Liverpool Women's
NHS Foundation Trust

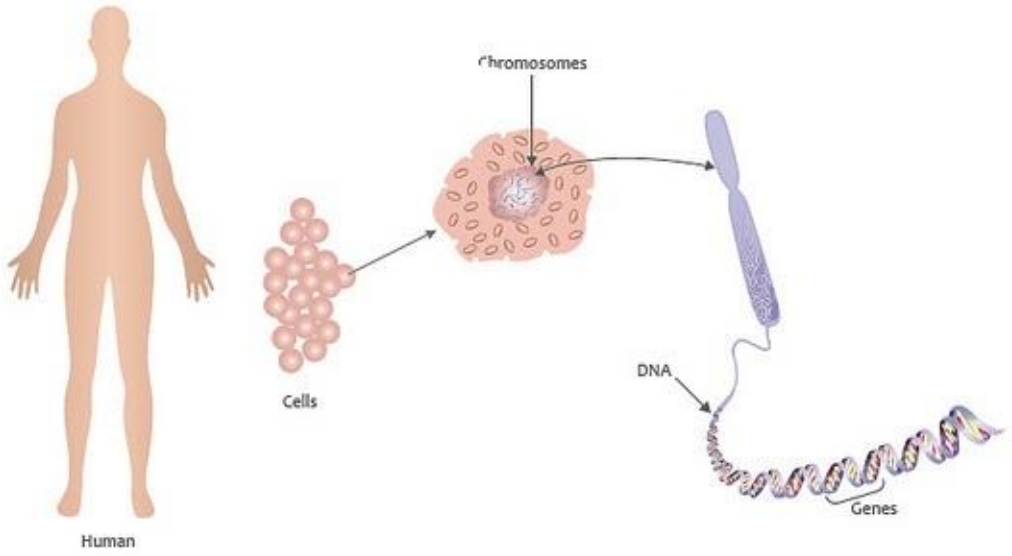
Predictive testing for a Breast Cancer 1(BRCA1) gene alteration: Information for families where an altered cancer gene has been found and who are considering undergoing predictive testing

Cancer is common in the general population with 1 in 2* people being diagnosed with a cancer in their lifetime. Approximately 1 in 7* women will be diagnosed with breast cancer and most cancer occurs just by chance. Our suspicions of an inherited explanation for the cancers in a family are raised if the same or related cancers occur in several family members on the same side of the family, usually across different generations and at a younger age than expected. This is why genetic testing would be offered to a family.

*Cancer Research UK (2015) estimated lifetime risk of being diagnosed, people born after 1960.

What are genes and chromosomes?

Humans are made up of trillions of cells. At the centre of almost all of your cells is a ball-shaped structure called the nucleus, inside of which are 46 thread-like structures called chromosomes. Chromosomes are long strands of DNA (**D**eoxyribo**N**ucleic **A**cid). It is estimated that if a strand of DNA was stretched out, it would be around two meters long, even though the average cell is smaller than a pinhead.



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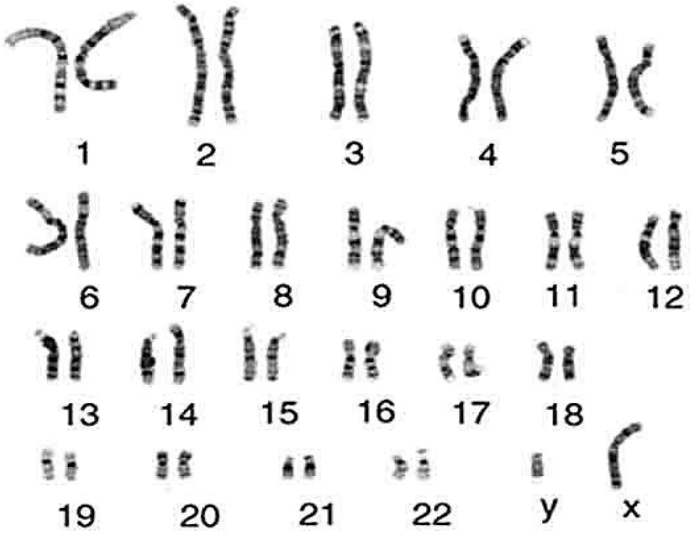
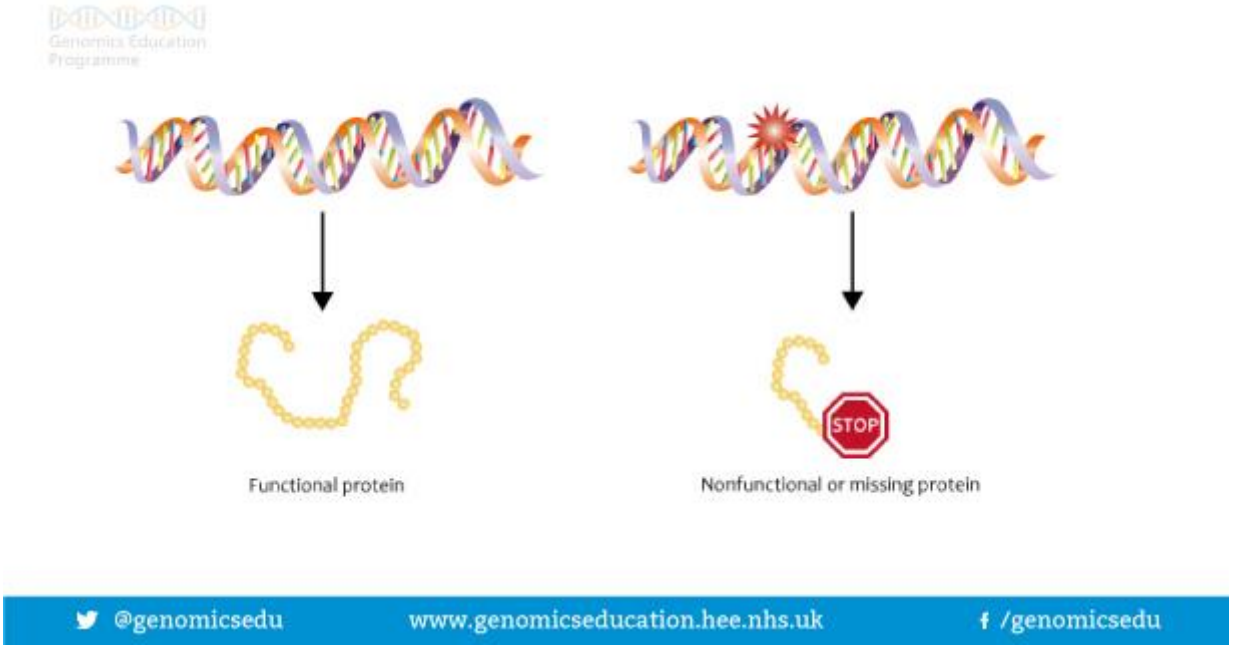


Image Source: https://cpmc.coriell.org

We have 23 pairs of chromosomes; one of each pair is inherited from your mother and one of each pair from your father. Chromosomes 1-22 are arranged in size order with number 1 being the largest and 22 the smallest. The 23rd pair of chromosomes determines a person's sex. Most males are XY and most females are XX. Chromosomes contain an estimated 20-30,000 pairs of genes that make us who we are. As we have pairs of chromosomes we therefore have pairs of genes.

Genes are often called the blueprint for life because they tell each of your cells what to do and when to do it. For example, some genes determine how tall you will be; some what colour your hair will be; some genes are responsible for maintenance in our bodies and some for our development, and so on. Genes do this by making proteins. In fact, each gene is really just a 'recipe' or a code for making a certain protein. In order for a gene to do the job it is supposed to do, the 'recipe' or code needs to be written correctly. If the 'recipe' is wrong, the protein is either not made, or is made incorrectly so cannot do the job it is supposed to do. This is sometimes called a gene alteration, a spelling mistake or a gene mutation.



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What is the role of the BRCA1 gene?

The role of the BRCA1 gene is to protect the body against developing cancer in certain areas of the body. BRCA1 genes are called tumour suppressor genes and the protein produced from them helps prevent cells from growing and dividing too rapidly or in an uncontrolled way. The pair of BRCA1 genes is found on chromosome 17.

What is the main cancer risks associated with having an altered BRCA1 gene?

Associated risks	General Population risk	With a BRCA1 gene alteration
Breast cancer	~ 15% = 1 in 7* women	60-80% lifetime risk
Ovarian cancer	~2% = 1 in 50* women	30-60% lifetime risk
Male breast cancer	Very low	0.1-1%
Prostate cancer	~18%*	Thought to be slightly above population risk

*Cancer Research UK (2015) estimated lifetime risk of being diagnosed, people born after 1960.

There may also be a small risk of developing other cancers but not enough to warrant additional screening. However, it would be important to have a low threshold for seeking medical help for any concerning or persistent symptoms.

What can be done to help manage these risks?

For each of the high risk cancers, screening and surgical options are discussed. Different options are available to men and women, and options can also differ dependent on what age you are.

Breast Screening

Women who have a BRCA1 gene alteration are offered high risk breast screening.

This involves:

- Annual magnetic resonance imaging (MRI) scan from 25-39 years
- Annual MRI AND mammography from 40-50 years
- Annual mammography from 51-71 years (some women may continue to receive MRI too)

Women who have a 50% chance of inheriting a BRCA1 gene alteration but choose not to have a genetic test will be offered the screening described above until the age of 50. These women will then need to have genetic testing in order to continue to receive high risk breast screening, otherwise they will join the NHS Breast Screening Programme for a mammogram every three years.

Most NHS routine or high risk breast screening stops after the age of 70 or in some places 73. You can still have screening after this, and can arrange an appointment by contacting your local breast screening unit. This is something we would recommend if you were a carrier of a BRCA1 gene alteration. We also suggest that women carry out monthly self-examination of the breasts.

Men are not offered any breast screening, but we suggest they check their chest and armpit areas and seek medical advice for any unusual lumps.

Breast Surgery

Women who have a BRCA1 gene alteration also have the option of having surgical removal of both breasts (bilateral mastectomy). Although this procedure could significantly reduce the risk of developing breast cancer it will not remove the risk entirely. We also recognise this is a radical step that requires careful consideration. Therefore women who choose this option are fully supported throughout the process and not rushed into making any decisions.

Ovarian Screening and Surgery

Ovarian screening involves regular blood tests approximately 3-4 times a year, to measure a marker in the blood called CA125 and also by annual ultrasound from the age of 35. However, ovarian screening does not reliably inform us of cancers early enough in order for them to be treated effectively.

Therefore, for women who are BRCA1 carriers, over the age of 35 and have completed their families we would encourage those to think about having their ovaries and fallopian tubes removed (bilateral salpingo-oophorectomy). This can significantly decrease the risk of developing ovarian cancer but, again the risk of cancer is never removed entirely.

There are clear advantages to having your ovaries and fallopian tubes removed, however they do need to be weighed with the potential disadvantage of being put into an early menopause and the possible need for hormone replacement therapy (HRT). The advantages and disadvantages of HRT could be further discussed with a gynaecologist if you choose to go ahead with this process.

Chemoprevention

Recent guidelines have suggested that ladies at high risk of breast cancer be offered chemo-prevention medications. Research suggests these medications can reduce the risk of developing breast cancer however they do have significant side effects. Please ask for a leaflet outlining the risks and benefits of chemoprevention if you think this is something you might be interested in.

Prostate screening for people with a BRCA1 gene alteration

Prostate screening should be undertaken annually from the age of 40 in people who have a BRCA1 gene alteration. This can be provided through the GP.

How are BRCA1 gene alterations passed down (inherited) through families?

The way BRCA1 gene alterations are inherited is called DOMINANT inheritance. This is caused by an alteration in only one copy of the BRCA1 gene. Even though we each have 2 copies of the BRCA1 gene the normal copy cannot compensate for the altered copy and a person with one altered BRCA1 gene has an increased risk of developing cancer.

If a parent carries an altered BRCA1 gene, each of their children has a 50%, or 1 in 2 chance of inheriting the altered gene and therefore having an increased risk of developing cancer. For each child, regardless of their sex, the risk is the same = 50%.

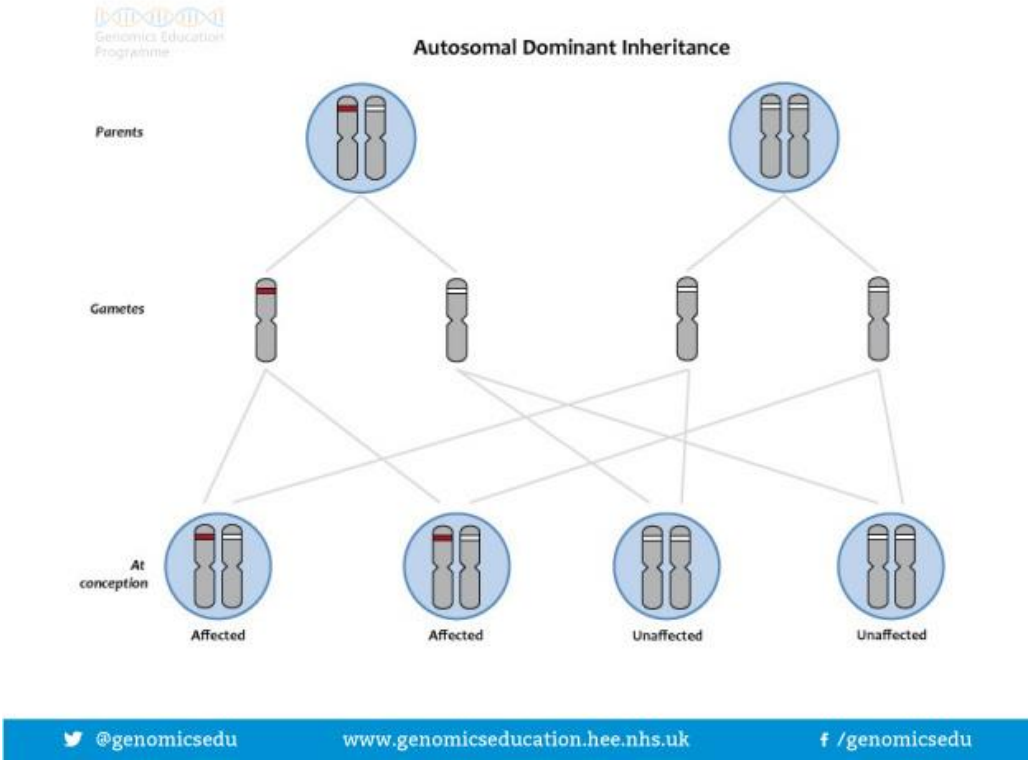

Image source: https://www.genomicseducation.hee.nhs.uk/image-library/

What is predictive testing?

Predictive testing is offered to family members who are known to be at risk of inheriting a gene alteration that has been identified in the family but are currently well. Predictive testing is usually offered over a series of appointments to allow the opportunity to consider options and choices with time for reflection in-between. How many appointments a person requires varies considerably from person to person and is negotiated on an individual basis with your genetic counsellor team. The overall aim of the predictive testing process is to help prepare you for your results whatever they are.

- **What are the issues to think about when deciding whether or not to have a gene test?**

A genetic test can establish whether you have an alteration in a gene which could affect your health. It can be difficult to make a decision about whether or not to have a genetic test. We all have gene alterations and many of these do not affect our health. It is still quite unusual for a person to know they have an alteration in a specific gene.

There are reasons for and against having a genetic test. Within one family, relatives often have different views. You should try to make your own decision, without feeling pressured from relatives or other influences.

You will have plenty of opportunity to talk through the issues surrounding the test with the genetic counsellor or doctor.

- **How do you think you would cope if the test were to show that you have inherited the altered gene?**

For some people, knowing that they have the altered gene is preferable to living with uncertainty. Having a genetic test enables them to make decisions about the future and about screening and measures to reduce their risk. Other people may prefer not to have the test because they may feel very anxious if the test shows that they have the altered gene.

- **How do you think you would cope if the test were to show that you have not inherited the altered gene?**

Perhaps surprisingly, it can often take people some time to get used to the knowledge that they do **not** have the altered gene. This can be particularly difficult when other relatives have a different result. People who do not have the altered gene have the same chance of developing cancer as other people in the general population.

- **If the test were to show that you have the altered gene, this would mean that your children would also be at risk of having the altered gene. How do you think you might feel about this?**

Having a genetic test may be important to other people, such as your children. It will help them to understand their own risk and if necessary make choices about screening and risk reducing options.
It can be very difficult knowing that you could have passed on an altered gene to your children. This can be hard to deal with even if you know that you had no control over which genes you passed on.

- **If you were to have the test, would you want to tell anyone the test results?**

It is important to think about who you would want to know about your test as it is very personal information. Many people who attend our clinic find that it helps to confide in a partner, trusted friend or relative.

- **Would having the test affect your ability to get life or medical insurance?**

At present, if you have already obtained your insurance, having the test should not affect your current policies. However, it is not possible to know whether it will affect your ability to get or to change insurance policies in the future.

- **Would having the test affect your employment?**

If the test shows you have the altered gene it would be your decision whether or not to inform your present employers. Some employers might ask about this if you apply for a new job.

It is important that each family member makes the decision that is best for them. We will support you whether you decide to have the test or whether you decide against having the test. It is your decision!

- **What happens if I choose to go ahead and have a test?**

-After you have the opportunity to discuss the positives and negatives of predictive testing, if you wish to have the test you will be asked to read and sign a consent form and a small blood sample will then be taken.

- Once the blood is taken, the laboratory staff would test the sample to find out whether or not you have inherited the altered gene known in your family.

-Test results are usually available 4-6 weeks after having your blood taken and you can choose to have your results over the phone or in a clinic appointment.

IF, FOR SOME REASON YOU, HAVE NOT RECIEVED YOUR RESULTS WITHIN 4-6 WEEKS AS EXPECTED PLEASE CALL THE LIVERPOOL CENTRE FOR GENOMIC MEDICINE ON 0151 802 5008. Please remember to have your G number and W number handy for this call so we can quickly and correctly identify you.

- **What Happens If I Choose Not To Go Ahead With Having A Test?**

We may still recommend screening to you as explained earlier in this leaflet.

You can change your mind and decide not to have the test at any time before the result is given.

Other Factors to Consider

Insurance and Genetics

For some types of insurance it is necessary to provide medical information, including genetic information, to the insurers in order for them to set up your policy and work out your premiums. The types of policy that require a medical history or genetic test are likely to be, life cover, critical illness insurance and income protection insurance.

We would suggest that if yourself or family members are considering taking out new insurance policies in the future that consideration be given to the possible affect genetic test results could have on the ability to gain insurance or the premiums charged. Genetic test results do not affect insurance policies already in place.

The Association of British Insurers (ABI) has a Code of Practice 'The Concordat and Moratorium on Genetic and Insurance'.

- *Insurance companies cannot ask for the **Predictive Genetic Test** results of individuals or family members* (unless for Huntington Disease over £500,000). *A Predictive Genetic Test is where an individual has a family member with a genetic condition, but who personally has no symptoms, signs or abnormal medical tests consistent with the condition at time of testing.*

- *If a family member has been diagnosed with a genetic condition based on a **Diagnostic Genetic Test** then you or family members will need to mention this when asked to provide your family's medical history. In many cases Diagnostic Genetic Testing is used to confirm a diagnosis when a particular condition is suspected because of symptoms, signs or abnormal non-genetic tests including unusual findings on a routine blood test or other test.*

Sources of further information on Insurance and Genetics:

The Association of British Insurers Genetics Frequently Asked Questions
https://www.abi.org.uk/products-and-issues/topics-and-issues/genetics/genetics-faqs/

Genetic Alliance UK (Charity) Genetics & Insurance
http://www.geneticalliance.org.uk/information/living-with-a-genetic-condition/insurance-and-genetic-conditions/

Family planning

Everyone who has an inherited genetic condition can choose from a variety of options to ensure they do not pass it on. It is a highly personal decision and there is certainly no expectation that couples have to do anything to prevent passing on a BRCA1 gene alteration, but for couples who wish to consider this, some of the choices can include:

- **Preimplantation genetic diagnosis (PGD)**

  PGD involves the use of assisted reproductive technology (ART), which is also offered to couples with fertility problems. The aim is to obtain and fertilize a number of eggs. Once fertilized, the embryos develop for six days and then a number of cells are removed from each embryo. The genetic material (DNA or chromosomes) within each cell is then tested for the genetic or chromosome abnormality. Up to two unaffected embryos are then transferred to the uterus with the hope that they will implant and form a pregnancy. If successful, the baby should not be affected by the disorder it was tested for.

More information can be obtained here: http://www.pgd.org.uk

- **Adoption**
- **Sperm or egg donation**: dependent on who carries the gene alteration.

Our experience is however that very few couples who carry a BRCA1 gene alteration choose any of the above options.

Oral Contraceptives

There have been a number of studies looking at the relationship between taking oral contraceptives and breast cancer risk but unfortunately the findings can often differ between different studies. However, overall, we know that taking the combined oral contraceptive pill (COC) increases the risk of breast cancer in all women. The risk appears to be confined to current and recent use and the risk drops once you stop taking the pill, and will return to normal after a number of years without use. It is felt that 10 years after stopping the COC, the breast cancer risk is the same as if you had never taken it at all.

One study showed an increased risk of breast cancer under the age of 40 to women who were carriers of a BRCA1 gene alteration (Narod SA et al (2002) Oral Contraceptives and the Risk of Breast Cancer in BRCA1 and BRCA2 Mutation Carriers, J Natl Cancer Inst 94:1773-9).

Use of COC also reduces the risk of ovarian cancer proportionally to the duration of use but should never be prescribed for this reason only.

There is no evidence regarding progesterone only contraceptives and breast cancer risk associated with family history.

You should discuss the use of oral contraceptives with your GP to weigh up the risks and benefits to help you make the decision that is right for you. You may also want to look at the Cancer Research UK website for further information.

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Useful websites

Genetic Alliance UK	www.geneticalliance.org.uk
Cancer research group UK (CRUK)	www.cruk.org.uk
National Institute for Health Care and Excellence (NICE)	www.nice.org.uk/Guidance/CG41

If you need more advice about any aspect of BRCA1 predictive testing, you are welcome to contact:

Liverpool Centre for Genomic Medicine
Liverpool Women's Hospital NHS Foundation Trust
Crown Street
Liverpool
L8 7SS
Telephone: 0151 802 5001 or 5008 Email: lwft.clingen@nhs.net

This leaflet can be made available in different formats on request. If you would like to make any suggestions or comments about the content of this leaflet, then please contact the Patient Experience Team on 0151 702 4353 or by email at pals@lwh.nhs.uk

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