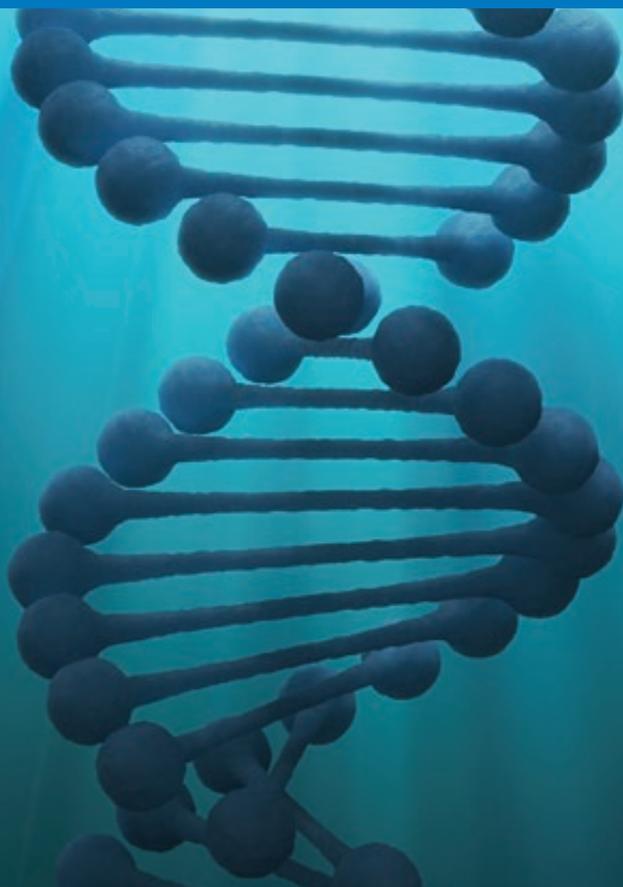


Hereditary non-polyposis colorectal cancer (HNPCC)/ Lynch syndrome

Information for patients



This booklet has been written for people with a strong family history of bowel cancer which may be due to an inherited tendency. It answers some of the common questions you may have about hereditary non-polyposis colorectal cancer (HNPCC).

HNPCC is often referred to as Lynch syndrome, after the doctor who first described it. It was given this rather long-winded name to distinguish it from another type of hereditary bowel cancer known as familial adenomatous polyposis – FAP where many polyps are found in the bowel.

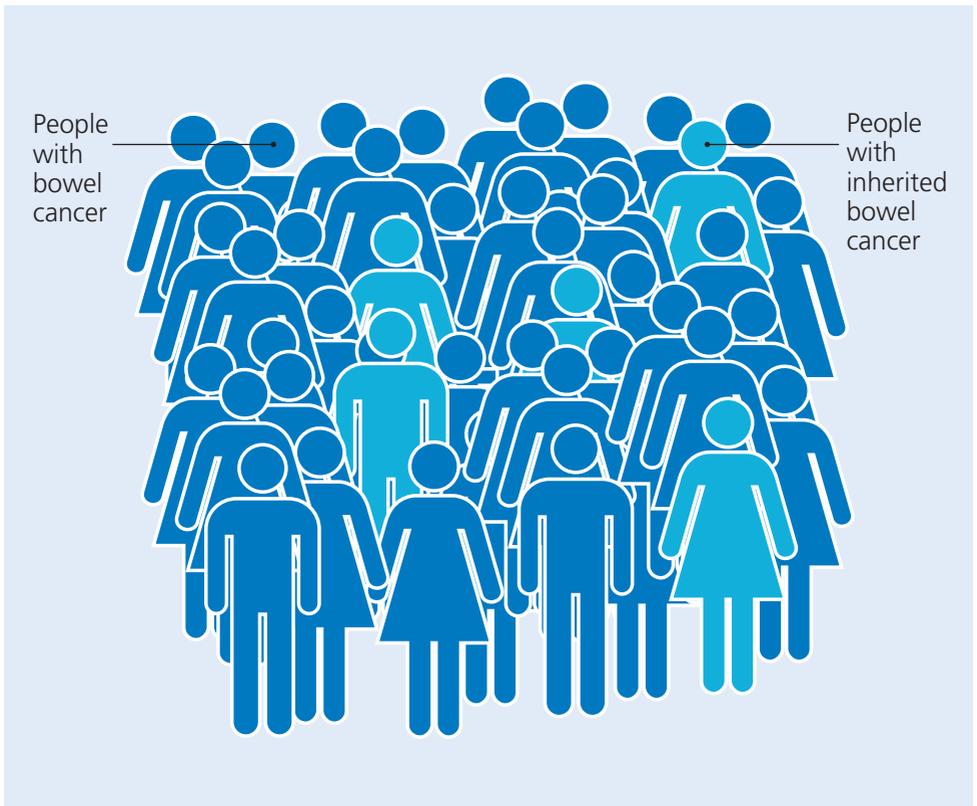
It was originally thought that there are no polyps present in this secondary type, thus the name non-polyposis, but it has since been discovered that polyps are present, but in much smaller numbers.

It is important to note that HNPCC and FAP are totally unrelated and that one cannot develop into the other form.

Inherited bowel cancer

In about 5 to 10% of people with bowel cancer (also known as colorectal cancer), the development of the cancer is thought to be due to a strong inherited factor. This factor is usually an alteration (mutation) in a gene which has been inherited from a parent.

Several different genes have been identified that are associated with a significantly increased risk of developing bowel cancer and HNPCC is the most common inherited genetic predisposition to bowel cancer.



Polyps

Most bowel cancers are thought to start as a polyp; a small growth on the lining of the bowel. Most polyps are harmless and non-cancerous (benign), but some may grow over several years and develop into a cancer. Certain types of polyps, called adenomas, can turn into a cancer if left to grow.

Genes

Our bodies contain thousands of coded messages called genes which send instructions to our body on how to function; for example what colour to make our eyes or how tall we will grow.

There are also genes that are involved in repairing the damage to our bodies that occurs during normal daily life. If some of these genes don't work properly then damage can build up and eventually cells may become cancerous.

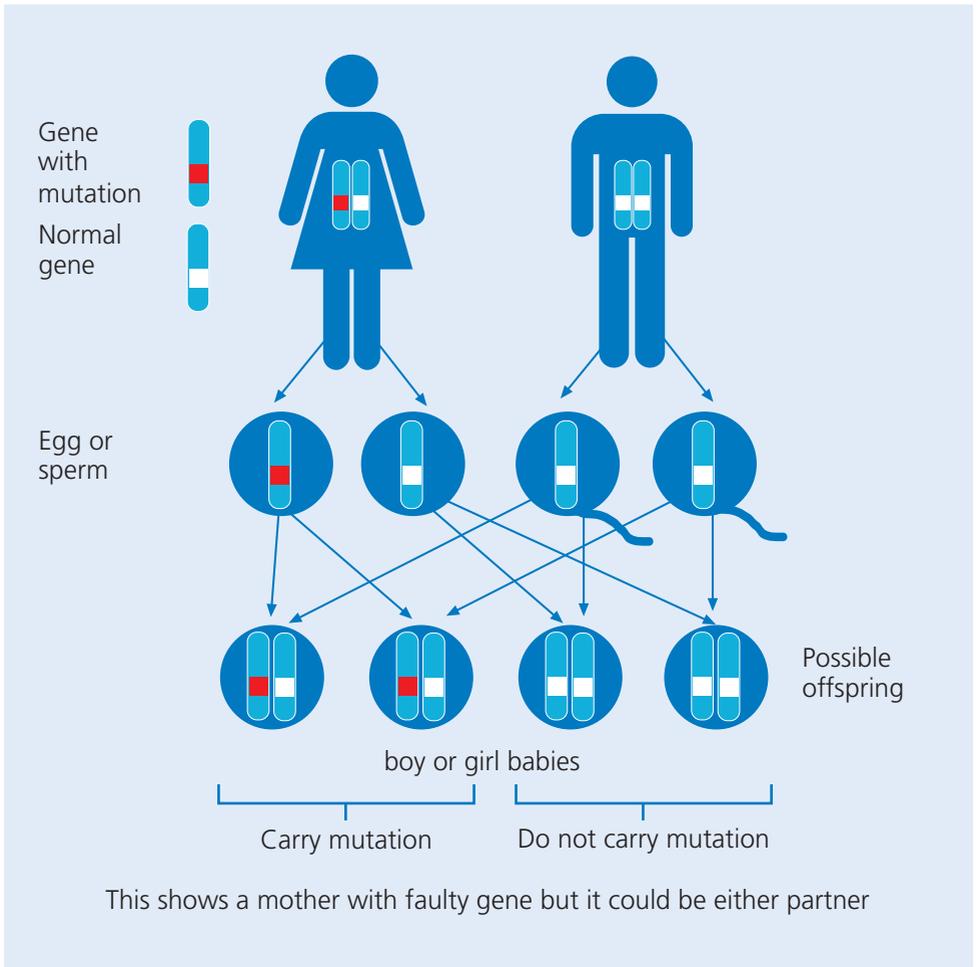
Gene mutations

You may hear many different words used to describe a gene that is not working properly. A gene may be said to be faulty, altered or changed. The technical term would be to say that there is a gene mutation. This means that the instruction the gene sends to the body may be different, just as a spelling mistake may alter the meaning of a word.

Inheritance

All our genes come in pairs and we get one copy from our mother, the other copy from our father. When we have children, we pass just one of each pair the other comes from the other parent.

If a person has an gene mutation, they will also have a second normal copy of the gene. Therefore each of his or her children has a one in two (50%) chance of inheriting the mutation. If a person has not inherited a mutation, then they cannot pass it on to their children.



HNPCC gene mutations

The genes associated with HNPCC are usually involved in repairing damage within our bodies. When a mutation is present in one of these genes, the gene does not work properly and cannot repair any damage. If damage accumulates the risk of developing cancer increases. Mutations in the HNPCC genes are primarily associated with an increased risk of bowel cancer.

Women who carry a mutation in an HNPCC gene have an increased risk of developing cancer of the lining of the womb (endometrium) and a slightly increased risk of developing ovarian cancer. In some families with HNPCC, other rare cancers are seen more frequently than in the general population.

Please ask your doctor or genetic counsellor to discuss this with you. If you have several closely related family members (such as sisters, brothers, a parent, grandparent, aunts/uncles who are blood relatives) with bowel or womb cancer, and if their cancers occurred at a young age, this may be suggestive of HNPCC. However, even if this is the case, you may not have inherited it.

Genetic testing

A person's genetic material (DNA) can be looked at in a blood sample. However, because only a small proportion of people with bowel cancer will have an HNPCC gene mutation, the test is only offered to people with a very strong family history. Without this, the test is unlikely to show any mutations. Also, the test is technically difficult and it can take a long time for results to become available. There are five genes known to be associated with HNPCC and there are probably several other genes that cause bowel cancer still to be discovered.

If genetic testing is indicated in your family, a family member who has had bowel or endometrial cancer should be tested first. If a mutation is found in one of the HNPCC genes, testing can then be offered to other family members to look for the same mutation. Once a gene mutation is found in a family, looking for the same mutation in other family members is relatively easy and takes less time.

Cancer risks

The risk of developing bowel and/or womb cancer is high if you inherit an HNPCC mutation, but it's not inevitable. Some people have a gene mutation and never develop cancer, whereas other people with the same mutation may develop multiple cancers. At present, we do not know why some people develop cancer and some do not.

You may never develop cancer. 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 chance that the disease can be cured if detected and treated early.

Without appropriate bowel screening, the risk of developing bowel cancer in your lifetime may be as high as four out of five (80%). However, the risk of bowel cancer in women with HNPCC is thought to be lower. The risk for women with HNPCC of developing womb cancer is between 40% and 60%.

MLH1 gene lifetime cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	22-52%	27-69%	7% (male) 5% (female)
Womb cancer	14-55%	men do not have a womb	2-3% (female)
Ovarian cancer	4-6%	men do not have ovaries	1-2% (female)

MSH2 gene lifetime cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	22-53%	27-69%	7% (male) 5% (female)
Womb cancer	14-15%	men do not have a womb	2-3% (female)
Ovarian cancer	8-11%	men do not have ovaries	1-2% (female)

MSH6 gene lifetime cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	20-25%	22-44%	7% (male) 5% (female)
Womb cancer	40-50%	men do not have a womb	2-3% (female)
Ovarian cancer	4-6%	men do not have ovaries	1-2% (female)

PMS2 gene lifetime cancer risks

	Female carriers	Male carriers	Chance in the general population
Colorectal cancer	11-15%	15-20%	7% (male) 5% (female)
Womb cancer	12-15%	men do not have a womb	2-3% (female)
Ovarian cancer	not known	men do not have ovaries	1-2% (female)

Prevention

At present, there is no guaranteed way of preventing bowel cancer, but with screening it is possible to detect the signs of cancer early and remove them. For example, if any polyps are identified on the lining of the bowel, these can be removed before they turn into cancer.

People who have an inherited HNPCC gene mutation may consider removing part of the bowel, or their womb and ovaries as a preventative measure; this is called risk-reducing surgery. There are also some studies underway on different types of drugs that may decrease the risk of developing bowel and womb cancers.

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 be removed there and then.

It is necessary to prepare the bowel by emptying it before the test. The hospital will give you details about what you need to do when you are given your appointment. This will need to be done once every one to two years. At present, we do not have methods of screening that are proven to be effective at detecting the early signs of womb or ovarian cancers, but screening may be available as part of research studies. Please ask us about these.

If you have not inherited a familial HNPCC gene mutation it is still possible to get cancer, although the risk is much the same as in the general population. Every person has about a 5-7% chance of developing bowel cancer, so even with a negative predictive genetic test there is still a chance of developing bowel cancer.

Benefits of genetic testing

People who have a mutation in an HNPCC gene are at increased risk of developing cancer. Knowing your risks may help you make decisions about your life and the options available to manage your cancer risks. For some people, it is also important for them to know whether they have inherited a familial mutation rather than live with the uncertainty.

Close blood relatives of individuals who have an HNPCC gene mutation may have inherited it. Each family member can be informed of their risk and offered genetic counseling, appropriate screening and/or predictive genetic testing. If you have a negative predictive genetic test, you will not need any additional screening.

Considerations

If a mutation is found that increases your risk of developing cancer it might in the future affect your ability to get insurance (such as health, life or disability cover). You may want to review your insurance before testing. You should talk to your doctor about how the information will be kept in your medical records; 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.

It is important that you do not withhold information asked for on your application as it may make your policy void. You may wish to look at different insurance company's information before choosing a particular company or consult an independent insurance advisor.

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

Genetic testing in a family can affect other family members. They may need to be told that they too are at increased risk or unexpected information may be revealed; for example, someone may disclose that a family member is adopted. Therefore, genetic testing may sometimes affect relationships within families.

You may choose not to have genetic testing. Whether or not you are tested, you should talk to your doctor about starting a programme to detect cancer early.

Further information

The team involved in your care is:

Consultant:

Tel No:

Genetic counsellor:

Tel no:

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

- **Wessex Clinical Genetics Service**

Princess Anne Hospital
Coxford Road
Southampton
SO16 5YA

Telephone: **023 8120 6170**

Website: **www.uhs.nhs.uk/genetics**

This booklet was written by:

Wessex Clinical Genetics Service
Princess Anne Hospital
Coxford Road
Southampton
SO16 5YA

**If you need a translation of this document,
an interpreter or a version in large print,
Braille or on audiotape, please telephone
023 8120 4688 for help.**

www.uhs.nhs.uk/genetics

© 2016 University Hospital Southampton NHS Foundation Trust. All rights reserved.
Not to be reproduced in whole or in part without the permission of the copyright holder.

Version 5. Published May 2016. Due for review May 2019. GEN008.01