Appendix A: Summary of evidence from surveillance

4-year surveillance (2017) – Familial breast cancer (2013) NICE guideline CG164

Summary of evidence from surveillance

The clinical significance of a family history of breast cancer

Q – 01 Accuracy of family history

- **Family history-taking and initial assessment in primary care**
- **Family history-taking in secondary care**
- **Family history-taking in a specialist genetic clinic**

Recommendations derived from this review question

1.1.1 When a person with no personal history of breast cancer 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. [2004]

1.1.2 Healthcare professionals should respond to a person who presents with concerns but should not, in most instances, actively seek to identify people with a family history of breast cancer. [2004]

1.1.3 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. [2004]

1.1.4 A person should be given the opportunity to discuss concerns about their family history of breast cancer if it is raised during a consultation. [2004]

1.1.5 A second-degree family history (that is, including aunts, uncles and grandparents) should be taken in primary care before explaining risks and options. [2004]

1.1.6 A second-degree family history needs to include paternal as well as maternal relatives. [2004]

1.1.7 Asking people to discuss their family history with relatives is useful in gathering the most accurate information. [2004]

1.1.8 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. [2004]

1.1.9 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 ancestry[1]. [2004]

1.1.10 A family history should be taken when a person with no personal history of breast cancer presents with breast symptoms or has concerns about relatives with breast cancer. [2004]

1.1.11 A third-degree family history should be taken in secondary care where possible and appropriate. [2004]

1.1.12 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. [2004]

1.1.13 A third-degree family history should be taken in a specialist genetic clinic for a person with no personal history of breast cancer, if this has not been done previously. [2004]

1.1.14 For accurate risk estimation, the following are required:

- age of death of affected and unaffected relatives
- current age of unaffected relatives. [2004]

1.1.15 In general, it is not necessary to validate breast cancer-only histories (via medical records/cancer registry/death certificates). [2004]

1.1.16 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). [2004]

1.1.17 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with risk-reducing surgery. [2004]

1.1.18 Abdominal malignancies at young ages and possible sarcomas should be confirmed in specialist care. [2004]

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

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

One RCT[1] was identified which tested a breast cancer risk assessment and education intervention in women (n=1235). The study found that the intervention resulted in increased discussion about family cancer history, high-risk clinics and genetic counselling/testing compared to control.

4-year surveillance summary

A topic expert highlighted an RCT[2] (n = 3786) examining the effect of a web-based history-taking tool on family communication. The intervention named 'Family HealthWare' is a self-administered, web-based tool that assesses familial risk for a range of hereditary illness including breast and ovarian cancer, and provides a personalised prevention plan based on familial risk. Authors do not report (from an assessment of the abstract) on what the control group received. The follow-up time was 6 months. Results indicated that communication between family members was significantly more likely in the intervention group, but only for those who were not communicating at baseline. For those who were already communicating at baseline, there was no significant effect of the intervention.

Topic expert feedback

Recommendation 1.1.2 states that healthcare professionals should respond to a person who presents with concerns but should not, in most instances, actively seek to identify people with a family history of breast cancer. A topic expert highlighted a potential inequality issue with this recommendation because there may be a risk that medically underserved populations may not be identified. It was suggested that there may be a role for a more proactive approach in some circumstances.

Impact statement

New evidence was identified to suggest that an educational intervention improved communication about family cancer history whilst assessing breast cancer risk. This evidence is consistent with the existing guideline which recommends taking a family history in primary care to assess breast cancer risk, and that tools should be made available to enable an accurate collection of family history information. It is also consistent with recommendation 1.1.7 which advises that people should be asked to discuss their family history with relatives. Therefore it is unlikely that the recommendations will be affected by the new evidence.

New evidence is unlikely to change guideline recommendations.

Q – 02 What are the optimal methods for assessing the carrier probability of people (whether or not they have a personal history of breast cancer) at different thresholds for genetic testing in women and men at risk of familial breast cancer?

Recommendations derived from this review question

1.1.19 When available in secondary care, use a carrier probability calculation method with demonstrated acceptable performance (calibration and discrimination) as well as family history to determine who should be offered referral to a specialist genetic clinic. Examples of acceptable methods include BOADICEA and the Manchester scoring system. [2013]

1.1.20 In a specialist genetic clinic, use a carrier probability calculation method with demonstrated acceptable performance (calibration and discrimination) to assess the probability of a BRCA1 or BRCA2 mutation. Examples of acceptable methods include BOADICEA and the Manchester scoring system. [2013]

1.1.21 If there are problems with using or interpreting carrier probability calculation methods, use clinical judgement when deciding whether to offer genetic testing. [2013]

Surveillance decision

This review question should not be updated.

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A cohort study[3] (n = 146) evaluated the validity of the risk assessment model 'BRCAPRO' on men who presented for genetic counselling and testing. Results indicated that the BRCAPRO score was significantly higher for patients who tested positive for a BRCA mutation. The area under the receiver operating characteristics curve was 0.83 for all patients for the BRCAPRO score to predict the risk of carrying a BRCA mutation. At a cut-off point of 30.02%, the sensitivity, specificity, positive predictive value and a negative predictive value were 0.74, 0.81, 0.67 and 0.86 respectively.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence was found on the use of the risk assessment model BRCAPRO to assess

carrier probability in men. This is in line with recommendation 1.1.19 which currently advises the use of a carrier probability calculation method with demonstrated acceptable performance when deciding who should be offered referral to a specialised genetic clinic. It is therefore unlikely that the new evidence will impact recommendations.

New evidence is unlikely to change guideline recommendations.

Q – 03 Communicating cancer risk and carrier probability

Recommendations derived from this review question

1.1.22 People should be offered a personal risk estimate but information should also be given about the uncertainties of the estimation. [2004]

1.1.23 When a personal risk value is requested, it should be presented in more than one way (for example, a numerical value, if calculated, and qualitative risk). [2004]

1.1.24 People should be sent a written summary of their consultation in a specialist genetic clinic, which includes their personal risk information. [2004]

Surveillance decision

No new information was identified at any surveillance review.

This section of the guideline should not be updated.

Information and support

Q – 04 Patient information and support

Recommendations derived from this review question

1.2.1 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. [2004]

1.2.2 To ensure a patient-professional partnership, patients should be offered individually tailored information, including information about sources of support (including local and national organisations). [2004]

1.2.3 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). [2004]

1.2.4 Standard information should be evidence based wherever possible, and agreed at a national level if possible (NICE's information for the public provides a good starting point). [2004]

1.2.5 Standard information should not contradict messages from other service providers, including commonly agreed information across localities. [2004]

Box 1: Information provision for people with concerns about familial breast cancer risk

Standard written information for all people
• 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 (women only) ◊ lifestyle, including diet, alcohol, etc ◊ breastfeeding, family size and timing (women only). • Contact details of those providing support and information, including local and national support groups. • People 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 people 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 people 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 genetics service) and what may happen at each level.
For people being referred back to primary care
• Standard written information (as above). • Detailed information about why secondary or a specialist genetics 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 people 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 people being referred to a specialist genetic clinic
• 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 genetics service, including counselling and genetic testing.

For people being cared for in a specialist genetic clinic

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

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

An RCT[4] (n = 207) examined the effectiveness of a telephone-based peer-delivered intervention in reducing distress among women with a BRCA mutation. The intervention lasted 4 months and was delivered by trained peer volunteers who contacted women to provide informational, emotional and practical support. The intervention was compared to a usual care control and the follow-up period was post-intervention and 2 months later. Results indicated that at both follow-up points there was a greater decrease in distress scores in the intervention group compared to the control group. There was also a greater reduction in unmet information needs and 'Cognitive Appraisals about Genetic Testing' stress subscale scores for the intervention group compared to control.

4-year surveillance summary

An RCT[5] (n = 197) investigated the effect of a tailored pre-counselling informative website on patient experience in people preparing for breast cancer genetic counselling. Participants were randomised to the usual care group or the intervention and completed questionnaires pre and post counselling and at one year follow-up. Results indicated that at one year follow-up, the intervention group reported significantly more positive experiences with the counselling and higher perceived personal control. There were no significant differences between groups for measures of recall, knowledge, anxiety, cancer worry, risk perception alignment and adherence to breast surveillance advice.

An RCT[6] (n = 158) examined the effects of a 10-week cognitive behavioural stress management group intervention on distress among women with a family history of breast cancer. The intervention was compared to waitlist control group. Results indicated that compared to control, the intervention group had significantly lower post-treatment depressive symptoms and perceived stress.

A quasi-experimental study[7] (n = 97) examined the effect of stress management group counselling on stress levels of women with a family history of breast cancer. The intervention consisted of 6 sessions lasting 90 minutes and results were compared to a no treatment control group. Follow-up time is not specified. Results indicated that the intervention group had significantly different stress management scores in favour of the intervention group.

An RCT[8] (n = 150) examined the effect of a decision aid on decision making and psychosocial functioning in women with a BRCA mutation with no previous diagnosis of cancer. The intervention group was compared to a usual care control group and all participants were followed up at 3, 6 and 12 months. The results indicated that at 6 and 12 month follow-up, mean cancer-related distress scores were significantly lower in the intervention group compared to the control group. Decisional conflict scores declined over

time in both groups, with no significant differences between groups.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence was identified to suggest that telephone peer interventions and decision aids reduce distress in women with a BRCA mutation. There was also evidence to suggest that stress management programmes had a positive impact on depressive symptoms and stress control. Whilst the guideline does not currently recommend specific interventions to support people at high risk of developing breast cancer, it does recommend offering patients individually tailored information, including information about sources of support (recommendations 1.2.1-1.2.5). It is therefore unlikely that the guideline will be impacted.

New evidence is unlikely to change guideline recommendations.

Care of people in primary care

Q – 05 Care and management in primary care

Recommendations derived from this review question

1.3.1 People without a personal history of breast cancer 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[2], 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). [2004]

1.3.2 People who do not meet the criteria for referral should be cared for in primary care by giving standard written information. [2004]

[2] In most cases, this will equate to less than a 3% 10-year risk of breast cancer at age 40 years.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Q – 06 Referral from primary care

1.3.3 People without a personal history of breast cancer 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. [2004]

1.3.4 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). [2004]

1.3.5 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 person is not sufficiently reassured by the standard information provided. [2004]

1.3.6 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). [2004]

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A study[9] aimed to validate the 6-Point Screening Tool to identify low-income women at high risk of familial breast cancer. Scores were compared to genetic counsellors'

recommendations for referral (n = 744) as well as the Referral Screening Tool (RST) (n = 1425) which is a validated instrument. Results indicated that compared to genetic counsellors' recommendations, the 6-Point Screening Tool had low sensitivity but high specificity. Compared to the RST, the 6-Point Screening Tool had high sensitivity and high specificity.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence was identified to support the use of a brief screening tool to identify low income women at high risk of breast cancer and to aid referral decision-making. The guideline does not currently make any recommendations on the use of screening tools during referral from primary care. Instead, the choice to refer someone from primary care is based on personal and family history (see recommendations 1.3.3-1.3.6). Until there is a consistent evidence base in this area, it is unlikely that the recommendations will be affected.

New evidence is unlikely to change guideline recommendations.

Q – 07 Patient education and information

Recommendations derived from this review question

1.3.7 Women who are being referred to secondary care or a specialist genetic clinic should be provided with written information about what happens at this stage. [2004]

1.3.8 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. [2004]

1.3.9 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. **[2004]**

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Care of people in secondary care and specialist genetic clinics

Q – 08 Care and management approach in secondary care

Recommendations derived from this review question

1.4.1 Care of people in secondary care (such as a breast care team, family history clinic or breast clinic) should be undertaken by a multidisciplinary team. It should include the following:

- written protocols for management
- central, standardised resources
- mammographic surveillance available to standard of the national breast screening programmes[3]
- access to surveillance [2013]
- access to a team offering risk-reducing surgery
- standardised written information
- designated/lead clinicians
- a designated contact for primary care
- a designated contact in a specialist genetic clinic
- audit
- clinical trials access
- access to psychological assessment and counselling
- information about support groups and voluntary organisations
- administrative support. [2004]

1.4.2 People who meet the following criteria should be offered secondary care and do not require referral to a specialist genetic clinic:

- 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 a specialist genetic clinic) or a family history pattern is likely to give risks of greater than 3–8% risk in the next 10 years for women aged 40 years, or a lifetime risk of 17% or greater but less than 30%[4]

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). [2004]

1.4.3 People whose risk does not meet the criteria for referral to secondary care (see recommendation 1.3.3) can be referred back to primary care:

- with appropriate information being offered and
- support mechanisms (for example, risk counselling, psychological counselling and risk management advice) need to be identified, and should be offered to people not eligible for referral and/or surveillance on the basis of age or risk level who have ongoing concerns. [2004]

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

- 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) [2004] 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) [2004] or
  - ◊ four relatives diagnosed with breast cancer at any age (at least one must be a first-degree relative). [2004] 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 [2004] or
  - ◊ two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years [2004] or
  - ◊ another ovarian cancer at any age. [2004] or
- Families affected by 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 50 years [2004] or
  - ◊ one first-degree or second-degree relative diagnosed with bilateral cancer and one first or second degree relative diagnosed with breast cancer at younger than an average age of 60 years. [2004] 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 [2004] or
  - ◊ two first-degree or second-degree relatives diagnosed with breast cancer at younger than an average age of 60 years. [2004] or
- A formal risk assessment has given risk estimates of:
  - ◊ a 10% or greater chance of a gene mutation being harboured in the family (see recommendations 1.5.8–1.5.13) [2013] or
  - ◊ a greater than 8% risk of developing breast cancer in the next 10 years [2004] or
  - ◊ a 30% or greater lifetime risk of developing breast cancer. [2004]

1.4.5 Clinicians should seek further advice from a specialist genetics service for families containing any of the following, in addition to breast cancers:

- triple negative breast cancer under the age of 40 years [2013]
- Jewish ancestry [2004]

- sarcoma in a relative younger than age 45 years [2004]
- glioma or childhood adrenal cortical carcinomas [2004]
- complicated patterns of multiple cancers at a young age [2004]
- very strong paternal history (four relatives diagnosed at younger than 60 years of age on the father's side of the family). [2004]

1.4.6 The management of high-risk people may take place in secondary care if they do not want genetic testing or risk-reducing surgery and do not wish to be referred to a specialist genetics service. [2004]

1.4.7 Following initial consultation in secondary care, written information should be provided to reflect the outcomes of the consultation. [2004]

1.4.8 Care of people referred to a specialist genetic clinic should be undertaken by a multi-disciplinary team. In addition to having access to the components found in secondary care, it should also include the following:

- clinical genetic risk assessment
- verification for abdominal malignancies and possible sarcomas. [2004]

[3] National breast screening programmes: England – NHS Breast Screening Programme (NHSBSP); Wales – Breast Test Wales; Northern Ireland – NI Breast Screening Programme.

[4]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 be calculated for the age range 40–49.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Q – 09 Genetic counselling for people with no personal history of breast cancer

Recommendations derived from this review question

1.4.9 Women with no personal history of breast cancer meeting criteria for referral to a specialist genetic clinic should be offered a referral for genetic counselling regarding their risks and options. [2004]

1.4.10 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. [2004]

1.4.11 Predictive genetic testing should not be offered without adequate genetic counselling. [2004]

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

One RCT[10] was identified which assessed the effect of a website providing computer-tailored information and a question prompt sheet to

individuals prior to receiving breast cancer genetic counselling (n=192). Compared to usual care, those receiving the intervention more often shared their agenda, directed the communication and paraphrased the counsellors' words.

The results of a RCT[11] showed that uptake of BRCA1/2 testing was lower following telephone genetic counselling than in-person counselling for women at risk for BRCA1/2 mutations (n=988), although telephone counselling was non-inferior in terms of psychosocial outcomes. Another RCT[12] of participants without newly diagnosed or metastatic cancer (n=669) also found that BRCA1/2 test uptake was lower following telephone genetic counselling compared to in-person counselling. However, telephone counselling was non-inferior to in-person counselling in terms of knowledge, perceived stress and satisfaction.

4-year surveillance summary

A secondary analysis from an RCT[13] (n = 669) examined the predictors of genetic testing in a trial of in-person and telephone-based genetic counselling in women at high risk of developing breast or ovarian cancer. The results of the original trial indicated that participants receiving telephone counselling were significantly less likely to be tested, compared to those receiving in-person counselling. Results from the secondary analysis on the predictors of this effect indicated that women from minority groups receiving telephone counselling were least likely to complete testing.

A one year follow-up[14] to the RCT[11] discussed in the previous (2-year) surveillance was identified. Results indicated that at one year follow-up, telephone counselling was still non-inferior to in-person counselling for all psychosocial outcomes including anxiety, cancer-specific distress, perceived personal control and decisional conflict. Results also indicate that test uptake was significantly lower for telephone counselling compared to in-person counselling.

An RCT[15] (n = 554) examined the patient perceptions of telephone compared to in-person genetic counselling. Participants were women at high risk of developing breast or ovarian cancer. Results indicated that those receiving telephone counselling rated the sessions as significantly more convenient than the women receiving in-person counselling. However, levels of support and emotional recognition were rated significantly lower in the telephone counselling group.

A topic expert highlighted a study[16] (n = 3628) which aimed to identify factors associated with the use of BRCA testing in the US and assess whether delivery of genetic counselling adheres to professional guidelines. The study also measured the impact of genetic counselling on patient-reported outcomes. Participants in the study were women whose clinicians ordered BRCA testing. Results indicated that only 36.8% of the women reported receiving genetic counselling prior to testing and the most common reason for lack of counselling was no clinician referral. For the women who did receive genetic counselling, they demonstrated a significantly greater knowledge and expressed a greater understanding of BRCA mutations. They also had significantly higher satisfaction ratings.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence was identified which compared the effectiveness of genetic counselling via telephone with in-person sessions. In general, results showed that people were less likely to attend genetic testing after telephone counselling compared to in-person sessions. Those receiving telephone counselling were also reported to have received lower levels of support. Currently the guideline recommends that all women referred to a specialist genetic clinic should be offered a referral for genetic counselling however there are no recommendations about methods of delivering counselling. Telephone genetic counselling is not routinely offered in the UK and the majority of the new evidence originates from US studies. Therefore it is unlikely that the new evidence will impact recommendations.

Evidence was highlighted by a topic expert which indicated that in the US only a small proportion of patients are referred to genetic counselling prior to BRCA testing, but no evidence was identified to suggest that this is the case in England. Recommendation 1.4.11 currently states that predictive genetic testing should not be offered without adequate genetic counselling.

New evidence is unlikely to change guideline recommendations.

Genetic testing

Q – 10 Genetic testing for people with a family history but no personal history of breast cancer

Q – 11 Mutation tests

Recommendations derived from these review questions

1.5.1 All eligible people should have access to information on genetic tests aimed at mutation finding. [2004]

1.5.2 Pre-test counselling (preferably two sessions) should be undertaken. [2004]

1.5.3 Discussion of genetic testing (predictive and mutation finding) should be undertaken by a healthcare professional with appropriate training. [2004]

1.5.4 Eligible people 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. [2004]

1.5.5 Tests aimed at mutation finding should first be carried out on an affected family member where possible. [2004]

1.5.6 If possible, 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) (see recommendations 1.5.8–1.5.13). [2004]

1.5.7 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. [2004]

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A cost effectiveness study[17] was identified which aimed to evaluate the long-term cost-effectiveness of BRCA testing in women with epithelial ovarian cancer. Results indicated that BRCA testing of all women with epithelial ovarian cancer was cost-effective, with an incremental cost-effective ratio of £4,339 per quality-adjusted life year. The result was primarily driven by fewer cases of breast cancer and ovarian cancer and associated reductions in mortality.

Topic expert feedback

Topic experts noted that currently the only guidance is for tests of BRCA1, BRCA2 and P53 mutations and that new panel tests have now been developed which include at least a further four genes. It was also suggested that SNP tests should also be used to assess risk.

However, a topic expert also highlighted that new panel tests may lead to the discovery of lower penetrance breast cancer susceptibility loci which may complicate service delivery because options post-testing are less clear. The costs of the panel tests were noted to now be a similar price to BRCA1 and BRCA2 tests.

It was noted that the results of the 100,000 Genomes Project may mean a group of individuals may be found to have the BRCA1 and BRCA2 mutations without a family history of the disease. It was highlighted that this could have a significant impact on service delivery and that the penetrance of mutations ascertained this way will likely be lower, leading to a misleadingly high breast cancer prediction rate.

Impact statement

Evidence was identified to suggest that BRCA testing of all women with epithelial ovarian cancer is a cost-effective strategy. This evidence is based on one study whose sample size and data source are not reported in the abstract, making the validity of the findings unclear. The guideline currently recommends offering genetic testing in specialist genetic clinics to a person with breast or ovarian cancer if their combined BRCA1 and BRCA2 mutation carrier probability is 10% or more (see recommendation 1.5.11). Under this recommendation, the majority of women with ovarian cancer will be referred for BRCA testing therefore it is unlikely that the guideline will be impacted at this point. Until there is further evidence in this area with consistent results, the recommendation will remain unchanged.

Many topic experts noted the increasing popularity of multigene panel tests now available. This information has been passed onto the Diagnostics Assessment Programme at NICE to consider drafting guidance in this area. However, without a defined intervention to assess, such as a specific gene panel product, and because there is a lack of evidence indicating the benefit of testing for other high risk genes in this population, it is not possible to pursue diagnostic guidance further at this time.

New evidence is unlikely to change guideline recommendations.

Q – 12 What is the carrier probability at which genetic testing should be offered to people who are (a) unaffected but with a family history of breast, ovarian or related cancer; (b) Unaffected with a family history and no living relative; (c) affected patients?

Recommendations derived from this review question

1.5.8 Discuss the potential risk and benefits of genetic testing. Include in the discussion the probability of finding a mutation, the implications for the individual and the family, and the implications of either a variant of uncertain significance or a null result (no mutation found). [2013]

1.5.9 Inform families with no clear genetic diagnosis that they can request review in the specialist genetic clinic at a future date. [2013]

1.5.10 Clinical genetics laboratories should record gene variants of uncertain significance and known pathogenic mutations in a searchable electronic database. [2013]

1.5.11 Offer genetic testing in specialist genetic clinics to a relative with a personal history of breast and/or ovarian cancer if that relative has a combined BRCA1 and BRCA2 mutation carrier probability of 10% or more. [2013]

1.5.12 Offer genetic testing in specialist genetic clinics to a person with no personal history of breast or ovarian cancer if their combined BRCA1 and BRCA2 mutation carrier probability is 10% or more and an affected relative is unavailable for testing. [2013]

1.5.13 Offer genetic testing in specialist genetic clinics to a person with breast or ovarian cancer if their combined BRCA1 and BRCA2 mutation carrier probability is 10% or more. [2013]

Surveillance decision

This review question should not be updated.

2-year surveillance summary

Evidence relevant to this review question was used in the update of the NICE guideline on early and locally advanced breast cancer: diagnosis and treatment (CG80) in 2017. See more details on this update decision in the 2-year surveillance review.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No relevant topic expert feedback was identified.

Impact statement

No new evidence was identified in the 4-year surveillance review and there is no impact on the guideline at this time.

New evidence is unlikely to change guideline recommendations.

Q – 13 Does knowing the mutation status of a patient at or soon after cancer diagnosis affect the different cancer treatment options and/or does it usefully inform immediate decisions about risk-reducing options?

Recommendations derived from this review question

1.5.14 Offer people eligible for referral to a specialist genetic clinic a choice of accessing genetic testing during initial management or at any time thereafter. [2013]

1.5.15 Offer fast-track genetic testing (within 4 weeks of a diagnosis of breast cancer) only as part of a clinical trial. [2013]

1.5.16 Discuss the individual needs of the person with the specialist genetics team as part of the multidisciplinary approach to care. [2013]

Surveillance decision

This review question should not be updated.

2-year surveillance summary

A RCT[19] (n=265) assessing the impact of rapid genetic counselling and testing on newly diagnosed breast cancer patients' choice of surgery was identified. The study found no difference between rapid testing and usual care in uptake of direct bilateral mastectomy (BLM) or delayed contralateral prophylactic mastectomy. However, only a minority of patients in the intervention group received DNA test results prior to surgery. Per-protocol analysis indicated that patients who received

test results before surgery opted for direct BLM more often than those who received usual care.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

No relevant topic expert feedback was identified.

Impact statement

There is limited evidence from one study which suggests that rapid genetic counselling and testing influences decisions about risk-reducing surgery.

During development of the original guideline the committee agreed that there was insufficient evidence to say whether knowledge of mutation status before making decisions about risk-reducing mastectomy influenced outcome. There was also no evidence that a delay in genetic testing at diagnosis of breast cancer affected overall survival. As such, no recommendations were made for fast track genetic testing outside the context of a clinical trial. A recommendation for further research in this area was made in order to determine the benefits and harms of creating rapid access to genetic testing, in particular the optimum model for service delivery, clinical and cost effectiveness, uptake and patient experience. Whilst the new evidence suggests genetic testing may usefully inform treatment decisions, further consistent evidence is needed to demonstrate that fast track testing is beneficial before it can be considered for inclusion within CG164.

New evidence is unlikely to change guideline recommendations.

Q – 14 Who should discuss the implications of genetic testing with the patient and when is the most appropriate time for such a discussion to occur?

Recommendations derived from this review question

1.5.17 Offer detailed consultation with a clinical geneticist or genetics counsellor to all those with breast cancer who are offered genetic testing, regardless of the timeframe for testing. [2013]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Surveillance and strategies for early detection of breast cancer

Q – 15 Breast awareness

Recommendations derived from this review question

1.6.1 Women at increased risk of breast cancer should be 'breast aware' in line with Department of Health advice for all women. [2004]

Surveillance decision

This review question should not be updated.

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

An RCT[20] (n = 37) aimed to (1) evaluate the feasibility of Clinical nurse specialist-led (CNS) breast self-examination (BSE) education as part of BRCA surveillance; and (2) to evaluate the effects and feasibility of additional written information leaflets concerning BSE. The participants were women with a BRCA mutation. Participants in both the intervention and control groups were educated about BSE by a CNS, with the intervention group receiving additional written BSE instructions. Follow-up time was 3 months. Results indicated that a significant increase in the self-reported frequency of BSE after CNS-led education was shown. However, authors report that BSE frequencies did not significantly differ between groups. Before the education, the main reason for not performing BSE was that women had felt unable to perform BSE. Patient satisfaction with the CNS-led education was high.

Topic expert feedback

No relevant topic expert feedback was identified.

Impact statement

New evidence was identified to suggest that addition of written information leaflets concerning BSE to CNS-led BSE education had no effect on the frequency of BSE so it is unlikely that the guideline will be impacted. The guideline currently recommends that women at increased risk of breast cancer should be 'breast aware' in line with the Department of Health advice, which includes extensive guidance on how to perform self-examination.

New evidence is unlikely to change guideline recommendations.

Q – 16 What are the specific surveillance needs of women with a family history who have no personal history of breast cancer?

Q – 17 What are the specific surveillance needs of people with a personal history of breast cancer and a familial risk, who have not undergone a risk-reducing bi-lateral-mastectomy?

Recommendations derived from these review questions

1.6.2 Do not routinely offer ultrasound surveillance to women at moderate or high risk of breast cancer but consider it:

- when MRI surveillance would normally be offered but is not suitable (for example, because of claustrophobia)
- when results of mammography or MRI are difficult to interpret. [2013]

1.6.3 Offer annual mammographic surveillance to women:

- aged 40–49 years at moderate risk of breast cancer
- aged 40–59 years at high risk of breast cancer but with a 30% or lower probability of being a BRCA or TP53 carrier

- aged 40–59 years who have not had genetic testing but have a greater than 30% probability of being a *BRCA* carrier
- aged 40–69 years with a known BRCA1 or BRCA2 mutation. [2013]

1.6.4 Offer mammographic surveillance as part of the population screening programme to women:

- aged 50 years and over who have not had genetic testing but have a greater than 30% probability of being a TP53 carrier
- aged 60 years and over at high risk of breast cancer but with a 30% or lower probability of being a BRCA or TP53 carrier
- aged 60 years and over at moderate risk of breast cancer
- aged 60 years and over who have not had genetic testing but have a greater than 30% probability of being a BRCA carrier
- aged 70 years and over with a known BRCA1 or BRCA2 mutation. [2013]

1.6.5 Consider annual mammographic surveillance for women:

- aged 30–39 years at high risk of breast cancer but with a 30% or lower probability of being a BRCA or TP53 carrier
- aged 30–39 years who have not had genetic testing but have a greater than 30% probability of being a BRCA carrier
- aged 30–39 years with a known BRCA1 or BRCA2 mutation
- aged 50–59 years at moderate risk of breast cancer. [2013]

1.6.6 Do not offer mammographic surveillance to women:

- aged 29 years and under
- aged 30–39 years at moderate risk of breast cancer
- aged 30–49 years who have not had genetic testing but have a greater than 30% probability of being a TP53 carrier
- of any age with a known TP53 mutation. [2013]

1.6.7 Offer annual MRI surveillance to women:

- aged 30–49 years who have not had genetic testing but have a greater than 30% probability of being a *BRCA* carrier
- aged 30–49 years with a known *BRCA1* or *BRCA2* mutation
- aged 20–49 years who have not had genetic testing but have a greater than 30% probability of being a *TP53* carrier
- aged 20–49 years with a known *TP53* mutation. [2013]

1.6.8 Consider annual MRI surveillance for women aged 50–69 years with a known TP53 mutation. [2013]

1.6.9 Do not offer MRI to women:

- of any age at moderate risk of breast cancer
- of any age at high risk of breast cancer but with a 30% or lower probability of being a BRCA or TP53 carrier
- aged 20–29 years who have not had genetic testing but have a greater than 30% probability of being a BRCA carrier
- aged 20–29 years with a known BRCA1 or BRCA2 mutation
- aged 50–69 years who have not had genetic testing but have a greater than 30% probability of being a BRCA or a TP53 carrier, unless mammography has shown a dense breast pattern
- aged 50–69 years with a known BRCA1 or BRCA2 mutation, unless mammography has shown a dense breast pattern. [2013]

Also see Summary of recommendations on surveillance for women with no personal history of breast cancer.

1.6.10 Ensure that all women with breast cancer are offered annual mammography for 5 years for follow-up imaging, in line with the NICE guideline on early and locally advanced breast cancer. In conjunction with follow-up, women who remain at high risk of breast cancer and have a family history should receive surveillance as outlined in recommendations 1.6.11–16.15. [2013]

1.6.11 Offer annual mammographic surveillance to all women aged 50–69 years with a personal history of breast cancer who:

- remain at high risk of breast cancer (including those who have a BRCA1 or BRCA2 mutation), and
- do not have a TP53 mutation. [2013]

1.6.12 Offer mammography as part of the population screening programme for all women aged 70 years and over with a personal history of breast cancer who:

- remain at high risk of breast cancer (including those who have a BRCA1 or BRCA2 mutation), and
- do not have a TP53 mutation. [2013]

1.6.13 Offer annual MRI surveillance to all women aged 30–49 years with a personal history of breast cancer who remain at high risk of breast cancer, including those who have a BRCA1 or BRCA2 mutation. [2013]

1.6.14 Do not offer MRI surveillance to any women aged 50 years and over without a TP53 mutation unless mammography has shown a dense breast pattern. [2013]

1.6.15 Consider annual MRI surveillance for women aged 20–69 years with a known TP53 mutation or who have not had a genetic test but have a greater than 30% probability of being a TP53 carrier. [2013]

1.6.16 Ensure that surveillance for people with a personal history of breast cancer who remain at moderate risk of breast cancer is in line with the NICE guideline on early and locally advanced breast cancer. [2013]

1.6.17 Offer support (for example, risk counselling, psychological counselling and risk management advice) to women who have ongoing concerns but are not eligible for surveillance additional to that offered by the national breast screening programmes[5]. [2004, amended 2013]

1.6.18 Before decisions on surveillance are made, discuss and give written information on the benefits and risks of surveillance, including:

- the possibility that mammography might miss a cancer in women with dense breasts and the increased likelihood of further investigations [2013]
- possible over diagnosis
- the risk associated with exposure to radiation
- the possible psychological impact of a recall visit. [2004, amended 2013]

1.6.19 Review eligibility for surveillance if family history changes (for example, if another member of the family develops breast cancer or a mutation is identified). [2013]

1.6.20 At the start of a surveillance programme and when there is a transition or change to the surveillance plan, give women:

- information about the surveillance programme, including details of the tests, how often they will have them and the duration of the programme
- information about the risks and benefits of surveillance
- details of sources of support and further information. [2006, amended 2013]

1.6.21 Ensure that women know and understand the reasons for any changes to the surveillance plan. [2006, amended 2013]

1.6.22 For women under 50 years who are having mammography, use digital mammography at centres providing digital mammography to national breast screening programme standards. [2013]

1.6.23 Ensure that individual strategies are developed for all women having mammographic surveillance and that surveillance is:

- to national breast screening programme standards
- audited
- only undertaken after written information is given about risks and benefits. [2013]

1.6.24 Ensure that MRI surveillance includes MRI of both breasts performed to national breast screening programme standards. [2006, amended 2013]

1.6.25 When women not known to have a genetic mutation are referred to a specialist genetic clinic, offer them assessment of their carrier probability using a carrier probability calculation method with acceptable performance (calibration and discrimination) to determine whether they meet or will meet the criteria for surveillance. (An example of an acceptable method is BOADICEA.) [2013]

1.6.26 Do not offer surveillance to women who have undergone a bilateral mastectomy. [2013]

[5]National breast screening programmes: England – NHS Breast Screening Programme (NHSBSP); Wales – Breast Test Wales; Northern Ireland – NI Breast Screening Programme.

Surveillance decision

These review questions should not be updated.

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A comparative study[21] (n = 1951) investigated the additional contribution of mammography to screening accuracy in BRCA mutation carriers screened with MRI at different ages. Results indicated that in BRCA mutation carriers of all ages, adding mammography to MRI did not significantly increase screening sensitivity. However, in women younger than 40 years with a BRCA2 mutation, additional mammography increased sensitivity by 34.5%, and that approximately one third of the cancers detected were identified by mammography only. However, a review of the full text indicates that the increase in sensitivity that the addition of mammography caused was non-significant.

A comparative study[22] (n = 559) evaluated the breast cancer screening efficacy of mammography, ultrasound, and MRI in high risk women either with a BRCA mutation or a high familial risk. Results indicated that the sensitivity of MRI was significantly higher than that of mammography and ultrasound. Age, mutation status, and breast density had no influence on the sensitivity of MRI and did not affect the superiority of MRI over mammography or ultrasound.

Topic expert feedback

It was highlighted that some patient organisations have reported an ongoing issue with screening of people at moderate risk of breast cancer, with ongoing confusion about what should be happening in this area.

There was also concern about the strength of the evidence relating to moderate risk women. It was suggested that this could mean that the recommendations for this group will not be implemented resulting in inequitable service provision.

Some topic experts noted that ultrasound should be considered for women with dense breast tissue who are not eligible for MRI.

It was also suggested that women aged 35-39 with an enhanced familial risk of breast cancer should be considered for mammographic

screening. An ongoing trial (FH02 study) was highlighted which assesses this area.

A potential equality issue was raised whereby surveillance may be implemented in an inconsistent way, depending on funding in the area.

Impact statement

New evidence was identified which suggested that for women under 40 years with a BRCA2 mutation, the addition of mammographic surveillance to MRI increased the sensitivity of the screen, with a third of breast cancers in this group being identified by mammography only. The guideline currently recommends considering annual mammographic surveillance for women aged 30-39 with a known BRCA mutation (see recommendation 1.6.5). However, this evidence is not in line with recommendation 1.6.6, which advises not to offer mammographic surveillance for women aged 29 years and under. This is unlikely to affect the guideline because the change in sensitivity caused by additional mammographic surveillance was non-significant.

There was new evidence to suggest that MRI screening is superior to mammography and ultrasound in detecting cancers in high risk women (either with a BRCA mutation or with a family history).The guideline currently recommends MRI surveillance for women but only if they are any of the following: aged 30-49 and have not had genetic testing but have a greater than 30% probability of being a BRCA carrier; aged 30–49 years with a known BRCA1 or BRCA2 mutation; aged 20–49 years who have not had genetic testing but have a greater than 30% probability of being a TP53 carrier; aged 20–49 or 50-69 years with a known TP53 mutation (see recommendations 1.6.7-1.6.8).

The new evidence is based on one study and it is unclear from the abstract what age group was included in the study. Therefore before further evidence is available which can confirm these findings, it is unlikely that the guideline will be affected.

Clinical feedback indicated that there they may be issues regarding the implementation of the recommendations for surveillance of moderate risk women. However, no further evidence was provided which would impact on the current recommendations for women at moderate risk of breast cancer which state: offer annual mammographic surveillance to women aged 40-49 years; consider annual mammographic surveillance for women aged 50-59 years; and offer mammographic surveillance as part of the population screening programme to women aged 60 years and over.

Topic experts highlighted a need for ultrasound to be considered in women with dense breasts who are not eligible for MRI. No evidence was identified in this area so it is unlikely that the recommendations will change, however we will log this issue and review the area again at the next surveillance point.

An ongoing trial was highlighted which examines the need for mammographic surveillance of women aged 35-39 years at moderate risk of breast cancer. The guideline currently recommends considering annual mammographic surveillance for women aged 50-59 years at moderate risk. The trial has been added to our event tracker and the impact on CG164 will be reviewed once the main results have been published.

New evidence is unlikely to change guideline recommendations.

Q – 18 **Risk reduction and treatment strategies**:

- **Risks associated with family history**
- **Menstrual and reproductive factors**
- **Reproductive and fertility issues**
- **Sub-fertility and induced ovulation**
- **Hormonal contraceptives**
- **Breast feeding**
- **Hormone replacement therapy (HRT)**
- **Alcohol consumption**
- **Smoking**
- **Weight and physical activity**

Recommendations derived from this review question

1.7.1 People should be provided with standardised written information about risk, including age as a risk factor. [2004]

1.7.2 Modifiable risk factors should be discussed on an individual basis in the relevant care setting. [2004]

1.7.3 Healthcare professionals should be able to provide information on the effects of hormonal and reproductive factors on breast cancer risk. [2004]

1.7.4 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. [2004]

1.7.5 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. [2004]

1.7.6 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. [2004]

1.7.7 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. [2004]

1.7.8 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. [2004]

1.7.9 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. [2004]

1.7.10 Women with a family history of breast cancer who are considering taking, or already taking, HRT should be informed of the increase in breast cancer risk with type and duration of HRT. [2004]

1.7.11 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). [2004]

1.7.12 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. [2004]

1.7.13 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 moderate or high risk (see also recommendations 1.7.53 and 1.7.54). [2004]

1.7.14 Alternatives to HRT should be considered for specific symptoms such as osteoporosis or menopausal symptoms (see also recommendations 1.7.53 and 1.7.54). [2004]

1.7.15 Consideration should be given to the type of HRT if it is being considered for use in conjunction with risk-reducing gynaecological surgery. [2004]

1.7.16 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. [2004]

1.7.17 Women should be advised not to smoke, in line with current health advice. [2004]

1.7.18 Women should be advised on the probable increased postmenopausal risk of breast cancer from being overweight. [2004]

1.7.19 Women should be advised about the potential benefits of physical exercise on breast cancer risk. [2004]

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A meta-analysis[24] of 8 cohort studies and 4 case-control studies (n = 358,955) examined the relationship of dietary and serum linoleic acid level with breast cancer risk in women. Results indicated that there were no significant associations between breast cancer risk and dietary linoleic acid intake or serum linoleic acid level.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

There was new evidence which suggested that there was no significant associations between breast cancer risk and dietary linoleic acid intake or serum linoleic acid level. The guideline does not currently make any recommendations on this and therefore it is unlikely that the new evidence will impact recommendations.

New evidence is unlikely to change guideline recommendations.

Q – 19 What is the effectiveness of chemoprevention for the reduction of the incidence of breast cancer in people with a family history of breast, ovarian or related (prostate/pancreatic) cancer?

Recommendations derived from this review question

1.7.20 Healthcare professionals within secondary care or specialist genetic clinics should discuss the absolute benefits and risks of options for chemoprevention with women at high or moderate risk of breast cancer. Discussion, using a decision aid, should include the following to promote shared decision-making and informed preferences:

- the reduced risk of invasive breast cancer
- the lack of effect on mortality
- the side effects of the different options
- alternative approaches, such as surveillance alone and, for women at high risk, risk-reducing surgery.

Women should all be given information in an accessible format. [2013, amended 2017]

1.7.21 Offer tamoxifen[6] for 5 years to premenopausal women at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer. [2017]

1.7.22 Offer anastrozole[7][8] for 5 years to postmenopausal women at high risk of breast cancer unless they have severe osteoporosis. [2017]

1.7.23 For postmenopausal women at high risk of breast cancer who have severe osteoporosis or do not wish to take anastrozole:

- offer tamoxifen[6] for 5 years if they have no history or increased risk of thromboembolic disease or endometrial cancer, or
- consider raloxifene[9] for 5 years for women with a uterus if they have no history or increased risk of thromboembolic disease and do not wish to take tamoxifen. [2017]

1.7.24 Do not offer chemoprevention to women who were at high risk of breast cancer but have had bilateral risk-reducing mastectomy. [2013, amended 2017]

1.7.25 Consider tamoxifen[6] for 5 years for premenopausal women at moderate risk of breast cancer, unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer. [2017]

1.7.26 Consider anastrozole[7][8] for 5 years for postmenopausal women at moderate risk of breast cancer unless they have severe osteoporosis. [2017]

1.7.27 For postmenopausal women at moderate risk of breast cancer who have severe osteoporosis or do not wish to take anastrozole:

- consider tamoxifen[6] for 5 years if they have no history or increased risk of thromboembolic disease or endometrial cancer, or
- consider raloxifene[9] for 5 years for women with a uterus if they have no history or increased risk of thromboembolic disease and do not wish to take tamoxifen. [2017]

1.7.28 Do not continue chemoprevention beyond 5 years in women with no personal history of breast cancer. [2013, amended 2017]

1.7.29 Inform women that they should stop tamoxifen[6] at least:

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

[6] At the time of publication (March 2017), tamoxifen did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[7] At the time of publication (March 2017), anastrozole did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

[8] The summary of product characteristics for anastrozole indicates that women with osteoporosis or at risk of osteoporosis should have their bone mineral density assessed when starting treatment and then at regular intervals. Treatment or prophylaxis for osteoporosis should be started when needed and carefully monitored.

[9] At the time of publication (March 2017), raloxifene did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

Surveillance decision

This review question should not be updated.

2-year surveillance summary

These review questions were updated in 2017. Evidence identified in 2-year surveillance review was available for consideration in the update.

4-year surveillance summary

A meta-analysis[25] of 4 studies (n not reported) examined whether adjuvant tamoxifen treatment for breast cancer is associated with reduced contralateral breast cancer risk in patients with the BRCA mutation. Results indicated that tamoxifen was significantly associated with the reduced risk of contralateral breast cancer among BRCA mutation carriers.

Topic expert feedback

A topic expert noted that there is a variation in the prescribing of tamoxifen and raloxifene across hospitals, particularly for women at moderate risk.

Impact statement

New evidence was identified to suggest that treatment with tamoxifen was significantly associated with the reduced risk of contralateral breast cancer. This is supportive of recommendations 1.7.21, 1.7.23, 1.7.25 and 1.7.27 which cover chemo-preventative treatment with tamoxifen in various groups.

It was noted that there may be some variation in the prescribing of tamoxifen and raloxifene, however we did not find any evidence in this area. This issue has been logged for consideration again at the next surveillance point.

New evidence is unlikely to change guideline recommendations.

Q – 20 Risk-reducing mastectomy for women with no personal history of breast cancer

Recommendations derived from this review question

1.7.30 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. [2004]

1.7.31 Bilateral mastectomy should be raised as a risk-reducing strategy option with all women at high risk. [2004]

1.7.32 Women considering bilateral risk-reducing mastectomy should have genetic counselling in a specialist cancer genetic clinic before a decision is made. [2004]

1.7.33 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). [2004]

1.7.34 Family history should be verified where no mutation has been identified before bilateral risk-reducing mastectomy. [2004]

1.7.35 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with bilateral risk-reducing mastectomy. [2004]

1.7.36 Pre-operative counselling about psychosocial and sexual consequences of bilateral risk-reducing mastectomy should be undertaken. [2004]

1.7.37 The possibility of breast cancer being diagnosed histologically following a risk-reducing mastectomy should be discussed pre-operatively. [2004]

1.7.38 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. [2004]

1.7.39 A surgical team with specialist oncoplastic/breast reconstructive skills should carry out risk-reducing mastectomy and/or reconstruction. [2004]

1.7.40 Women considering bilateral risk-reducing mastectomy should be offered access to support groups and/or women who have undergone the procedure. [2004]

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

A study[26] was identified which found that there was a reduced risk of death from breast cancer following contralateral mastectomy compared with unilateral mastectomy in women with a BRCA1 or 2 mutation and a family history of breast cancer (n=390).

4-year surveillance summary

A meta-analysis[27] of 4 studies (n = 2635) aimed to clarify the role of bilateral risk-reducing mastectomy (BRRM) in reducing breast cancer risk in women with BRCA mutations. Results indicated that there was a significant risk reduction of breast cancer incidence in BRCA mutation carriers receiving BRRM.

A meta-analysis[28] of 15 studies (n not reported) aimed to investigate the effectiveness of prophylactic surgeries implemented in women with a BRCA mutation. The results indicated that bilateral prophylactic mastectomy (BPM) was associated with a decreased breast cancer risk in BRCA mutation carriers. Contralateral prophylactic mastectomy (CPM) was found to significantly decrease contralateral breast cancer incidence in BRCA mutation carriers. All-cause mortality was found to be significantly lower for patients who underwent CPM. The association between all-cause mortality and BPM was not significant.

A systematic review[29] of 22 studies (n not reported) examined the effect of BPM on quality of life in women at high risk of developing breast cancer. Results indicated that post-BPM, patients were satisfied with the outcomes and report high psychosocial well-being and positive body image. The authors report that sexual well-being and somatosensory function are the most negatively affected.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence was identified which suggests that contralateral and bilateral mastectomy reduces the risk of death and reduces the risk of breast cancer. Further evidence was found to suggest that women undergoing bilateral mastectomy were satisfied with the outcome and reported high psychosocial well-being. The new evidence is in line with the guideline which currently recommends bilateral mastectomy as a risk-reducing strategy option for all women at high risk of breast cancer.

New evidence is unlikely to change guideline recommendations.

Q – 21 Risk-reducing oophorectomy for women with no personal history of breast cancer

Recommendations derived from this review question

1.7.41 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. [2004]

1.7.42 Information about bilateral oophorectomy as a potential risk-reducing strategy should be made available to women who are classified as high risk. [2004]

1.7.43 Family history should be verified where no mutation has been identified before bilateral risk-reducing oophorectomy. [2004]

1.7.44 Where no family history verification is possible, agreement by a multidisciplinary team should be sought before proceeding with bilateral risk-reducing oophorectomy. [2004]

1.7.45 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. [2004]

1.7.46 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. [2004]

1.7.47 The effects of early menopause should be discussed with any woman considering risk-reducing bilateral oophorectomy. [2004]

1.7.48 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. [2004]

1.7.49 Women considering risk-reducing bilateral oophorectomy should have access to support groups and/or women who have undergone the procedure. [2004]

1.7.50 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. [2004]

1.7.51 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. [2004]

1.7.52 Women undergoing bilateral risk-reducing oophorectomy should have their fallopian tubes removed as well. [2004]

Surveillance decision

This section of the guideline should not be updated.

2-year surveillance summary

A prospective study[30] was identified which found that prophylactic oophorectomy reduced the risk of ovarian, fallopian tube or peritoneal cancer in women with a BRCA1 or BRCA2 mutation (n=5783).

4-year surveillance summary

A meta-analysis[28] of 15 studies (n not reported) aimed to investigate the effectiveness of prophylactic surgeries implemented in women with a BRCA mutation. The results indicated that prophylactic bilateral salpingo-oophorectomy (PBSO) was associated with a decreased breast cancer risk in BRCA mutation carriers. PBSO was found to be associated with significantly lower all-cause mortality in BRCA mutation carriers both with and without cancer.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

The new evidence is consistent with the current guideline recommendations for bilateral oophorectomy as a potential risk-reducing strategy for women who are classified as high risk.

New evidence is unlikely to change guideline recommendations.

Q – 22 What are the risks and benefits of HRT for women under the age of 50, with a BRCA1 or BRCA2 mutation who have undergone a bilateral salpingo-oophorectomy?

Recommendations derived from this review question

1.7.53 When women with no personal history of breast cancer have either a BRCA1 or BRCA2 mutation or a family history of breast cancer and they have had a bilateral salpingo-oophorectomy before their natural menopause, offer them:

- combined HRT if they have a uterus
- oestrogen-only HRT if they don't have a uterus

up until the time they would have expected natural menopause (average age for natural menopause is 51–52 years). [2013]

1.7.54 Manage menopausal symptoms occurring when HRT is stopped in the same way as symptoms of natural menopause. [2013]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Q – 23 What level of risk indicates that risk reducing surgery is a viable option?

Recommendations derived from this review question

1.7.55 Refer women with a personal history of breast cancer who wish to consider risk-reducing surgery for appropriate genetic and psychological counselling before surgery. [2013]

1.7.56 Discuss the risks and benefits of risk-reducing mastectomy with women with a known or suspected BRCA1, BRCA2 or TP53 mutation. [2013]

1.7.57 For a woman considering risk-reducing mastectomy, include in the discussion of risks and benefits:

- the likely prognosis of their breast cancer, including their risk of developing a distal recurrence of their previous breast cancer
- a clear quantification of the risk of developing breast cancer in the other breast

- the potential negative impact of mastectomy on body image and sexuality
- the very different appearance and feel of the breasts after reconstructive surgery
- the potential benefits of reducing the risk in the other breast and relieving the anxiety about developing breast cancer. [2013]

1.7.58 Give all women considering a risk-reducing mastectomy the opportunity to discuss their options for breast reconstruction (immediate and delayed) with a member of a surgical team with specialist skills in oncoplastic surgery or breast reconstruction. [2013]

1.7.59 Ensure that risk-reducing mastectomy and breast reconstruction are carried out by a surgical team with specialist skills in oncoplastic surgery and breast reconstruction. [2013]

1.7.60 Offer women who have BRCA1, BRCA2 or TP53 mutations but who decide against risk-reducing mastectomy, surveillance according to their level of risk. [2013]

1.7.61 Discuss the risks and benefits of risk-reducing bilateral salpingo-oophorectomy with women with a known or suspected BRCA1, BRCA2 or TP53 mutation. Include in the discussion the positive effects of reducing the risk of breast and ovarian cancer and the negative effects of a surgically induced menopause. [2013]

1.7.62 Defer risk-reducing bilateral salpingo-oophorectomy until women have completed their family. [2013]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Q – 24 What are the factors that indicate that offering risk reducing surgery is not appropriate?

Recommendations derived from this review question

1.7.63 Do not offer risk-reducing surgery to people with comorbidities that would considerably increase the risks of surgery. [2013]

1.7.64 Do not offer risk-reducing surgery to people who have a limited life expectancy from their cancer or other conditions. [2013]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Q – 25 What is the effectiveness of mastectomy compared with breast conserving surgery plus radiotherapy for people with newly diagnosed breast cancer or high grade ductal carcinoma in situ (DCIS) with a TP53 mutation or at high risk of TP53 mutation?

Recommendations derived from this review question

1.7.65 When a person has invasive breast cancer or ductal carcinoma in situ and is known to have a TP53 mutation or a 30% probability of a TP53 mutation:

- inform them of all the possible treatment options
- make sure they know about the uncertainties associated with these treatment options
- inform them of the risks associated with each treatment (for example, the risk of recurrence, the risk of new primary breast cancer and the risks of malignancy associated with radiotherapy and chemotherapy). [2013]

1.7.66 Offer people with invasive breast cancer or ductal carcinoma in situ and a 30% probability of a TP53 mutation, genetic testing to help determine their treatment options. [2013]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Editorial and factual corrections identified during surveillance

There are no editorial or factual corrections to make.

Research recommendations

Prioritised research recommendations

At 4-year and 8-year surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. We may then propose to remove research recommendations from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full versions of the guideline. See NICE's research recommendations process and methods guide 2015 for more information.

These research recommendations were deemed priority areas for research by the Guideline Committee; therefore, at this 4-year surveillance review time point a decision will be taken on whether to retain the research recommendations or stand them down.

We applied the following approach:

- New evidence relevant to the research recommendation was found and an update of the related review question is planned.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database. If needed, a new research recommendation may be made as part of the update process.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.
  - The research recommendation will be retained because there is evidence of research activity in this area.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database because further research is unlikely to impact on the guideline.
- Ongoing research relevant to the research recommendation was found.
  - The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.
- No new evidence relevant to the research recommendation was found and no ongoing studies were identified.
  - The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.
- The research recommendation would be answered by a study design that was not included in the search (usually systematic reviews or randomised controlled trials).
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.
- The new research recommendation was made during a recent update of the guideline.
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

RR – 01 **Further research is recommended into developing and validating models for calculating carrier probability, which incorporate additional data, such as the molecular pathology of tumours and the prevalence of mutations in different ethnic groups.**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 02 **Research is recommended to determine the benefits and harms of creating rapid access to genetic testing for people with newly diagnosed breast cancer. This research should address the optimum model for service delivery and organisation, the clinical and cost effectiveness of such a change, uptake outcomes and patients' experience.**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

A RCT[19] was identified that assessed the impact of rapid genetic counselling and testing on newly diagnosed breast cancer patients' choice of surgery. The study found no difference between rapid testing and usual care in uptake of direct bilateral mastectomy (BLM) and delayed contralateral prophylactic mastectomy.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 03 **Research is recommended to establish the risk and benefits of MRI surveillance compared with mammography in women over 50 years with a personal history of breast cancer. Studies should include sub-analysis for breast density.**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

RR – 04 **What is the clinical and cost effectiveness of aromatase inhibitors (particularly exemestane and letrozole) compared with tamoxifen and raloxifene for reducing the incidence of breast cancer in women with a family history of breast or ovarian cancer?**

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

RR – 05 Further research is recommended to compare psychosocial and clinical outcomes in women who choose and women who do not choose to have risk-reducing surgery.

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

RR – 06 What is the prevalence of *BRCA1* mutations in unselected basal phenotype breast cancer compared with unselected triple negative breast cancer?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

Other research recommendations

The following research recommendations were not deemed as priority areas for research by the guideline committee.

RR – 07 Research is recommended as part of a trial of fast track genetic testing to determine:

- **which members of the multidisciplinary team should/could discuss fast track testing with people with newly diagnosed breast cancer**
- **the best way of providing information about fast track genetic testing to people with newly diagnosed breast cancer**
- **the psychosocial impact of receiving information about genetic testing within 4 weeks of a diagnosis of breast cancer**
- **the short, medium and long-term psychosocial impact of undergoing fast track genetic testing.**

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 08 Research is recommended to assess the benefit of MRI surveillance in terms of mortality of all ages for people with a personal history of breast cancer.

New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

RR – 09 Prospective and retrospective international collaborative studies are recommended to assess the risks and benefits of radiotherapy and chemotherapy for people with a TP53 mutation.

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

This research recommendation will be considered again at the next surveillance point.

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