or taped) as well as the actual content and form that should be provided (see box 1, page 11).
- 1.1.4 Standard information should be evidence based wherever possible, and agreed at a national level if possible (the Institute’s ‘Understanding NICE guidance’ provides a good starting point, see section 5.3).
- 1.1.5 Standard information should not contradict messages from other service providers, including commonly agreed information across localities.

Box 1 Recommendations for information provision

Standard written information for all women

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

For women cared for in primary care

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

For women being referred to secondary care

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

For women being referred back to primary care

- Standard written information (as above).
- Detailed information about why secondary care or a specialist genetic service are not needed.
- Advice to return to primary care to discuss any implications if there is a change in family history or breast symptoms develop.

For women being cared for in secondary care

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

For women being referred to tertiary care

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

For women being cared for in tertiary care

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

1.2 Breast awareness and examination

1.2.1 Women at increased risk of breast cancer should be 'breast aware' in line with Department of Health advice for all women (see www.cancerscreening.nhs.uk/breastscreen/breastaware.pdf).

1.3 Care of women in primary care

Many women with concerns about their family history present to their GP. Most women will be cared for in primary care, as they will not be at a risk level that requires specialist care. Provision of information, reassurance and support from primary care are crucial aspects of caring for women with concerns.

New The only intervention likely to be offered to a woman estimated to be at raised risk is mammographic surveillance. MRI may be offered to some women who are at high risk and who meet certain surveillance criteria.

As the benefit of surveillance varies with age (see section 1.4.4), a woman's age should be taken into account when considering referral from primary care. Following the advice of this guideline, a woman younger than age 30 years estimated to be at raised risk (for example, only one relative with breast cancer), will not in practice be offered any intervention. The woman and her GP may therefore decide that a referral would confer no benefit. Similarly, a woman older than age 50 years will already be eligible for 3-yearly mammographic surveillance and, if estimated to be at raised risk, would receive no additional intervention by referral.

Conversely, women in the 40–49 year age group who are estimated to be at raised risk may benefit most from a referral and increased mammographic surveillance.

Because of the benefits of MRI screening in younger women with dense breasts, women in the 20–49 age group who are estimated to be at high risk and meet certain criteria are likely to benefit most from increased MRI screening.

1.3.1 Family history taking and initial assessment

- 1.3.1.1 When a woman presents with breast symptoms or has concerns about relatives with breast cancer, a first- and second-degree family history should be taken in primary care to assess risk, because this allows appropriate classification and care.
- 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.
- 1.3.1.3 In some circumstances, it may also be clinically relevant to take a family history, for example, for women older than age 35 years using an oral contraceptive pill or for women being considered for long-term HRT use.
- 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.
- 1.3.1.5 A second-degree family history (that is, including aunts, uncles and grandparents) should be taken in primary care before explaining risks and options.
- 1.3.1.6 A second-degree family history needs to include paternal as well as maternal relatives.
- 1.3.1.7 Asking women to discuss their family history with relatives is useful in gathering the most accurate information.
- 1.3.1.8 Tools such as family history questionnaires and computer packages exist that can aid accurate collection of family history information and they should be made available.

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

- age of diagnosis of any cancer in relatives
- site of tumours
- multiple cancers (including bilateral disease)
- Jewish ancestry⁴.

1.3.2 Primary care management

1.3.2.1 Women can be cared for in primary care if the family history shows only one first-degree or second-degree relative diagnosed with breast cancer at older than age 40 years, provided that none of the following are present in the family history:

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

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, page 11).

1.3.3 Referral from primary care

For some women, further assessment of their family history in specialist care will allow a better understanding of its impact, if any, on their estimated level of risk. This might mean that a referral to secondary or other specialist care will allow that assessment to be considered. The referral criteria given are

⁴ Women with Jewish ancestry are around 5–10 times more likely to carry *BRCA1* or *BRCA2* mutations than women in non-Jewish populations.

examples of family histories that may result in a referral being offered; the examples are not exhaustive. Other patterns may also result in offers of referral, but this will usually be after consultation with the designated secondary care contact about uncertain or unusual patterns of cancer. The criteria are fairly inclusive so that high-risk families are not missed.

However, if there is only a single relative with breast cancer even at a young age (younger than 40 years) or two older female relatives (older than 50 years on average) with breast cancer, referral is unlikely to lead to additional surveillance if the woman is outside the 40–49 year age group.

1.3.3.1 Before a decision on referral is made, primary care professionals should note that a woman outside the 40–49 year age group who is estimated to be at raised risk (for example, she has only one relative with breast cancer diagnosed at any age, or she has two relatives diagnosed with breast cancer older than an average age of 50 years) will not generally be offered additional mammography.

1.3.3.2 Women at raised risk outside the 40–49 year age group may be referred for risk counselling and advice on risk management or consideration for prevention trials. Advice should be sought from the designated contact in secondary care about the appropriateness of referral.

1.3.3.3 Women who meet the following criteria should be offered referral to secondary care:

- one first-degree female relative diagnosed with breast cancer at younger than age 40 years, **or**
 - one first-degree male relative diagnosed with breast cancer at any age, **or**
 - one first-degree relative with bilateral breast cancer where the first primary was diagnosed at younger than age 50 years
- or**
- two first-degree relatives, or one first-degree **and** one second-degree relative, diagnosed with breast cancer at any age, **or**

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

or

- three first-degree or second-degree relatives diagnosed with breast cancer at any age.

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

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

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

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

1.3.4 Information for women who are being referred

1.3.4.1 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, page 11).

1.3.5 Information and ongoing support for women who are not being referred

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

1.3.6 Support for primary care

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

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

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

Service configurations will vary by locality. However, recommendations are presented for settings that are likely to be found in most localities. In specialist care settings, a wider range of healthcare professionals is available. This allows further assessment to be made if necessary and also ensures that different healthcare professionals are available to offer information and support that may be needed. In some instances, referral will be to take a more

complete history; this may then mean that some women are referred back to primary care while others may be offered specialist care.

1.4.1.1 Care of women in secondary care (such as a breast care team, family history clinic or breast clinic which can be shared between trusts) should be undertaken by a multidisciplinary team. It should include the following:

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

1.4.2 Family history taking in secondary care

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.

1.4.2.2 A third-degree family history should be taken in secondary care where possible and appropriate.

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.

1.4.3 Management in secondary care

The criteria given are examples of family histories. Other patterns may also equate to raised risk (that is, a 10-year risk of 3–8% for women aged 40–49 or a lifetime risk of 17% or greater but less than 30%) which would be appropriate for care in secondary care. Consultation with the designated tertiary care contact about uncertain or unusual patterns of cancer will help in decision making where appropriate.

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

- one first-degree relative diagnosed with breast cancer at younger than age 40 years, **or**
- two first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 50 years, **or**
- three first-degree or second-degree relatives diagnosed with breast cancer at an average age of older than 60 years, **or**
- a formal risk assessment (usually carried out in tertiary care) or a family history pattern is likely to give a 10-year risk of 3–8% for women aged 40–49 years⁵, or a lifetime risk of 17% or greater but less than 30%

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

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

⁵ For the purpose of these calculations, a woman's age should be assumed to be 40 for a woman in her forties. A 10-year risk should then be calculated for the age range 40–49.

1.4.3.2 Women whose risk is less than that in recommendation 1.4.3.1 can be referred back to primary care (see recommendation 1.3.2.1), with appropriate information being offered (see box 1, page 11, and recommendation 1.3.5.1).

1.4.4 Surveillance

New For this updated guideline issued by NICE, new studies published since May 2004 were appraised. The Guideline Development Group (GDG) considered this evidence in the context of other available evidence.

The research evidence base for mammographic and MRI surveillance for women at particular risk levels and different age groups is incomplete, both for women in the general population as well as for women at risk because of a family history. Thus a considerable degree of uncertainty still exists about who should receive mammographic and MRI screening, at what age, and at what interval.

In some areas, knowledge exists that allows a better understanding of the likely benefits or disadvantages for particular groups. For example, the density of breast tissue in younger women (particularly in women aged younger than 30 years) means that informative mammograms are unlikely to be produced. In addition, the benefits of mammographic surveillance for women aged 50 years and older in the general population have been shown in many studies. Although there is still a relative lack of evidence for women with a family history, it is assumed that mammographic surveillance is of benefit to women in this category.

There is uncertainty, however, about the benefits of mammographic surveillance for women aged 30–49 years. There is some evidence to suggest a possible benefit in women at raised risk or greater aged 40–49 years, and an NHS-funded study is further evaluating this. Therefore, mammographic surveillance for this age group is being recommended in this guideline. This advice may change when definitive evidence is obtained. There is virtually no evidence in the 30–39 year age group and as such, screening should only be carried out as part of ethically approved and audited studies in this age group.

Recent evidence has suggested that MRI increases the sensitivity of breast cancer screening, although this is at the expense of specificity. This additional sensitivity has the potential to identify cases earlier which should lead to more promising prognoses. Similarly, evidence has suggested that MRI is more effective than mammography in screening younger groups of women, because of breast tissue density issues. Therefore, MRI surveillance for younger women who are at high risk of breast cancer and who meet certain criteria is being recommended in this guideline.

The benefit of MRI screening has to be contrasted between different groups of women, taking into consideration the issues surrounding specificity and the number of false positive results and the resulting increase in cost of those incorrectly brought back for further investigation.

In making any surveillance decision, the benefits and risks of each intervention must be considered. These include the possibility that further investigations may be needed, causing discomfort and worry, and the possible effects of additional radiation from mammography to those who may be more susceptible to radiation risks.

It is recommended that participation in available studies is encouraged and that MRI and mammography data should be collected for audit purposes. This information will build the evidence base and will help to develop future recommendations. Research is ongoing in several of these areas and as findings emerge the recommendations should be reconsidered in the light of those findings.

When calculating a woman's 10-year risk, her age should be assumed to be 30 for a woman in her thirties and 40 for a woman in her forties. A 10-year risk should then be calculated for the age range 30–39 and 40–49, respectively.

- 1.4.4.1 Before decisions on surveillance are made, written patient information and discussion should be offered. This should:
- reflect the possible reduced sensitivity of mammographic detection of the younger age group with dense breasts and the increased potential for further investigations
 - discuss the potential advantages and disadvantages of mammographic surveillance for early detection of breast cancer, including:
 - radiation risks
 - the possible psychological impact of a recall visit.
- 1.4.4.2 Mammographic surveillance should not be available for women younger than age 30 years.
- 1.4.4.3 For women aged 30–39 years satisfying referral criteria for secondary or specialist care, mammographic surveillance should be carried out:
- only as part of a research study (ethically approved) or nationally approved and audited service
- and**
- individualised strategies should be developed for exceptional cases, such as:
 - women from families with *BRCA1*, *BRCA2* or *TP53* mutations
 - women with equivalent high breast cancer risk.
- 1.4.4.4 Support mechanisms (for example, risk counselling, psychological counselling and risk management advice) need to be identified and should be offered to women not being offered mammographic surveillance who have ongoing concerns.
- 1.4.4.5 All women satisfying referral criteria to secondary or specialist care (at raised risk or greater) should be offered mammographic surveillance from age 40 years.

1.4.4.6 **New** Women who have been referred to a clinical genetics centre who are not known to have a genetic mutation should be offered an assessment of their 10-year breast cancer risk using a validated risk assessment tool (for example, Tyrer-Cuzick or BOADICEA^{6,7}) to assess whether they are or will be eligible for MRI.

1.4.4.7 For women aged 40–49 years at raised risk or greater, mammographic surveillance should be:

- annual
- to NHS Breast Screening Programme standards
- audited
- part of the NHS Research and Development Health Technology Assessment programme evaluation of mammographic surveillance of women younger than age 50 years with a family history wherever possible
- only undertaken after provision of written information about the positive and negative aspects of surveillance.

⁶ Antoniou A, Pharoah PD, Narod S et al (2003) Average risks of breast and ovarian cancer associated with *BRCA1* or *BRCA2* mutations detected in case Series unselected for family history: a combined analysis of 22 studies. *American Journal of Human Genetics* 72: 1117–1130.

⁷ Amir E, Evans DG, Shenton A et al (2003) Evaluation of breast cancer risk assessment packages in the family history evaluation and screening programme. *Journal of Medical Genetics* 40: 807–814.

- 1.4.4.8 For women aged 50 years and older, surveillance should be:
- as part of the NHS Breast Screening Programme, screened every 3 years
 - more frequent mammographic surveillance should take place only as part of a research study (ethically approved) or nationally approved and audited service
- and
- individualised strategies should be developed for exceptional cases, such as:
 - women from families with *BRCA1*, *BRCA2* or *TP53* mutations
 - women with equivalent high breast cancer risk.
- 1.4.4.9 **New** When mammography is recommended in women under 50, digital mammography should be used in preference to conventional mammography at centres where this is available to NHS Breast Screening Programme standards.
- 1.4.4.10 **New** At entry to an MRI surveillance programme, and at each subsequent change in the programme, women should be provided with a documented plan which includes:
- a clear description of the method(s) and intervals, including the risks and benefits
 - the reasons for any changes to the surveillance plan
 - sources of support and further information.
- 1.4.4.11 **New** Women who are known to have a genetic mutation should be offered annual MRI surveillance if they are:
- *BRCA1* and *BRCA2* mutation carriers aged 30–49 years
 - *TP53* mutation carriers aged 20 years or older.

1.4.4.12 **New** MRI surveillance should be offered annually when indicated.

From 30–39 years:

- to women at a 10-year risk of greater than 8%⁸

From 40–49 years:

- to women at a 10-year risk of greater than 20%, or
- to women at a 10-year risk of greater than 12% where mammography has shown a dense breast pattern⁹.

1.4.4.13 **New** Women who have not been tested but have a high chance of carrying a *BRCA1* or *TP53* genetic mutation should be offered annual MRI surveillance from 30–49 years if they are at:

- a 50% risk of carrying one of these mutations in a tested family, or
- a 50% risk of carrying a *BRCA1* or *TP53* mutation in an untested or inconclusively tested family with at least a 60% chance of carrying a *BRCA1* or *TP53* mutation (that is, a 30% risk of carrying one of these mutations themselves).

1.4.4.14 **New** MRI of both breasts should be performed to high quality standards ensuring both high temporal and spatial resolution. Dynamic sequences are recommended post contrast. They should be double-read where possible.

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

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

A genetic test would usually be required to determine a 10-year risk of 20% or greater in women aged 40–49 years.

*All relatives must be on the same side of the family and one must be a mother or sister of the woman.

⁹ As defined by the 3-point mammographic classification used by UK breast radiologists (Breast Group of the Royal College of Radiologists 1989).

- 1.4.4.15 **New** MRI and any accompanying mammography data should be collected for audit purposes to support a national database.
- 1.4.4.16 **New** On the basis of current evidence, ultrasound should not be used in routine surveillance practice but may have a role in problem-solving mammographically or MRI-detected abnormalities.

1.4.5 Referral to tertiary care

Women who are estimated to be at high risk (that is, a 10-year risk at age 40–49 years of greater than 8% or a lifetime risk of 30% or greater, or a 20% or greater chance of a faulty *BRCA1*, *BRCA2* or *TP53* gene in the family) should be referred to a specialist genetics clinic in tertiary care.

The referral criteria given in this guideline are **examples** of family histories which may equate to levels of risk described on page 8 in order that women are referred and assessed appropriately. Other patterns may also be appropriate for referral. Consultation with the designated tertiary care contact about uncertain or unusual patterns of cancer will help in decision making where appropriate.

- 1.4.5.1 Women who meet the following referral criteria should be offered a referral to tertiary care.
- At least the following female breast cancers only in the family:
 - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 50 years (at least one must be a first-degree relative), **or**
 - three first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years (at least one must be a first-degree relative), **or**
 - four relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative).

or

- Families containing one relative with ovarian cancer at any age **and**, on the same side of the family:
 - one first-degree relative (including the relative with ovarian cancer) or second-degree relative diagnosed with breast cancer at younger than age 50 years, **or**
 - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years, **or**
 - another ovarian cancer at any age.

or

- Families containing bilateral cancer (each breast cancer has the same count value as one relative):
 - one first-degree relative with cancer diagnosed in both breasts at younger than an average age of 50 years, **or**
 - one first-degree or second-degree relative diagnosed with bilateral breast cancer **and** one first-degree or second-degree relative diagnosed with breast cancer at younger than an average age of 60 years.

or

- Families containing male breast cancer at any age **and** on the same side of the family, at least:
 - one first-degree or second-degree relative diagnosed with breast cancer at younger than age 50 years, **or**
 - two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years.

or

- A formal risk assessment has given risk estimates of:
 - a 20% or greater chance of a *BRCA1*, *BRCA2* or *TP53* mutation being harboured in the family, **or**
 - a greater than 8% chance of developing breast cancer age 40–49 years, **or**
 - a 30% or greater lifetime risk of developing breast cancer.

- 1.4.5.2 Clinicians should seek further advice from a specialist genetics service for families containing any of the following, in addition to breast cancers:
- Jewish ancestry
 - sarcoma in a relative younger than age 45 years
 - glioma or childhood adrenal cortical carcinomas
 - complicated patterns of multiple cancers at a young age
 - very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family).
- 1.4.5.3 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 specialist genetics service.
- 1.4.5.4 Following initial consultation in secondary care, written information should be provided to reflect the outcomes of the consultation (see box 1, page 11).
- 1.4.6 Care of women in tertiary care**
- 1.4.6.1 Care of women referred to tertiary care should be undertaken by a multidisciplinary team. In addition to having access to the components found in secondary care, it should also include the following:
- clinical genetic risk assessment
 - verification for abdominal malignancies and possible sarcomas.
- 1.4.7 Family history taking in tertiary care**
- 1.4.7.1 A third-degree family history should be taken in tertiary care, if this has not been done previously.

- 1.4.7.2 For accurate risk estimation, the following are required:
- 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).
- 1.4.7.4 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).
- 1.4.7.5 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk-reducing surgery.
- 1.4.7.6 Abdominal malignancies at young ages and possible sarcomas should be confirmed in specialist care.

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.

1.4.8 Genetic counselling

Genetic counselling can be very important in helping a woman understand the role of both her family history and lifestyle on her risk of breast cancer. Counselling provides information about the individual woman's risk level; enables discussion of available options; helps the woman to make choices about the course of action that seems most appropriate; and assists the woman in adjusting to her risk and its implications.

- 1.4.8.1 Women meeting criteria for referral to tertiary care should be offered a referral for genetic counselling regarding their risks and options.
- 1.4.8.2 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.
- 1.4.8.3 Predictive genetic testing should not be offered without adequate genetic counselling.

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.
- 1.4.9.2 When a personal risk estimate is requested, it should be presented in more than one way (for example, a numerical value, if calculated, and qualitative risk).
- 1.4.9.3 Women should be sent a written summary of their consultation in a specialist genetics clinic, which includes their personal risk information.

1.4.10 Genetic testing

Genetic testing is only appropriate for a small number of women from high-risk families and should begin with an affected relative. It is a two-stage process.

Stage one: mutation searching/screening on an affected relative

Genetic testing in a family starts by testing an individual with cancer (affected family member) for mutations in *BRCA1*, *BRCA2* or *TP53*. A positive test will usually mean that other unaffected family members can be tested for the identified mutation.

If the search for a mutation in the affected family member proves negative, the results are deemed inconclusive for the family, who therefore will not know whether there is a faulty gene in the family.

The number of families in which a gene test can be developed will depend on the threshold for testing. It is estimated that with full gene testing on an affected relative and the 20% threshold, a mutation will be found in about one in three families. Therefore, in two out of three high-risk families, a predictive test can not be offered even after testing an affected family member because no mutation can be found.

Stage two: predictive testing (tests on unaffected individuals)

Once a mutation has been identified in an affected family member a definitive genetic test (mutation test) can be made available to all blood relatives. About two in three women test negative for the gene fault in clinical practice.

A woman testing negative for a known genetic mutation in the family will have no risk of transmitting the gene fault to her children. The assumption is that she is likely to be at about population-level risk of developing breast (or ovarian) cancer. Interventions such as early screening and risk-reducing surgery will no longer be appropriate. She can be referred back to primary care and cared for as all women in the general population.

Testing an unaffected individual without pre-testing an affected family member

If a faulty gene has not previously been identified by testing an affected relative, a negative full screen for a mutation (for example, *BRCA1*, *BRCA2* or *TP53*) in an unaffected family member is likely to be uninformative. This is because the majority of families, even those qualifying for testing, will not have a detectable mutation. In these circumstances, testing will not affect the risk estimate of breast cancer in the unaffected individual and will therefore not provide reassurance or change management decisions. Hence, this guideline recommends that testing begins with the affected individual.

- 1.4.10.1 All high-risk women should have access to information on genetic tests aimed at mutation finding.
- 1.4.10.2 Pre-test counselling (preferably two sessions) should be undertaken.
- 1.4.10.3 Discussion of genetic testing (predictive and mutation finding) should be undertaken by a health professional with appropriate training.
- 1.4.10.4 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 results.

Mutation tests

- 1.4.10.5 Tests aimed at mutation finding should first be carried out on an affected family member where possible.
- 1.4.10.6 Women from families with a 20% or greater chance of carrying a mutation such as *BRCA1*, *BRCA2* or *TP53* should have access to testing.
- 1.4.10.7 The development of a genetic test for a family should usually start with the testing of an affected individual (mutation searching/screening) to try to identify a mutation in the appropriate gene (such as *BRCA1*, *BRCA2* or *TP53*).
- 1.4.10.8 A search/screen for a mutation in a gene (such as *BRCA1*, *BRCA2* or *TP53*) should aim for as close to 100% sensitivity as possible for detecting coding alterations and the whole gene(s) should be searched.

1.4.11 Risk-reducing surgery

Risk-reducing surgery is only appropriate for a small proportion of women with a family history of breast cancer. Women considering this option may need

considerable time and support in making decisions about risk-reducing surgery and may need reassurance that a short delay will not significantly affect their chances of developing cancer. Decisions need to be taken only after careful assessment of all implications, including the recognition that:

- there may be uncertainty about their absolute risk due to incomplete or uncertain information
- risk-reducing surgery does not eliminate all risk of breast cancer
- the interventions themselves have other risks associated with them, as with all surgical interventions.

1.4.11.1 In services offering risk-reducing surgery, the following should be available:

- facilities to verify family history and clinical genetic risk assessment
- **New** facilities for appropriate imaging (mammography +/- MRI)
- psychological assessment and counselling
- information about support groups
- oncoplastic/breast reconstructive skills.

1.4.11.2 If risk-reducing surgery is being considered, and no mutation has been identified, clinicians should seek confirmation of family history (via medical records/cancer registry/death certificates).

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

1.4.12 Bilateral risk-reducing mastectomy

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

1.4.12.2 Bilateral mastectomy should be raised as a risk-reducing strategy option with all women at high risk.

- 1.4.12.3 Women considering bilateral risk-reducing mastectomy should have genetic counselling in a specialist cancer genetics clinic before a decision is made.
- 1.4.12.4 Discussion of individual breast cancer risk and its potential reduction by surgery should take place and take into account individual risk factors, including the woman's current age (especially at extremes of age ranges).
- 1.4.12.5 Family history should be verified where no mutation has been identified before bilateral risk-reducing mastectomy.
- 1.4.12.6 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with bilateral risk-reducing mastectomy.
- 1.4.12.7 Pre-operative counselling about psychosocial and sexual consequences of bilateral risk-reducing mastectomy should be undertaken.
- 1.4.12.8 The possibility of breast cancer being diagnosed histologically following a bilateral risk-reducing mastectomy should be discussed pre-operatively.
- 1.4.12.9 All women considering bilateral risk-reducing mastectomy should be able to discuss their breast reconstruction options (immediate and delayed) with a member of a surgical team with specialist oncoplastic or breast reconstructive skills.
- 1.4.12.10 A surgical team with specialist oncoplastic/breast reconstructive skills should carry out risk-reducing mastectomy and/or reconstruction.
- 1.4.12.11 Women considering bilateral risk-reducing mastectomy should be offered access to support groups and/or women who have undergone the procedure.

1.4.13 Risk-reducing bilateral oophorectomy

- 1.4.13.1 Risk-reducing bilateral oophorectomy is appropriate only for a small proportion of women who are from high-risk families and should be managed by a multidisciplinary team.
- 1.4.13.2 Information about bilateral oophorectomy as a potential risk-reducing strategy should be made available to women who are classified as high risk.
- 1.4.13.3 Family history should be verified where no mutation has been identified before risk-reducing bilateral oophorectomy.
- 1.4.13.4 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk-reducing bilateral oophorectomy.
- 1.4.13.5 Any discussion of bilateral oophorectomy as a risk-reducing strategy should take fully into account factors such as anxiety levels on the part of the woman concerned.
- 1.4.13.6 Healthcare professionals should be aware that women being offered risk-reducing bilateral oophorectomy may not have been aware of their risks of ovarian cancer as well as breast cancer and should be able to discuss this.
- 1.4.13.7 The effects of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy.
- 1.4.13.8 Options for management of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy, including the advantages, disadvantages and risk impact of HRT.
- 1.4.13.9 Women considering risk-reducing bilateral oophorectomy should have access to support groups and/or women who have undergone the procedure.

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

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

1.4.13.12 Women undergoing bilateral risk-reducing oophorectomy should have their fallopian tubes removed as well.

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

Evidence was sought that might show whether the risks for women with a family history 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, extrapolation of findings from general populations was undertaken.

Overall, the risk factors for developing breast cancer for women with a family history are the same as for women in the general population. However, the impact of these risk factors, both positive and negative, is likely to be greater for women with a family history because of their greater risk of developing breast cancer. Healthcare professionals should discuss these issues fully so that the woman understands what she can and cannot do to modify her risk of breast cancer, and the effect this will have on her risk of other diseases and conditions.

Many of the risk factors are not modifiable (for example, the age when periods started) or are difficult to change (for example, age at first pregnancy).

However for some women, changing behaviours, such as lifestyle factors, will affect their overall breast cancer risk.

In some instances, such as for women estimated to be at very high risk, the risk associated with family history is such that lifestyle changes will have little impact on risk.

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 (see box 1, page 11).
- 1.5.1.2 Modifiable risk factors should be discussed on an individual basis with each woman in the relevant care setting.

1.5.2 HRT

- 1.5.2.1 Women with a family history of breast cancer who are considering taking, or are already taking, HRT should be informed of the increase in breast cancer risk with type and duration of HRT.
- 1.5.2.2 Advice to individual women on the use of HRT should vary according to the individual clinical circumstances (such as asymptomatic menopausal symptoms, age, severity of menopausal symptoms, or osteoporosis).
- 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. Oestrogen-only HRT should be prescribed where possible.
- 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 age 50 years if at raised or high risk.
- 1.5.2.5 Alternatives to HRT should be considered for specific symptoms such as osteoporosis or menopausal symptoms.
- 1.5.2.6 Consideration should be given to the type of HRT if it is being considered for use in conjunction with risk-reducing gynaecological surgery.

1.5.3 Hormonal contraceptives

- 1.5.3.1 Advice to women up to age 35 years with a family history of breast cancer should be in keeping with general health advice on the use of the oral contraceptive pill.
- 1.5.3.2 Women aged over 35 years with a family history of breast cancer should be informed of an increased risk of breast cancer associated with taking the oral contraceptive pill, given that their absolute risk increases with age.
- 1.5.3.3 For women with *BRCA1* mutations, the conflicting effects of a potential increased risk of breast cancer under the age of 40 years and the lifetime protection against ovarian cancer risk from taking the oral contraceptive pill should be discussed.
- 1.5.3.4 Women should not be prescribed the oral contraceptive pill purely for prevention of cancer, although in some situations reduction in ovarian cancer risk may outweigh any increase in risk of breast cancer.
- 1.5.3.5 If a woman has a *BRCA1* mutation and is considering a risk-reducing oophorectomy before the age of 40 years, the oral contraceptive pill should not be prescribed purely for the reduction in ovarian cancer risk.

1.5.4 Breastfeeding

- 1.5.4.1 Women should be advised to breastfeed if possible because this is likely to reduce their risk of breast cancer and is in accordance with general health advice.

1.5.5 Alcohol consumption

- 1.5.5.1 Women with a family history should be informed that alcohol may increase their risk of breast cancer slightly. However, this should be considered in conjunction with any potential benefit of moderate

alcohol intake on other conditions (such as heart disease) and adverse effects associated with excessive alcohol intake.

1.5.6 Smoking

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

1.5.7 Weight and physical activity

1.5.7.1 Women should be advised on the probable increased postmenopausal risk of breast cancer associated with being overweight.

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

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.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from www.nice.org.uk/CG041.

The scope of this guideline was care and classification of women at risk of breast cancer because of a family history of breast or ovarian cancer. It does not cover women who have diagnosed breast cancer. The guideline covers women aged 18 years and older; it does not refer to men but the recommendations will be pertinent. 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.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Primary Care to develop the original guideline (CG 14) and this update. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information in the booklet: 'The guideline development process: an overview for stakeholders, the public and the NHS' (2006), which is available from www.nice.org.uk/guidelinesprocess or by telephoning 0870 1555 455 (quote reference N1113).

3 Implementation

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health', issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG041).

- Costing tools:
 - costing report to estimate the national savings and costs associated with implementation.
 - costing template to estimate the local costs and savings involved.

Suggested audit criteria based on the key priorities for implementation are listed in appendix D of this document (see page 49), and can be used to audit practice locally.

The original costing report and costing template for NICE clinical guideline 14 can be found on the NICE website (www.nice.org.uk/CG041).

4 Research recommendations

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

- The benefit of surveillance with MRI in the over 50 age group.
- The benefit of digital mammography in women at increased risk.

5 Other versions of this guideline

5.1 *Full guideline*

The full guideline, 'Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care (update)' contains details of the methods and evidence used to update section 1.4.4.

For details of the evidence for the other recommendations, see the full version of NICE clinical guideline 14 (www.nice.org.uk/CG041). It is published by the National Collaborating Centre for Primary Care, and is available from www.rcgp.org.uk/nccpc, our website (www.nice.org.uk/CG041fullguideline) and the National Library for Health (www.nlh.nhs.uk).

5.2 *Quick reference guide*

A quick reference guide for healthcare professionals is available from www.nice.org/CG041quickrefguide

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1130).

5.3 'Understanding NICE guidance'

Information for patients and carers ('Understanding NICE guidance') is available from www.nice.org.uk/CG041publicinfo

For printed copies, phone the NHS Response Line on 0870 1555 455 (quote reference number N1131).

6 Related NICE guidance

Cancer service guidance

Improving outcomes in breast cancer. *NICE cancer service guidance* (2002). Available from www.nice.org/csgbc

Technology appraisal guidance

Docetaxel for the adjuvant treatment of early node-positive breast cancer. *NICE technology appraisal guidance* no. 109 (2006). Available from www.nice.org/TA109

Paclitaxel for the adjuvant treatment of early node-positive breast cancer. *NICE technology appraisal guidance* no. 108 (2006). Available from www.nice.org/TA108

Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer. *NICE technology appraisal guidance* no. 107 (2006). Available from www.nice.org/TA107

Guidance on the use of capecitabine for the treatment of locally advanced or metastatic breast cancer. *NICE technology appraisal guidance* no. 62 (2003). Available from www.nice.org/TA062

Guidance on the use of trastuzumab for the treatment of advanced breast cancer. *NICE technology appraisal guidance* no. 34 (2002). Available from www.nice.org/TA034

Guidance on the use of vinorelbine for the treatment of advanced breast cancer. *NICE technology appraisal guidance* no. 54 (2002). Available from www.nice.org/TA054

Guidance on the use of taxanes for the treatment of breast cancer. *NICE technology appraisal guidance* no. 30 (2001). Available from www.nice.org/TA030

NICE is developing the following guidance (details available from www.nice.org.uk).

- Early breast cancer: diagnosis and treatment. *NICE clinical guideline* (publication expected July 2008).
- Advanced breast cancer: diagnosis and treatment. *NICE clinical guideline* (publication expected July 2008).
- Gemcitabine for advanced/metastatic breast cancer. *NICE technology appraisal guidance* (publication date to be confirmed).

7 Updating the guideline

NICE clinical guidelines are updated as needed so that recommendations take into account important new information. We check for new evidence 2 and 4 years after publication, to decide whether all or part of the guideline should be updated. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

Appendix A: The Guideline Development Group

The GDG members of the original guideline were reconvened under the same chairmanship for the update. New members were also invited to join. The GDG members are listed below.

NICE clinical guideline 14

Professor Gareth Evans (Chair)

Consultant Clinical Geneticist, St Mary's Hospital, Manchester

Nasim Bahar

Patient Representative

Professor Doug Easton

Principle Research Fellow, Cancer Research UK

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

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 Sue Barter

Radiologist, Cambridge Breast Unit, Addenbrooke's Hospital, Cambridge

Update

Dr Cristina Parsons Perez

Senior Genetics, Policy and Information Officer, Breakthrough Breast Cancer

Dr Ken Young

Consultant Physicist, National Co-ordination Centre for the Physics of Mammography, Royal Surrey County Hospital NHS Trust, Guildford,

Prof Fiona Gilbert

Radiologist, Foresterhill Aberdeen

National Collaborating Centre for Primary Care

Richard Norman

Health Economist, NCC for Primary Care

Gill Ritchie

Systematic Reviewer, NCC for Primary Care

Yolanda Jozeph

Project Manager, NCC for Primary Care

Nancy Turnbull

Chief Executive, NCC for Primary Care

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The Panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Professor Mike Drummond (Chair)

Director, Centre for Health Economics, University of York

Mr Barry Stables

Patient/Lay Representative

Dr Robert Walker

Clinical Director, West Cumbria Primary Care Trust

Dr John Harley

Clinical Governance and Prescribing Lead, North Tees Primary Care Trust

Appendix C: The algorithms

Pathways for care can be found in the quick reference guide, available at www.nice.org.uk/CG041quickrefguide. Printed copies of the quick reference guide are available from the NHS Response Line (telephone 0870 1555 455 and quote reference number N1130).

Appendix D: Audit criteria

The measures that could be used as a basis for audit are included in the table below.

Criterion	Standard	Exception	Definition of terms
Standard written information should be developed for use in primary, secondary and tertiary care	100% of centres should provide this information	Nil	Written information that will provide consistent advice to women, including risk and breast awareness information, lifestyle advice, etc
Local protocols should be developed with clear referral mechanisms between primary, secondary and tertiary care and with appropriate facilities	100% of organisations should have local protocols	Nil	
Information should be provided about the potential advantages and disadvantages of mammographic surveillance	100% of women who are offered mammographic surveillance	Nil	Information includes written information and discussion on: <ul style="list-style-type: none"> • reduced sensitivity in younger breasts • radiation risks • the possible psychological impact of a recall visit
Risk-reducing surgery should be managed by a multidisciplinary team	The small proportion of women who are from high-risk families	Nil	Risk-reducing surgery refers to bilateral mastectomy and oophorectomy. A multidisciplinary team should include: <ul style="list-style-type: none"> • facilities to verify family history and clinical genetic risk assessment • mammography before surgery • psychological assessment and counselling • information about support groups • oncoplastic/breast reconstructive skills.
MRI should be offered to those who meet the appropriate age and risk criteria	Number (proportion) receiving screening who do and do not meet criteria	Nil	
Centres should record details of tumour size, grade and lymph node status and whether the cancer was a prevalent, incident or interval cancer so that sensitivity and specificity can be calculated	Proportion detected at screening and proportion of interval cancers	Nil	Number of true positive, false positive, true negative, false positive test results

Calculation of compliance

Compliance (%) with each measure described in the table above is calculated as follows:

$$\frac{\text{Number of patients whose care is consistent with the criterion *plus* number of patients who meet any exception listed}}{\text{Number of patients to whom the **measure** applies.}} \times 100$$

Clinicians should review the findings of measurement, identify whether practice can be improved, agree on a plan to achieve any desired improvement and repeat the measurement of actual practice to confirm that the desired improvement is being achieved.