

Costing report

Familial breast cancer

Published: June 2013

<http://guidance.nice.org.uk/CG164>

Following a review of the guideline in 2017, the costing tools remain valid to support the implementation of the guideline

This costing report accompanies the clinical guideline: 'Familial breast cancer: classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer' (available online at <http://guidance.nice.org.uk/CG164>).

Issue date: June 2013

This report is written in the following context

This report represents the view of NICE, which was arrived at after careful consideration of the available data and through consulting with healthcare professionals. It should be read in conjunction with the NICE guideline. The report and template are implementation tools and focus on the recommendations that were considered to have a significant impact on national resource utilisation.

The cost and activity assessments in the report are estimates based on a number of assumptions. They provide an indication of the likely impact and are not absolute figures. Assumptions used in the report are based on assessment of the national average. Local practice may be different from this, and the template can be amended to reflect local practice.

Implementation of this report is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this costing tool should be interpreted in a way that would be inconsistent with compliance with those duties.

National Institute for Health and Care Excellence

Level 1A
City Tower
Piccadilly Plaza
Manchester M1 4BT

www.nice.org.uk

© National Institute for Health and Care Excellence, 2013. All rights reserved. This material may be freely reproduced for educational and not-for-profit purposes. No reproduction by or for commercial organisations, or for commercial purposes, is allowed without the express written permission of NICE.

Contents

Executive summary.....	4
<i>Significant resource-impact recommendations</i>	4
<i>Net resource impact</i>	4
<i>Local costing template</i>	7
1 Introduction.....	8
1.1 <i>Supporting implementation</i>	8
1.2 <i>What is the aim of this report?</i>	8
1.3 <i>Epidemiology of familial breast cancer</i>	9
1.4 <i>Current service provision</i>	9
2 Costing methodology.....	12
2.1 <i>Process</i>	12
2.2 <i>Scope of the cost-impact analysis</i>	12
2.3 <i>General assumptions made</i>	15
2.4 <i>Basis of unit costs</i>	16
3 Significant resource-impact recommendations.....	17
3.1 <i>Carrier probability at which genetic testing should be offered</i>	17
3.2 <i>Annual surveillance for women with a personal history of breast cancer</i>	22
3.3 <i>Chemoprevention</i>	24
3.4 <i>Benefits and savings</i>	31
4 Sensitivity analysis	33
4.1 <i>Methodology</i>	33
4.2 <i>Impact of sensitivity analysis on costs</i>	34
5 Impact of guidance for commissioners	35
6 Conclusion.....	36
6.1 <i>Total cost per 100,000 for England</i>	36
6.2 <i>Next steps</i>	37
Appendix A. Approach to costing guidelines.....	38
Appendix B. Results of sensitivity analysis	39
Appendix C. References	40

Executive summary

This costing report looks at the resource impact of implementing the NICE guideline 'Familial breast cancer' (updated in 2013) in England.

The costing method adopted is outlined in appendix A; it uses the most accurate data available, was produced in conjunction with key clinicians, and reviewed by clinical and financial professionals.

Significant¹ resource-impact recommendations

This report focuses on the recommendations that are considered to have the greatest resource impact, and therefore require the most additional resources to implement or can potentially generate the biggest savings. They are:

- Carrier probability at which genetic testing should be offered (recommendations 1.5.11 and 1.5.12).
- Chemoprevention for women with no personal history of breast cancer (recommendations 1.7.21, 1.7.22 and 1.7.23).

Net resource impact

It is anticipated that the lower carrier probability of 10% (currently 20%) at which genetic testing should be offered is likely to result in additional costs. The recommendations on chemoprevention may result in additional costs, but these costs may be partly offset by savings from preventing breast cancer. The annual change in resource use arising from implementing the recommendations considered in the costing analysis is summarised below.

¹ The following impacts have been defined as significant:

- where the number of people affected by the guidance recommendations is estimated to be over 300 (equivalent to 1 patient per 170,000; in practice, smaller populations may have no patients or possibly more than 1, particularly if it is a disease that runs in families and there is a cluster in 1 area)
- where initial costing work indicates that the national cost is more than £1 million (equivalent to £2000 per 100,000 population).

Summary of the resource impact per 100,000 population

	Current cost (£000s)	Proposed cost (£000s)	Change in cost (£000s)
Genetic testing	5.3	10.0	4.7
Chemoprevention cost ¹	0	0.2	0.2
Total	5.3	10.2	4.9
¹ Because of the low incidence of familial breast cancer, a population size of 100,000 would not show potential savings from chemoprevention. For some larger populations (including at a national level) a saving would be shown in the costing template.			

Recommendations that may have a resource impact at a local level

Depending on local practice, the following recommendations may have a resource impact at a local level:

- 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 (recommendation 1.6.11).
- 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 (recommendation 1.6.13).

The timeframe for implementation may vary for each element of the guidance, particularly in relation to access to MRI scanning, in which there is wide variation in practice. Administration of chemoprevention may not be costly to implement. However difficulty may lie with discussing and agreeing chemoprevention with healthy women at increased risk of developing breast cancer, and prescribing drugs outside their UK marketing authorisation. Implementing the guidance may mean an increase in the number of genetic tests carried out. It is anticipated that there is sufficient capacity available at the specialist centres for genetic testing.

Benefits and savings

Implementing the clinical guideline may result in the following savings and benefits:

- There are benefits to genetic testing, whether a person receives a positive or negative result. The potential benefits of a negative result include giving people a sense of relief and avoiding costs for preventative surveillance, tests or surgery. A positive result can bring relief from uncertainty and allow people to make informed decisions about their future, including taking steps to reduce their cancer risk, which could lead to avoiding costly treatments.
- The recommendations on chemoprevention could reduce the number of women at high risk who go on to develop breast cancer. This is likely to result in savings in costs associated with surgery, radiotherapy, chemotherapy and drug administration. It is estimated that treatment costs for an invasive breast cancer are around £12,700 in total per person over a 12-month period.
- The recommendations on annual surveillance for people with a personal history of breast cancer (recommendations 1.6.11 and 1.6.13) would make practice more equitable. Expert opinion suggests that currently annual surveillance is mainly offered to unaffected women who are at high risk. Women with a personal history may be offered mammography as part of the population screening programme (for unaffected women without a family history), which is every 3 years.
- Early detection could prevent more serious metastatic cancers that may have treatment costs of around £25,000 (these costs include chemotherapy with trastuzumab [herceptin], surgery, drugs to prevent infection, skeletal-related events and pain reduction).
- For women who take hormone replacement therapy (HRT) in line with recommendation 1.7.53, there may be some savings arising from fewer cases of osteoporosis, fewer GP visits and lower incidence of

cardiovascular disease because of the protective effects of HRT. Examples of costs that could be avoided are:

- Weighted average cost for an admission to hospital relating to a cardiovascular disease event is £4,574 (NICE clinical guideline 67).
- The cost of osteoporotic fragility fractures ranges from £2,381 (wrist) to £6,816 (hip) (NICE technology appraisal guidance 160 and 161).

Local costing template

The costing template produced to support this guideline enables organisations in England, Wales and Northern Ireland to estimate the impact locally and replace variables with ones that depict the current local position. A sample calculation using this template showed that additional costs of around £4,900 (relating to genetic testing and chemoprevention) could be incurred for a population of 100,000.

1 Introduction

1.1 *Supporting implementation*

1.1.1 The NICE clinical guideline on familial breast cancer is supported by the following implementation tools available on our website www.nice.org.uk/guidance/CG164:

- costing tools
 - a national costing report; this document
 - a local costing template; a spreadsheet that can be used to estimate the local cost of implementation
- a behind the evidence podcast (and transcript) – aimed at the changes for genetics services / counsellors
- a surveillance table as a standalone tool
- a baseline assessment tool

Please note audit support is provided via current national audits.

1.2 *What is the aim of this report?*

1.2.1 This report provides estimates of the cost per 100,000 population arising from implementation of guidance on familial breast cancer in England. These estimates are based on assumptions made about current practice and predictions of how current practice might change following implementation.

1.2.2 The focus of the costing work is on those recommendations that are new and those that have been updated since publication of NICE clinical guideline 41, and are likely to have a significant cost impact. In addition to this, the costing tools have looked at areas highlighted by Guideline Development Group (GDG) members for which implementation of previous NICE guidance on familial breast cancer has been inconsistent.

- 1.2.3 This report aims to help organisations plan for the financial implications of implementing NICE guidance.
- 1.2.4 This report does not reproduce the NICE guideline on familial breast cancer and should be read in conjunction with it (see www.nice.org.uk/guidance/CG164).
- 1.2.5 The costing template that accompanies this report is designed to help those assessing the resource impact at a local level in England, Wales or Northern Ireland.

1.3 *Epidemiology of familial breast cancer*

- 1.3.1 Familial breast cancer typically occurs in people with an unusually high number of family members affected by breast, ovarian or a related cancer. If more cases of breast, ovarian or a related cancer are seen in a family than would be expected by chance alone, this can be a sign that genes have caused or contributed to its development. A small proportion of familial breast cancers may be caused by a mutation in genes that predispose people to developing cancers. About 5% of all breast cancers arise from a mutation in a high-penetrance breast cancer-predisposing gene such as *BRCA1*, *BRCA2* or *TP53* (Antoniou et al. 2003). Inherited *BRCA1* and *BRCA2* mutations also account for 10–15% of ovarian cancers (Campeau et al. 2008).
- 1.3.2 Based on UK incidence data, a woman aged 20 who has no affected relatives has a 7.8% probability of developing breast cancer by the age of 80; with 1 affected relative this probability rises to 13.3% and with 2 affected relatives to 21.1% (Collaborative Group on Hormonal Factors in Breast Cancer 2001).

1.4 *Current service provision*

Genetic testing

- 1.4.1 Expert opinion suggests that implementation of NICE clinical guideline 41 has been inconsistent. Genetic testing for *BRCA1* and *BRCA2* mutations in people with no personal history of breast cancer is still largely driven by the finding of a *BRCA1* or *BRCA2* mutation in a family member with breast or ovarian cancer. In many but not all genetic testing centres, the threshold for testing has decreased from a 20% likelihood of *BRCA1* or *BRCA2* mutation to 10% because high throughput and more rapid testing are available.
- 1.4.2 Implementing the guidance is likely to increase the number of people offered genetic testing. This is because of the lower probability thresholds at which testing is recommended – from a 20% to a 10% likelihood of being a *BRCA1/2* carrier (recommendation 1.5.11), and extending tests to unaffected relatives (if an affected relative is unavailable for testing – recommendation 1.5.12).

Chemoprevention

- 1.4.3 Chemoprevention prevents breast cancer by using hormone therapy to interfere with oestrogen's ability to stimulate the growth of breast cancer cells. Although chemoprevention was investigated in CG41, no recommendations were made on this topic. Since then, 2 trials reviewed for CG41 have published updated results with longer follow-up times. For women at high risk of breast cancer, the evidence of benefit from chemoprevention is sufficiently strong to outweigh the potential harms of side effects. The new recommendations on chemoprevention for women with no personal history of breast cancer (recommendations 1.7.21, 1.7.22 and 1.7.23) are likely to lead to a significant change in practice. However there is a high level of uncertainty about initial prescribing rates and the uptake of chemoprevention in women with no personal history of breast cancer (Keogh et al. 2009).

Surveillance

- 1.4.4 All women aged 50-70 years are invited for breast screening every 3 years as part of the NHS Breast Screening programme. The age range is currently being extended to 47-73 years. For women with no personal history of breast cancer but who are at moderate to high risk, surveillance may take place annually. It is not anticipated that implementing the updated recommendations on surveillance for this group would result in a significant change in practice.
- 1.4.5 At present, women with a personal history of breast cancer are offered mammographic surveillance; however practice varies as to the frequency. For this group mammography may be offered annually or biennially for between 3 and 5 years and some for longer than this (National Collaborating Centre for Cancer 2013). It has been shown that overall mammography has a lower performance for women with a personal history of breast cancer than for women with no personal history. MRI has been shown to be more sensitive than mammography, especially in high-risk populations such as people with a *BRCA1/2* mutation who are aged 30–49 years (Duffy et al. 2010).
- 1.4.6 Implementing the recommendation on annual MRI surveillance for women aged 30–49 years with a personal history of breast cancer (recommendation 1.6.13) may increase activity at MRI centres and increase costs. However because of wide variations in practice (as highlighted in the GDG survey – see NICE guideline p47), this would need to be assessed locally.
- 1.4.7 For women aged 50–69 years with a personal history of breast cancer, there may be also be a change in the numbers who are seen annually for mammographic surveillance (recommendation 1.6.11). Practice is likely to vary; any changes to practice can be assessed using the costing template.

2 Costing methodology

2.1 *Process*

- 2.1.1 We use a structured approach for costing clinical guidelines (see appendix A).
- 2.1.2 We have to make assumptions in the costing model. These are tested for reasonableness with members of the GDG and key clinical practitioners in the NHS.
- 2.1.3 Local users can assess local cost impact, using the costing template as a starting point, and update assumptions to reflect local circumstances.

2.2 *Scope of the cost-impact analysis*

- 2.2.1 The guideline offers best practice advice on familial breast cancer.
- 2.2.2 The guidance does not cover:
 - children and young people (under 18 years)
 - men, except for the consideration of risk thresholds for genetic testing.

Therefore, these issues are outside the scope of the costing work.

- 2.2.3 We worked with the GDG and other professionals to identify the recommendations that would have the most significant resource impact (see table 1). Costing work has focused on these recommendations.

Table 1 Recommendations with a significant resource impact

Recommendation	Recommendation number	Guideline key priority?
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 <i>BRCA1</i> and <i>BRCA2</i> mutation carrier probability of 10% or more. [new 2013]	1.5.11	✓
Offer genetic testing in specialist genetic clinics to a person with no personal history of breast or ovarian cancer if their combined <i>BRCA1</i> and <i>BRCA2</i> mutation carrier probability is 10% or more and an affected relative is unavailable for testing. [new 2013]	1.5.12	✓
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 <i>BRCA1</i> or <i>BRCA2</i> mutation) and do not have a <i>TP53</i> mutation. [new 2013]	1.6.11	✓
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 <i>BRCA1</i> or <i>BRCA2</i> mutation. [new 2013]	1.6.13	✓
Offer tamoxifen for 5 years to pre-menopausal 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. [new 2013]	1.7.21	✗
Offer tamoxifen for 5 years to post-menopausal women without a uterus and at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or they have a past history of endometrial cancer. [new 2013]	1.7.22	✗
Offer either tamoxifen or raloxifene for 5 years to post-menopausal women with a uterus and at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer. [new 2013]	1.7.23	✓

2.2.4 Ten of the recommendations in the guideline have been identified as key priorities for implementation, and 5 of these are also among the 10 recommendations considered to have a significant resource

impact. Two recommendations listed in the table above relating to chemoprevention are not key priorities but may have a significant resource impact. The other 5 key priority recommendations are not included in table 1 because they are not anticipated to have significant resource impact. The reasons for this are explored below.

- 2.2.5 The key priority recommendation on using an acceptable carrier probability calculation and assessment of family history to determine referral to specialist care (recommendation 1.1.19) should not result in a significant impact on resources. Implementing this recommendation is likely to refine referrals to specialist care by providing quick guidance for clinicians to determine which families need referring for *BRCA1/2* mutation testing and which gene to test first.
- 2.2.6 The key priority recommendation on information and support (recommendation 1.2.2) is not likely to have significant impact on costs because this can be part of clinical consultations. Providing information on national and local organisations is also likely to be part of current practice.
- 2.2.7 The key priority recommendations on surveillance for women with no personal history of breast cancer and who are at moderate to high risk (recommendations 1.6.3 and 1.6.7) are aligned with the current NHS breast screening programme for these groups. (NHS Breast Screening Programme 2011). The programme has adopted previous NICE guidance on familial breast cancer (NICE clinical guideline 41). The costing work for NICE clinical guideline 41 found that following recommendations on annual surveillance with MRI and/or mammography would mean screening an additional 2500 women annually at an additional cost of £0.9 million nationally. It is therefore not anticipated that the updated recommendations would have a significant cost impact.

- 2.2.8 For women considering bilateral risk-reducing mastectomy, the opportunity to discuss their breast reconstruction options with a member of the surgical team (recommendation 1.7.38) is unlikely to result in a significant cost impact. This is because each type of reconstruction has risks and benefits that are normally discussed with the surgeon who advises on the best approach.
- 2.2.9 We have limited the consideration of costs and savings to direct costs to the NHS that will arise from implementation. We have not included consequences for the individual, the private sector or the not-for-profit sector. If applicable, any realisable cost savings arising from a change in practice have been offset against the cost of implementing the change.

2.3 *General assumptions made*

- 2.3.1 The model is based on annual incidence of breast cancer in women and men and ovarian cancer by age group applied to population estimates. These are taken from data produced by the Office for National Statistics (2010) on the average number of new cases per year.
- 2.3.2 To estimate the incidence of breast and ovarian cancer that have an inherited component, the costing model uses data sources taken from the full guideline (see notes to table 2).

Table 2 Breast and ovarian cancer annual cases per 100,000 population by age group, and annual number of cases per 100,000 population that have an inherited component

Age	Breast cancer cases	Ovarian cancer cases	Inherited – breast cancers ¹	Inherited – ovarian cancers ²	Total inherited cancers
20–29	0	0	0	0	0
30–39	5	1	0	0	0
40–49	14	1	1	0	1
50–59	24	2	1	0	1
60–69	27	3	1	1	2
70 and over	29	5	2	1	3
Total women	100	12	5	2	7
Men 18+	1		0		

¹Inherited breast cancer incidence 5%: Antoniou et al. (2003).
²Inherited ovarian cancer incidence 10–15%: Campeau et al. (2008)

2.3.3 In a national context, applying the figures above to the population in England produces 56,000 cases of breast cancer in women per year and 366 cases in men. For ovarian cancer this is 7100 cases per year. Of these figures, those that have a high risk inherited component are 2800 cases of breast cancer in women; 18 cases of breast cancer in men and 1000 cases of ovarian cancer.

2.4 Basis of unit costs

2.4.1 If a national tariff price or indicative price exists for an activity, this has been used as the unit cost. This has then been inflated by the national average market forces factor.

2.4.2 Using these prices ensures that the costs in the report are the cost to the commissioners for cancer services of commissioning predicted changes in activity at the tariff price, but they may not represent the actual cost to provider organisations delivering the activity.

- 2.4.3 For new or developing services for which there is no national average unit cost, organisations already undertaking this activity have been asked their current unit cost.

3 Significant resource-impact recommendations

3.1 *Carrier probability at which genetic testing should be offered*

Genetic testing at specialist centres

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 (recommendation 1.5.11).

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 (recommendation 1.5.12).

Background

- 3.1.1 Mutations in several genes are known to be associated with an inherited risk of breast cancer. Of the known genes, inherited mutations *BRCA1* and *BRCA2* are the most common cause of a high lifetime risk of breast cancer of between 40% and 85%, depending on gene and context. Female mutation carriers also have a high risk of ovarian cancer (10–60%, depending on the gene involved), whereas male carriers of *BRCA2* mutations have an increased risk of prostate cancer (an estimated 25% risk for *BRCA2* carriers) and breast cancer (8% for *BRCA2*) (Familial breast cancer update – full cost effectiveness and evidence review report 2013).

Assumptions made

- 3.1.2 The health economics supporting the guidance estimates that about 5% of all breast cancers arise from a high risk cancer-predisposing gene such as *BRCA1*, *BRCA2* and *TP53* (Antoniou et al. 2003). For ovarian cancer, this is between 10 and 15% (Campeau et al. 2008). The higher estimate of 15% is used in the standard assumptions based on expert opinion. These percentages have been applied to annual incidence rates for cancer in each age group (see table 2 above). Therefore it is assumed that 5% of breast cancer cases and 15% of ovarian cancer cases are identified as having a family history of breast or ovarian cancer.
- 3.1.3 It is assumed that these people are likely to have been identified under accepted risk-scoring models as carrying a gene mutation that increases their chances of developing breast cancer (this is defined in the guidance as a mutation carrier probability of 10% or more). Therefore using the percentage of cancers caused by predisposing genes (5% breast cancers, 15% ovarian cancers) as a proxy, we can estimate the potential numbers that could be offered genetic testing for *BRCA1*, *BRCA2* or *TP53* genetic mutation. This produces 5 people per 100,000 population (see table 2 above).
- 3.1.4 Using the estimates from the health economics, it is assumed that there are on average 2 unaffected relatives who may be offered testing per affected woman found positive. Unaffected relatives would be eligible for testing because they have a carrier probability of 10% or more, and the affected family member is unavailable for testing. Using this assumption a further 14 people per 100,000 population could be offered testing.
- 3.1.5 The full guideline includes survey data from GDG members. These showed that 46% of those surveyed already use a threshold of 10% or greater to offer genetic testing to an affected woman. A

proportion of people choose not to undergo genetic testing: for affected individuals the estimate from the full cost-effectiveness report has been used (table 1.4: Schwartz et al. 2004). This assumes 86% of affected individuals take up the genetic test. This produces an estimate of 39.56% for those who are offered and who take up the test.

- 3.1.6 When a test could not be offered to an affected individual in the first instance, over 65% of the cancer geneticists surveyed had offered *BRCA1/2* full gene mutation testing to some unaffected individuals with a family history of breast, ovarian or related cancers in the past year. Around 48% of unaffected individuals take up genetic testing (Evans et al. 2009). This gives an estimate of 31% of unaffected individuals who are offered and who take up a genetic test. These figures have been used as standard assumptions in the costing model to estimate current activity and costs.
- 3.1.7 In order to estimate the increase in activity and cost impact of the new recommendations, we have predicted that the guidance would align practice; therefore the remaining proportion of geneticists (54%) would offer genetic testing at the 10% or greater (rather than 20% or greater) threshold to an affected woman or man. The same uptake of 86% is assumed (see section 3.1.4).
- 3.1.8 For unaffected relatives, it is assumed that 100% would be offered a genetic test at a 10% or greater threshold and that around 50% would choose to take up the test. This is based on assumptions in the Familial breast cancer update – full cost effectiveness and evidence review report (2013) (table 1.4 Evans et al. 2009). The uptake estimates for unaffected relatives are lower because predictive testing has substantial implications that would have psychosocial and emotional impact, particularly for carriers who may not have completed their families. These estimates may vary significantly; variations are shown in the sensitivity analysis. Table 3 shows the estimated change in the number of people

referred for genetic testing per 100,000 population as a result of implementing the guidance.

Table 3 Estimated increases in activity for the number of people tested at lower threshold per 100,000 population

	People eligible for testing	Current numbers tested at lower thresholds	Future numbers tested at lower thresholds	Change
Affected people ¹	7	3	6	3
Unaffected relatives ²	14	4	7	3
Total	21	7	13	6
¹ The number of affected people eligible for testing is taken from table 2. This is the sum of inherited breast cancer cases = 5 plus inherited ovarian cancer cases = 2. ² It is assumed there are 2 unaffected relatives who would be tested for each affected person (this is an average estimate taken from the health economics supporting the guidance)				

Costs of diagnostic genetic testing

3.1.9 The cost of genetic testing is made up of 2 components. The laboratory cost and the cost of counselling. Counselling usually involves a risk assessment based on the individual's personal and family history. There are also discussions about the medical implications of a positive or a negative result, the psychological risks and benefits of genetic results and the risk of passing a mutation to children.

3.1.10 The laboratory costs of genetic testing are different for an affected individual and an unaffected relative. This is because a full genetic test is needed to identify whether there is a genetic mutation in an affected person and the type of mutation, whereas for an unaffected relative the type of mutation may already be known. Therefore the test would identify whether the gene mutation has been passed on to the relative.

3.1.11 The laboratory costs of genetic testing (based on GDG expert opinion) are estimated to be £700 for an affected individual and

£240 for a family member. The full cost-effectiveness evidence review also assumes 2 counselling sessions are needed for an affected individual and 3 are needed for an unaffected relative. Table 4 shows the estimated cost of genetic testing included in the costing template.

Table 4 Unit cost assumptions used for genetic testing

	Unit cost £	Units	Total cost £
Affected people			
Laboratory cost of test	700	1	700
Counselling cost per hour ¹	125	2	250
Total			950
Unaffected relatives			
Laboratory cost of test	240	1	240
Counselling cost per hour ¹	125	3	375
Total			615
¹ Counselling cost taken from PSSRU 12-hourly rate for a Band 7 to Band 8 counsellor in primary medical care – client contact			

Cost summary

- 3.1.12 Genetic testing at lower carrier probability thresholds would align current practice and is likely to increase activity in genetic testing at specialist centres.
- 3.1.13 The net cost of genetic testing at specialist centres is summarised in table 5.

Table 5 Estimated increases in cost of genetic testing at lower carrier probability thresholds per 100,000 population

		Current		Proposed		Change	
	Unit cost £	Numbers of patients	Cost (£000)	Numbers of patients	Cost (£000s)	Numbers of patients	Cost (£000s)
Affected people	950	3	2.6	6	5.7	3	3.1
Unaffected relatives	615	4	2.7	7	4.3	3	1.6
Totals		7	5.3	13	10.0	6	4.7

Other considerations

3.1.14 Lowering the testing thresholds may increase the number of preventative surgeries (mastectomy, salpingo-oophorectomy) carried out. This may increase costs in the short term; however there are significant long-term benefits from reducing cancer incidence and cases of advanced cancer. Estimating the number of additional surgeries in the short term would be difficult because of the personal nature of decisions. As an example of costs, the cost of mastectomy including reconstruction surgery is £6,504 (2013/14 mandatory tariff code JA16Z), which is significantly less than the estimated average cost of treating an invasive cancer of £12,700 (this includes the cost of surgery, chemotherapy and radiotherapy – see table 7).

3.2 *Annual surveillance for women with a personal history of breast cancer*

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

- remain at high risk of breast cancer (including those who have a *BRCA1* or *BRCA2* mutation), **and**
- do not have a TP53 mutation (recommendation 1.6.11).

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 (recommendation 1.6.13).

Background

- 3.2.1 Women who are affected by primary breast cancer are at an increased risk of developing second breast cancers in the remaining breast tissue. Those women with a family history are at even higher risk. Since the publication of CG41, studies have found that MRI screening is more sensitive than mammography, especially in high-risk populations such as *BRCA1/2* carriers (Duffy S. W. et al. FH01 study 2010). MRI surveillance is recommended for women aged 30–49 years because the breast tissue at that age is too dense for mammography to be effective.
- 3.2.2 Systems for breast cancer surveillance vary significantly across England (NHS Breast Screening Programme 2011). Women with a personal history and a family history need to be identified correctly and need to have more intensive surveillance than other groups.

Assumptions made

- 3.2.3 Because of wide variation in practice, it has been challenging to produce standard assumptions for current activity. A section has been included in the costing template to assist with local estimates. This section could be used to estimate potential increases in activity as a result of implementing the new recommendations.

Cost of MRI scan and mammography

- 3.2.4 The unit cost of an MRI scan is £250. This is from the 2013/14 mandatory tariff (code RA05Z) 'Magnetic resonance imaging scan 2–3 areas with contrast'. The unit cost of mammography is estimated at £53. This is for digital mammography. In the absence of a mandatory tariff and reference cost, we have used the unit cost in the costing report for Venous thromboembolic diseases (NICE

clinical guideline 144; 2012). These costs can be amended to reflect local estimates.

3.3 Chemoprevention

Offer tamoxifen for 5 years to pre-menopausal 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 (recommendation 1.7.21).

Offer tamoxifen for 5 years to post-menopausal women without a uterus and at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or they have a past history of endometrial cancer (recommendation 1.7.22).

Offer either tamoxifen or raloxifene for 5 years to post-menopausal women with a uterus and at high risk of breast cancer unless they have a past history or may be at increased risk of thromboembolic disease or endometrial cancer (recommendation 1.7.23).

Background

3.3.1 Since the publication of CG41, 2 trials have been published on chemoprevention. These have provided high-quality evidence that shows tamoxifen is effective in reducing breast cancer incidence when used for chemoprevention in pre- and post-menopausal women who do not have a diagnosis of breast cancer (Fisher et al. 2005; Cuzick et al. 2007). There was also high-quality evidence to suggest that raloxifene has similar effectiveness to tamoxifen when used for chemoprevention in post-menopausal women with a uterus who do not have a diagnosis of breast cancer (Vogel et al. 2006).

Assumptions made

3.3.2 It is assumed that chemoprevention is not current practice for women with no personal history of breast cancer and therefore all costs are incremental. To estimate the number of unaffected women who may be eligible to receive chemoprevention with either

tamoxifen or raloxifene it is assumed that the average of 2 unaffected relatives per affected person could be used (this can be amended to reflect local estimates in the template). This gives a figure of 14 people per 100,000 (in line with the potential numbers who may be eligible for genetic testing – see table 3 above). The proportion of unaffected relatives who may be carriers of the *BRCA1*, *BRCA2* or *TP53* gene is assumed to be 50%. This is based on expert opinion. Therefore 7 unaffected women per 100,000 population could be carriers of high-risk genes.

- 3.3.3 For some women, chemoprevention may not be a suitable option. Reasons may include a past history of endometrial cancer or thromboembolic disease. Some women may also choose to have risk-reducing surgery as their cancer prevention method. Therefore it is assumed in the costing template that 20% of eligible women may take up chemoprevention. This means around 1 woman per 100,000 population will take up chemoprevention.
- 3.3.4 Chemoprevention may not work in certain circumstances; in which case treatment is stopped after 1 year. Expert opinion suggests that 20% of women stop due to side effects and 20% stop due to no effect on mammographic density. For a population of 100,000, due to small numbers, the costing template does now show that any women continue chemoprevention for 5 years. For some larger populations (including at a national level) the costing template will show the numbers of women who continue chemoprevention for 5 years.
- 3.3.5 It is assumed that unaffected relatives who are at risk are not currently offered chemoprevention. It is not known what proportion of women would take treatment with tamoxifen and what proportion would of post menopausal women take up raloxifene. Uptake of tamoxifen and raloxifene in post-menopausal women is therefore assumed to be split 50/50. These figures can be amended locally.

- 3.3.6 Treatment is assumed to take place with tamoxifen and raloxifene. It is recognised that prescribing these drugs as indicated in the guidance is outside their UK marketing authorisation.

Cost of chemoprevention

- 3.3.7 The annual cost of tamoxifen is £36 (electronic drugs tariff 2012/13). The annual cost of raloxifene is £222 (electronic drugs tariff 2012/13) [accessed 13 February 2013].
- 3.3.8 The costing template shows the annual costs of chemoprevention as the year-5 ongoing cost after the guidance is implemented. The 5-year ongoing cost takes into account women who receive chemoprevention for 1 year (see section 3.3.4).
- 3.3.9 In addition to drug costs, a 6-monthly visit to the GP/clinic is needed to monitor treatment and give women a repeat prescription. The cost of a GP visit is estimated to be £40 per 11.7-minute consultation (Curtis 2012). For women who stop treatment after a year, the annual cost is £80, for women who continue treatment for 5 years; the total cost is £400.
- 3.3.10 The estimated cost of chemoprevention is summarised in table 6.

Table 6 Cost of chemoprevention per 100,000 population

	Annual cost £	Women who stop treatment after 1 year	Cost (women who stop treatment) £	Women who continue treatment for 5 years	Cost (women who continue treatment) £	Annual ongoing cost after year 5 £
Tamoxifen						
Pre-menopause ¹	36	0	0	0	0	0
Post-menopause ¹	36	1	18	0	0	0
Raloxifene						
Post-menopause	222	1	111	0	0	0
Subtotal		1	129	0	0	0
GP visits	80	1	80	0	0	00
Total			209		0	209

¹The age of pre-menopause is taken to be women aged 20–49 years. The age of post-menopause is taken to be from age 50 years onwards.

Because of a low incidence and small population, for a population of 100,000 people, the costing template does not show that there are any women or costs who continue chemoprevention for 5 years.

Other considerations

3.3.11 There were side effects reported in the trials with tamoxifen and raloxifene. Some side effects were less serious, such as increased frequency of hot flushes (with both drugs) and vaginal discharge (especially with tamoxifen). These were the most commonly reported side effects and for some women these could lead to more frequent visits to primary care. Because of the low patient numbers involved, this is not estimated to have a significant cost impact.

3.3.12 Potentially more serious side effects such as endometrial cancer and thromboembolic disease were also reported. An absolute increased risk of 1.4 cases of endometrial cancer per 1,000 women per year was seen only among women taking tamoxifen in the BCPT trial, whereas no increased risk incidence was reported for women taking raloxifene. Put another way, for each 714 women taking tamoxifen for 5 years, 1 woman would be newly diagnosed with endometrial cancer (Redmond et al. 1993). Because of the low numbers estimated to use tamoxifen over 5 years, it is not estimated that this would have significant local cost impact.

- 3.3.13 Other adverse events such as deep vein thrombosis (DVT) occurred at annual rates of 1.1 per 1,000 women under the age of 50 years and 1.5 for women aged 50 years and over. Raloxifene was also associated with an elevated risk of DVT; however because of the low numbers, this is not estimated to have a significant local cost impact.
- 3.3.14 There may be a cost impact because of the need to educate healthcare professionals and women eligible to receive treatment on the potential risks and benefits of using these drugs for this purpose. Costs will depend on local circumstances. Flexibility is provided in the costing tool to estimate these costs locally.

Potential savings

Background

- 3.3.15 The results from 2 randomised trials showed a risk reduction for preventing breast cancer of 50% for women taking tamoxifen (Vogel et al. 2006) and 38% for women taking raloxifene (Vogel et al. 2010). These figures have been adjusted to take into account expert opinion, the risk reduction for tamoxifen is reduced to 45% and for raloxifene this is reduced to 33.5%. Evidence from the trials shows that tamoxifen is effective in reducing breast cancer incidence when used for chemoprevention in pre-menopausal women who do not have a diagnosis of breast cancer. The evidence also showed that tamoxifen and raloxifene have similar effectiveness when used for chemoprevention in post-menopausal women who do not have a diagnosis of breast cancer.

Assumptions made

- 3.3.16 In order to estimate the number of cancer cases prevented each year, the increased annual incidence of breast cancer in people who are at high risk needs to be identified. Based on UK incidence data, a woman aged 20 who has no affected relatives has a 7.8%

probability of developing breast cancer by the age of 80; with 1 affected relative it is 13.3%, and with 2 affected relatives this rises to 21.1% (Collaborative Group on Hormonal Factors in Breast Cancer 2001). For women with affected relatives, the costing work assumes a midpoint of these 2 figures, which is 17%. This is because it is difficult to estimate the number of women who have 1 or 2 affected relatives.

- 3.3.17 The midpoint figure of 17% needs to be adjusted by the general population risk of a woman developing breast cancer who has no affected relatives. This is estimated to be 7.8% – see section 3.3.15 above (baseline risk in general population). The difference between the 2 figures is the increased annual probability of women who are at high risk of developing breast cancer; this is 9.2%.
- 3.3.18 The proportion of post-menopausal women treated with tamoxifen or raloxifene is assumed to be a 50/50 split. It is assumed that all pre-menopausal women are treated with tamoxifen.
- 3.3.19 A risk reduction of 45% has been assumed for tamoxifen (Vogel et al. 2006 – adjusted per expert opinion) and a risk reduction of 33.5% is assumed for raloxifene (Vogel et al. 2010 adjusted per expert opinion). Applying these assumptions to a per 100,000 population would not result in any cancer cases avoided because the numbers are very low. Using the England population, the estimated number of breast cancer cases avoided per year is 16 when using the above assumptions. This would have the effect of reducing hereditary breast cancer incidence by 0.03% (using the annual incidence figure of 2,652 cases – see section 2.3.3).

Savings

- 3.3.20 There are different combinations of treatment that could be used to treat breast cancer, depending on which stage the cancer is detected. Table 7 shows a typical example of a breakdown of costs, which are based on the economic model supporting the

guidance. The costs relate to breast cancer detected at an early invasive or invasive stage.

Table 7 Example of potential costs of breast cancer treatment

Description	Unit cost £	Units	Total £
Breast surgery (weighted average cost) ¹	2,783	1	2,783
Adjuvant radiotherapy (fractions) ²	123	15	1,845
Chemotherapy delivery – first attendance ³	482	1	482
Chemotherapy delivery – subsequent cycles ⁴	321	5	1,605
Chemotherapy – drug costs ⁵	289	6	1,736
Other drug costs			
Neulasta ⁶	686	6	4,118
Dexamethasone ⁷			13
Ondansetron ⁷			101
Maxolan ⁷			8
Endocrine therapy – anastrozole ⁸	1.85	13	24
Total			12,715
¹ This is a weighted average using HES activity data for breast surgery 2011/12 and national tariff 2013/14 for codes JA06Z, JA09D and JA16Z ² Tariff 2013/14 code SC23Z Adjuvant radiotherapy – 15 fractions ³ Tariff 2013/14 code SB14Z Deliver complex chemotherapy, including prolonged infusional treatment at first attendance ⁴ Tariff 2013/14 Deliver subsequent elements of a chemotherapy cycle ⁵ Drug costs for Epirubicin, cyclophosphamide and fluorouracil (assumption this is the standard regimen based on TA109 Breast cancer (early) – docetaxel) ⁶ Standard treatment to reduce infection risk because of chemotherapy-induced neutropenia price taken from electronic drug tariff 2013 ⁷ Full cost-effectiveness evidence review and reports – familial breast cancer (table 1.13 costs included in cancer treatment micro-costing) ⁸ Endocrine therapy – anastrozole, unit cost from eMC dictionary of medicines 2013, 1mg once daily (annual cost)			

3.3.21 Not all women benefit from chemoprevention. Using the above assumptions, for every 27 women who take chemoprevention for 5 years, 1 breast cancer case could be avoided. Applying these assumptions to the England population, around 17 cases of breast cancer could be avoided each year. This could reduce breast cancer incidence rates and result in annual savings of around £0.2 million with net annual costs of chemoprevention estimated at £0.3 million. Although these figures are not significant nationally, there are the potential benefits of avoiding cancer in some high-risk

women, and that women may be offered an alternative to radical surgery, which carries its own risks and is a huge psychological and physical challenge.

Other considerations

- 3.3.22 Chemoprevention may reduce the number of risk-reducing surgeries carried out; however this is likely to be over a longer period. This would be difficult to predict because there are many factors that affect the decision on which prevention course is the best option. These factors include age, level of cancer risk, the strength of the benefits and significance of the possible harms, and any contraindications to treatment. Chemoprevention could be a more acceptable option for women at increased risk of breast cancer.
- 3.3.23 Despite the high-quality evidence of the efficacy of tamoxifen and raloxifene for breast cancer prevention, uptake in other countries, even among very high-risk women, is much lower than anticipated. Barriers include the applicability of the trial findings to the population of women seen by clinicians; the potential side effects; and that neither drug has a marketing authorisation for chemoprevention in women who do not have a diagnosis of breast cancer. Uptake may increase as a result of implementing the guidance, but this is difficult to predict. The sensitivity analysis uses the uptake range gathered from expert opinion.

3.4 *Benefits and savings*

Genetic testing

- 3.4.1 There may be savings as a result of genetic testing. This would identify family members who are not carriers of *BRCA1/2* or *TP53* genes and therefore who would not need annual surveillance, preventative surgery, tests and chemoprevention. Savings would

be hard to quantify because of the different prevention options available and individual circumstances.

- 3.4.2 For people who are at increased risk, this would allow them to make decisions to reduce their cancer risk and could help avoid costly treatments. Savings would be difficult to quantify because they depend on a number of variables, including the stage of the cancer and the type of treatment needed.

HRT for women with no personal history of breast cancer who have bilateral salpingo-oophorectomy before the natural menopause

- 3.4.3 Although it reduces cancer risk, bilateral salpingo-oophorectomy is not without consequences, particularly those relating to oestrogen deprivation from surgically induced menopause. Oestrogen deprivation also leads to loss of bone mineral density and risk of osteoporosis and bone fracture (Jones et al. 1985; Cummings et al. 1998), and may shorten lifespan through an earlier onset of cardiovascular disease (Howell and Evans 2011).
- 3.4.4 HRT reduces symptoms associated with menopause in some women, and protects against bone density loss. For women with no personal history of breast cancer who have either a *BRCA1* or *BRCA2* mutation, HRT is recommended in line with recommendation 1.7.53. There may be some savings associated with fewer cases of osteoporosis, fewer GP visits and lower incidence of cardiovascular disease because of the protective effect of HRT. Examples of costs that could be avoided are:
- Weighted average cost for an admission to hospital relating to a cardiovascular disease event is £4,574 (NICE clinical guideline 67).
 - The cost of osteoporotic fragility fractures ranges from £2,381 (wrist) to £6,816 (hip) (NICE technology appraisal guidance 160 and 161).

- 3.4.5 Current practice varies, and predicting savings for this group of women would be challenging. The recommendation on HRT (recommendation 1.7.53) would align practice and is likely to have no significant cost impact.

4 Sensitivity analysis

4.1 *Methodology*

- 4.1.1 There are a number of assumptions in the model for which no empirical evidence exists; these are therefore subject to a degree of uncertainty.
- 4.1.2 Appropriate minimum and maximum values of variables were used in the sensitivity analysis to assess which variables have the biggest impact on the net cost or saving. This enables users to identify the significant cost drivers.
- 4.1.3 It is not possible to arrive at an overall range for total cost because the minimum or maximum of individual lines are unlikely to occur simultaneously. We undertook one-way simple sensitivity analysis, altering each variable independently to identify those that have greatest impact on the calculated total cost.
- 4.1.4 Appendix B contains a table detailing all variables modified, and the key conclusions drawn are discussed below.
- 4.1.5 The variables which have the greatest sensitivity ratio are discussed below. The sensitivity ratio allows comparison of the variables by analysing the percentage changes in the variables and outturn. The closer the ratio is to 1, the more sensitive the overall cost is to fluctuations in the variable.

4.2 *Impact of sensitivity analysis on costs*

Percentage of unaffected people who are offered and who take up genetic testing at the lower carrier probability threshold of 10%

- 4.2.1 The most sensitive variable which has the highest sensitivity ratio of 0.92 is the percentage of unaffected people who take up a genetic test at the lower carrier probability threshold of 10%. Varying this from the standard assumption of 50% to a minimum of 40% and a maximum of 60% produces costs per 100,000 of £4,000 and £5,800 respectively. This variable is sensitive because it determines the number of unaffected people tested.

Potential number of relatives who may be eligible for genetic testing

- 4.2.2 Varying the number of relatives per person who may be eligible for genetic testing per person with family history of breast or ovarian cancer from the standard assumption of 2 to a minimum of 1 and a maximum of 3 produces costs per 100,000 population of £4,100 and £7,800 respectively. This variable has a lower sensitivity ratio of 0.76. The variable is sensitive because it is a key driver for activity numbers.

Percentage of breast cancers that have an inherited component

- 4.2.3 Varying the percentage of breast cancers that have an inherited component from the standard assumption of 5% to a minimum of 3% and a maximum of 7% produces costs per 100,000 population of £3,500 and £6,300 respectively. The variable has a lower sensitivity ratio of 0.71. The variable is sensitive because it drives the numbers offered genetic testing.

Estimated percentage of women who take up chemoprevention

- 4.2.4 Varying the percentage of women who take up chemoprevention from the standard assumption of 20% to a minimum of 10% and a maximum of 50% produces costs per 100,000 population of £4,900

and £7,200 respectively. The variable has a low sensitivity ratio of 0.23.

5 Impact of guidance for commissioners

5.1.1 The cost of genetic testing is outside the Payment by Results tariff. Surveillance using MRI falls within the mandatory tariff (code RA05Z). Chemoprevention using hormone therapy (tamoxifen and raloxifene) is likely to fall under programme budgeting category 2F Cancers and tumours – breast and 2G Cancers and tumours – gynaecological.

5.1.2 The commissioning arrangements for cancer services are described as follows:

- Clinical commissioning groups (CCGs) commission services for patients with common cancers (which includes breast and gynaecological cancers) with the exception of radiotherapy, chemotherapy and specialist interventions listed under specific cancers. It is therefore anticipated that genetic testing would be commissioned by clinical commissioning groups (CCGs) under section 111 Specialist genetic services (all ages). MRI services would be commissioned by CCGs under section 105 Specialist cancer services (adults). This is because breast cancer is a common cancer that falls within the remit of CCGs. In addition, the referrer for genetic testing is likely to be a primary or secondary/tertiary care clinician referring from a service that is not commissioned the NHS commissioning board.
- NHS England is the commissioner for chemotherapy for common cancers, this includes drug costs, procurement and delivery of chemotherapy.

- 5.1.3 The guideline is likely to have an impact on specialist genetic clinics in terms of increased activity for genetic testing, and an impact on primary care services relating to additional GP visits needed for women who take up chemoprevention. Depending on where genetic counselling takes place, there may also be a resource impact on services providing genetic counselling. Genetic testing may also increase the number of preventative surgeries carried out in secondary care. This is difficult to predict because there may also be a reduction in surgeries as a result of identifying women who are not carriers of high-risk genes.
- 5.1.4 Implementing the guidance may reduce the incidence of familial breast cancer. This supports the national outcomes framework in respect of preventing people from dying prematurely (under 75 mortality from cancer).

6 Conclusion

6.1 *Total cost per 100,000 for England*

- 6.1.1 Using the significant resource-impact recommendations shown in table 1 and assumptions specified in section 3, we have estimated the annual impact of implementing these recommendations in England to be a cost of around £4,900 per 100,000 population. Table 8 shows the breakdown of cost of each significant resource-impact recommendation.
- 6.1.2 The costs presented are estimates and should not be taken as the full cost of implementing the guideline.
- 6.1.3 Implementing the recommendations on genetic testing, surveillance and chemoprevention is likely to produce savings as a result of avoiding breast cancer. These could be significant, particularly where the cancer is first diagnosed when it is at an invasive stage. There are also wider savings such as sickness absence, care costs

and benefit payments to someone who has breast or ovarian cancer.

Table 8 Summary of the resource impact per 100,000 population

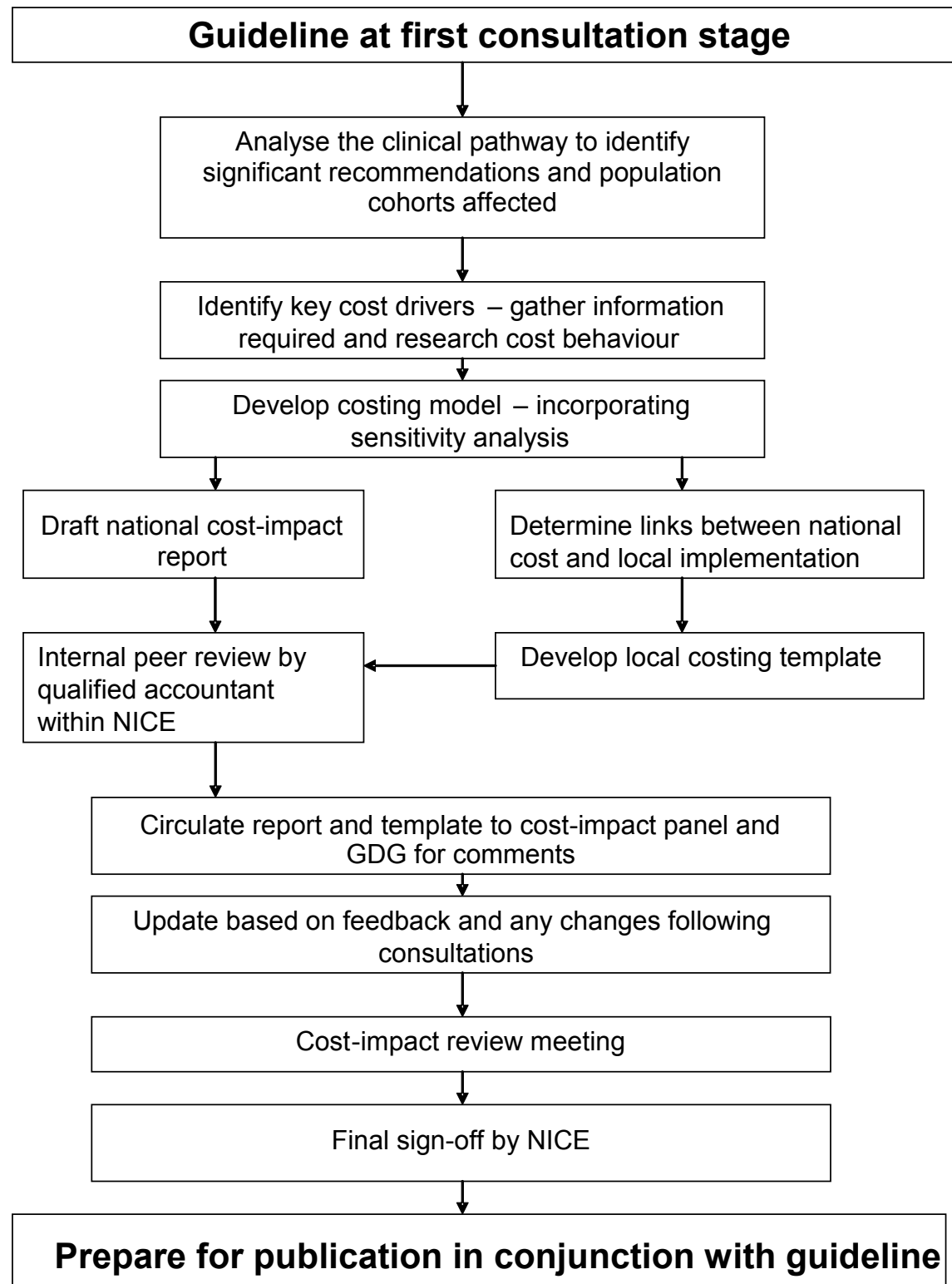
	Current cost (£000)	Proposed cost (£000)	Change in cost (£000)
Genetic testing	5.3	10	4.7
Chemoprevention cost ¹	0.0	0.2	0.2
Total	5.3	10.2	4.9
¹ Because of the low incidence of familial breast cancer, a population size of 100,000 would not show potential savings from chemoprevention. For some larger populations (including at a national level) a saving would be shown in the costing template.			

6.1.4 The timeframe for implementation may vary for each element of the guidance, particularly in relation to access to MRI scanning where there is wide variation in practice. The recommendations on chemoprevention may not be costly or difficult to implement. However difficulty may lie with discussing chemoprevention with healthy women at increased risk of developing breast cancer. Implementing genetic testing at the lower probability thresholds could be achievable in the short term by using more rapid testing available at laboratories.

6.2 Next steps

6.2.1 The local costing template produced to support this guideline enables organisations such as primary care trusts or health boards in Wales and Northern Ireland to estimate the impact locally and replace variables with ones that depict the current local position. A sample calculation using this template showed that a population of 100,000 could expect to incur additional costs of £4,900. Use this template to calculate the cost of implementing this guidance in your area.

Appendix A. Approach to costing guidelines



Appendix B. Results of sensitivity analysis

	Baseline value	Minimum value	Maximum value	Recurrent costs				Sensitivity ratio
				Baseline costs (£000's)	Minimum costs (£000's)	Maximum costs (£000's)	Change (£000's)	
Percentage of breast cancers that have an inherited component (driver for numbers offered genetic testing).								
Percentage of ovarian cancers that have an inherited component (driver for numbers offered genetic testing).	5%	3%	7%	4.9	3.5	6.3	2.8	0.71
Potential number of relatives per person who may be eligible for genetic testing per person with family history of breast or ovarian cancer								
Estimated percentage who take up chemoprevention	15%	10%	20%	4.9	4.5	5.3	0.8	0.24
Percentage of people who are offered and who take up genetic testing at lower carrier probability threshold of 10%.								
Proportion who stop chemoprevention after 1 year (due to no change in condition)	2	1	3	4.9	4.1	7.8	3.7	0.76
Proportion who receive chemoprevention for 5 years	20%	10%	50%	4.9	4.9	7.2	2.3	0.23
Uptake of tamoxifen (post-menopause)								
Uptake of raloxifene (post-menopause)	50%	40%	60%	4.9	4.0	5.8	1.8	0.92
Risk reduction from chemoprevention – tamoxifen (cases prevented)								
Risk reduction from chemoprevention – raloxifene (cases prevented)	45%	40%	50%	4.9	4.9	4.9	0.0	0.00
Cost of a genetic test - affected people								
Cost of genetic counselling - affected people	33.5%	29%	38%	4.9	4.9	4.9	0.0	0.00
Cost of a genetic test - unaffected people	£ 700	£ 600	£ 800	4.9	4.6	5.2	0.6	0.43
Cost of genetic counselling - unaffected people	£ 250	£ 150	£ 350	4.9	4.6	5.2	0.6	0.15
Cost of genetic counselling - unaffected people	£ 240	£ 140	£ 340	4.9	4.6	5.2	0.6	0.15
Chemoprevention - tamoxifen annual cost	£ 375	£ 275	£ 475	4.9	4.6	5.2	0.6	0.23
Chemoprevention - raloxifene annual cost	£ 36	£ 26	£ 46	4.9	4.9	4.9	0.0	0.00
Potential savings - cost of a cancer case avoided	£ 222	£ 122	£ 322	4.9	4.9	4.9	0.0	0.00
	£ 12,715	£ 6,715	£ 18,715	4.9	4.9	4.9	0.0	0.00

Appendix C. References

Antoniou A, Pharoah PD, Narod S et al. (2003) Average risks of breast and ovarian cancer associated with *BRCA1* or *BRCA2* mutations detected in 29 case series unselected for family history: a combined analysis of 22 studies. *American Journal of Human Genetics* 72(5): 1117–30

Campeau PM, Foulkes WD, Tischkowitz MD (2008) Hereditary breast cancer: new genetic developments, new therapeutic avenues. *Human Genetics* 124(1): 31–42

Collaborative Group on Hormonal Factors in Breast Cancer (2001) Familial breast cancer: collaborative 15 reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast 16 cancer and 101,986 women without the disease. *Lancet* 358: 1389–99

Cummings SR, Browner WS, Bauer D et al. (1998) Endogenous hormones and the risk of hip and vertebral fractures among older women. Study of Osteoporotic Fractures Research Group. *New England Journal of Medicine* 339(11): 733–8

Curtis L (2012) Unit costs of health and social care. Personal Social Services Research Unit, University of Kent

Duffy SW, Mackay J, Thomas S et al. (2010) Mammographic surveillance in women younger than 50 years who have a 12 family history of breast cancer: tumour characteristics and projected effect on mortality in the 13 prospective, single-arm, FH01 study. *The Lancet Oncology* 11: 1127–34

Evans et al. (2009) Full cost effectiveness evidence review supporting the guidance (see table 1.4) (2013).

Howell A, Evans DG (2011) Hormone replacement therapy and breast cancer. *Recent Results Cancer Research* 188: 115–22

Jones KP, Ravniker VA, Tulchinsky D et al. (1985) Comparison of bone density in amenorrheic women due to athletics, weight loss, and premature menopause. *Obstetrics and Gynecology* 66: 5–8

Keogh LA, Hopper JL, Rosenthal D et al. (2009) Australian clinicians and chemoprevention for women at high familial risk of breast cancer. *Hereditary Cancer in Clinical Practice* 7: 9

National Collaborating Centre for Cancer (2013) Familial breast cancer: classification and care of women at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer. Full cost effectiveness evidence review and reports

NHS Breast Screening Programme (2011) [NHS Breast Screening Programme annual review](#) [online] [Accessed March 2013]

NICE clinical guideline 41 (2006) Familial breast cancer: the classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care

NICE clinical guideline 41 (2006) Costing template and report

Office for National Statistics (2010) [Cancer statistics: registrations series MB1](#) [online] [Accessed March 2013]

Redmond CK, Wickerham DL, Cronin W et al. (1993) The NSABP breast cancer prevention trial (BCPT): a progress report. [Abstract] *Proceedings of the American Society of Clinical Oncology* 12: A-78, 69

Schwartz M, Lerman C, Brogan B et al. (2004) Impact of *BRCA1/BRCA2* counselling and testing on newly diagnosed breast cancer patients. *Journal of Clinical Oncology* 22(10): 1823–9

Vogel VG, Constantino JP, Wickerman DL et al. (2006) Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP study of Tamoxifen and Raloxifene (STAR) P-2 trial. *JAMA* 295(23): 2727–41

Vogel VG, Constantino JP, Wickerman DL et al. (2010) Update of the national surgical adjuvant breast and bowel project study of tamoxifen and raloxifene (STAR) P-2 trial: preventing breast cancer. *Cancer Prevention Research* 3(6): 696–706