

The ROYAL MARSDEN
NHS Foundation Trust

A Beginner's Guide to *BRCA1* and *BRCA2*

Patient Information



NHS

Contents

	Page
Introduction	
What does it mean to have a <i>BRCA</i> gene mutation?	1
Background information about the <i>BRCA1/2</i> genes	2
Screening	
Managing your risk of breast cancer	4
Managing your risk of ovarian cancer	8
Reducing risk	
Risk-reducing mastectomy	11
Risk-reducing ovarian surgery and surgical menopause	13
Sharing information with your family	
General issues	24
Who is at risk of having the faulty gene in my family?	26
Men and <i>BRCA</i> genes: What do men need to know?	29
Predictive genetic testing	31
A letter for your relatives	33
Passing on the cancer gene: How to tell the family	37
Talking to children and young people about <i>BRCA</i>	40
Adoption	45
Predictive genetic testing and insurance	46
Did you know?	
Family Planning	49
Pre-implantation Genetic Diagnosis	51
<i>BRCA</i> genes and the Ashkenazi Jewish population	53
Current studies and trials	54
New cancer treatment options for <i>BRCA</i> carriers	55
Organ donation	57
Where can I get more information?	59

Acknowledgements

We would like to express our gratitude to Macmillan Cancer Support who provided funding for the pilot phase of this project. Macmillan Cancer Support improves the lives of people affected by cancer. They provide practical, medical, emotional and financial support and push for better cancer care.

Introduction

What does it mean to have a *BRCA* gene mutation?

This information pack was put together to provide answers to some of the many questions people have when they receive the news that they are *BRCA* gene mutation carriers. Healthcare professionals working in Cancer Genetics have met many people who are *BRCA* carriers and we can share our experience to some extent. We can provide information and make referrals to other healthcare professionals. We can tell you that other people in your situation have had similar feelings and anxieties but we do not truly know what it is like for you and how it may affect your life.

Many people have questions that, for the time being, cannot be answered fully because we are still studying the *BRCA* genes and their impact. One of the challenges that *BRCA* carriers face is coping with the uncertainty of what the future holds, both for you and your family. You may be asked to make life-changing decisions about cancer screening and risk-reducing surgery without the benefit of all the facts you would like. This may be difficult and could cause you to feel quite anxious, frustrated or even angry at times. It may take you some time to feel that you have absorbed enough information to feel confident about your decisions.

Unlike other health-related issues there is an extra set of challenges for *BRCA* gene mutation carriers - the risks for your relatives. If you are the first person in the family to have been diagnosed with a *BRCA* gene mutation you will have to find a way to share this information with your family. Even if you aren't the first person in the family to be tested there may be family pressures to face. Will relationships be affected if one person has a positive gene test and their relative has a negative result? What about starting a new relationship – when do you tell someone and what do you say? What if you have young children or are planning a family?

We hope that this guide will be useful in providing you with some of the information you need and also help you to think about questions you may wish to discuss with your family and the genetics department. If you have any comments about the guide do let us know. We would like to make this booklet as useful and accessible as we can to support you and your relatives.



Background information about the *BRCA1* and *2* genes

Is breast cancer inherited?

Generally speaking, cancer is not an inherited illness. Breast cancer is common, affecting about 1 in 8 women at some point during their life, more commonly after the menopause. It isn't unusual to have a relative who has been affected by breast cancer. Most breast cancer occurs sporadically or 'out of the blue'.

However, we know that faulty genes are the underlying cause for about 5–10% (5 to 10 in 100) of breast cancers. There are two genes that, if mutated, greatly increase an individual's chance of developing breast and ovarian cancer. These are known as *BRCA1* (Breast Cancer 1) and *BRCA2* (Breast Cancer 2) genes. These two genes account for approximately a fifth (20%) of familial breast cancers. Research to identify new genes that also contribute to a high risk of breast cancer or modify the risk associated with a *BRCA1/2* mutation is ongoing.

What are breast cancer genes?

Genes are pieces of the DNA code that we inherit from our parents. We have two copies of each gene: one copy is inherited from our mother and one from our father. We have about 20,000 genes, each with a specific function that helps our bodies grow and function normally. Some genes work to protect against cancer by correcting damage that can occur in the DNA during cell division. *BRCA1* and *BRCA2* are two examples of these tumour suppressor genes. If an individual has a mutation in a *BRCA1/2* gene they have a greatly increased risk of developing breast and ovarian cancer. The *BRCA1/2* mutation does not cause cancer to occur on its own. The individual is at greater risk of developing cancer because their cells' ability to repair DNA damage may be impaired by the *BRCA1/2* mutation. It is the accumulation of DNA damage which causes a cell to change into a cancerous cell. We do not yet fully understand the whole process that changes a normal cell into a cancerous cell. We also do not yet understand why the *BRCA1/2* mutations primarily give a high risk of breast, ovarian and prostate cancers, rather than other types of cancer.

What are the cancer risks associated with *BRCA1/2*?

Gene	<i>BRCA1</i>	<i>BRCA2</i>
Breast cancer, in unaffected women (up to age 80)	60–90%	45–85%
Women with breast cancer (unilateral)	50%	50%
Lifetime risk of a new cancer in the other breast	5 year risk of new breast cancer ~10%	5 year risk of new breast cancer ~ 5–10%
Ovarian cancer, lifetime risk	40–60% Risk increases from age 40	10–30% Risk increases from mid 40s
Male breast cancer, lifetime risk	0.1–1%	5–10%
Prostate cancer, lifetime risk	~10% Similar to population risk	20–25%

Risk of developing breast cancer by age

Current age	<i>BRCA1</i>		<i>BRCA2</i>	
	Approximate remaining lifetime risk to 80 years	Approximate 5 year risk	Approximate remaining lifetime risk to 80 years	Approximate 5 year risk
20–25	70%	5%	70%	1%
26–30	70%	5%	70%	2%
31–35	65%	5%	65%	5%
36–40	65%	10%	65%	5%
41–45	60%	10%	60%	10%
46–50	55%	15%	55%	10%
51–55	50%	15%	50%	10%
56–60	40%	10%	50%	10%
61–65	30%	10%	45%	15%
66–70	25%	10%	35%	15%



Screening

Managing your risk of breast cancer

Women who are carriers of a *BRCA* gene mutation have an increased risk of developing breast cancer during their lifetime.

What is my risk compared with other women?

Women in the UK have a 1 in 8 or 12.5% chance, on average, of developing breast cancer in their lifetime. Women with one or two close relatives affected with breast cancer have a lifetime risk of 17-30%, depending on the specific family history. Women who have a *BRCA1* gene mutation have a 60-90% lifetime risk and women who have a *BRCA2* gene mutation have a 45-85% lifetime risk. Women with *BRCA* mutations have an increased risk of developing breast cancer at a younger age. Also, *BRCA* mutation carriers who have had breast cancer have a higher risk of developing another new breast cancer, compared to women who develop sporadic breast cancer in the general population.

How can I manage my risk of developing breast cancer?

There are two approaches to managing your risk. You can choose to have cancer screening such as mammography to try to detect breast cancer at an early stage so it is possibly easier to treat. You can choose to have risk-reducing surgery to remove your breast tissue, before the diagnosis of breast cancer. Screening does not prevent or reduce the risk of breast cancer. Surgery has potential side effects that need careful consideration. Many women choose to have screening initially and some may also consider risk-reducing surgery.

Clinical trials are examining whether drugs can be given to try to prevent breast cancer in those who are at increased risk. This is known as chemoprevention. The National Institute for Clinical Excellence (NICE) is in the process of updating its guidance for the management of women at high risk of developing breast cancer. The new guidelines are due to be agreed and published in 2013 and may contain advice around chemoprevention.

There is no 'right' choice. Everyone has to decide which option is best for them. We can help you make that decision by ensuring you have accurate information and by referring you to speak to the appropriate specialists.

What breast cancer screening is recommended for *BRCA* mutation carriers?

Breast awareness: This involves being aware of changes in the breast and feeling the breast with the flat of the hand in a systematic way once a month 5-10 days after you have finished your period. It is also important to take time to look at your breasts in different positions. If there are any changes at all you should inform your doctor. All women should practice this from their early 20s.

Breast screening: Mammography is offered annually from age 40–70.

Magnetic resonance imaging: MRI is a new form of breast screening that is being introduced for young women at increased risk of breast cancer. It is a more sensitive screening technique, compared with mammography in women under 50. It is currently recommended that women, who are known carriers of either *BRCA1* or *BRCA2* mutations, aged 30–50 have annual MRI screening.

If I have breast cancer what is the chance that it will be detected on a mammogram?

Mammography has been shown to be effective in detecting breast cancer in women over 50. If a woman over 50 has breast cancer there is about 85% chance that mammography will detect it. This is called the sensitivity of the test. There is less evidence available about the sensitivity of mammography in women under 50. For example, in some studies of women aged 40-49 the sensitivity of mammography ranged from 62-76%. The sensitivity of mammography in young *BRCA* carriers (aged 35-49) has been demonstrated to be around 40%. This difference in sensitivity is one of the reasons we suggest that women have annual mammography rather than every two or three years.



If I have breast cancer what is the chance that it will be detected on a MRI scan?

Studies on young women (aged 35-49) who carry *BRCA* mutations have demonstrated that MRI screening is more effective at detecting breast cancer than mammography (77% versus 40%). Also, studies showed that combining both MRI and mammography screening improves the detection rate for both *BRCA1* and *BRCA2* mutation carriers to 94%. One drawback of MRI screening is that there is a higher recall rate to investigate abnormalities that may not be cancer, compared with mammography. Further research is ongoing into the usefulness of MRI screening for *BRCA* mutation carriers.

What does it mean if I am called back for another scan?

If something unusual is found on your mammogram or MRI scan you will be recalled for further examinations to clarify what the abnormality is. It is not unusual to be recalled following your first mammogram or MRI. After your first screening examination the doctors will have images to compare, making it easier to tell if further investigations are needed. You may be recalled because of suspicious results or technical issues. If you are recalled you may have a clinical exam, a mammogram taking views from different angles, an ultrasound scan and, if needed, a biopsy to determine the nature of the abnormality. Not everyone who is recalled will be diagnosed with breast cancer but the extra investigations can be uncomfortable and it can be a stressful time waiting for the results. This is why it is important that a screening test is good at detecting cancer when it is present and has a low recall rate.

Why can't I have the ultrasound scans to screen for breast cancer?

Studies have shown that an ultrasound scan is not an effective tool for routine screening for breast cancer. Ultrasound examinations are used to clarify the finding of a clinical breast examination, mammogram or MRI scan, where a lump or thickened area has been detected. It is also used when biopsies are taken.

What choices can you make to help to reduce your risk of developing breast cancer?

Risk-reducing surgery: Women who have risk-reducing mastectomies reduce their risk of developing breast cancer to less than 5% over their lifetime, which is less than the risk in the general population. Women who have their ovaries removed before the menopause reduce their risk of developing breast cancer by up to 50%, even when hormone replacement therapy is given.

Lifestyle and diet: Currently there is no definitive scientific evidence to suggest that there are specific lifestyle or dietary factors that reduce or increase the risk of breast cancer for *BRCA* carriers. Many scientific studies in the general population have shown that limiting alcohol consumption, maintaining a healthy weight, being physically active, and breast feeding can help women to reduce their overall risk of developing breast cancer. Having a healthy diet that includes plenty of fruit and vegetables, pulses and whole grain foods can help you maintain a healthy weight.

The Pill: There may be a small increase in breast cancer risk if the oral contraceptive pill is used for more than four years but evidence is still being gathered on this. It is not known if the mini-pill is a safer than the combined pill but it is one alternative that women may consider. Another alternative is the Mirena coil. We advise that women discuss their contraception with their GP to assess the range of options.

HRT: Studies have shown that women who take hormone replacement therapy (HRT) after the natural menopause (especially the combined HRT, rather than oestrogen only HRT) have a slightly increased risk of developing breast cancer compared with women who do not take HRT. However once women stop taking HRT their risk goes back to normal within 5 years of stopping HRT. We do not know if this same effect occurs in *BRCA* mutation carriers. However women who have risk-reducing surgical removal of their ovaries (bilateral salpingo-oophorectomy) at a younger age are usually offered HRT to prevent significant menopausal symptoms. Evidence indicates that these women still have reduction in breast cancer risk (despite taking HRT) if their ovarian surgery is undertaken before age 50.



Managing your risk of ovarian cancer

Women who are carriers of a faulty *BRCA* gene have an increased risk of developing ovarian cancer during their lifetime.

What is my risk compared with other women?

On average women have about a 2% chance of developing ovarian cancer in their lifetime. Women with a close relative affected with ovarian cancer may have a slightly increased risk of around 4-5%. Women who have a faulty *BRCA1* gene have a 40-60% lifetime risk of developing ovarian cancer. Women who have a faulty *BRCA2* gene have a 10-30% lifetime risk of developing ovarian cancer.

The risk of developing ovarian cancer starts to increase from around the age of 40 for *BRCA1* carriers and in the mid 40s for *BRCA2* carriers.

What are the symptoms of ovarian cancer?

It is important to be aware of ovarian cancer symptoms and discuss them with your GP. Ovarian cancer was once known as a “silent” disease, because its symptoms can be vague. Evidence now shows that any of the following three symptoms, if they occur on most days may suggest ovarian cancer:

- persistent pelvic and abdominal pain
- increased abdominal size or persistent bloating (not bloating that comes and goes)
- difficulty eating, and feeling full quickly

Occasionally, women may also experience other symptoms, such as urinary symptoms, changes in bowel habit, extreme fatigue or back pain, on their own or at the same time as those listed above. These symptoms are unlikely to be ovarian cancer, but may be present in some women with the disease. If you regularly experience any of these symptoms and they're not normal for you, see your GP.

There is a further leaflet available on:

www.nhs.uk/conditions/cancer-of-the-ovary/pages/symptoms.aspx

Is ovarian cancer screening available?

Currently there is no proven test or group of tests that reliably diagnoses ovarian cancer at an early stage. Therefore no routine screening for ovarian cancer is currently available.

Is there any research into ovarian screening?

A large study called the UK Familial Ovarian Cancer Screening Study (UKFOCSS) recruited patients from 2002–2011 to look at how to screen high risk women for ovarian cancer. They expect to report their findings about the effectiveness of their screening technique in 2013/14. It takes a long time to study a new screening technique in order to get meaningful results.

How did the UKFOCSS screen women for ovarian cancer?

Women aged 35 and over were recruited to this study. They were offered annual ovarian ultrasound examinations and blood tests to measure a protein called CA125 three times a year. The ultrasound aims to detect changes in the size and appearance of the ovaries. The CA125 protein level is often raised in women who have ovarian cancer. The study was trying to see if small increases in the CA125 level were an indicator of early signs of ovarian cancer and to determine how often the CA125 would have to be measured, in order to detect ovarian cancer at an early stage.

Have there been any results from the study yet?

The early results from the study indicate that if a woman has normal CA125 levels and a normal scan it is unlikely that she has ovarian cancer at the time the tests are done. However, women on the study who were diagnosed with ovarian cancer were not all detected at an early stage of the disease. Further research and analysis is needed before we know if ovarian screening is effective in improving survival from ovarian cancer.



Why can't I have the ultrasound and blood test anyway?

The problem with having these tests without knowing if they actually work as a screening test is the risk of a false positive result – women may get results which initially appear abnormal and need further, possibly invasive testing to clarify the results. This can be very stressful for women even when they get a normal result at the end of their investigations. The other problem is that this test may be falsely reassuring and women may discount the option of risk-reducing surgery if they are having these tests. We can only offer a screening test if it has a good rate of detecting cancers at an early stage and a low false positive rate – meaning that it doesn't identify too many women incorrectly as having signs of ovarian cancer.

What is available then?

We know that taking the oral contraceptive pill is protective against developing ovarian cancer. However, if women with *BRCA* mutations take the pill for an extended period of time (more than four years), it may slightly raise their risk of developing breast cancer.

The other option women can consider is having risk-reducing surgery to remove their ovaries and fallopian tubes, before any cancer is diagnosed.

Reducing risk

Risk-reducing mastectomy

Women who have a faulty *BRCA1* or *BRCA2* gene may choose to have screening to manage their increased risk of breast cancer. However the main drawback to screening is that it does not prevent cancer. If a woman wishes to reduce her risk of developing breast cancer she could consider risk-reducing mastectomies. This is the surgical removal of breast tissue to try to prevent the development of cancer. There are various types of operations, but, in general, as much breast tissue as possible is removed. There will be some breast tissue remaining but the lifetime risk of breast cancer would generally be reduced by 90-95%. Women who have the risk-reducing surgery will no longer need annual mammographic screening because they will have very little breast tissue left. Reconstructive surgery can be offered at the same time as the risk-reducing mastectomies.

Making a decision to have risk-reducing surgery is very personal and very complex. There are many factors to consider. There are decisions to be made about the type of surgery you wish to have. The surgical team will explain the options to you over several appointments. You will have a chance to look at pictures with the breast nurse and speak with a clinical psychologist about the potential emotional impact of the surgery. One advantage of having risk-reducing surgery is that you can pick a time to have surgery and make arrangements in advance regarding work and childcare for your recovery period.

A booklet called ***Understanding Risk-reducing Breast Surgery – Prophylactic Mastectomy and Reconstruction*** produced by Macmillan Cancer Support provides information about many aspects of this surgery, for women who are considering this option. The booklet includes information about the surgery, reconstruction techniques, recovery, possible complications, the emotional effects of having the surgery and sources of additional information. If you are interested in finding out more about having risk-reducing surgery you can ask for a referral to the breast team. You would be under no obligation to go ahead with the surgery. We recognise as much information as possible is needed before this type of decision is made.



Breast surgery options for women affected with breast cancer

For *BRCA* carriers, the risk of cancer recurring in the affected breast is not significantly increased compared to other women with the same type of breast cancer, but the risk of developing a new tumour in the other (unaffected) breast is greater. This risk is about 50% if women are followed up to age 80. Having both breasts removed (bilateral mastectomy with reconstruction) will reduce this long-term risk to less than 5%. It will avoid the need for future breast screening by mammograms and MRI (magnetic resonance imaging). This surgery minimises the likelihood of needing treatment for a new cancer in either breast. It may provide an improved sense of control over risk and may avoid the worry associated with having breast imaging.

We do not know, however, that mastectomies are necessary to maximise a woman's survival chances. This is because many factors may influence an individual's long term survival such as treatment including chemotherapy and other follow-up such as breast imaging which aims to find new cancers (if they occur) as early as possible.

Some *BRCA* carriers (or other women at high risk) feel that mastectomies (usually with reconstruction) are not for them. They prefer to have lumpectomy, radiotherapy and then breast screening. There are a number of factors to consider in making such a surgical choice. These include how a woman feels about the impact of surgery on her body image and relationships. The decision-making involves discussions with different health professionals to help a woman decide what choice is best for her.

Some women may choose to have lumpectomy and radiation as their initial treatment and to think about further surgery later to both breasts. This is an option, although the skin elasticity after radiation can be less which can affect the type of reconstructive choices available.

Risk-reducing ovarian surgery and surgical menopause

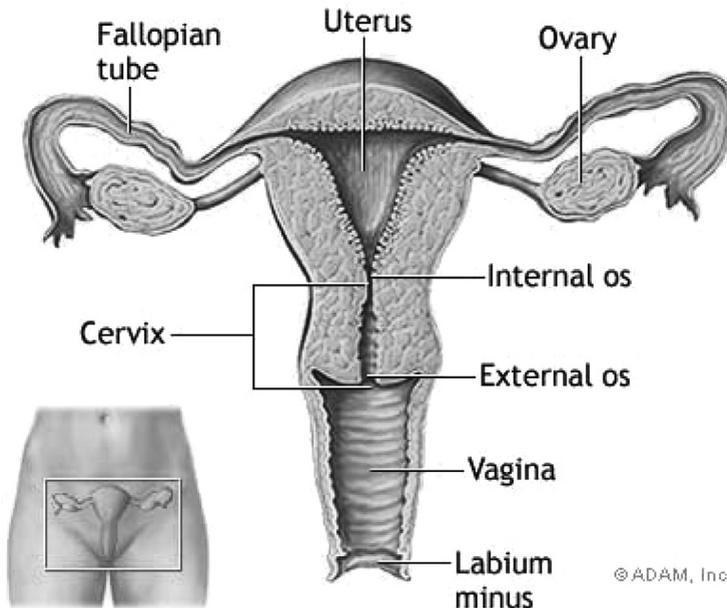
What is a risk-reducing bilateral salpingo-oophorectomy (BSO)?

A risk-reducing bilateral salpingo-oophorectomy (BSO, Bilateral (both sides) salpingo- (fallopian tube), oophor- (ovaries), ectomy (excision of)) is the surgical removal of a woman's ovaries and fallopian tubes before an ovarian cancer has occurred. This surgery is carried out to reduce the risk of developing ovarian or fallopian tube cancer.

How do the ovaries normally work?

Normally a woman has two ovaries and each month an egg is released from one of the ovaries. If the egg is fertilised a pregnancy may result. If a pregnancy does not occur, the lining of the womb (uterus) falls away and the woman has her period.

As well as storing and producing eggs, ovaries produce the female sex hormones called oestrogen and progesterone. These hormones cause a woman's breasts to develop, help make periods regular and work to build up the lining of the womb each month





to support a pregnancy (if it occurs). The ovaries also produce a hormone called testosterone that influences hair growth and sex drive (libido). As a woman ages and gets closer to the menopause, the ovaries make less of these hormones and her periods gradually stop. For most women this usually happens between the early-40s and mid-50s.

Who is offered a risk-reducing BSO?

Some women, for example *BRCA* mutation carriers, are advised to consider risk-reducing BSO because they have a high risk of developing cancer of the ovaries. In this situation it is also recommended that the fallopian tubes be removed at the same time, as this tissue is similar to that of the ovaries. Women may choose to have risk-reducing BSO after they have considered their individual risk of ovarian cancer against the risks of the surgery, the risk of premature menopause and depending on personal circumstances, such as their family planning situation.

What is the risk of ovarian cancer for *BRCA* carriers?

Women who have a *BRCA1* mutation have a lifetime risk of 40-60% of developing ovarian cancer. Their risk of ovarian cancer starts to increase in the early-40s. Women who have a *BRCA2* mutation have a lifetime risk of 10-30% of developing ovarian cancer. Their risk of ovarian cancer starts to increase in the mid-40s.

Are there other risk management options available?

- **Screening**

Unlike surgery, screening does not reduce the risk of developing ovarian cancer. The aim of screening is to detect ovarian cancer at an early stage. Currently in the UK ovarian screening is not offered to women through the NHS because we do not know if it is effective. A large study was carried out to evaluate whether screening is useful in detecting ovarian cancer. This study was called The UK Familial Ovarian Cancer Screening Study (UKFOCSS). The results of this study will help to determine whether screening should be offered as a clinical service.

- **The oral contraceptive pill**

The oral contraceptive pill has been shown to reduce the risk of ovarian cancer by a factor of about a half when taken for several years. However, the oral contraceptive pill is also known to increase the risk of breast cancer slightly if taken for more than four years. The benefits and risks of taking the pill as a risk-reducing option should be carefully discussed with your doctors. The most effective way to minimise ovarian cancer risk is still a risk-reducing BSO as this reduces the risk to less than 5%.

What if I prefer not to choose any of these options?

After discussion with your doctor you may decide that none of these options are appropriate for you at this time. It may be that you are younger than the recommended age for surgery, or it may be that you wish to stay fertile as you have not completed your family. It is important to make the decision that is right for you and this decision can be discussed with your doctor, nurse or genetic counsellor at any time.

For women who choose not to have surgery there are certain advantages and disadvantages that need to be considered. The advantages include that you will remain fertile (if you have not yet gone through the menopause) and that there are no side-effects (see “complications of surgery” below). The disadvantage of not having surgery is that it is not easy to recognise the signs and symptoms of ovarian cancer during the early stages. If ovarian cancer does occur and is only found at an advanced stage, it is much more difficult to treat effectively.

When should I consider having risk-reducing surgery?

The age at which a woman's risk of developing ovarian cancer becomes significant will vary depending on her family history and which gene fault is present.

- The risk of ovarian cancer in women who carry a *BRCA1* or *BRCA2* gene fault does not begin to rise markedly until about the age of 40 for *BRCA1* carriers and in the mid-40s for *BRCA2* carriers. Risk-reducing BSO is generally performed in women in their early to mid-40s.

- For most women, the value of risk-reducing BSO before the age of 40 is minimal. However, a very small group of women, who have a strong family history of cancer of the ovaries before the age of 40, can be offered risk-reducing BSO earlier.

How is risk-reducing BSO performed?

There are two main surgical ways of removing the ovaries; keyhole (laparoscopy) or open surgery (laparotomy). Both are carried out under general anaesthetic. Whichever approach is used, after the operation both ovaries and tubes will be sent to a laboratory to check if ovarian cancer is already present. You will get an outpatient appointment about four weeks after the procedure to discuss the final pathology results.

- **Laparoscopy or ‘keyhole’ surgery:** Most risk-reducing BSOs are done using this method. A small 1cm cut (incision) will be made in the belly button (umbilicus) through which a camera will be inserted. Carbon dioxide gas is used to inflate the abdomen so that the surgeon will be able to see the pelvic organs. The laparoscope relays pictures to a television screen and the surgeon is able to view the internal organs and abdomen. These images give the surgeon an external view of the pelvis from where they can carry out this procedure. A further two or three small incisions will then be made in the lower abdominal wall to create space for the safe insertion of instruments with which the surgeon will remove the ovaries and tubes. While this is a standard procedure used by gynaecological surgeons it should be noted that different surgeons use slightly different techniques. Some women feel some discomfort after surgery, mainly shoulder pain or bloating related to the use of the carbon dioxide gas. As with all operations, it is normal to feel tired for a day or two after the surgery.
- **Laparotomy or ‘open’ surgery:** This procedure involves the removal of the ovaries by a larger cut in the lower abdomen, usually along the bikini line. One in 20 women who opt for ‘keyhole’ surgery have an open incision performed instead as it may not be possible to perform the procedure with the laparoscope. Women who are more likely to need an open

incision include those who are overweight, those in poor general health, who have had previous operations on their abdomen, who have had a hysterectomy, women with a disease known as endometriosis and women with a condition known as pelvic inflammatory disease.

How do the two methods compare?

Keyhole surgery usually involves one overnight stay in hospital. Some keyhole surgery may be carried out as a day case, if this is considered appropriate for the patient. The average hospital stay for open surgery (when keyhole surgery is not considered the appropriate procedure for the patient) is increased to about five nights. The average return to normal activity is two to three weeks for keyhole surgery compared with about four to six weeks for open surgery. These figures are averages and this does vary a lot between different people depending on their usual work, family and exercise commitments. Both procedures take about the same operating time. Patients often ask when they can travel after surgery, in particular travel by plane. This does need to be discussed before the procedure due to the variations in patients' age, general health, post-operative recovery and their lifestyle commitments.

What other procedures are carried out?

The womb is not usually removed as part of the risk-reducing BSO operation, although some women with a history of gynaecological problems may consider having a hysterectomy (removal of the womb) during the surgery.

A hysterectomy is a bigger operation and may lengthen the hospital stay and time spent getting better. Some gynaecologists prefer to obtain a sample of lining from the womb (endometrium) during the procedure, known as curettage.

Before the procedure it is common practice to carry out a transvaginal ultrasound scan to assess the womb and ovaries and a blood test to check the levels of an ovarian tumour marker called CA125. If the surgery is delayed following these investigations, for whatever reason, the gynaecologist may wish to repeat both investigations before the new surgery date.

Who should carry out the operation?

The operation is not carried out by one person but by a team. A consultant gynaecology surgeon is usually head of that team. In the UK, that consultant would usually be a member or a fellow of the Royal College of Obstetricians and Gynaecologists (RCOG) and be on the specialist register of the General Medical Council (GMC). In addition, the RCOG issue certificates to surgeons who demonstrate that they have trained in laparoscopic surgery.

What are the complications of risk-reducing BSO?

There are complications associated with any type of surgery. The main possible complications are infection of the bladder, wound or urine, bleeding at the time of surgery requiring a blood transfusion, or the formation of blood clots. There is also a risk of herniation from the small abdominal incisions (so-called port sites) and damage to surrounding organs like viscera, bowel or bladder resulting in laparotomy (open procedure) to repair them. Fortunately these complications are relatively rare. Women at greater risk of complications include those with other illnesses, those who are overweight, those who smoke and those who have had previous surgery. You should discuss your own individual risk with your surgeon.

What are the advantages of risk-reducing BSO?

- Risk-reducing BSO minimises the lifetime risk of ovarian cancer to less than 5% in some studies.
- If a woman with a *BRCA1* or *BRCA2* alteration has a risk-reducing BSO performed before they reach the menopause then studies have shown that they may also reduce their risk of breast cancer by half.

What are the disadvantages of risk-reducing BSO?

- While risk-reducing BSO minimises the risk of ovarian cancer, it cannot reduce the risk by 100%. On very rare occasions it is not possible to remove all ovarian tissues due to scar tissue (adhesions). Another rare situation is that women may develop cancer of the lining of the abdominal wall (peritoneum). This type of cancer is clinically identical to ovarian cancer.

- Once the ovaries are removed, a woman is no longer fertile and is unable to have children naturally.
- Women choosing to have risk-reducing BSO before the menopause may experience the symptoms of a surgical menopause, which is described below. Some may have no significant symptoms at all; it varies greatly from person to person.

Surgical menopause

The most significant side-effect of BSO is the experience of going through the menopause. The menopause is the time in a woman's life when she stops having periods. While this usually only affects women who have not yet gone through the menopause, some women who are going through the menopause may find their symptoms get worse after the surgery. The natural menopause is usually very gradual, giving a woman time to adjust to the changes that are happening to her body. However, when the menopause occurs because the ovaries are surgically removed the symptoms can be quite severe and women may have a delay before receiving HRT while waiting for pathology results.

What is the menopause?

According to the British Menopause Society, the menopause is the permanent cessation of periods that results from the loss of ovarian activity. The ovaries stop producing an egg every month and the woman stops menstruating. The average age of menopause in the UK is 52. Menopause before the age of 45 is known as early or premature menopause. The process is usually gradual, as the ovaries slowly stop producing hormones, but if the ovaries are surgically removed then menopause will be immediate.



Menopausal symptoms:

Not all women experience the same type or severity of symptoms. Some of the issues reported by women are listed below. It is important to remember that only a minority of women have very severe symptoms or many symptoms at the same time.

- Hot flushes and accompanying sweats, often at night (75% of women experience this, more so in the first two years, but 20-50% continue long term)
- Headaches, lack of concentration/memory, low mood, insomnia
- Uncharacteristic tiredness, anxiety and irritability
- Palpitations, panic attacks
- Loss of bone mass or pain in joints
- Vaginal dryness/itching, reduced sex drive
- Dry skin, brittle hair, thinner hair, weight gain
- Stress and urge incontinence, urinary tract infections

How will menopause affect me?

It is difficult to predict how menopause will affect you as an individual. Menopausal symptoms do not run in the family, although the age of menopause can. Women experience menopause very differently, even within the same family. Treatment will be individualised and based on personal symptoms.

How does menopause affect bone health?

It is normal to lose bone density as women get older. Oestrogen works to ensure that calcium is not lost and protects against thinning of the bones. Osteoporosis is when the bones become weak and more likely to break. Often there are no signs of osteoporosis and it is only found after someone has a fracture, maybe after a fall. There are several risk factors for osteoporosis, including family history, low body weight, diet/nutritional deficiencies, smoking, some medications like corticosteroids, and premature menopause. If you have your ovaries removed

before 50, you should have your GP organise a bone density test (DEXA scan) at the time of surgery (baseline) and then every three to five years. If the bone density is low, the test should be repeated two-yearly. Treatment for low bone density can include a recommendation to eat healthily, take regular weight-bearing exercise and sometimes medication.

How does menopause affect heart health?

Oestrogen helps to control the level of cholesterol and other fats in the blood. After the menopause, the drop in oestrogen levels means fats could build up in the blood vessels of the heart, contributing to the development of coronary heart disease. Lifestyle advice and medication may be given to control the level of cholesterol and fats in the blood.

What is Hormone Replacement Therapy (HRT)?

Hormone Replacement Therapy (HRT) replaces the hormones such as oestrogen and progesterone that are lost when a woman has her ovaries removed. HRT comes in many preparations, some containing both oestrogen and progesterone (combined HRT) and some contain oestrogen alone (for women who have had a hysterectomy).

Should I take Hormone Replacement Therapy?

If you have your ovaries removed before age 50 and you have never had breast cancer, HRT is likely to be recommended for you. Studies have shown that HRT is safe in *BRCA* mutation carriers who have an early menopause after surgery. You might have to wait several weeks before starting the HRT while the tissue from your operation is checked for any signs of cancer. If you are near to the age of 50 then you might decide with your doctor to wait and see how your symptoms are and consider treatment options. If you have had breast cancer that was hormone (oestrogen/progesterone receptor) positive, you might be taking hormone therapy such as tamoxifen. Your oncologist will probably suggest that you do not take HRT, although if there are significant symptoms affecting your quality of life then discussion should be held with your treating team.



Does HRT increase breast cancer risk?

Some members of the public and health care professions still associate HRT with negative outcomes. It is important to distinguish between women taking HRT for many years after the natural menopause from young women taking HRT because they had early menopause (including spontaneous/medically or surgically induced). Having your ovaries removed before age 50 is known to protect against breast cancer. It is important to remember that the level of hormones in the HRT will be much less than the ovaries would have been making naturally if a woman still had her ovaries. Studies show that risk-reducing BSO before the age of 50 overall decreases the risk of breast cancer in high-risk women even when they take HRT. HRT is safe and recommended in young women to help offset the risk of other potential health problems.

What other options are available and how should I choose?

This should be done in consultation with a health care professional. You might need to try different options before finding the right treatment for you. If women are having significant menopause symptoms they can be referred to a specialist menopause clinic for advice.

There are many different preparations of HRT and several non-hormonal treatment options. Selecting the most appropriate solution may be an ongoing process, depending on your symptoms and how you react to treatment.

Aerobic exercise can improve quality of life and psychological health in women with hot flushes as well as help with low mood and insomnia. Infrequent high impact exercise can actually make symptoms worse, and it appears preferable to have regular, sustained activity (such as swimming or running). Occasionally women can feel tired and depressed as a result of low testosterone; so-called female androgen deficiency syndrome and this can be treated with testosterone replacement therapy. Venlafaxine is an anti-depressant that can help with low libido; this should only be considered after careful discussion with your doctor. Avoiding or

reducing alcohol or caffeine can help with hot flushes and sweats. Yoga and relaxation techniques such as massage or reflexology help some women to manage stress. If vaginal dryness is a problem, lubricants could be helpful.

The options for treating symptoms are normally addressed post-operatively once pathology results are available as it is impossible to know what symptoms each woman will experience after her surgery. Advice can be provided by your gynaecologist, your CNS, your GP or through a specialist menopause clinic.

Where can I get more information about menopause?

The Menopause Matters website has information, a magazine, an online forum and links to other sources of information:
www.menopausematters.co.uk

Where else can I find information concerning risk-reducing BSO?

The decision to undergo risk-reducing BSO can be a difficult one to make. There are many advantages and possible disadvantages to be weighed up including the effects on body image and lifestyle. It is important that the decision you make is the right one for you and that you have access to all the information you need to make the decision about whether to have surgery. This leaflet has covered most aspects of risk-reducing BSO. More detailed information is normally specific to individuals and best discussed with your surgeon, genetics doctor or genetic counsellor, oncologist, your family doctor or clinical nurse specialist.



Sharing information with your family

General issues

Who needs to know that a *BRCA* gene mutation has been identified?

During your genetic counselling session the doctor or the genetic counsellor will go through your family tree with you to identify who is at risk of inheriting the faulty *BRCA* gene. Cancer susceptibility due to a faulty *BRCA1* or *BRCA2* gene is inherited. Your close relatives (brothers, sisters and your children) will have a 50% chance of inheriting the faulty *BRCA* gene. In most families it will be easy to predict if the faulty *BRCA* gene came down through your mother's or your father's family because of the family history of cancer. The only way to prove this is to test family members to see who has the faulty gene. Only your relatives from that side of the family will have a risk of inheriting the faulty *BRCA* gene.

What do I tell people?

You will have received quite a lot of information about the *BRCA* gene, your risks and your options. It can be a bit daunting to know how to share all this information with someone else. Many people worry that they will be asked questions and they won't know the answers. Your genetics unit will not approach your relatives about your result, so usually it is you who would provide this initial information about the presence of a faulty *BRCA* gene to the family. The geneticists can provide you with a 'To Whom it May Concern' letter for you to share with your relative(s) which contains all the required information so that they can ask for a referral from their GP to their local genetics unit.

Why do other people in my family need this information?

Genetic information is different from most medical information an individual receives, because it is not only relevant to the individual but also to their family members. Genetic information can provide an explanation as to why someone has a particular health problem, but it can also predict future poor health or the risk of having a child affected with a particular genetic problem. If

someone is aware that they have an increased risk of developing cancer, they have the chance to make choices about genetic testing, cancer surveillance or preventative surgery. They may also decide to make changes to their lifestyle to help decrease their risk of developing cancer, and they may wish to consider the family planning implications and insurance issues. Knowing about the risk gives your relatives a chance to take action to reduce their risk of getting cancer or help ensure that cancer is detected at an early stage so it can be treated more effectively.

When should I share this information?

There is probably no 'right' time to tell people. Sometimes families are aware of the testing process and are waiting to hear the results. Other people choose to wait until they know their results before they mention it to anyone else. There will be a variety of factors that affect your decision to share this news, for example you may need time to get used to the information first, or someone may have been bereaved recently and you may feel it is better to wait a bit. Sometimes people are too young to be told everything or maybe you are waiting until you have the chance to see someone in person rather than telling them over the telephone or by mail. Women can start breast screening from 30 years of age so if your female relative is over 30 she could start breast cancer screening right away if she is at risk of having the faulty *BRCA* gene. Anyone in the family who has been affected with breast, prostate or ovarian cancer should be told as soon as possible because their doctors may need this information to make appropriate treatment decisions. It is important to highlight that women who are closely related (sister, daughter) to a person with a faulty *BRCA* gene can also have cancer screening, without undergoing genetic testing. We realise that not everyone wishes to have the genetic test.

How can I avoid upsetting my relative?

Many people are concerned that sharing this information will cause their relative to feel very anxious or guilty and responsible for causing this upset. It is always difficult to share 'bad' news. It might be useful to think of other times that you have had to share bad news, how you did it and what you learned from that



experience. It may be useful if you think about this information in a positive light; that members of your family, with this information, are in a better position to make choices that could reduce their risk of cancer or ensure it is detected as early as possible. It is important to remember that if someone has this *BRCA* gene mutation it is nobody's fault – we cannot control which genes were passed on to our children. It is also important to remember that if someone has a faulty *BRCA* gene they have always had it since the moment they were conceived, so what is different now is that we can identify it and give people options to manage their risk.

Where can I get help with telling my family?

The genetics team can help you to identify who needs to be informed in your family and provide you with a 'To Whom It May Concern' letter. We can provide you with a copy of a letter that was written by a lady with *BRCA* gene mutation to her family, which is an example of how someone else in your situation chose to share information. There is a resource list which can direct you and your family to additional sources of information. It can be a burden to have this responsibility. Perhaps there is someone else within your family that you could share the information with and who could then help by taking on some of the responsibility of telling other people within the family. In some families we see the information being passed on to one generation and it is then passed down within family units. The genetics team can discuss strategies for sharing information with you to make it as easy as possible.

Who is at risk of having the faulty *BRCA* gene in my family?

If you are a *BRCA* mutation carrier, your close relatives have a 50/50 risk of having the faulty *BRCA* gene. The faulty gene would have been present in your family for many generations; it is not new within your family. It is only that we are now able to identify who actually carries the faulty gene. You would have inherited the *BRCA* mutation from either your mother or your father. This faulty *BRCA* gene causes the increased risk of developing cancer.

Your brothers and sisters:

Your brothers and sisters each have a 50/50 risk of having the faulty *BRCA* gene. Each person would need to have genetic testing to determine if they have the faulty *BRCA* gene or not. You cannot predict if someone has the gene on the basis of their brothers' or sisters' genetic test results or if people look alike in the family.

Your children:

Your children (or future children) each have a 50/50 risk of having the faulty *BRCA* gene. We do not offer predictive testing to children because screening or risk-reducing treatment is not generally needed or available for children. Once they are older, each of your children could choose to have genetic testing to find out if they have inherited the faulty *BRCA* gene or not.

Your extended family:

The faulty *BRCA* gene would either have come down through your mother's or your father's family. So if you inherited the faulty *BRCA* gene from your mother, for example, then only your aunts, uncles and cousins on your mother's side of the family are at risk of having the faulty *BRCA* gene.

Does the faulty *BRCA* gene skip a generation?

The faulty gene does **not** skip a generation. Not all individuals with a *BRCA* mutation will develop cancer (particularly men). For this reason, it may look as if the mutation has skipped but in reality it was present in the previous generation.

Is the faulty gene only important if you are a woman?

When thinking about who is at risk of having the mutation in the family it does not matter if you are a man or a woman. Both men and women have *BRCA1* and *BRCA2* genes and men can also carry a faulty *BRCA1/2* gene. The risk of developing cancer for men is not as great as it is for women but they can still pass the faulty *BRCA* gene on to their offspring.



How do I know who to tell about the gene?

When you have your appointment in the genetics clinic the doctor or counsellor will go through your family tree with you and explain who is at risk of having the faulty *BRCA* gene and who is not at risk. We can provide you with a letter that explains about the gene fault for you to share with your at-risk relatives so they can decide if they want to have a genetics appointment to find out more information.

What does ‘dominant inheritance’ mean?

You may have heard the term ‘dominant inheritance’ at your genetics appointment when the doctor or the counsellor was describing how the gene mutation is passed down within the family. When we understand how a gene is passed down in a family we can then determine who is at risk of having the faulty gene within the family.

We have about 20,000 genes. These genes are the instructions that our bodies need to develop and function normally. All genes come in pairs; we get one copy from our mother and the matching copy from our father.

A dominant condition is one where a person only needs one of the two genes to have a mutation, in order to be affected. In a *BRCA* carrier, having one faulty (mutated) copy is enough for someone to have the increased risk of developing breast, ovarian and prostate cancer, even though the other copy of the gene, which they inherited from their other parent, works normally.

Therefore we know that if a person carries a *BRCA* mutation there is a 1 in 2 or 50% chance they will pass the faulty copy of the gene to their offspring; hence the 50% risk for children of *BRCA* carriers. We can also work out the risk to extended family by looking at how they are related to the *BRCA* carrier in the family.

Men and *BRCA* Genes: What do men need to know?

Everyone has two copies of the *BRCA1* gene and two copies of the *BRCA2* gene. These genes are part of our normal complement of genes. Genes are the individual instructions which make our bodies develop and function normally. The *BRCA* genes' role is to help the body correct mistakes that occur in the DNA code during cell division and therefore help to prevent cancer. If someone has a faulty copy of either the *BRCA1* or *BRCA2* gene it means that their body is less efficient at correcting mistakes that occur when cells divide and are therefore at a higher risk of developing cancer during their lifetime. For reasons we do not fully understand, *BRCA1/2* gene faults mainly cause an increased risk of breast and ovarian cancer.

Many people mistakenly believe that either men don't carry *BRCA* genes at all or that having a faulty *BRCA* gene is not relevant to men within the family. This is not true. Men have *BRCA* genes; they can carry faulty *BRCA* genes. They will have a slightly increased risk of developing certain types of cancer and they can pass on the faulty gene down to both sons and daughters.

What are the cancer risks for men who have a faulty *BRCA* gene?

Men who have a *BRCA* gene mutation have a slight increase in breast and prostate cancer risk as adults, and this is seen mainly in men with a change in the *BRCA2* gene. Men who have a *BRCA1* gene mutation have a 0.1-1% risk of breast cancer and a prostate cancer risk which is similar to (or may be slightly more than) the population risk. A man with a *BRCA2* gene mutation may have a 5-10% lifetime breast cancer risk and 20-25% lifetime risk of prostate cancer.

Can men be referred to genetics clinics for information about testing and cancer surveillance?

Yes, men can ask their GP or hospital consultant to refer them to their local genetic service to discuss their family history, the option of genetic testing and arrange appropriate cancer surveillance plans.



What are the risks to the children of men who have a faulty *BRCA* gene?

Men who carry a faulty *BRCA* gene have a 50-50 risk of passing the faulty gene to their children. The risk of inheriting the faulty gene is the same for both sons and daughters. However, daughters who inherit the faulty gene have a higher risk of developing cancer during their lifetime, compared with sons, because the risks are greater for women than men. Women need earlier and more frequent cancer surveillance.

What cancer surveillance can be offered to men who have a faulty *BRCA* gene?

Male carriers of *BRCA* mutations are advised to practise breast awareness and to inform their doctors of any changes in texture of breast tissue (due to the small risk of male breast cancer). They may also be offered the opportunity to take part in a research project which is looking at the efficacy of prostate screening using PSA blood tests annually from the age of 40 to 69. There is a small risk of some other cancers for which screening is not usually considered to be useful. However, this is individualised depending on the family history. As in all cases, men (and women) are advised not to smoke. If there are any new symptoms they should discuss this with their doctor without delay.

How common is prostate cancer?

Prostate cancer is the most common cancer in men in the UK. Cancer Research UK estimates that 1 in 9 men may be affected by prostate cancer in their lifetime and usually after the age of 70 years.

It is thought that only about 1–2% of prostate cancer that are diagnosed under in patients age 65 are caused by a *BRCA1* or *BRCA2* mutation.

How do you screen for prostate cancer?

Screening for prostate cancer currently consists of a Prostate Specific Antigen (PSA) test, which is a blood test, and sometimes in combination with an examination of the prostate gland.

Screening is not currently offered in the UK to all men within a National Screening Programme because its benefits are uncertain but some men choose to discuss the pros and cons of having a yearly PSA test with their GP once they are over the age of 50 years. The Department of Health screening committee is waiting for the results of a large research study (called ProtecT) that has been funded by the Department of Health before a decision is made about whether all men should be offered screening.

PSA alone is currently not recommended for screening in the UK because men with prostate cancer may not have a raised PSA and 2 out of 3 men with a raised PSA do not have prostate cancer. There is uncertainty about the best way to treat early prostate cancer. The treatments can cause unpleasant side effects.

Is prostate cancer screening available for men with *BRCA1* and 2 mutations?

As faults in the *BRCA1/2* genes may increase the risk of prostate cancer the IMPACT study is conducting a multi-centre international study of prostate cancer screening in men with mutations in *BRCA1* or *BRCA2*. It is offering prostate screening to men aged between 40 and 69 and who are from a family who are known to have a fault in either *BRCA1* or *BRCA2*. Men who have tested negative for the gene fault can take part to act as a 'control' group. More information can be obtained from www.impact-study.co.uk.

Predictive genetic testing

What does predictive genetic testing mean?

This term refers to a genetic test that is offered to someone who is healthy (for example, has not had a diagnosis of breast or ovarian cancer). The purpose of the test is to determine if the person has inherited the faulty *BRCA* gene that has already been identified in one of their close relatives. It is called a predictive test because if the person has the faulty *BRCA* gene it means that they have an increased risk of developing these cancers over their lifetime. Not everyone who has a faulty *BRCA* gene goes on to develop cancer but the risk is increased.



Who can have predictive testing?

Close relatives of an individual with a faulty *BRCA* gene can ask to be referred to their local genetics service by their GP to discuss the option of genetic testing. Your genetic doctor or genetic counsellor will go through the family tree with you to show you who in your family is at risk of having the faulty *BRCA* gene. We do not offer predictive genetic testing to children because this is an adult onset disorder so cancer screening or interventions are not necessary for children.

What happens when someone is referred for genetic testing?

If someone is coming for a predictive genetic test they may have one or two appointments to discuss the issues around testing, depending on their age and their understanding of the genetic information.

The first step for the genetics department is to confirm that there is a faulty *BRCA* gene in the family and obtain a copy of the relative's *BRCA* mutation report from the genetics centre where they had their test. If the report is not available then predictive genetic testing may not be possible. At their first appointment the doctor or counsellor will explain what the faulty gene is, how it is inherited, the associated cancer risks, and their risk of having the faulty gene and options for cancer screening or risk-reducing options. They will also discuss whether or not the individual wants to have a test at this point in their life, who they have for support and whom they have told about the test. We also discuss how a positive or negative result will impact on their lives and their relationships within the family. A letter summarising the consultation is sent to the individual after the clinic appointment. If they decide to have the test, results are given a few weeks later at an appointment (which is usually face-to-face, rather than by telephone). Individuals are welcome to bring a friend or relative with them to the results appointment for support.

What if someone doesn't want genetic testing?

Not everyone who is at risk of having a faulty *BRCA* gene wishes to have a predictive genetic test. Even if someone doesn't want

genetic testing it is still useful to talk to him or her in the genetics clinic. We can explain the options and give them a chance to ask any questions. If people are at 50% risk of having a faulty *BRCA* gene they are still eligible for extra cancer surveillance, such as breast screening from age 30, even if they don't want testing.

Does predictive genetic testing have a negative impact on insurance?

Sometimes people worry that if they have a genetic test they will have problems taking out life insurance. There is an agreed code of practice amongst insurance companies that that results of predictive testing for high risk cancer genes will not be used by ABI insurers to determine premiums or eligibility for life insurance. This agreement was recently extended until 2017. Further information can be found on the website: www.abi.org.uk

Planning to emigrate?

If you are planning to emigrate to a new country it would be good to check with that country's relevant office to determine if having a predictive genetic test could impact either your emigration application or your ability to obtain health insurance and/or health care provision before undertaking genetic testing.

A letter for your relatives (*BRCA1*)

As a result of genetic testing, a change (mutation) has been found in the *BRCA1* gene within your family. We have asked a relative to pass this letter on to you.

What does this *BRCA1* gene mutation mean for my family?

Genes are pieces of the DNA code that we inherit. The *BRCA1* gene has a role in protection against certain cancer risks. We all have two copies of the gene, one inherited from each parent.

A woman who has a *BRCA1* mutation (that is a change in the code where the gene does not function properly) has an increased risk of breast and ovarian cancer. A man with a *BRCA1* mutation may have a slight increase in breast and prostate cancer risk. A parent



(male or female) who has a *BRCA1* mutation has a 50% (1 in 2) chance of passing it on to a child (boy or girl). Cancer risk is not, however, usually increased in childhood for boys or girls.

Can I be tested for this *BRCA1* gene mutation?

Yes. Your GP can refer you to your local genetics centre. Predictive genetic testing (after a genetic consultation) is available to adult family members (blood relatives) to see if they have inherited the mutation in the *BRCA1* gene. This information can then guide advice on cancer screening (and cancer risk-reduction options).

What if I don't want genetic testing?

We know that some people may choose not to know if they have the *BRCA1* mutation but would still like to have advice, for example, on cancer screening. We are happy to have consultations with such family members. They can be offered cancer screening even if untested (if they are close relatives of someone who is known to have the *BRCA1* mutation).

What cancer screening is offered to people who have the *BRCA1* mutation?

Breast awareness: This involves being aware of changes in the breast and feeling the breast with the flat of the hand in a systematic way once a month, 5-10 days after the end of the menstrual period. It is also important for women to take time to look at their breasts in different positions. If there are any changes at all a doctor should be informed. We would recommend that all women practise this from their early-20s. Breast cancer is very rare in male *BRCA* carriers but any lumps in breast tissue should be reported to a doctor.

Mammographic screening and MRI (for women): We would recommend annual mammography from age 40. Between the ages of 30 and 50 years, we also advise breast MRI screening (magnetic imaging).

Surgical choices: If a woman who has the *BRCA1* mutation would like information on how breast and/or ovarian surgery can reduce cancer risks, then this is also covered in a genetics consultation.

The referral process to surgeons and other professionals involved in helping with these decisions can be explained.

Prostate screening: Researchers are studying whether prostate cancer screening is necessary and effective in male *BRCA1* carriers, using PSA blood tests annually from age 40 and we can provide more information on this if required.

Is any other type of cancer screening needed or available?

The need for any other cancer screening in the family can be reviewed if there are any other types of cancer in the family.

How do I access genetic advice?

If you would like to discuss cancer screening or genetic testing or both, we would recommend that you ask your GP for a referral to a Cancer Genetics Clinic. Genetics centres can be identified from the British Society of Human Genetics: www.bshg.org.uk.

A letter for your relatives (*BRCA2*)

As a result of genetic testing, a change (mutation) has been found in the *BRCA2* gene within your family. We have asked a relative to pass this letter on to you.

What does this *BRCA2* gene mutation mean for my family?

Genes are pieces of the DNA code that we inherit. The *BRCA2* gene has a role in protection against certain cancer risks. We all have two copies of the gene - one inherited from each parent.

A woman who has a *BRCA2* mutation (i.e. a change in the code where the gene does not function properly) has an increased risk of breast and ovarian cancer. A man with a *BRCA2* mutation may have a slight increase in breast and some increased prostate cancer risk. A parent (male or female) who has a *BRCA2* mutation has a 50% (1 in 2) chance of passing it on to a child (boy or girl). Cancer risk is not however usually increased in childhood for boys or girls.



Can I be tested for this *BRCA2* gene mutation?

Yes. Your GP can refer you to your local genetics centre. Predictive genetic testing (after a genetic consultation) is available to adult family members (blood relatives) to see if they have inherited the mutation in the *BRCA2* gene. This information can then guide advice on cancer screening (and cancer risk-reduction options).

What if I don't want genetic testing?

We know that some people may choose not to know if they have the *BRCA2* mutation but would still like to have advice e.g. on cancer screening. We are happy to have consultations with such family members. They can be offered cancer screening even if untested (if they are close relatives of someone who is known to have the *BRCA2* mutation).

What cancer screening is offered to people who have the *BRCA2* mutation?

Breast awareness: This involves being aware of changes in the breast and feeling the breast with the flat of the hand in a systematic way once a month, 5-10 days after the end of the menstrual period. It is also important for women to take time to look at their breasts in different positions. If there are any changes at all a doctor should be informed. We would recommend that all women practise this from their early-20s. Breast cancer risk is only slightly increased in male *BRCA2* carriers but any lumps in breast tissue should be reported to a doctor.

Mammographic screening and MRI (for women): We would recommend annual mammography from age 40. Between the ages of 30 and 50 years, we also advise breast MRI screening (magnetic imaging).

Surgical choices: If a woman who has the *BRCA2* mutation would like information on how breast and/or ovarian surgery can reduce cancer risks, then this is also covered in a genetics consultation. The referral process to surgeons and other professionals involved in helping with these decisions can be explained.

Prostate screening: Researchers are studying whether prostate

cancer screening is necessary and effective in male *BRCA2* carriers, using PSA blood tests annually from age 40 and we can provide more information on this if required.

Is any other type of cancer screening needed or available?

The need for any other cancer screening in the family can be reviewed if there are any other types of cancer in the family.

How do I access genetic advice?

If you would like to discuss cancer screening or genetic testing or both, we would recommend that you ask your GP for a referral to a Cancer Genetics Clinic. Genetics centres can be identified from the British Society of Human Genetics: www.bshg.org.uk

Passing on the cancer gene: How to tell the family

Sharing information about a *BRCA* gene within the family can be a challenge. There is no single right or wrong way of telling relatives about this news. Sometimes it is useful to know how other people have dealt with the same issue as it may give you some ideas about how to approach the topic.

The following article is an excerpt from a book written by a *BRCA1* carrier.

Recent legislation allows couples to eliminate the cancer gene when a child is conceived. This new ruling created a dilemma for our family. We had previously agreed that there would be no need to worry the younger members about our family cancer until about their late 20s, unless they themselves raised the subject. The picture was now quite different. Any affected family member could now choose to avoid having a pregnancy that would result in a baby who had inherited our family's cancer gene. Naturally, my four nephews and nieces aged 18–22 could only make decisions about this if they were fully informed well before their first pregnancy. I also wrote a paper that could be given to each of them if appropriate. I thought it might be easier to have the information

applicable directly to our own family circumstances. This is it:

“For most people who get cancer, it occurs without warning, seemingly out of the blue. However, a small proportion of cancers, particularly breast and ovarian cancer, do run in some families and are associated with particular genes. *BRCA1*, a breast cancer gene, is one of these and runs in the Bryan family. It can be inherited and passed on, by either male or female members. Children whose mother or father carries the cancer gene will have a 50:50 chance of inheriting the gene. As this cancer only involves breasts and ovaries, it rarely affects men. Nor had there, until recently, been any way of knowing whether a man had inherited the cancer gene unless one of his daughters developed that kind of cancer. Grandpa’s mother, Silver Bryan, and your great-aunt, Grandpa’s sister, Sylvia Wevill, developed cancer of the ovary. So did a number of more distant cousins. However, we did not know whether Grandpa had inherited the cancer gene until Bunny got cancer of the ovary. Soon after that, it became possible to positively identify the gene through a blood test. Felicity and I then arranged to have this blood test and found that we too, like Bunny, were positive. If a woman has the cancer gene, she will not necessarily develop cancer. There is, however, about an 80% chance that she will do so at some stage in life unless she takes action to avoid it. At what age the cancer appears can vary widely. In our family, no one has had it before they were 40. Felicity and I had our ovaries removed once we knew we didn’t want, or couldn’t have, any more children. Unfortunately, Felicity later developed breast cancer. Luckily, this was caught early and treated. I avoided getting ovarian or breast cancer by having everything at risk removed. Whether the cancer in my pancreas is related to our *BRCA1* family gene is not known. It is apparently quite rare.

Some people prefer not to find out whether they have the gene. Clearly, such people will not want to have the test. Others think it helps to know. If, for example, the test proves negative, you can feel reassured and needn’t worry any more about it. If you find you do carry the gene, a number of things can be done to prevent any danger of the cancer becoming a serious problem. Women can have frequent screenings of ovaries and breast by ultrasound to

detect any cancer as early as possible. Ovaries are more difficult to screen than breasts, so to be (almost) completely safe, ovaries probably need to be removed by your early 40s. As both Felicity and Bunny carried the gene, all four of you have a 50:50 chance of carrying it too. You could all be negative and therefore in the clear. But, equally, you could all have the bad luck of carrying it. The most likely situation is that some of you will have it and others not. Until this year, there has been no hurry for you even to think about the chances. Even if you were found to be positive, there was nothing that needed to be done or even considered until your late 30s. The situation has now changed. If you carry the cancer gene, it is now possible to avoid passing it on to any child you may have. A child conceived by someone who carries the cancer gene, either in an egg or a sperm, has a 50:50 chance of inheriting that gene. You all four, therefore, need at least to know about this new option before you think of getting pregnant. You can avoid having a child with the cancer gene by taking advantage of a new procedure – Pre-implantation Genetic Diagnosis, or PGD. This is done using IVF, in vitro fertilisation, or the “test tube” method. After several eggs have been collected from the woman and fertilised by sperm, the resulting embryos can be tested for the gene. Only an embryo that is negative for the cancer gene would be transferred to the womb. Many people will not want to even consider PGD, but it is important that you at least know what options are available. Over the next 20 years, there are likely to be many improvements in the detection and treatment of cancer and the chance of dying will certainly decrease. By how much and when unfortunately no one can say.”

All four took the information seriously, but without undue alarm. Their first reaction was that they would probably go ahead and be tested when practicable. They all understood about the option of PGD and embryo selection. We of the older generation needed to remind ourselves of the importance of confidentiality. The young all know that their parents and I are happy to talk about any concerns they may have. But the decisions they are to make are theirs, not ours. This applies not only to what they decide and do, but also to what they reveal and to whom. For a family that talks openly about personal matters, this will require restraint from



us. We should not inquire about their plans. They have a right to choose how much they reveal and to whom. And we have no right to expect or request more.'

Excerpt from *Singing the Life: The Story of a Family Living in the Shadow of Cancer* by Elizabeth Bryan. We are grateful to the publishers and Dr. Bryan's family for their permission to print and distribute this passage.

Talking to children and young people about *BRCA*

Many parents find the prospect of talking to their children about the presence of a faulty *BRCA* gene within the family difficult and distressing. Studies show that parents' first instinct is to protect their children and they find it difficult to know what and when they should tell their children. Parents are often dealing with their own concerns about their health and future wellbeing, and can feel a sense of guilt that their children may also be at risk.

What helps children and young people?

In most cases, children cope better when the family is more willing to discuss what is happening to different members. Talking to children helps them feel valued and respected and helps them cope better than when they are left feeling confused and unsure how or what to ask.

Children get information from many places including school, television and friends. They are likely to already have some knowledge about cancer and possibly about hereditary cancer. By talking to them, you can help them sort out what is accurate and what is inaccurate and clarify things they are not sure about.

Children will probably be most worried about their parent developing cancer so they will need reassurance and reminders that having the *BRCA* gene mutation does not always result in cancer. However, knowing you carry the gene mutation means that you can have regular tests to ensure that if a cancer arises it can be detected very early on and treated.

When is a good time to tell your children?

There is no 'right' age but try not to keep secrets. Children and young people place great emphasis on trust and honesty from parents. Children often observe changes in their parent's behaviour and may try asking questions or may be waiting for you to discuss what is happening. Watch for any changes in your child's behaviour, it may indicate that they are worried or concerned about what they have observed or overheard.

By the age of 8 years, children learn not to ask difficult questions unless their parent(s) gives them permission because they fear upsetting their parent(s). Therefore, you may have to prompt your child, and let them know you are willing to talk with them about the *BRCA* gene. This applies to older children too.

What information do you tell children?

Try to respond to children's questions, using language appropriate to their age. Providing small amounts of information gradually is likely to help children understand and cope best. Check on the question being asked so that you find out what your child actually wants to know.

Explain and provide the name '*BRCA* gene' - children cope better because knowing the name allows them to discuss it with you, and this knowledge gives them a sense of control. Parents often place a positive emphasis on the importance of knowing about the *BRCA* gene because it means there are improved screening and perhaps treatment options. When children become adults, there may also be even better treatments available, which you can explain to your child.

Communication tips

- Children and young people prefer informal discussion often while doing other things together, for example, driving, cooking or gardening.
- Check their understanding because children worry about upsetting their parents and so may not always ask.

- 
-
- Talking about *BRCA* is an ongoing discussion rather than a one-off conversation. Like adults, children probably need information given to them more than once. They may need time to digest information and then want to come back and discuss it with you.
 - Discuss information young people find on the internet or in newspapers.
 - Discuss emotions – provide reassurance they are not alone.
 - Explain parents' behaviour if they are anxious or upset.
 - Being with peers, for example cousins, in similar circumstances might be helpful.
 - Support and guide decision-making, especially with young people, who usually like to make their own decisions but with advice from parents.
 - If you do not know the answer, explain some questions do not have answers or that you will try to find out for your child.
 - Agree appropriate times to discuss *BRCA* and cancer if your child asks questions at inopportune moments.

What are children likely to know about genes and inheritance?

8-11 years: They have a very basic understanding of heredity and that they share characteristics with parents and they may talk about genes but not fully understand what they are. Often children of this age cope with simple explanations in response to their questions and are not easily upset, although you may have to reassure them that having an altered *BRCA* gene is not the same as having cancer. Children and young people can easily confuse this so it often needs repeating throughout development into adulthood.

12-14 years: Children are beginning to develop more insight about heredity, will begin to recognise that you having the gene mutation may have implications for them but will usually cope well if you explain there is only 50% chance of them having the *BRCA* gene alteration.

15-17 years: Children recognise the risks to their parent, themselves and often their future children and can begin to

consider genetic testing. By this age, young people will be learning about *BRCA* and other hereditary diseases in school curricula.

Most children are quite pragmatic in response to genetic risk in families affected by inherited genetic conditions. Children and young people are often focused on developing friendships, school and their personal interests so do not dwell on the risk.

What helped parents talk to their children?

It has been observed that the following points helped parents talk to their children:

- Younger children do not have the experience to recognise and anticipate the fuller implications so there is a gradual realisation.
- Not feeling under pressure to talk before an impending event, for example, a school science lesson.
- Talking was a relief for parents and ultimately easier than keeping the secret.
- Parents can be the role models for young people – giving them insight into how to cope with the risk.
- Recognising siblings may all have different needs, trying to find out what each understands at different times in their development.
- Ensuring children and young people understand a positive genetic test is not a cancer diagnosis – some get quite confused about this.
- Belief in a child's right to know.
- Support of other family members, friends and health professionals.
- Attendance at support groups gave focus to regular discussion with children and young people with parents discussing where they were going and what had been discussed when they returned.

Preparing to talk to your children

It might be worth considering the following benefits and drawbacks in preparing to talk to your child but try to take naturally occurring opportunities where possible.

Benefits	Drawbacks
<ul style="list-style-type: none">• Makes family closer• Support for children• Gives insight and helps them realise that parents being upset about <i>BRCA</i> is not down to them or their behaviour. It is 'no fault' of theirs• Confidence to talk to close friends• Children and young people feel valued by parent(s)• Allows discussion of altered <i>BRCA</i> and cancer risk without centralising it to life• A shared reality and understanding helps children and young people cope• Reduces risk of children getting inaccurate information from elsewhere.	<ul style="list-style-type: none">• It can be emotionally taxing dealing with questions• Children and young people can remind you about <i>BRCA</i>, when you do not want to be reminded• Questions can arise at inopportune moments – explain when it is appropriate to discuss it• Wanting to talk to peers but networks can be limited• Can affect schoolwork for a short time (but so can worrying about what is happening in their family if there is secrecy).

Alison Metcalfe & Gill Plumridge (June 2010 Version 2)

Adoption

Is it possible to share the *BRCA* information with a relative who was adopted out of the family?

Yes, NHS Adoption services do provide assistance to families to pass on important hereditary (genetic) medical information to individuals who have been adopted.

What information is required?

If an individual wants to request help in passing on details about a serious genetic condition, they can write to the NHS Adoption Service directly. They need to provide the information from the adoption certificate (for example, the post-adoptive name). A letter from a GP or consultant is also required explaining the medical condition. However, the GP/consultant letter must not quote any of the personal identifying details, such as name, date of birth etc. A covering letter will be sent from the adoption office to accompany this letter. If the sought person has died, the GP/consultant's letter is returned to individual who requested assistance.

What if the post-adoptive details aren't known?

If an individual does not have or cannot get a copy of the adoption certificate they can contact their local social services department. All social services departments have links with accredited intermediary agencies who can request the details from the adoption section of the General Registry Office (GRO), which is the only department that have the records to link the birth name with the adoptive name. If the agency is able to trace the person, the individual seeking to pass information on to the adopted person will then be advised to send a request letter with the doctor's letter to the NHS Adoption Service (see above). Individuals seeking to share genetic information will not be provided with any personal details of the adoptive person. The intermediary agency will then assist the NHS Adoption Service to pass on information.



Would this service allow us to get in touch directly with our adopted relative?

No, this service does not facilitate any contact between the birth family and the adopted person.

What can an adopted person do if they wish to contact their birth family to share genetic information?

If an individual has been adopted and wishes to share genetic information with their birth family the NHS Adoption Service can also assist in passing on the information. Adoptive individuals do not have to reveal any identifying information. Accredited intermediary agencies can also help adopted adults check if they have a significant family history of cancer or a genetic disorder.

Website: <http://www.ic.nhs.uk/services/nhs-adoptions-service/passing-on-vital-medical-information>

Predictive genetic testing and insurance

This information is for people who are considering having a predictive genetic test for an adult onset condition such as an inherited cancer syndrome. A brief outline of the current agreements regarding the use of genetic test information by insurers is provided. If you have specific questions about your own circumstances we advise you to speak to an approved financial advisor.

What is the current law on the use of genetic test information?

Currently, there is no law in the UK that explicitly prevents discrimination on the basis of genetic differences. However, both Government and insurers have a common interest in people knowing they can take out insurance with confidence and so they set up an agreement on genetic tests and insurance. The concordat and moratorium enables people to take out substantial amounts of insurance without having to disclose the results of genetic tests used to predict the likelihood they will get an illness in the future due to a faulty gene. It runs for a set period with a planned review to ensure that the interests of both consumers and insurers are

taken into account. Reviews are needed because geneticists can only see so far ahead and new discoveries in genetic science are happening all the time. The moratorium runs to 2017 with the next review due in 2014.

How does this agreement affect me if I have a predictive genetic test?

According to the agreement there are ten commitments on the information to be sought from customers:

- Customers will not be asked to undergo a predictive genetic test, disclose a family member's test result or diagnostic genetic test acquired as part of clinical research; or disclose any predictive genetic test results that are made available after their policy has started, for as long as that policy is in place.
- Customers will not be required to disclose results of predictive genetic tests for cancer risk genes, for example, *BRCA1* and *BRCA2*.
- There is a detailed process for resolution of disputes and complaints, which can involve the independent Arbitration Service (www.arbitrators.org) or Financial Ombudsman Service.
- Insurers will continue to use family history information to assess risk and underwrite policies. This practice is not affected by these agreements.
- Insurers may agree to take favourable predictive test results into account, to offset the family history information when setting the premium (underwriting).
- Insurers will not use predictive genetic test results to underwrite travel insurance, private medical insurance or any other one-off or annual policy, or for long-term care policies.

***BRCA* carriers affected with cancer**

If you are buying new insurance products after a diagnosis of cancer and you have had a diagnostic genetic test, insurance companies are entitled to ask for this information just as they may request information about your treatment or surgery. This



scenario is not included in the moratorium on predictive testing because you are already affected by the condition. (Predictive testing refers to testing individual who do not have symptoms of the genetic disorder at the time of testing.) However, you only have to answer the questions that they ask you honestly. Please see the information produced by the Genetic Alliance or speak with a financial advisor if you need more information about your circumstances.

Where can I get further information?

- Association of British Insurers (ABI): www.abi.org.uk
020 7600 3333
- Department of Health – to request a copy of the Concordant and Moratorium on Genetics and Insurance: 020 792 1518
- Macmillan Cancer Support: www.macmillan.org.uk
- The Genetic Alliance have a patient leaflet relating to all aspects of insurance questions:
<http://www.geneticalliance.org.uk/insurance.htm>

Did you know?

Family Planning

If you are found to have a *BRCA* mutation before you have your family you may have some questions about risk for your future children and you may wish to know if anything can be done to minimise this risk. Anyone with an inherited condition has a risk of passing it on to their children. The risk depends on the specific genetic condition, as there are several ways an inherited condition can be passed on in a family.

If you have a *BRCA* mutation, it is a dominant condition. Therefore there is a 50-50 or 50% or 1 in 2 chance that each of your children could inherit the *BRCA* mutation. This risk is the same for each pregnancy. The concept of dominant inheritance is explained in more detail in an earlier section of this booklet.

Everyone who has a genetic condition can choose from a variety of family planning options and each option has pros and cons. It is a highly personal decision for you and your partner and many factors will influence your choice. There is no right or wrong decision – you have to make the choice that best suits your circumstances, feelings and beliefs.

In summary the options are:

1. Have your children without any intervention. Each child would have a 50% chance of inheriting the *BRCA* mutation and if they inherited the mutation they would be at an increased risk of developing cancer as an adult.
2. Some couples decide not to have a family at all because they are very concerned by the risk of passing on the *BRCA* mutation.
3. Adoption – some couples may chose to adopt a baby to avoid the risk of passing the *BRCA* mutation to the next generation.
4. Egg or sperm donation – some couples chose to use donor eggs (if mum is the *BRCA* carrier) or donor sperm (if dad is the *BRCA* carrier) to avoid passing the *BRCA* mutation to the next generation.

- 
-
5. Prenatal testing – some couples may chose to get pregnant naturally and have a test during the pregnancy to see if the baby has inherited the *BRCA* mutation. The couple would plan to continue the pregnancy if the baby has not inherited the *BRCA* mutation. However, if the baby has inherited the *BRCA* mutation, they would choose to end (by a termination) the pregnancy.
 6. Pre-implantation genetic diagnosis (PGD) (for further information see below) – some couples may choose this option to avoid passing the *BRCA* mutation to their offspring and avoid considering prenatal testing and possibly termination. There is no guarantee this technique will result in a successful pregnancy and funding for it on the NHS may not be available to all patients.

Some of these options may seem drastic at first glance. Please bear in mind that these are the options for couples at risk of passing any genetic condition to their children. Some genetic conditions cause severe learning or physical disabilities, or often both and some genetic conditions may be life-limiting meaning that the child would not survive into adulthood due the condition. For most genetic conditions there is no cure and limited options to treat the symptoms.

In our experience talking to couples about family planning, most choose to have their family without any intervention. If anyone expresses an interest in finding out more about any of the other options we can help make referrals or direct people to the appropriate services. We are happy to talk about these options in more detail at a genetic counselling appointment, if you would find that helpful.

As we get asked about PGD often we have provided a brief overview of it here; as well as websites to get more detailed information.

Pre-implantation Genetic Diagnosis (PGD)

What is it?

It is a technique used to select embryos that have not inherited the gene mutation which causes the genetic illness or cancer predisposition in a family.

Why would people consider having PGD?

Some couples wish to ensure that they avoid passing on a gene mutation to their children. They want to be confident that their children won't be affected with the genetic illness or cancer predisposition (although it is important to point out that a risk of cancer would still be present in a child without the genetic mutation, just like for everyone else). Alternatives to PGD could include prenatal testing and termination of affected pregnancies or using donor sperm/eggs or adoption or deciding not to have children.

How is it done?

PGD is carried out in conjunction with an IVF (in vitro fertilisation) procedure. The egg and sperm cells are collected from each parent and the embryos are created outside the woman's body. The embryos are then tested for the genetic mutation in the family. Only embryos that have not inherited the genetic mutation are selected to be implanted.

Who can have PGD?

If an individual has a specific gene mutation that is known to cause a predisposition to cancer they may be able to have PGD. If there is a strong family history of cancer, but no gene mutations have been identified or genetic testing is not possible in your family, then PGD is not an option. Couples who are referred to the PGD centre at Guy's and St Thomas' NHS Foundation Trust will need to provide DNA samples from specific relatives in order to undertake the testing. If this is not possible, we can help identify another PGD centre that may be able to offer direct mutation testing.



If you have had cancer and stored embryos prior to treatment and your treatment has left you unable to have children naturally, we would not recommend PGD treatment. For example if you only have 6-7 stored embryos and these embryos represent your only chance to have your own biological child, PGD treatment may mean that all embryos are tested but not suitable for use, either because they are all affected or not suitable for implantation.

What about funding?

The PGD centre will apply for funding on your behalf. It is possible that funding for PGD for adult onset conditions such as *BRCA* may be limited in the future. Couples are unlikely to obtain NHS funding if they already have living unaffected children, or if the mother's BMI is greater than 30, or the mother is older than 39 years. If couples are considering self-funding the cost of one cycle is currently about £9000.

Where can I find out more about PGD?

If you are interested in considering this option, please ask to be referred to a PGD centre. There is one NHS PGD centre in London which offers testing for inherited cancer syndromes. At your first appointment they will discuss all aspects of PGD, including fertility assessment, funding applications, licence applications, time frame, risks and success rates. It can take 1–2 years from the first appointment to treatment, so you may wish to ask for an initial consultation long before you actually want to start your family.

Please refer to the centre's website for more detailed information.

The Centre for Pre-Implantation Genetic Diagnosis:
www.pgd.org.uk

BRCA genes and the Ashkenazi Jewish population

How common are faulty *BRCA* genes in the Ashkenazi population?

In the general population, around 1 in 800 individuals have a fault (mutation) in one of their *BRCA* genes but it is more common in some population groups. It is estimated that as many as 1 in 40 individuals of Ashkenazi Jewish descent have a *BRCA* gene alteration. There are 3 common *BRCA* alterations in the Ashkenazi Jewish population (2 in *BRCA1*, 1 in *BRCA2*), which account for almost all (>96%) of the *BRCA* gene alterations in the Jewish population.

What kind of family history might be significant?

The indications in a family history that there may be a faulty *BRCA* gene are:

- Many relatives on the same side of the family with breast and/or ovarian cancer.
- Several close relatives affected with breast cancer at a young age.
- A close relative with cancer in both breasts, or breast and ovarian cancer.
- Breast cancer diagnoses in male relatives.

Who can have genetic testing?

Over 1000 *BRCA* gene mutations have been found in the general population (non-Jewish) and testing is offered only to individuals with a strong family history. As only three gene mutations account for most of the *BRCA*-associated risk in Ashkenazi Jewish individuals, and positive results can be associated with a less strong family history, testing is less complex and can be offered to individuals with a weaker family history of breast and ovarian cancer. Ashkenazi Jewish individuals who are found not to have one of these three gene mutations have a very small chance of carrying a *BRCA* gene alteration. Testing for a rare *BRCA* mutation



may be offered to those with cancer who also have a strong family history of breast and/or ovarian cancer.

How can I find out more about genetic testing?

If you are concerned about your family history of cancer and wish to find out more about genetic testing, your GP can refer you to the local genetics service for an appointment.

Current studies and trials

Individuals attending the cancer genetics clinic will be offered an opportunity to take part in appropriate research trials. This leaflet is designed to give some general information about taking part in research. Specific details about research projects that are currently open can be obtained from the genetics team.

Taking part in research

Taking part in research studies is voluntary and if you prefer not to take part in research that is not a problem at all. We invite everyone we meet in the clinics, who is eligible, to take part in research. If you would prefer that we didn't ask you then please let one of the clinicians know so that we can make a note of your preference. We have many research projects running at one time, and it is likely that you will be invited to take part in several studies. You will be given an information sheet about each study and given as much time as you need to think about whether you would like to take part in the study. You will also be given the opportunity to ask any questions about the research project, including any benefits or disadvantages of taking part. With all research, if you decide to take part, you are free to withdraw at any time, without giving a reason and this would not affect the standard of care you receive.

Confidentiality

If you decide to take part in a research project any information you give us for the purposes of the study will be treated like all medical information. It will be kept strictly confidential and will be accessible only to the immediate study team. Information is stored

on databases adhering to guidelines set out in the Data Protection Act. If specimens (for example, blood or urine) are obtained from you as part of the study they will be stored using identifying codes that will be known only by the research team. If you decide to withdraw from a study and you would like us to destroy any samples that you have provided for research we will be happy to do so.

Types of research project

- Epidemiological studies: studies looking at the interaction of environmental, lifestyle and genetic factors in the development of cancer
- Screening studies: studies looking at new methods of screening for cancer
- Psychosocial studies: studies looking at the emotional and societal impact of disease
- Drug trials: studies looking at the use of new drugs in the treatment or prevention of cancer
- Tissue bank: the storage of samples in a sample bank for future research

New cancer treatment options for *BRCA* carriers

It can sometimes be useful for the oncology team to know if patients have a *BRCA* mutation so they can take this into account when considering options for treatment trials. If you are seeking information on cancer research trials you should discuss this with your oncology team and you can refer to these websites: www.cancerhelp.org.uk/trials and www.cancer.gov/clinicaltrials

Patients may be referred to be considered by their treating oncology teams if the teams feel that these drugs may be useful after more established treatments have been tried. It is important to note that trials for any drug may not be open to new patients at the time you may be discussing treatment trials with your oncologist.



Currently *BRCA* carriers who develop cancer are initially given the same chemotherapy treatment options as people who develop cancer out of the blue. We know that *BRCA* carriers in some situations have more benefit from certain standard therapies than women with non-hereditary cancer. For example, *BRCA* carriers with ovarian cancer receiving standard platinum treatments have higher response rates and longer times to relapse than women with non-hereditary cancer. Studies are examining how *BRCA*-related tumours respond to standard treatments and to new agents including those designed specifically to target the *BRCA*-mutated cancer cells.

Examples of relevant trials include:

The TNT Trial

This is a trial for women who have certain types of breast cancer, including women who have a *BRCA* gene mutation. It is based on new research findings, which suggest that for people who have a *BRCA* gene mutation and whose breast cancer has returned, chemotherapy treatment with carboplatin may work better than a standard breast cancer chemotherapy treatment (docetaxel). In order to find out whether giving carboplatin to women with hereditary breast cancer will be of more benefit than docetaxel, one group of women in the study will have carboplatin and the other group will have docetaxel. Anyone not responding to their treatment can then receive the alternative drug. The differences between the two groups will then be compared. You may be able to take part in the trial if you have a mutation in the *BRCA1* or *BRCA2* gene and you have had breast cancer in the past that has now come back. This is called recurrent, relapsed, secondary or metastatic breast cancer. (Source: <http://www.cancerbackup.org.uk/Treatments/Trials/BRCAtrial>)

Trials of PARP Inhibitors

These drugs act by blocking a particular pathway of DNA repair. Tumour cells that arise in *BRCA* carriers already have problems with another DNA repair pathway in which the *BRCA* genes work. By blocking a second pathway it is expected that this will make it hard for such tumour cells to survive as they will have difficulty

copying their genetic material accurately during tumour cell division.

Studies at The Royal Marsden and The Institute of Cancer Research have shown promising results with PARP inhibitors in patients with *BRCA*-related advanced ovarian and breast cancers. The PARP inhibitors are generally well tolerated. Large international studies are currently being conducted in patients with ovarian and breast cancer, including combinations of PARP inhibitors with other drugs. It is possible that there may be trials in the future for people with early stage breast or ovarian cancer but researchers are still determining the effectiveness of these drugs and their long term side effects.

Organ donation

Can I still be on an organ donor?

BRCA carriers have asked if they can still register to be an organ donor, given their *BRCA* status and/or personal history of cancer. The NHS Organ Donation information team provided the following information:

There are only two conditions where organ donation is ruled out completely. A person cannot become an organ or tissue donor if they have been diagnosed with HIV or have, or are suspected of having, Creutzfeld-Jakob disease (CJD). Cancer is one of the diseases that can be passed from donor to the recipient. However the risk that this will happen depends to some extent on the type of cancer, the treatment received and the length of time since the disease was diagnosed and treated. Corneas can always be used.

At the time that donation is being considered:

- The family would be asked about any history of cancer
- The medical records would be reviewed
- A report would be obtained from the GP although this is not always available pre-transplantation

So if the potential donor had been confirmed as having a genetic predisposition to cancer this would be reported as part of the



assessment process pre-donation and would be included as part of the information provided to the transplant surgeon. A decision will then be made by a healthcare professional, at the time of death, about whether or not the organs can be used.

How can I register to be an organ donor?

If you do decide to register please make sure that you have informed your family, both so that they are aware of your wishes and to ensure the information about your genetic status is available for the assessment. People can sign up to the register at the following web page:

http://www.uktransplant.org.uk/ukt/how_to_become_a_donor/registration/consent.jsp

Where can I get more information?

This list of resources is intended to help you find further information or additional sources of support. Some patients may find these websites, books and charities helpful, but not all information will be relevant to all individuals.

Please consider the source of the material, for example clinical practice in the US may differ to clinical practice in the UK. Responsibility for the content of the website remains with the organisation that publishes the website.

Books:

- *Singing the Life: The Story of a Family Living in the Shadow of Cancer* by Elizabeth Bryan Vermilion (2008) ISBN-13: 978-0091917166
- *Am I Next In Line?: How I Conquered My Risk Of Hereditary Breast And Ovarian Cancer* by Monique Achtman (2006) ISBN-13: 978-0973373202
- *Positive Results: Making the Best Decisions When You're at High Risk of Breast or Ovarian Cancer* by Joi Morris & Ora Gordon Prometheus Books (2011) ISBN 978-1-59102-776-8
- *Apron Strings: Inheriting Courage, Wisdom And... Breast Cancer* by Diane Tropea Greene Books (2007) ISBN-13: 978-1568251080
- *Pretty is What Changes* by Jessica Queller Spiegel & Grau; (2008) ISBN-13: 978-0385520409
- *Why I wore Lipstick to my Mastectomy* by Geralyn Lucas St. Martin's Griffin (2005) ISBN-13: 978-0312334468
- *Previvors: Facing the Breast Cancer Gene and Making Life Changing Decisions* by Dina Roth Port (2010) ISBN-13: 978-1583334058
- *The Genesis Breast Cancer Prevention Diet: The Plan Every Woman Should Follow for Weight Loss and Optimum Health* by Michelle Harvie & Roy Ackermann Rodale International Ltd (2006) ISBN-13: 978-1405093460



Charities and support groups:

- Macmillan Cancer Support
www.macmillan.org.uk
Free phone information line: 0808 808 0000
- FORCE: a support group for BRCA carriers based in America
www.facingourrisk.org
- BrCa Umbrella Support and Social Network: an online support forum for BRCA carriers
<http://brcaumbrella.ning.com/>
- BRCA Scoop: a US website with information about the latest research into BRCA/12 genes
<http://brcascoop.com/>
- Pink Hope: an Australian website for BRCA carriers
www.pinkhope.org.au/
- Breakthrough Breast Cancer
www.breakthrough.org.uk/index.html
Free phone information line: 08080 100 200
- Breast Cancer Care
www.breastcancercare.org.uk/
Free phone information line: 0808 800 6000
- Facebook: there are several BRCA peer support groups on this social networking site
www.facebook.com
- The National Hereditary Breast Cancer Helpline and Information Centre
<http://breastcancergenetics.co.uk>
Helpline: 01629 813 000
- Ovacome: The Ovarian Cancer Support Network
www.ovacome.org.uk/
0845 371 0554
- Ovarian Cancer Action
www.ovarian.org.uk
Information line: 020 8238 7605

Websites for further information:

- Association of British Insurers (ABI)
www.abi.org.uk
020 7600 3333
- Genetic Alliance UK
www.geneticalliance.org.uk
- National Cancer Institute (US)
www.cancer.gov/cancertopics/types/breast
- Genetics Home Reference (US)
<http://ghr.nlm.nih.gov/condition=breastcancer>
- Cancer Research UK (CRUK)
www.cruk.org.uk
- National Institute for Health and Clinical Excellence (NICE
guidelines for familial breast cancer)
www.nice.org.uk/Guidance/CG41

Copyright © April 2013 The Royal Marsden NHS Foundation Trust
All rights reserved

Planned review April 2015

This booklet is evidence based wherever the appropriate evidence is available, and represents an accumulation of expert opinion and professional interpretation.

Details of the references used in writing this booklet are available on request from: The Royal Marsden Help Centre
Freephone: 0800 783 7176
Email: patientcentre@rmh.nhs.uk

The Royal Marsden NHS Foundation Trust
Fulham Road
London SW3 6JJ

www.royalmarsden.nhs.uk

No part of this booklet may be reproduced in any way whatsoever without written permission except in the case of brief quotations embodied in critical articles and reviews.

No conflicts of interest were declared in the production of this booklet.

The information in this booklet is correct at the time of going to print.



Printed by
Lundie Brothers Ltd.
Croydon, Surrey

GE-1200-02

The Royal Marsden publishes a number of booklets and leaflets about cancer. Here is a list of information available to you.



Diagnosis

- A beginner's guide to the *BRCA1* and *BRCA2* genes
- CT scan
- MRI scan
- Ultrasound scan



Treatment

- Central venous access devices
- Chemotherapy
- Clinical trials
- Radiotherapy
- Radionuclide therapy
- Your operation and anaesthetic



Supportive Care

- After treatment
- Coping with nausea and vomiting
- Eating well when you have cancer
- Infection Prevention and Control
- Lymphoedema
- Support at home
- Your guide to support, practical help and complimentary therapies



Your hospital experience

- Help Centre for PALS and patient information
- How to raise a concern or make a complaint
- Your comments please
- Your health information, your confidentiality



Life demands excellence

