Liverpool Women's
NHS Foundation Trust

Genetic testing for Lynch Syndrome
Information for people who have had a cancer and are eligible for genetic testing for Lynch Syndrome

Introduction

Cancer is common in the general population with 1 in 2* people being diagnosed with a cancer in their lifetime 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.

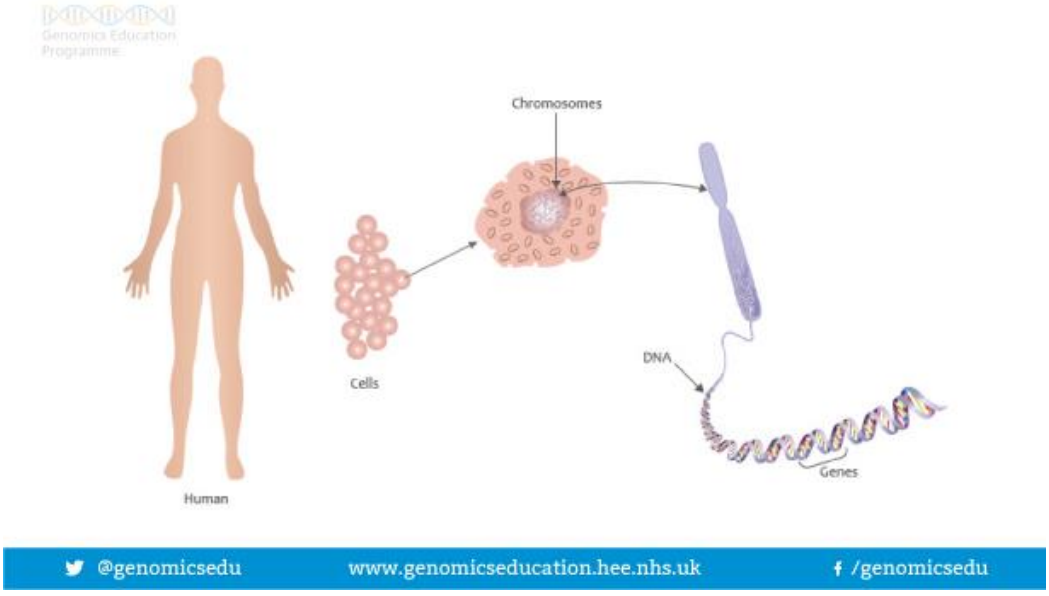


Image source: https://www.genomicseducation.hee.nhs.uk/image-library/

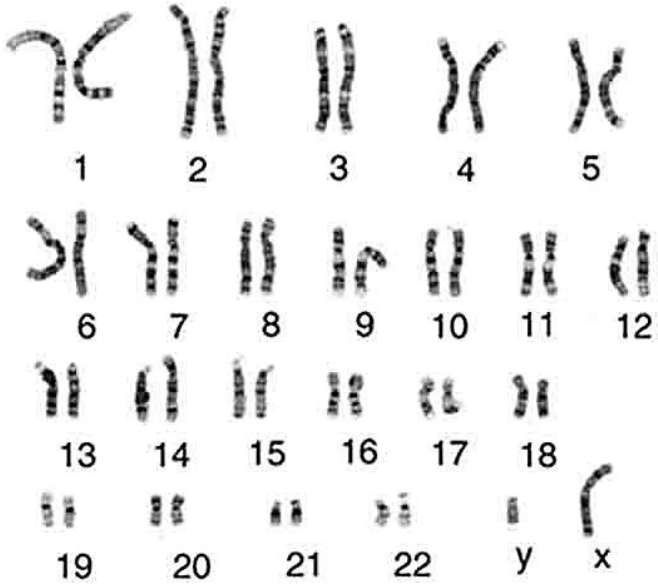
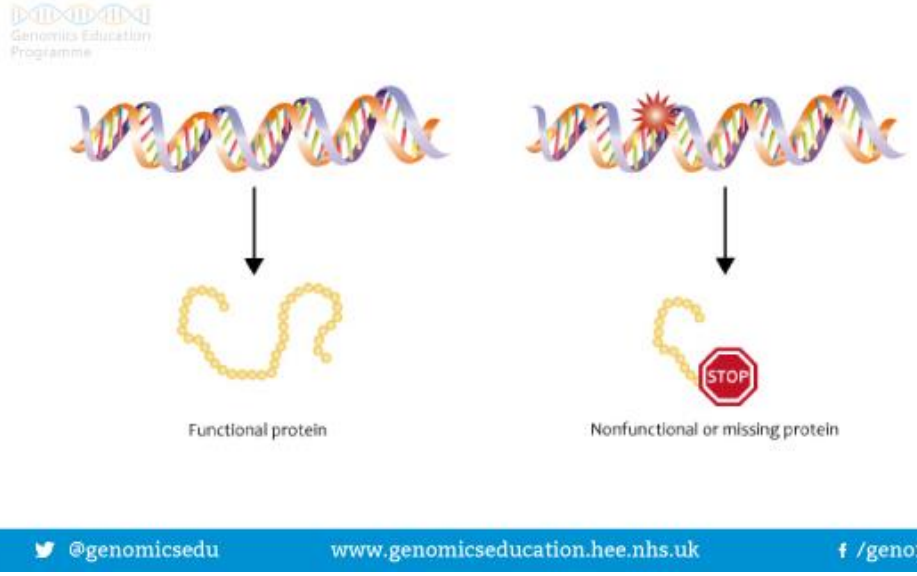


Image Source: https://cpmc.coriell.org

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, a gene may act by being 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 Lynch Syndrome?

Lynch syndrome is a hereditary condition that causes people to have an increased risk of developing certain types of cancer and is caused by a gene alteration. Lynch syndrome also used to be known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC).

What genes are associated with Lynch Syndrome?

There are currently 4 genes that we know of that, if they are altered, can be associated with the development of Lynch syndrome. These genes are known as MLH1, MSH2, MSH6 and PMS2. In fact we all have 2 copies each of these genes and they have a very important role to protect certain parts of our body from developing cancer. These genes are called mis-match repair genes and help protect us from developing cancer by detecting and correcting errors that can occur in DNA when cells copy themselves (DNA replication errors). They are like a quality control system that will either repair the mistakes in the DNA or gets rid of the cell with the mistake to stop it being copied anymore. If there is an alteration in one of our Lynch syndrome genes this quality control system is less effective and the person then has an increased *susceptibility* to developing cancer. But having an alteration in a Lynch syndrome gene does not mean a person will definitely go on to develop cancer.

What are the main cancer risks associated with having a Lynch Syndrome gene alteration?

There is a high risk of bowel cancer, with women having the additional risk of gynecological cancers including endometrial (womb) and ovarian cancer. Each of the genes associated with Lynch Syndrome carry different cancer risks.

There may also be a small risk of developing other cancers including kidney (renal) cancer and pancreatic cancer but not enough to warrant routine screening unless there is a family history.

What can be done to help manage these risks?

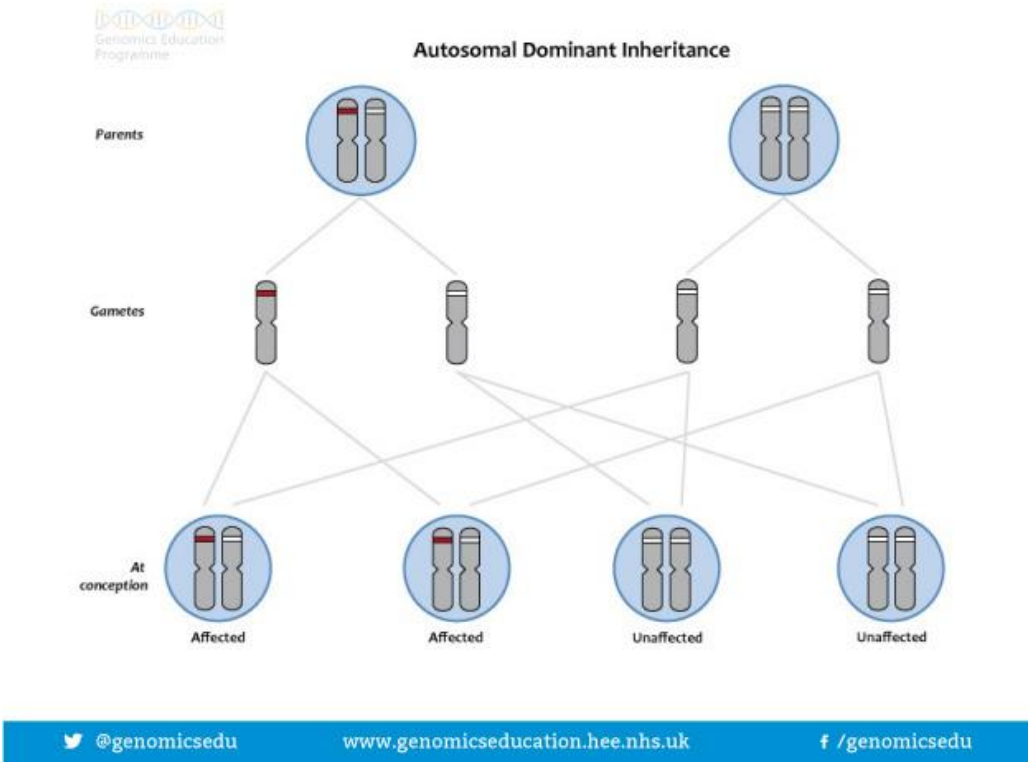
Symptom awareness, aspirin use, screening or surgical options may be suitable. Different options are available to men and women, and options can also differ dependent on what age you are.

Choices and options will be discussed in detail if genetic testing shows you have Lynch Syndrome.

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

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

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



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If I undergo testing for a Lynch syndrome gene alteration what will my results show?

Your results will show one of 3 things:

1. **A gene alteration is identified in your sample that is known to be disease causing (pathogenic).** This is highly likely to be the reason for the cancers in the family. If you **have had** a cancer this is called diagnostic testing. It also means you remain at risk of developing other cancers associated with having a Lynch syndrome gene alteration. Finding a gene alteration allows other family members to be offered 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 a person for their results whatever they are.

2. **No gene alteration is identified.** This does not mean there is not an inherited genetic explanation for the cancers in the family but it may be that within the confines of current technology we have been unable to detect a gene alteration or, that there may be an alteration in a gene that we do not yet know about and, therefore, cannot test for. Regardless of the results of any genetic testing we may still make screening recommendations for family members based on the family history to help protect their health.

3. **A gene change has been found but we are not sure if it is significant or not.** This is also sometimes called an unclassified variant (UV) or a variant of unknown significance (VUS). Finding this may mean we have to undertake more testing in the family or that we may need to look at the UV again sometime in the future to see if any further information about it is available. This will be discussed with you in more detail should this be the case.

*****NB: *The finding of a pathogenic (disease causing) gene alteration is based on current knowledge. Very occasionally, new information in the future may mean that our understanding of the significance of a specific gene alteration may change.*****

What are the issues to think about when deciding whether or not to go ahead with genetic testing?

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. Some of the things people may consider include:

- ***Do I need to tell people I am considering genetic testing?***

It is entirely up to you whether or not you choose to tell anyone you are going ahead with genetic testing. It is often useful to have someone to accompany you to your appointments so that you have another 'set of ears' to hear the information and discussions that you have had. They can also be useful as a support for any discussions away from the appointment and should be someone you trust. People often choose this to be their partner, a close friend or another family member. However, if you choose to bring a family member it is important to remember the discussions you have in clinic are likely to have implications for them as well and they may not be prepared for this. Our experience, however, has demonstrated that families are often aware of the cancers and may already be asking questions about why and so it may be that an opportunity to discuss this within the family could happen quite naturally anyway.

Other people would rather wait until there is something to know before discussing things with the wider family, whilst other people prefer to discuss things as the process goes along to help prepare the family for any news. There are no right or wrong answers and we are happy to discuss how to involve your family if you wish.

- ***Do my family need to know about any results I receive from genetic testing?***

Genetic testing provides information for the individual but also will provide information for the rest of the family. If genetic testing identifies a gene alteration in you we would assume that you had inherited it from either your mother or father. Altered genes can often be passed down through families over generations without being noticed. Therefore, finding a gene alteration in you will have implications for other family members as well. So sharing genetic information in a family is really important. It can provide family members with a real opportunity to protect their health by

enrolling in screening programmes to detect cancers as early as possible or even surgical options to help reduce the risk of developing cancer in the first place.

Sometimes people may think if genetic testing does not show anything then there is nothing to tell anyone. However, knowing what is happening in the family can prevent work being repeated as sometimes lots of family members are asking the same questions. It is also very important to remember that, regardless of the results of any genetic testing, the family history itself may mean family members are at a higher risk of cancer anyway and opportunities to protect their health can be offered to them.

- ***How can I share this information?***

On a practical level, you will have this leaflet to share with them and we will also provide a letter after your clinic appointment detailing any other issues discussed.

If a gene alteration is found we will provide you with a 'relative's letter' detailing that a gene alteration has been identified in the family, that they are at risk and how to access testing. We will also guide you as to whom the letter should be passed on to.

On an emotional level, telling family members may be more difficult. You may be worried about upsetting them or have trouble deciding when the right time is. There really is no right or wrong answer to this but it is really useful to think about this before you get your test results and we are more than happy to discuss this with you further.

- ***Should I tell my children?***

As parents, we want to protect our children from things that we believe can harm them and sometimes this means that we try and 'hide' things we think may be difficult for them to cope with. However, we tend to underestimate what children have already picked up on and they are often aware of something going on anyway. They may have noticed letters from the hospital or overheard conversations, they may also pick up cues from adults that they should not ask any questions.

Children in this situation may imagine something really awful is going on, often much worse than the reality, and may even believe it is something bad they have done.

Children value being included and are helped by adults who are honest and direct with communication. It is not always easy but children often cope a lot better than we give them credit for.

Our experience has also shown us that the parents of adult children often do the same. We are happy to talk to you about sharing information with your children during your appointment.

- ***Who else should I tell?***

That is entirely up to you. There is generally no obligation to tell your employer but it might be useful if you anticipate you may need time off work to have screening.
Having friends to discuss this with is helpful for some people but it is important to be aware that people may have differences of opinion that could be in conflict with any decisions you have made.

However, for the majority of people, having discussions with other people is helpful and supportive.

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

After you have discussed what genetic testing could mean for you, you may decide to go ahead with testing. We will ask you to sign a consent form and we will take a blood sample from you. The laboratory team will then search through the Lynch syndrome genes in your blood sample to see if the code in any of these genes differs from that of a normal gene. The Lynch syndrome genes are large and can take a long time to be looked through. We would expect results to be ready in approximately 3-4 months but please remember sometimes it can be more and sometimes less.

You can discuss with your genetic counsellor or doctor how you wish to receive your results. Some people want their results by letter or over the telephone with the opportunity of a follow-up appointment to discuss any findings, whereas others prefer to come into clinic to have the opportunity to discuss the implications of any findings and next steps. This is entirely up to you and will be discussed during your appointment.

IF, FOR SOME REASON YOU, HAVE NOT RECIEVED YOUR RESULTS WITHIN 3-4 MONTHS 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 will make screening recommendations for your relatives based on the family history of cancer.
-We will not be able to offer predictive testing to your relatives.

Attending clinical genetics does not oblige you to go ahead with testing and, if you do go ahead and change your mind about receiving your results, you can do so until you are ready.

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/

We hope you find this leaflet useful and please do not hesitate to discuss any of the issues identified in this leaflet with the genetics practitioner that is looking after you:

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

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

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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Liverpool
L8 7SS
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