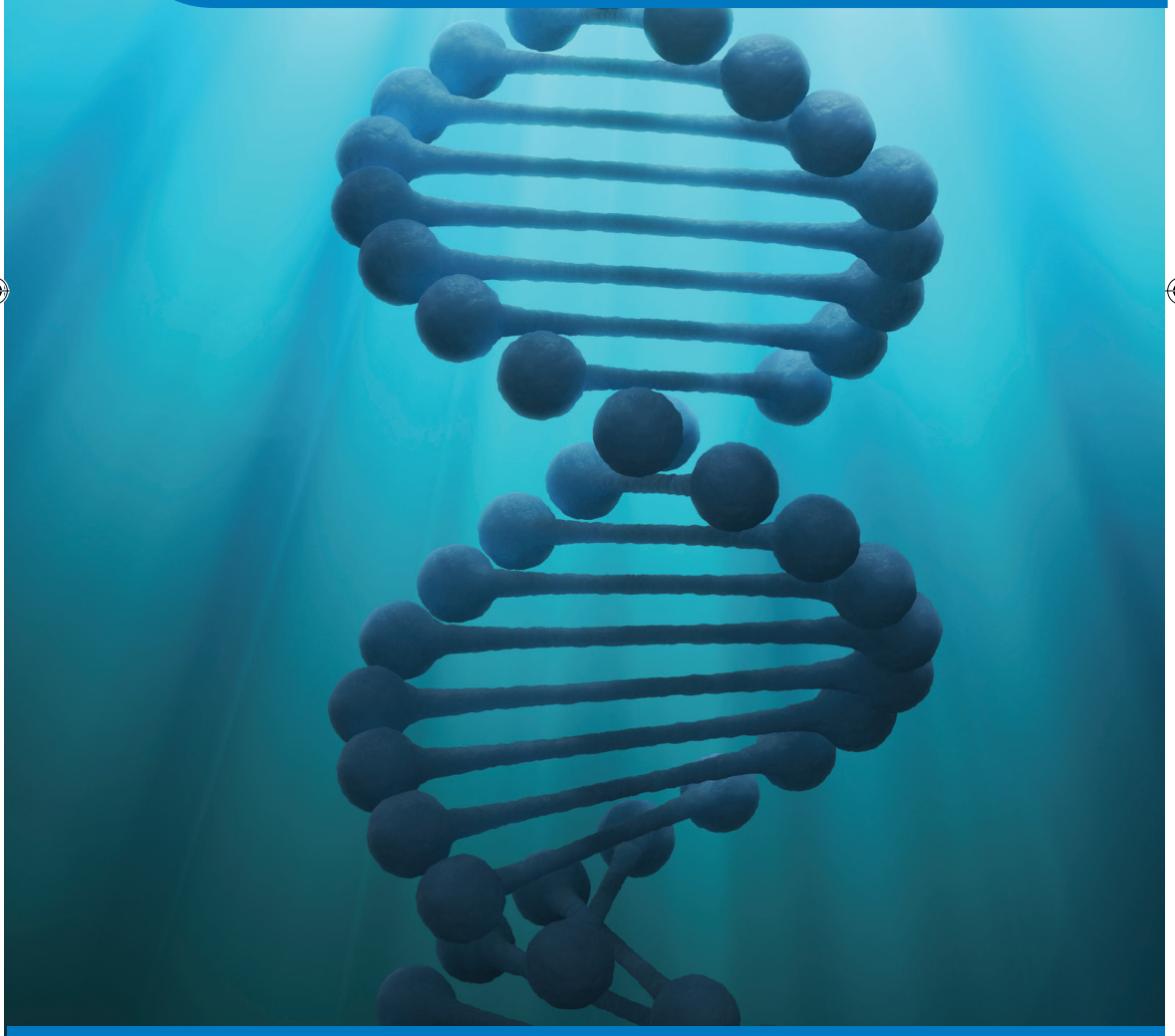
NHS
University Hospital Southampton
NHS Foundation Trust

Lynch syndrome

Information for patients, families and carers



We have written this booklet for people who have a family history of bowel cancer which may be due to an inherited tendency. The most common inherited tendency for bowel cancer is known as 'Lynch syndrome'. We hope this booklet will help to answer some of the questions you may have about Lynch syndrome.

Lynch syndrome was named after the doctor who first described it. Scientists previously thought that there were no polyps present in Lynch syndrome, so it is sometimes known as `hereditary non-polyposis colorectal cancer' (HNPCC).

We now know that there are actually polyps present in Lynch syndrome, but in much smaller numbers than in familial adenomatous polyposis (another type of hereditary bowel cancer where many polyps are found in the bowel).

Inherited bowel cancer

Only around five to 10% of bowel cancers (also known as colorectal cancers) are thought to be caused by a strong inherited factor. This factor may be a variant (often referred to as a 'mutation' or an 'alteration') in a gene which has been inherited from a parent.

There are several genes that are associated with a significantly increased risk of developing bowel cancer. If you have inherited any of these gene variants, this is known as Lynch syndrome. Lynch syndrome is the most common inherited genetic predisposition to bowel cancer.

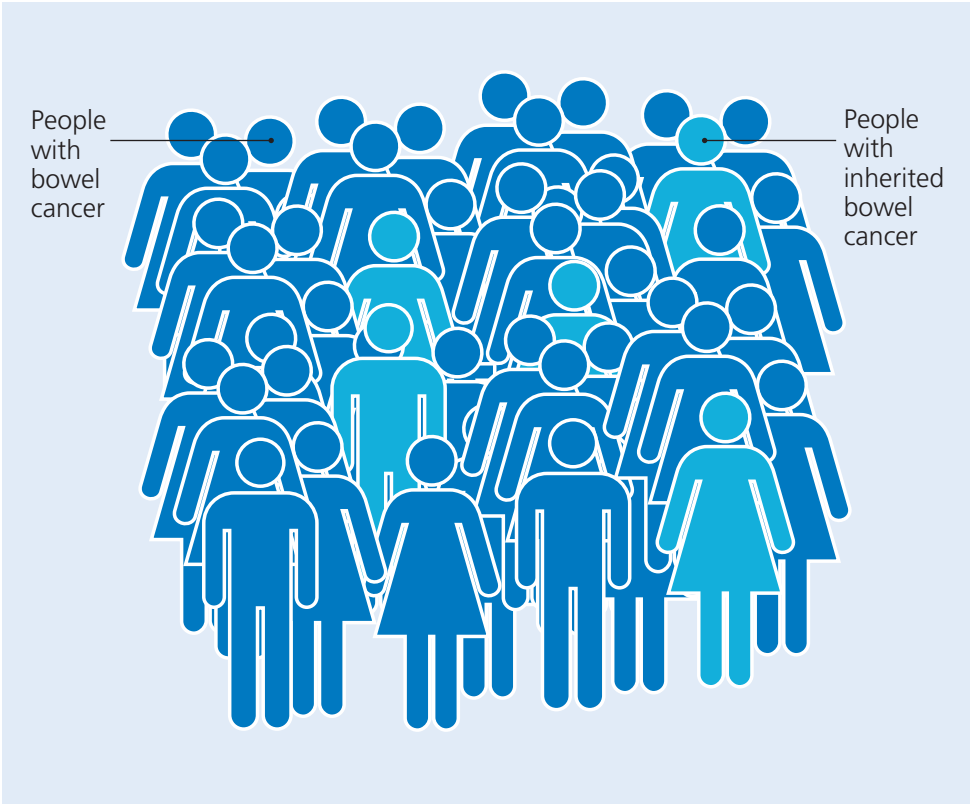


Diagram 1: This diagram shows that five in every 100 cases of bowel cancer have a strong inherited component.

Polyps

Scientists think that most bowel cancers start as a small growth on the lining of the bowel, known as a 'polyp'. Most polyps are harmless and non-cancerous (benign). Some types of polyps can turn into a cancer if they are left to grow for several years.

Genes

Genes are like coded messages which send instructions to your body about how to function (such as what colour your eyes will be, or how tall you will grow).

Some genes help to repair the normal, day-to-day damage that occurs in the cells that make up your body. If one of these genes doesn't work properly, damage can build up and cells may eventually become cancerous.

Gene variants

You may hear many different words used to describe a gene that is not working properly. A gene may be described as 'faulty', 'mutated', 'altered' or 'changed'. In this booklet we will use the term 'gene variant' or 'genetic variant'. Having a gene variant means that the instruction the gene sends to the body may be different, just as a spelling mistake may change the meaning of a word.

Inheritance

Our genes come in pairs. We get one copy from our mother and one copy from our father. When someone has biological children, they will pass on one copy of each pair. The child gets the other copy from the other parent.

If someone has a gene variant, they will also have a second copy of the gene which is working normally. Each of their children has a one in two (50%) chance of inheriting the variant. If they have not inherited a variant, they cannot pass it on to their own biological children.

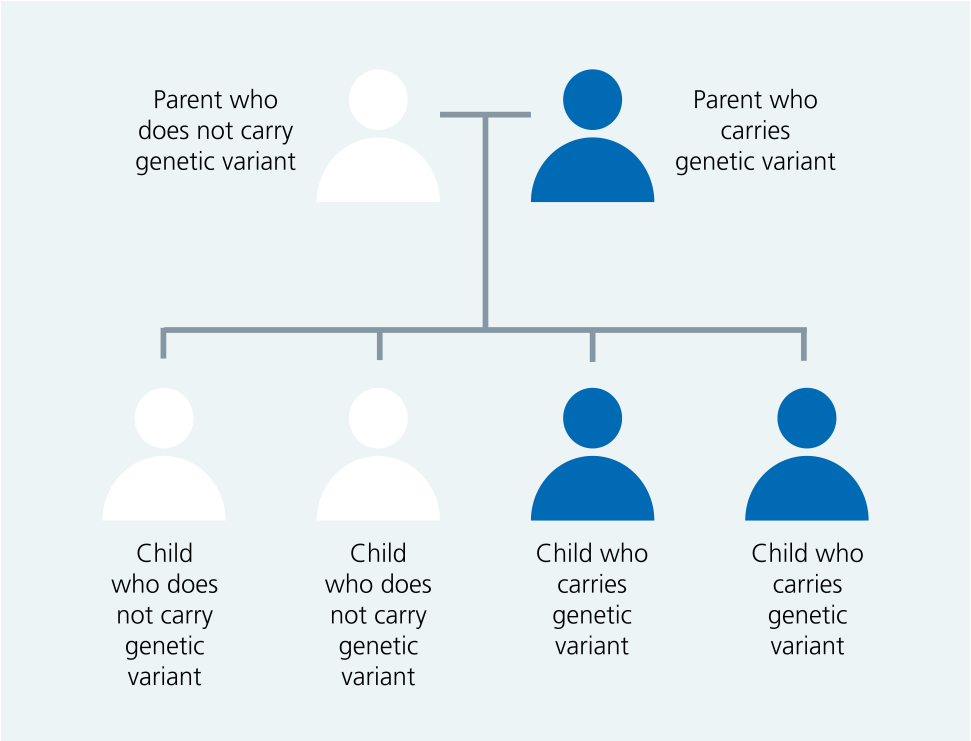


Diagram 2: Each child of someone with a MLH1, MSH2, MSH6 or PMS2 variant has a 50% (or one in two) chance of inheriting the gene variant. This is known as 'autosomal dominant inheritance'.

Lynch syndrome gene variants

The genes associated with Lynch syndrome usually help to repair damage within our cells. If one of the Lynch syndrome genes has a variant, the gene may not work properly and cannot repair damage as well as it normally would. Damage to the cells builds up over time, which increases the risk of developing cancer.

This means that men and women with Lynch syndrome gene variants have an increased risk of developing bowel cancer. Women who have a Lynch syndrome gene variant also have an increased risk of developing cancer of the lining of the womb (endometrium) and may also have an increased risk of developing ovarian cancer. In some families with Lynch syndrome, other rare cancers are seen more frequently than in the general population.

If you have several relatives (such as sisters, brothers, a parent or grandparent, aunts or uncles) who have developed bowel, womb or ovarian cancer, this may suggest that they have Lynch syndrome. Even if this is the case, you may not have inherited it. Please ask your genetic specialist for more information.

Genetic testing

A genetic test is a blood test to look for gene variants in someone's genetic material (DNA). Only a small number of people with bowel cancer will have a Lynch syndrome gene variant, so we usually only offer genetic testing to people with a strong family history of bowel cancer. It usually takes around two to three months to get the results from genetic testing, because there is a large amount of genetic code to analyse in the Lynch syndrome genes.

Genetic testing in a family usually starts with testing a family member who has a Lynch syndrome-related cancer. This is known as `diagnostic genetic testing'. It helps to provide the most informative result for the family. If we find a Lynch syndrome gene variant, we can then offer testing to other family members who have not had cancer, to look for the same variant. This is known as `predictive genetic testing'. It is relatively easy and takes less time than diagnostic testing.

Cancer risks

If you inherit a Lynch syndrome gene variant, your chance of developing bowel and/or womb cancer is higher but it's not inevitable. Some people have a gene variant and never develop cancer. Other people with the same variant may develop multiple cancers.

It is not possible to predict whether you will or will not develop cancer, or at what age. It is also important to remember that the risk of developing cancer is not the same as the risk of dying from the cancer. Even if a cancer develops, there is a good chance that the disease can be cured if detected and treated early.

Appropriate bowel screening increases the chance of finding a bowel cancer early, and treating it more effectively.

The risks are different in men and women with Lynch syndrome, and are different for each type of cancer. The lifetime cancer risks depend on the specific gene involved. These tables summarise the cancer risks associated with the main Lynch syndrome genes between the ages of 25 and 75 years.

MLH1 gene cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	48%	57%	7% (male) 6% (female)
Womb cancer	37%	Men do not have a womb	3% (female)
Ovarian cancer	11%	Men do not have ovaries	2% (female)

MSH2 gene cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	47%	51%	7% (male) 6% (female)
Womb cancer	49%	Men do not have a womb	3% (female)
Ovarian cancer	17%	Men do not have ovaries	2% (female)

MSH6 gene cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	20%	18%	7% (male) 6% (female)
Womb cancer	41%	Men do not have a womb	3% (female)
Ovarian cancer	11%	Men do not have ovaries	2% (female)

PMS2 gene cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	12%	13%	7% (male) 6% (female)
Womb cancer	13%	Men do not have a womb	3% (female)
Ovarian cancer	Similar to population risk	Men do not have ovaries	2% (female)

If you have not inherited a Lynch syndrome gene variant, it is still possible to develop cancer. Your risk will be similar to someone in the general population.

Prevention

People with Lynch syndrome can have bowel screening to detect bowel polyps early. This means that they can have the polyps removed before they turn into cancer.

Women who have a Lynch syndrome gene variant may want to consider having surgery to remove their womb and ovaries to reduce their risk of developing these types of cancer. This is known as `risk-reducing surgery'. We would offer this at an appropriate age, and we can discuss it with you at an appointment if appropriate.

Research has shown that people with Lynch syndrome can reduce their risk of developing cancer by taking aspirin daily. Talk to your GP before taking aspirin to see if it is suitable for you.

Scientists are still researching the most effective doses of aspirin, but the current recommended dose is:

- 150mg of aspirin per day for people who weigh less than 70kg
- 300mg of aspirin per day for people who weigh more than 70kg

Aspirin is available to buy `over the counter' in the UK.

Some people with Lynch syndrome have bacteria known as *Helicobacter pylori* (or *H. pylori*) in their stomachs. This bacteria doesn't often cause symptoms, but it increases the risk of ulcers and stomach cancer. A course of antibiotics can get rid of *H. pylori bacteria*, and reduce the associated risks. You can ask your GP to arrange a test for you which looks for *H. pylori.* They will prescribe antibiotics if you need them.

Screening

Bowel screening is done by a procedure called a colonoscopy. This is where a long flexible tube is passed up the back passage to look at the inside of the bowel. If polyps are found they can often be removed during the colonoscopy. People with Lynch syndrome are usually invited for a colonoscopy at least once every two years.

The screening involves emptying the bowel by using laxatives or an enema. The colonoscopy team will explain what you need to do before your colonoscopy appointment.

Scientists have not yet found an effective method of screening that can detect the early signs of womb or ovarian cancers. You may be able to take part in a research study which includes screening. Please ask your doctor or genetic specialist for more information.

Benefits of genetic testing

Knowing whether or not you have inherited a Lynch syndrome gene variant may help you make decisions about your life and how to manage your cancer risks. For some people, it is important for them to know whether they have inherited a familial variant rather than live with the uncertainty. The treatment options for people who develop bowel cancer may be different if the person has Lynch syndrome. Therefore, it may be helpful for people who have Lynch syndrome to discuss this with their oncology (cancer) team, or surgeon.

Close blood relatives of someone with a Lynch syndrome gene variant may have inherited it. These relatives can be told about their risk and offered genetic counselling, predictive genetic testing, and screening (if appropriate). Anyone who has not inherited the Lynch syndrome gene variant will not need any additional screening (unless there are other clinical reasons for screening).

Considerations

Insurance

There is currently an agreement in place with the Association of British Insurers (ABI) called the `Code on Genetic Testing and Insurance'. This states that people with a predictive genetic testing result (a result which tells them about their future cancer risks) do not have to tell any insurance company that is part of the ABI that they have had testing, or about the result.

However, you do have to disclose a diagnosis of cancer or any treatment that you are having. If you are having genetic testing because of a personal history of cancer, you may have to disclose the result.

You may wish to look at the information for different insurance companies before choosing a particular company, or consult an independent insurance advisor. You can find more information about the 'Code on Genetic Testing and Insurance' by visiting: **www.abi.org.uk/data-and-resources/tools-and-resources/genetics/code-on-genetic-testing-and-insurance/**

In the course of applying for insurance, people are often asked to sign forms that may give the insurance company access to your medical records. These may contain details of your genetic test. Talk to your genetic specialist about how the information will be kept in your medical records.

Impact on family members

People can experience a range of emotions when they are told they have a gene variant that increases their risk of cancer. Anger, shock, anxiety, worry about your health, and worry or guilt about possibly passing the gene variant on to your children are all normal reactions. Some people may feel guilty if they do not carry the gene variant when other close family members do. It is important to think about when might be the best time to have a genetic test.

Genetic testing in one person can have implications for other family members. Relatives may need to be told that they also have an increased risk. Unexpected information is sometimes revealed and this can affect relationships within families. For example, someone may disclose that a family member is adopted.

You may choose not to have genetic testing. Whether or not you are tested, you can talk to your genetic specialist about bowel screening.

Research

There are many research studies that involve individuals or families with Lynch syndrome, or a personal or family history of bowel cancer. If you are interested in taking part in research, please ask your genetic specialist if there are any research studies that you or your family are eligible for.

Research studies to consider

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Further information

The team involved in your care is:

Consultant:

Telephone:

Genetic counsellor:

Telephone:

If you need more advice or information about any aspect of Lynch syndrome please contact us at:

- **Wessex Clinical Genetics Service**
  Princess Anne Hospital
  Coxford Road
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  Telephone: **023 8120 6170**
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Version 6. Published January 2022. Due for review January 2025. 1431