This booklet has been written for people who have a personal or family history of breast and/or ovarian cancer that could be explained by an inherited factor. It has been written for use with a clinical genetics appointment and should answer some of your questions.

Is breast and/or ovarian cancer inherited?
Breast cancer is common and around 1 in every 9 women living in the UK will develop breast cancer in their lifetime. However, it not common for breast or ovarian cancer to be caused by a strong inherited factor. About 5% (1 in 20) of all breast cancers are caused by a strong inherited genetic factor and in these cases, a gene mutation plays a part. Ovarian cancer develops in around 1 in 80 women in their lifetime. Again, about 1 in 20 of these cases have a strong inherited component. We know of two genes that, if altered (i.e. the gene has a mutation), cause a substantially increased chance of developing breast, ovarian and prostate cancer. These genes are called BRCA1 and BRCA2.

What are BRCA1 and BRCA2?
BRCA1 and BRCA2 are genes that make proteins that play an important role in cell repair. A mutation can affect the function of the gene and this can increase the chance of developing breast, ovarian or prostate cancer. Individuals who carry a mutation in BRCA1 or BRCA2 are also more likely to develop cancer at a younger age.

How are the BRCA1 and BRCA2 genes inherited?
All our genes come in pairs and we inherit one copy from our mother and the other from our father. When we have children we randomly pass on one of each pair. If a person has a mutation in one copy of a particular gene pair, each of his or her children has a 50:50 (1 in 2) chance of inheriting it. The mutation can be inherited from either parent and males and females are equally likely to inherit a mutation.

If a person has not inherited a BRCA1/2 mutation, they cannot pass it on to their children.
How do I know whether a BRCA1/2 mutation is the cause of the cancers in my family?

If you have several closely related family members with breast, ovarian or prostate cancer, and if their cancers occurred at a young age, there may be a BRCA1 or BRCA2 gene mutation in your family. However, even if there is a mutation in your family, you may not have inherited it.
Can I have a test to see if the cancers in my family are due to a mutation in either BRCA1/2?
Possibly. A person’s genes can be examined from a blood sample. However, because only a small proportion of people with the above mentioned cancers will have a BRCA1 or BRCA2 mutation, and because the test can be difficult to interpret, at present, genetic testing is usually only offered to people with a very strong family history of breast/ovarian/prostate cancer.

If I do have a personal or family history of cancer, how do I go about testing?
We will usually need to start by obtaining a sample of blood from a person who has had breast/ovarian/prostate cancer. Several hundred different mutations are known in the BRCA1 and BRCA2 genes and ideally we need to find which, if any, mutation is present in your family before testing unaffected family members.

Finding the gene mutation in a family is the key to developing a genetic test for other family members. We know that at present we are not able to find all the causes of inherited breast cancer but our techniques are constantly improving and in years to come testing will be more straightforward.

I’ve heard of genetic variants, what are these?
Sometimes we find an alteration in the genetic code where we are not sure of its significance. This is called a variant of uncertain significance (VUS). If we are not certain that a particular gene alteration is the cause of the cancers in your family, we cannot offer genetic testing to predict the chance of cancer developing in other family members. We may however ask for extra samples from other family members to try and gather more information. These extra tests can often help to decide whether or not a VUS is the explanation for a family history of cancer.
What if a relative with breast/ovarian/prostate cancer is not available for testing, can I be tested even if I have never had cancer?
Testing can be difficult to interpret if we don’t know exactly which mutation is present in a family. If we test a person who has not had cancer and the test does not find a mutation, we cannot tell whether this is because they have not inherited the familial mutation or whether the test has just not been able to find a mutation that is actually present in their family. Without knowing the mutation present in your family, even if we tested you, we would not be able to reassure you that you have not inherited the mutation.

So testing is a two-stage process?
Yes. Usually the first step, the “diagnostic test” looks for a mutation in a person who has had cancer. If we cannot find a mutation, at present, testing may not be helpful for unaffected relatives. Testing is however constantly improving and a mutation may be found in the future. Therefore it is worth seeking an update from the genetics service every few years or earlier if there are further cases of cancer diagnosed in the family.

If we do find a mutation in a person with cancer we can then offer testing to unaffected relatives to see whether or not they have the same mutation. This is called a “predictive genetic test”. This second test is very accurate and takes just a few weeks. A predictive test in the presence of a known mutation in a family member helps give a person a better estimate of their future chance of cancer.

Does everyone who inherits a mutation in BRCA1 or BRCA2 mutation get breast or ovarian cancer?
No. The chance of developing these cancers is not 100%. We do not yet know why some people with a mutation develop cancer and some do not but lifestyle and other genetic factors are likely to play a role.
It is also important to remember that the chance of developing cancer is not the same as the chance of dying from cancer. Even if cancer develops, there is a chance that the disease can be cured if detected and treated early.
What are the chances of developing cancer with a mutation in BRCA1 or BRCA2?

### BRCA1 lifetime (up to 80 years) chances of developing cancer

<table>
<thead>
<tr>
<th></th>
<th>Female carriers</th>
<th>Male carriers</th>
<th>Chance in the general population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>60% - 80%</td>
<td>No known increase</td>
<td>11% (female) 0.5% (male)</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>40% - 60%</td>
<td>Men do not have ovaries</td>
<td>1-2% (female)</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Women do not have a prostate gland</td>
<td>10% - 15%</td>
<td>10%</td>
</tr>
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</table>

### BRCA2 lifetime (up to 80 years) chances of developing cancer

<table>
<thead>
<tr>
<th></th>
<th>Female carriers</th>
<th>Male carriers</th>
<th>Chance in the general population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>60% - 80%</td>
<td>5% - 10%</td>
<td>11% (female) 0.5% (male)</td>
</tr>
<tr>
<td>Ovarian cancer</td>
<td>10% - 30%</td>
<td>Men do not have ovaries</td>
<td>1-2% (female)</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Women do not have a prostate gland</td>
<td>20% - 30%</td>
<td>10%</td>
</tr>
</tbody>
</table>

There is also an increased chance of developing a second cancer. Please discuss this with your clinician.

Remember 10% means 1 person in every 10 will develop this cancer in their lifetime.
If I have not inherited a BRCA1/2 mutation can I still get cancer?
Yes, there is still a chance of developing cancer, because cancer can occur for other reasons that we do not yet understand (see chances of developing cancer in the general population in the table above). People who have not inherited a familial BRCA1 or BRCA2 gene mutation have a similar chance of developing cancer to someone in the general population.

Cancers that occur in the general population are more likely to develop at a later age than cancers due to a mutation in BRCA1 or BRCA2. More than half of all cancers diagnosed in the general population occur after 60 years of age.

Are BRCA1/2 the only genes that can cause hereditary breast cancer?
No, there are some other genes that increase the chance of developing breast cancer but most of these have lower cancer risks and it is not clear how these genes interact with each other. Therefore at present, testing these genes is less helpful. Research is however continually updating our knowledge in this area.

If I have a BRCA1/2 gene mutation when will I develop cancer?
Although you will have an increased chance, you may never develop cancer at all. It is not possible to predict whether you will or will not develop cancer or at what age you will develop it.

What can be done about the chance of developing breast cancer?
There are several checks you may want to discuss.

- **Breast examination**
In the past women were regularly examined by their doctor, or told to examine themselves once a month. Studies suggest that this is not an effective way of picking up breast cancer at an early stage. Instead women are advised to be aware of the normal shape and feel of their breasts and to report any changes that last for longer than one menstrual cycle to your doctor.
● **Mammography**
There is currently no clear evidence that mammography is effective in reducing the number of deaths from cancer in BRCA1 or BRCA2 gene carriers. However, mammography is offered to women at high genetic risk in most parts of the country from the age of 30-35, after discussion of the limitations, potential risks and benefits. Once a woman reaches the age of 50 she enters the National Breast Screening Programme where mammograms are offered every 3 years. Some women may be offered additional mammography after 50. Men are not offered mammograms as their chance is not increased to a level where this is recommended.

**Why doesn’t everyone have regular mammograms?**
In general, mammograms are more effective in picking up cancers in older women. In young women the pick up rate is much lower because the breasts are generally more dense than in postmenopausal women. Mammograms are X-rays, and too many X-Rays are known to sometimes increase a risk of cancer. Therefore, they are not usually done before the age of 35-40. Also, mammograms will miss a small proportion of cancers, even in the older breast, and so it is possible that you will be falsely reassured.

● **Magnetic Resonance Imaging (MRI)**
MRI is a newer method of screening that is sometimes offered alongside mammography from your thirties onwards. This will be discussed with you in more detail in the clinic.

● **Ultrasound scan of the breasts**
Some people believe that an ultrasound scan of the breast is better than mammograms for looking at young breasts. It is true that ultrasound does not carry the radiation risks that mammograms do, but it is not a good way to screen breasts that seem normal. It is good at looking in more detail at a lump that has been felt in the breast, but is not thought to be a useful screening tool.

● **Risk Reducing Breast Surgery (prophylactic mastectomy)**
This is the surgical removal of healthy breast tissue to prevent a cancer developing. This has been shown to reduce the chance of breast cancer, but it does not remove all the risk, as the surgery cannot remove every breast cell. It is a major operation that can have serious complications so it requires careful consideration.
What can be done about the chance of developing ovarian cancer?
In the past women have been offered a combination of an ultrasound scan and a blood test to look for cancer markers; however more recent research shows that these tests are poor at picking up ovarian cancer at an early stage. They may therefore lead to false reassurance.

- **Risk reducing removal of the ovaries (prophylactic salpingo-oophorectomy, BSO)**
  This is the surgical removal of healthy ovaries and fallopian tubes to prevent cancer developing. Having your ovaries removed reduces your risk of ovarian cancer but there is still a small chance of an ovarian-like cancer developing in the surrounding tissue that is left (estimated to be between 2-5% in your lifetime). As well as reducing your chance of ovarian cancer, prophylactic BSO may also help to reduce your chance of breast cancer if carried out before your natural menopause. Having your ovaries removed will however start an immediate menopause and you may therefore need some form of hormone replacement therapy (HRT). The advantages and disadvantages of this will be discussed with you. HRT is not recommended for women who have had breast cancer.

What about the contraceptive pill and my chances of cancer?
Research studies have shown that if you take the contraceptive pill for several years, this may slightly increase your future chance of breast cancer. It will also slightly decrease your chance of ovarian cancer. The risks are small and your will need to weigh up these risks with the reason for taking the pill (for example, preventing pregnancy or to control troublesome periods).

What about hormone replacement therapy (HRT) and my chances of cancer?
Long term (5 years or more) postmenopausal HRT use, will increase the chance of breast cancer slightly. Again this small risk must be balanced against, for example, the protection against bone thinning and menopausal symptoms that HRT provides.

Prostate cancer
There is no clear evidence about the effectiveness of prostate cancer screening, but there is research which you may be eligible to take part in.
Other cancers
In some families with BRCA1 and BRCA2 gene mutations we see an association with other cancers, but any increased chance is likely to be small.

Why would I consider predictive testing for a BRCA1 or BRCA2 mutation?
Knowing your future chance of developing cancer more accurately may help you with decisions about your life and allow you to make choices to manage your risks. However, it is important to know that at present there is no method of detection or prevention that has been proven to be completely effective. Some people would rather know whether they have inherited a BRCA1 or BRCA2 gene mutation than live with uncertainty. Others feel that knowing they carry a gene mutation whilst not knowing if and when it will cause cancer is not helpful.

Remember there is a 50% chance that the test will show that you have not inherited the mutation. In this situation, you cannot have passed it on to any of your children or future children. You will also not need any screening other than general population screening programmes. Remember “predictive” means a test on a person who has not had cancer but who is closely related to someone in whom a BRCA1 or BRCA2 gene mutation has been identified.

What are the risks of BRCA1/2 testing?
If a mutation is found that increases your chance of developing cancer some people may worry that genetic testing will affect their insurance prospects (e.g. health, life, disability). Currently the insurance industry has agreed it will not ask about genetic testing for the majority of policies, but this position may change in the future. You may want to review your insurance before testing. You can also talk to your doctor about how the information will be kept in your medical records.

Some people experience a range of emotions when they are told they have a gene mutation that increases their chance of cancer. Anger, shock, anxiety, worry about their health, worry or guilt about possibly passing the gene mutation on to children are all normal reactions. Some people may also feel guilty if they do not carry a familial gene mutation when other close family members do.
Remember that we can tell you that your chance of developing cancer is increased, but we cannot tell you for certain, when or even if, you will develop cancer.

Genetic testing in a family often affects other family members, as they may need to be told that they too are at increased risk of developing cancer. Sometimes, unexpected information may be revealed, for example, someone may disclose that a family member is adopted. Therefore, genetic testing may affect relationships within families.

**Is there an alternative to genetic testing?**
You may decide not to have genetic testing but whether or not you are tested, you should talk to your clinician about screening options.

**I’ve heard of research studies involving people with a family history of cancer, how can I find out more?**
There are several research studies that you may be able to take part in if you wish. It is important to remember that research studies may not benefit you directly, but may help future generations. Please talk to your clinician about all of these topics before deciding on a plan of action that is best for you.

**The team involved in your care are:**

Consultant: .................................................................................................................................

Tel No: ...........................................................................................................................................

Genetic Counsellor: ............................................................................................................................

Tel No: ............................................................................................................................................

**Please contact us on 023 8120 6170 if you have any other questions.**