Information Leaflet

Liverpool Women's NHS Foundation Trust

Genetic testing for Lynch Syndrome

Introduction

Cancer is common in the general population in the UK, with 1 in 2* people being diagnosed with some form of cancer during their lifetime. Most cancers are due to chance and/or environmental factors. For example, we know that the chance of developing cancer increases as we get older, and that lifestyle factors such as smoking, drinking alcohol and being overweight increase the chance of developing many cancers. Some cancers occur due to inherited genetic factors. We are more suspicious of there being an inherited cause for the cancers in a family if the same or related cancers occur across multiple generations, are diagnosed at younger than expected ages, with more people developing cancer than we would expect by chance.

*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 our 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.

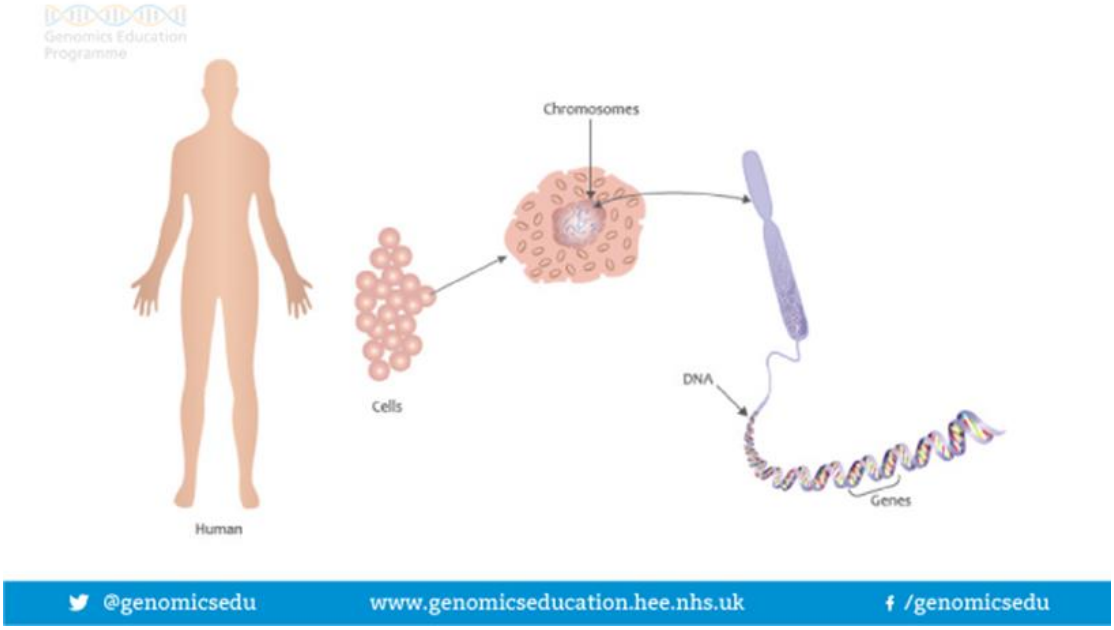


Image source: https://www.genomicseducation.hee.nhs.uk/image-library/

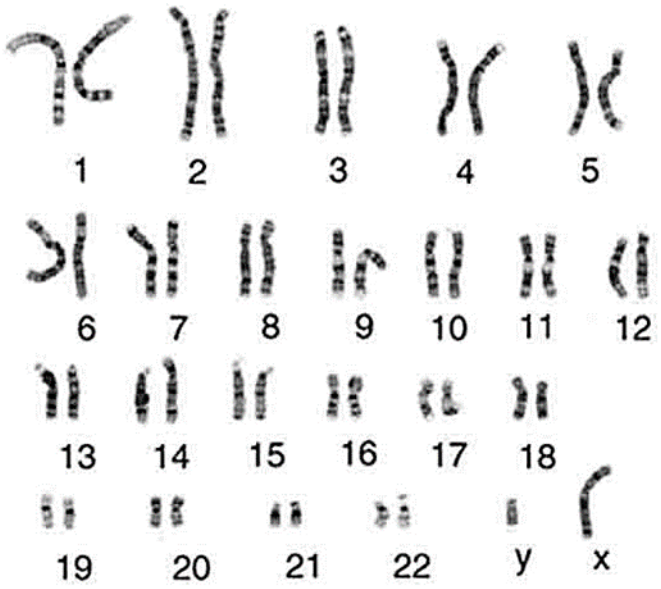
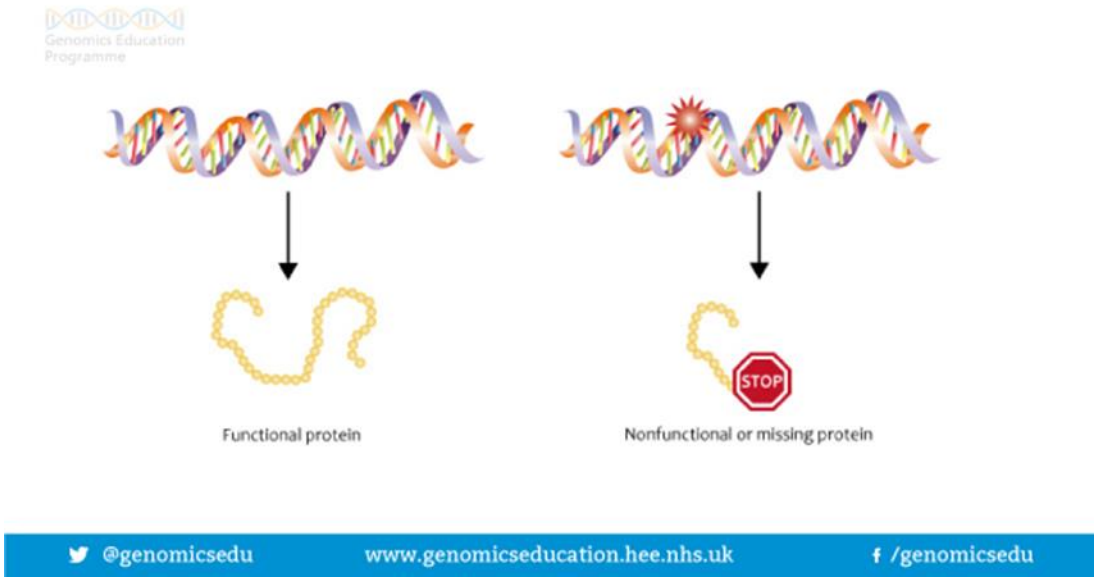


Image Source: https://cpmc.coriell.org

We have 23 pairs of chromosomes and one of each pair is inherited from each parent. Chromosomes contain an estimated 20-30,000 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. 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 variant, a spelling mistake or a mutation.



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What is Lynch syndrome?

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

There are currently 4 mismatch repair genes that we know of that act like a quality control system; MLH1, MSH2, MSH6 and PMS2. They help protect us from developing cancer by detecting and correcting errors that can occur in DNA when cells copy themselves (DNA replication errors). Having a pathogenic variant in one of these genes means that the quality control system is less effective, and the person has Lynch syndrome and so is more likely to develop certain types of cancer. Having Lynch syndrome does not mean a person will definitely go on to develop cancer.

Having Lynch syndrome causes a high chance of developing bowel cancer. People with Lynch syndrome who were assigned female at birth also have a high chance of endometrial (womb) cancer and often a high chance of ovarian cancer, depending on the particular gene in which the pathogenic variant is found. If a gene variant is found, gene-specific cancer risks can be provided. There may also be a slightly increased chance of developing other cancers including kidney (renal) cancer and pancreatic cancer, but not enough to warrant routine screening unless there is a family history.

Additional screening and/or risk-reducing measures may be advised depending on individual risks. Options will be discussed in detail if genetic testing shows you have Lynch syndrome.

How is Lynch syndrome passed down (inherited) through families?

Lynch syndrome is inherited in an autosomal dominant inheritance pattern. We have two copies of each of the mismatch repair genes and if one copy has a variant then this means the person has less protection against developing certain types of cancer and they have

Lynch syndrome. Each time someone with Lynch syndrome has a child, there is a 50% chance of passing on the working copy of the gene and a 50% chance of instead passing on the gene variant causing Lynch syndrome. Someone with Lynch syndrome has usually inherited this from one of their parents.

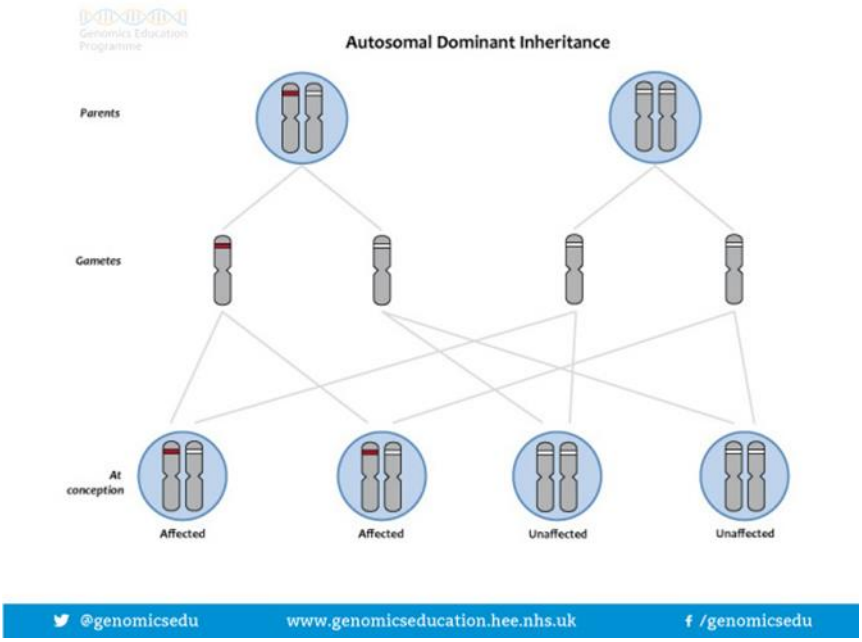

Image source: https://www.genomicseducation.hee.nhs.uk/image-library/

What might my genetic test results show?

Your results will show one of 3 things:

1. **A gene variant is identified in your DNA 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 have an increased chance of developing other cancers associated with Lynch syndrome. Predictive genetic testing can be offered to family members who may have inherited the family-specific gene variant
2. **No gene variants are identified.** This reduces the chance that you have Lynch syndrome but does not completely rule out there being an inherited genetic explanation for the cancers in the family. It may be that within the confines of current technology we have been unable to detect a gene variant, or you may have a variant in a gene we do not yet know about and therefore cannot test for. Taking these results into account, we may still make screening recommendations for family members based on the family history to help protect their health.
3. **A gene variant 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: Test results are *reported based on current knowledge. Very occasionally, new information in the future may mean that our understanding of the significance of a specific gene variant 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 a variant 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. There are reasons for and against having a genetic test. Within a 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 person to help process 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 may have implications for them as well and they may not be prepared for this. Our experience, however, has demonstrated that relatives are often aware of the cancers in the family and may already have questions, and so it may be that an opportunity to discuss this within the family could happen quite naturally anyway.

Some 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 could also provide information for the rest of the family. If genetic testing identifies a gene variant, we would assume that you had inherited it from one of your parents. Lynch syndrome can often be passed down through families over generations without being detected. Sharing genetic information in a family is really important because it provides family members with the 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 tests being repeated as sometimes lots of family members are asking the same questions. It is also very important to remember that, even if we do not find that you have Lynch syndrome, the family history itself may mean family members are at a higher risk of cancer 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 you are found to have Lynch syndrome, we will provide you with a 'Dear Family Member Letter' detailing that a gene variant 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 happy to discuss this with you further.

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

Parents naturally want to protect children from things that can harm them and sometimes this means that parents try and hide things they think may be difficult for their children 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 and may instead not feel able to share worries.

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 you will have a blood sample taken. The laboratory team will then search through the Lynch syndrome genes in your DNA 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.

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:

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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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