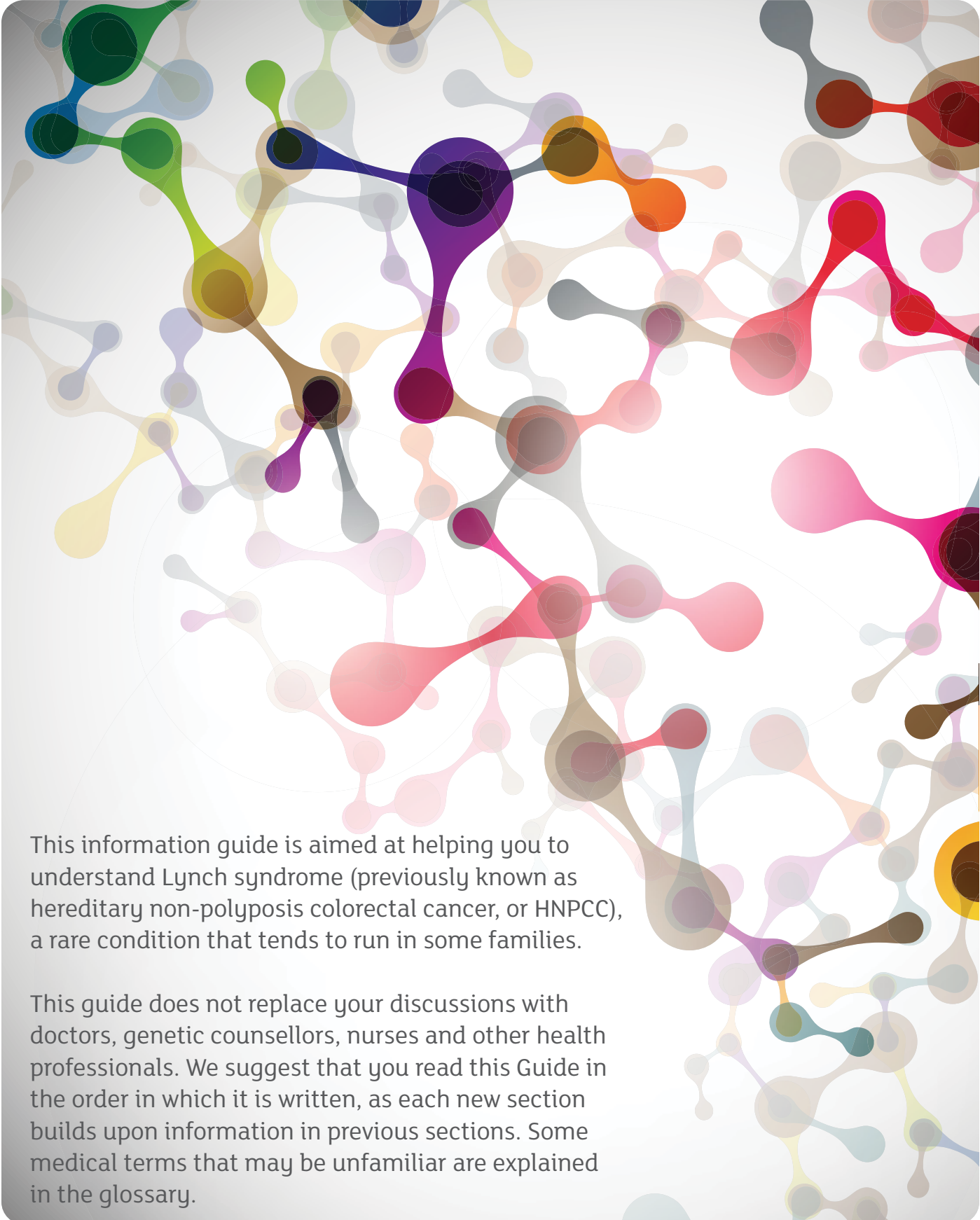


# Lynch syndrome

A guide for people with Lynch syndrome, and their family and friends



This information guide is aimed at helping you to understand Lynch syndrome (previously known as hereditary non-polyposis colorectal cancer, or HNPCC), a rare condition that tends to run in some families.

This guide does not replace your discussions with doctors, genetic counsellors, nurses and other health professionals. We suggest that you read this Guide in the order in which it is written, as each new section builds upon information in previous sections. Some medical terms that may be unfamiliar are explained in the glossary.

## 1. What is Lynch syndrome?

Lynch syndrome leads to a high risk for colorectal cancer, and some other cancers. Lynch syndrome is named after Dr Henry T. Lynch who described families with the condition. Lynch syndrome was previously known as HNPCC which stands for:

**H** stands for 'hereditary'.

This means that it can be passed from a parent to their child (inherited). People with this condition have not inherited cancer, but have inherited an increased risk of developing colorectal cancer and some other cancers. Still, sometimes people are the first in their family to develop Lynch syndrome.

**NP** stands for 'non-polyposis'.

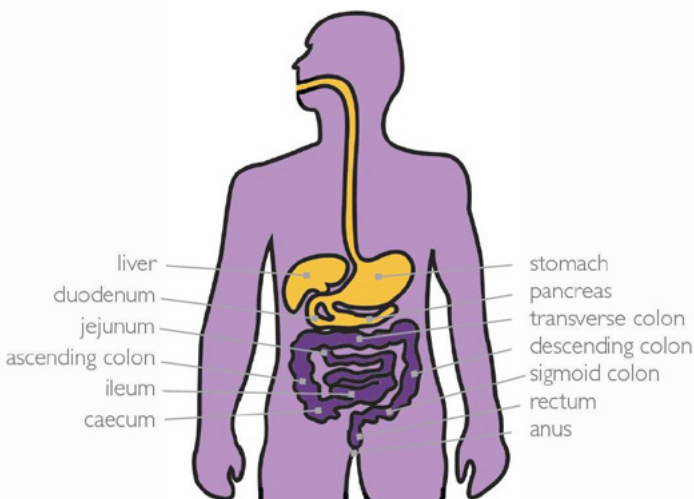
This indicates that Lynch syndrome is different from another hereditary condition called Familial Adenomatous Polyposis (FAP). People with FAP usually have hundreds of small growths, called polyps, on the lining of their bowel wall. Polyps do occur in Lynch syndrome but usually in much smaller numbers than in FAP.

**CC** stands for 'colorectal cancer' – that is, cancer of the colon or rectum, also known as large bowel cancer.

### The bowel

The bowel is part of the digestive system, or gut. The gut is the long tube that runs from your mouth, via your stomach and bowel, to your back passage (anus).

Food passes through the bowel, is digested and absorbed and the waste products are passed out as bowel motions.



The gut includes:

- The oesophagus, stomach and small bowel (the duodenum, jejunum and ileum) where food is digested and absorbed.
- The large bowel (the colon and rectum) where only water and salts are absorbed. The colon has different sections – caecum, ascending colon, transverse colon, descending colon and the sigmoid colon. The rectum leads to the outside of the body via the anus.

### What causes Lynch syndrome?

Every cell of the body carries a full set of instructions for growth and development called genes.

Occasionally some genes do not work properly because there is a fault in them. This fault is called a mutation.

Lynch syndrome arises when a gene contains a mutation that reduces its ability to prevent the growth of polyps and cancer in certain parts of the body.

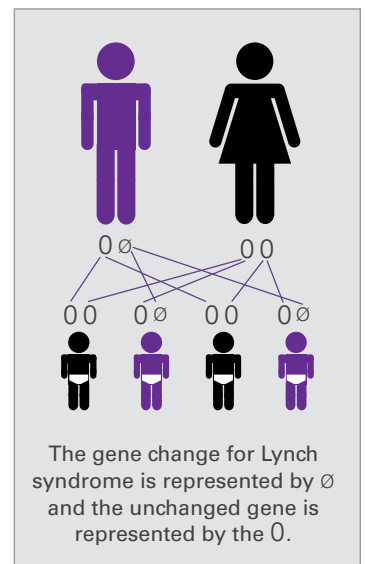
There are several known genes in which mutations can lead to Lynch syndrome. These genes are known as the 'mismatch repair' genes. Lynch syndrome is due to an inherited mutation in one of the mismatch repair genes.

### How is Lynch syndrome inherited?

Genes come in pairs. You inherit one copy of every gene from your mother and the other copy from your father. This is how a gene mutation can be passed on in a family.

If someone has a Lynch syndrome mutation, each of their children, regardless of their sex, has a 50% (one in two) chance of inheriting the mutation. This does not mean that 50% of the children will necessarily be affected, but that each child has a 50% chance of being affected.

This diagram shows the chance that each child has of inheriting the mutation. In this example, the father is carrying the Lynch syndrome mutation. When a baby is conceived, each parent passes on one copy of each of their genes to the baby. When one of the parents is carrying a mutation in one of the Lynch syndrome genes, represented here by the "ø" symbol, we see that there is a 50% chance that the baby will also carry this mutation.



If a person does not inherit the family Lynch syndrome mutation, then they cannot pass it on to their own children.

If someone has Lynch syndrome, it is possible that their brothers and sisters also have the condition. One of their parents could have the condition but may not know about it because they have not had any symptoms. The family should seek advice from genetic counselling professionals who know about Lynch syndrome and can advise the family on screening and testing.

### Cancers associated with Lynch syndrome

Some other forms of cancer are linked with Lynch syndrome. Cancer of the uterus/womb is the only one that occurs nearly as often as bowel cancer in some Lynch syndrome families.

Cancers shown in bold (below) are by far the most common in Lynch syndrome.

- **Large bowel** (colorectal)
- **Endometrium** (inner lining of uterus/womb. This is not cancer of the cervix)
- Ovary
- Stomach (gastric)
- Urothelial system: including renal pelvis (part of the kidney) and ureter (tube from kidney to bladder)
- Small bowel.

### Tumour tissue testing may assist the diagnosis of Lynch syndrome

If Lynch syndrome is suspected in your family then tests can be done on tissue from a cancer of a family member. These tests are looking for changes in the genetic information within a cancer cell and include:

- Microsatellite instability (MSI) testing, and/or
- Immunohistochemistry (IHC) testing. IHC is a staining test to check which genes are working in the tumour tissue.

### Your family may be at risk of having Lynch syndrome if any of the following features are present:

- At least three family members have had bowel cancer or one of the other cancers associated with Lynch syndrome, and one person is a close relative of the other two (i.e. parent/child/sibling).
- At least two successive generations are affected.
- At least one person was diagnosed at under 50 years of age.
- A person in the family with two or more bowel cancers, or bowel cancer and one of the other associated cancers.
- Familial Adenomatous Polyposis (FAP) has been excluded from the diagnosis.
- Testing on a cancer in the family has identified a problem (see more in the Tumour tissue testing section).

If you have a relative with Lynch syndrome you may be at risk. You might find it useful to contact your Family Cancer Clinic to discuss your family history and find out whether your family is at risk of Lynch syndrome. Contact details of your nearest Family Cancer Clinic are listed at the end of this information guide.

If the MSI test shows that the tumour cells are stable (no microsatellite instability) then it is less likely that the person has a mutation in one of the known Lynch syndrome genes. If the MSI shows that tumour cells are unstable, then Lynch syndrome is more likely. IHC testing can help identify which gene should be tested for the presence of a Lynch syndrome mutation.

### What can be done if someone has Lynch syndrome?

People with Lynch syndrome are at increased risk of developing cancer. A person with a proven diagnosis of Lynch syndrome has around a 30-50% chance of developing cancer (risks vary depending upon which gene is affected).

There is much that can be done to reduce cancer risk if someone has Lynch syndrome. This includes regular check-ups and, sometimes, individuals may consider preventative surgery.

## 2. Genetic testing for Lynch syndrome

### What does genetic testing involve?

Genetic testing is usually offered to families where there is a cancer history suggesting Lynch syndrome.

Whenever possible, tumour tissue testing is done first to clarify whether genetic testing is appropriate and which gene is likely to be affected. The particular mutation in the Lynch syndrome gene varies from one family to another.

The first step in each family is to try and find the family-specific Lynch syndrome gene mutation by first testing a blood sample from an affected person whose tumour testing showed a gene not working. This process of a "mutation search" may take considerable time, and it is not always possible to find the mutation that causes Lynch syndrome for a family. For this reason, a mutation search may be inconclusive.

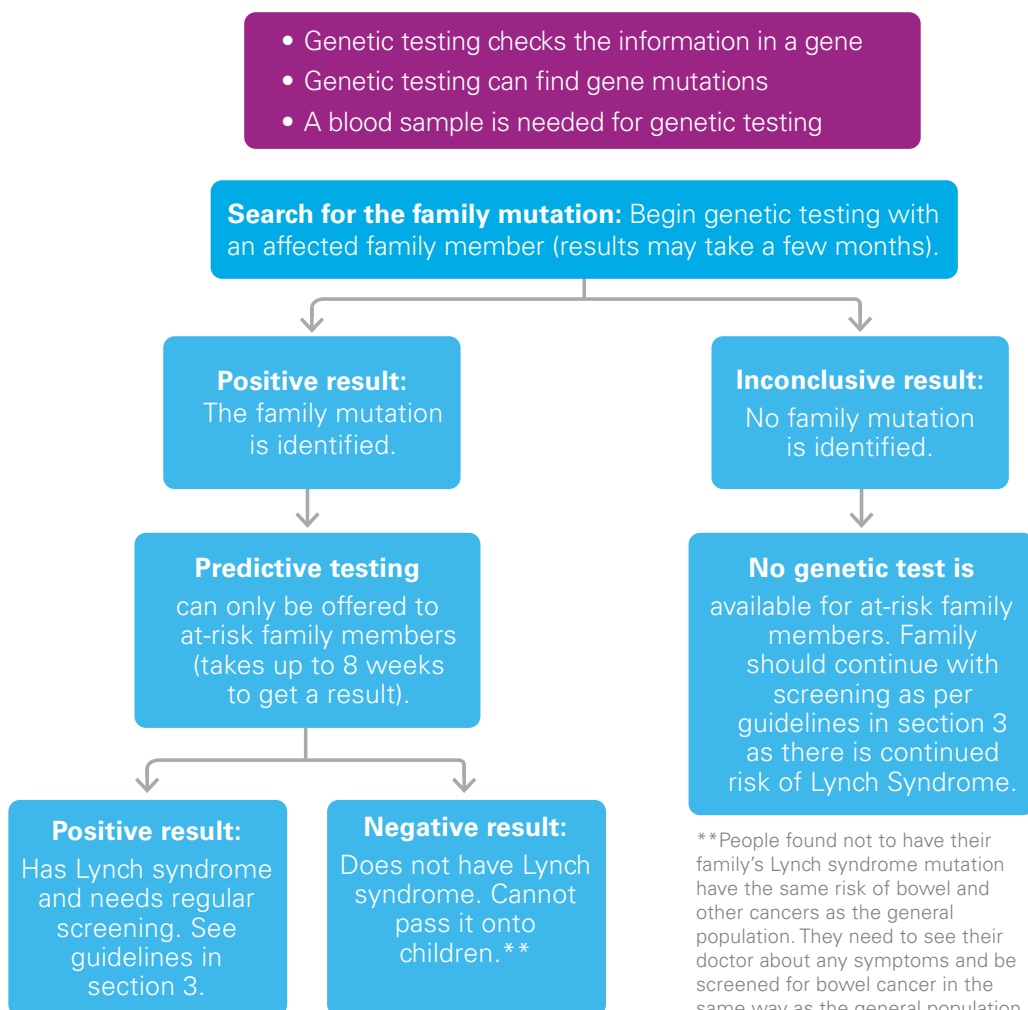
If, however, the family-specific gene mutation can be identified, then other at-risk relatives can have a blood test to see if they have inherited the family Lynch

syndrome mutation. This is called predictive testing. Results for predictive tests are available more quickly because we already know the family's specific Lynch syndrome mutation, so we know exactly where to look in the gene.

Genetic testing usually involves giving a small blood sample after written, informed consent is provided. Genetic counselling is offered before and after genetic testing by your Family Cancer Clinic.

If you have not inherited the family mutation, then you do not have Lynch syndrome. You do not need intensive screening, and your children are not at risk of inheriting Lynch syndrome from you.

Genetic testing in Australia is arranged through Family Cancer Clinics, where professionals make sure that people receive all the support and help they may need to make decisions about testing. Genetic testing through a Family Cancer Clinic is free.



### Genetic testing: Frequently asked questions

#### Can all families have the Lynch syndrome genetic test?

Not all families can have the Lynch syndrome genetic test because:

- Lynch syndrome genetic testing is only offered to families when the family history or tumour tissue testing suggests the possibility of Lynch syndrome.
- Sometimes a family thought to have Lynch syndrome has no living affected family member to test, or has some affected family members who are not interested in having genetic testing. This means that the family mutation cannot be identified, and at-risk relatives therefore cannot be offered predictive testing.
- In some families, even though a blood sample is available, the laboratory may not be able to find the family-specific Lynch syndrome gene mutation. This may be due to a type of mutation that is difficult to find and/or the possibility that there is a mutation in another gene not yet linked with Lynch syndrome.

#### What happens if I can't be gene tested?

If you are at risk of Lynch syndrome but you can't or don't wish to have genetic testing, you will need to have regular bowel examinations to check for polyps. Your treatment options then are the same as for everyone else with Lynch syndrome.

#### What if I don't have the family's Lynch syndrome gene mutation?

If you don't have the gene mutation found in other members of your family, you do not have Lynch syndrome and do not have the same high risk of developing bowel cancer.

Your children are not at risk of inheriting Lynch syndrome because you don't have the mutation to pass on to them.

Your children do not need to have the genetic test. You and your children no longer need to have screening for Lynch syndrome. If you have not inherited the family mutation it does not, however, mean that you will never develop bowel cancer, but that your chance of developing bowel cancer is the same as for the general population – about a 1 in 20 chance in your lifetime.

#### What if I do have the family Lynch syndrome gene mutation?

If the test finds that you have the family Lynch syndrome mutation then you have an increased risk of developing bowel cancer and an increased risk of some other cancers throughout your lifetime. You need to have regular check-ups to reduce your risk of developing cancer or to find cancer early if it has already developed.

For details about regular screening, see section 3 'Regular Check-ups'.

#### When can the test be done?

If the family-specific Lynch syndrome mutation is identified, family members (18 years and older) can have the test as soon as they wish. For people under the age of 18, parental consent may be required. There is no immediate benefit from genetic testing in childhood, so it is usually preferable for the individual to be old enough to have a say in whether or not they want to have the test. If you are concerned about this, talk it over with your genetic counsellor.

#### Who will know my test result?

Your personal test result is shared only with persons or organisations for whom you give consent.

#### The importance of talking it over

Before you have a genetic test, it is important to talk with a professional such as your doctor or genetic counsellor about the pros and cons of genetic testing. This may help you decide if genetic testing is right for you.

#### Insurance policies and genetic testing

If you are planning to have genetic testing, it is wise to discuss insurance issues with a genetic counsellor before testing.

A fact sheet about Life Insurance products and genetic testing in Australia can be found on the Centre for Genetics Education website.

#### I'm not sure I want to know

This is a common reaction. It may be helpful to consider the following points:

- If the test shows you do not have the family Lynch syndrome gene mutation, you will know that you have the same risk of developing bowel cancer as the general population but not the increased risk associated with being a Lynch syndrome mutation carrier. You will not need to have screening until the age recommended for the general population, unless symptoms arise. If you do not have Lynch syndrome, your children cannot inherit it from you.
- If the test shows you do have the family gene mutation, remember that people who have regular screening and removal of polyps have a lower risk of bowel cancer than those who do not have screening. Additional cancer screening tests may be advised. Also, cancers of the bowel and uterus diagnosed early can be treated very successfully.

### 3. Regular check-ups

Regular check-ups are recommended to detect and treat polyps and cancers early. Preventative surgery may also be advised.

#### Men and women with proven Lynch syndrome

For people with proven Lynch syndrome, the table below shows what check-ups or surgery are recommended to manage your cancer risk or chance of developing cancer.

Cancer type	Recommendation	
<b>For men and women</b>		
<b>Bowel (colorectal)</b>	Check-ups	Colonoscopy every 1–2 years is recommended from the age of 25 <sup>1</sup> . If someone in your family developed bowel cancer before the age of 30, then colonoscopy should start earlier in your family (i.e. 5 years younger than the age at which the person developed cancer). The frequency of colonoscopy may be reviewed at the age of 60, with a view to reducing frequency.
	Check-ups after surgery	Some people with Lynch syndrome may have bowel surgery. If you have had bowel surgery, check-ups of any remaining bowel every 12 months are recommended.
<b>Stomach (gastric)</b>	Check-ups	People who have a family history of gastric cancer, or those at high ethnic risk (eg. Chinese, Korean, Chilean or Japanese) may consider gastroscopy every two years from age 30.
<b>Urothelial system (including kidney and ureter)</b>	Check-ups	None. There is no evidence that regular check-ups of the urothelial system are of benefit. Instead, people with Lynch syndrome are encouraged to report any symptoms eg. blood in urine.
<b>For women</b>		
<b>Endometrial (uterine) and Ovarian</b>	Check-ups	None. There is no evidence that regular check-ups of the uterus and ovaries are effective in detecting these cancers early.
	Surgery	To reduce the risk of developing endometrial or ovarian cancer, women with Lynch syndrome are advised to undergo a hysterectomy, including removal of the ovaries. This may be done once childbearing is complete, or starting from around 40 years of age. <sup>2</sup>

1. For PMS2 mutation carriers, colonoscopy recommended from age 35 years.
2. For PMS2 mutation carriers, hysterectomy recommended from age 50 years.



Please visit [www.eviQ.org.au](http://www.eviQ.org.au) - Cancer Genetics section for the latest Lynch syndrome recommendations

Evidence shows that regular colonoscopy and removal of polyps improves outcomes in Lynch syndrome patients. There is some evidence that taking aspirin may reduce the risk of bowel cancer developing, however the appropriate dose is not yet defined.

### **Men and women at risk of (but not with proven) Lynch syndrome**

If you are at high risk of having Lynch syndrome (i.e. you have a parent, brother or sister with proven Lynch syndrome) you can have a genetic test to clarify your risk. If you do not wish to have genetic testing, you should follow the same advice as for someone with proven Lynch syndrome (see previous section).

Others at risk because of their family history should consider:

- Colonoscopy every 2 years.
- Faecal occult blood testing (FOBT) may be offered in intervening years.
- Other tests depend on the strength of family history of cancers in those organs.

### **Tests that may be used during regular check-ups**

#### **Colonoscopy**

A colonoscopy is an examination using video technology, in which the inner lining of the large bowel is inspected using a flexible tube with a light at the end. The tube is passed through the anus and moved through the bowel to enable the doctor to see along its full length. The bowel has to be empty, so some medication is usually given the day before to help you to empty your bowel. The examination generally takes about 30 minutes. It is done under sedation as a day procedure. If any polyps are seen, they can usually be removed at this time.

#### **Upper gastrointestinal endoscopy**

An upper gastrointestinal endoscopy examines the lining of the upper part of the gut using a similar type of technology to the colonoscopy. A tube is inserted through the mouth. Light sedation is often given to the patient. To ensure the stomach and upper gut are empty, no food or drink should be taken for several hours before the procedure.

## **Surgery**

### ***Surgery for bowel cancer***

Some people from a family with Lynch syndrome do not see a doctor until bowel cancer has already developed and it needs to be removed with surgery. The type of surgery will depend on the location of the cancer. Follow-up screening of the remaining bowel will be needed to detect any future abnormalities.

### ***The option of preventative surgery***

There is no clear agreement about the necessity for preventative bowel surgery in Lynch syndrome. Ask your specialist and the team at the local family cancer service about your particular situation.

People with Lynch syndrome and at-risk people should immediately tell their doctor about any symptoms of bowel problems such as rectal bleeding, indigestion, abdominal pain, changes to bowel habits (like prolonged constipation or diarrhoea) or genitourinary symptoms such as blood in the urine or abnormal bleeding from the vagina. In general, any persistent new symptoms should be discussed with your doctor.



**Please visit [www.eviQ.org.au](http://www.eviQ.org.au) -  
Cancer Genetics section for  
the latest Lynch syndrome  
recommendations**

### 4. Support and information

#### The NSW & ACT Hereditary Cancer Registry

The Hereditary Cancer Registry (HCR) was established to provide information and support to people affected by hereditary cancer, their family members who may be at risk, and their doctors in NSW and the ACT. While there are a number of hereditary related cancers, the conditions focussed on by the HCR include:

- Lynch syndrome (Hereditary Non-Polyposis Colorectal Cancer)
- Familial Adenomatous Polyposis – FAP
- Peutz-Jeghers Syndrome – PJS
- Juvenile Polyposis
- Other polyposis syndromes (i.e. Serrated Polyposis, Mixed Polyposis, MYH Associated Polyposis).

#### What does the Hereditary Cancer Registry do?

The HCR aims to assist people from families with a high risk of hereditary cancer to understand and manage their risk. It does this by:

- Building a complete picture of the condition in a family, assisting doctors to assess risks and plan screening and treatment.
- Developing knowledge about the incidence of hereditary cancer conditions in NSW and ACT.
- Contributing to better information, services and support for patients and their families.
- Providing a screening reminder service to registrants and their doctors.

The HCR offers an optional screening reminder service to assist registrants with keeping up to date with screening appointments. The HCR records registrants' contact details, family history, treatment, screening test results and details of any surgery that has been performed. All the information kept at the HCR remains strictly confidential. It is not given to anyone else, including other family members, without permission.

The information on the HCR database is an excellent starting point for national and international research into hereditary cancer syndromes such as Lynch syndrome. Information that is recorded on people or families is only used in statistical reports in which individuals cannot be identified. The HCR receives advice from a committee of clinical experts.

#### Why should I register and how do I register?

People from high-risk families are encouraged to register with the HCR to take advantage of the up-to-date information, screening reminder service and support provided by the registry. Registration is voluntary, and personal information is held confidentially under the NSW Health Information and Records Privacy Act. Registration can be completed using the registration form provided by your doctor or genetic counsellor, or contact the HCR for more information.

Other services offered by the NSW & ACT Hereditary Cancer Registry include:

- A screening reminder service for you and your doctor/s to help you keep track of your various appointments.
- Information about hereditary cancer, its prevention, treatment and management.
- Booklets and pamphlets about hereditary cancer conditions.
- Information about genetic services and tests.
- Linking separate branches of an extended family.
- Assistance with informing relatives of their risk by providing you with letters and other information about the family condition to pass on to them.
- Assistance with contacting support groups (cancer/genetics/ostomy).
- Assistance with passing on your hereditary information (with your consent) to interstate and overseas hereditary registers when you move.
- Referral to confidential telephone counselling.



#### For more information, contact the NSW & ACT Hereditary Cancer Registry:

**Phone:** 1800 505 644 **Fax:** 02 8374 3644 **Email:** [CINSW-HCR@health.nsw.gov.au](mailto:CINSW-HCR@health.nsw.gov.au)

**Mail:** Cancer Institute NSW, NSW & ACT Hereditary Cancer Registry,  
Locked Bag 2011, St Leonards NSW 1590

**Web:** [www.cancer.nsw.gov.au/data-and-statistics/cancer-registries/  
hereditary-cancer-registry](http://www.cancer.nsw.gov.au/data-and-statistics/cancer-registries/hereditary-cancer-registry)



### Support and information: Family Cancer Clinics

The staff at Family Cancer Clinics are trained to assist you with concerns about your family's history of cancer. Family Cancer Clinic staff can undertake a family risk assessment, provide you with screening recommendations, organise for you and your family to be seen by specialists and, if appropriate, organise genetic testing.

<b>Camperdown</b>	Hereditary Cancer Clinic Department of Cancer Genetics Level 2 Gloucester House Royal Prince Alfred Hospital Missenden Rd, Camperdown NSW 2050	(02) 9515 8780
<b>Darlinghurst</b>	Family Cancer Clinic Department of Medical Oncology Level 5, The Kinghorn Cancer Centre 370 Victoria Street, Darlinghurst NSW 2010	(02) 9355 5647
<b>Kogarah</b>	Genetic Counselling Service Cancer Care Centre, St George Hospital 1 Short Street, Kogarah NSW 2217	(02) 9113 3815
<b>Newcastle</b>	Hunter Family Cancer Service Cnr Turton & Tinonee Roads, Waratah NSW 2298	(02) 4985 3132
<b>Randwick</b>	Hereditary Cancer Clinic Prince of Wales Hospital High St, Randwick NSW 2031	(02) 9382 5107
<b>St Leonards</b>	Familial Cancer Service Dept Clinical Genetics Clinical Admin 3E Royal North Shore Hospital St Leonards NSW 2065	(02) 9463 1554
<b>Westmead</b>	Familial Cancer Service Crown Princess Mary Cancer Centre Westmead Hospital, PO Box 533, Westmead NSW 2145	(02) 8890 6947



#### For locations of Family Cancer Clinics in Regional NSW:

**Phone:** 1800 505 644

**Web:** [www.cancer.nsw.gov.au/learn-about-cancer/cancer-in-nsw/hereditary-cancers/cancer-genetics-counselling-services](http://www.cancer.nsw.gov.au/learn-about-cancer/cancer-in-nsw/hereditary-cancers/cancer-genetics-counselling-services)



#### An up-to-date list of Family Cancer Clinics can also be found on the Centre for Genetics Education website:

**Web:** [www.genetics.edu.au/genetic-services/cancer-genetics-clinics](http://www.genetics.edu.au/genetic-services/cancer-genetics-clinics)

**Other sources of support & information**

<p><b>Centre for Genetics Education</b></p>	<p>Information fact sheets and other information about hereditary cancer (including the booklet: Understanding genetic tests for Lynch syndrome – Information and decision aid) is available from the Centre for Genetics Education.</p>	<p>(02) 9462 9599 www.genetics.edu.au</p>
<p><b>Cancer Council Helpline</b></p>	<p>Cancer Council Helpline is a telephone information service provided by Cancer Council NSW for people affected by cancer.</p> <p>For the cost of a local call, you can talk about your concerns and needs confidentially with oncology health professionals. Helpline consultants can also put you in touch with appropriate services in your area.</p>	<p>13 11 20 www.cancer.org.au/about-cancer/patient-support</p>
<p><b>Genetic Alliance Australia (formerly AGSA)</b></p>	<p>For information about support groups contact Genetic Alliance Australia.</p>	<p>(02) 9295 8359 www.geneticalliance.org.au</p>
<p><b>eviQ Cancer Treatments Online</b></p>	<p>eviQ Cancer Treatments Online is a website that provides health professionals with current evidence-based, peer-reviewed, best-practice cancer treatment and information.</p> <p>The Cancer Genetics section of eviQ provides information about hereditary cancer conditions such as Lynch syndrome, including information sheets for people and families.</p>	<p>www.eviq.org.au (click on the Cancer Genetics tab)</p>

## 5. Glossary

### Adenoma

A non-cancerous tumour (growth). A type of polyp. It may turn into a cancer if not treated.

### Anus

The back passage. The opening of the bowel through which bowel motions are passed.

### Benign

Not cancer.

### Colon

The part of the large bowel between the end of the small intestine (the ileum) and the rectum. It is about 1.5 metres long.

### Colonoscopy

Examination of the large bowel using a thin flexible tube with a light at the end, called a colonoscope. It is passed through the anus and gently moved around so that, through it, the doctor can see the full length of the large bowel.

### Duodenum

The first 30 centimetres of the small bowel. The stomach empties into the duodenum.

### Gene

The parts of a cell that carry instructions on how the cell should grow and function. Each person has a set of many thousands of genes inherited from both parents. This set is found in every cell of the body.

### Ileum

The lower half of the small bowel, which joins up with the colon.

### Jejunum

The part of the small bowel below the duodenum and leading into the ileum.

### Large bowel

The colon and rectum.

### Malignant

Cancerous. Malignant (cancerous) cells can spread (metastasise) and eventually cause death if not treated.

### Mismatch repair genes

A set of genes whose job is to repair errors in DNA when cells divide. If one of the mismatch repair genes is not working properly, DNA errors accumulate in the cell, increasing the risk of cancer.

So far, four mismatch repair genes have been found to be associated with Lynch syndrome. The names of these four genes are hMLH1, hMSH2, hMSH6 and PMS2. There may be other genes associated with Lynch syndrome not yet discovered by scientists.

### Mutation

A change in a gene which may cause the gene to stop working properly.

### Polyp

An abnormal growth or lump in the bowel, often on a stalk, like a mushroom. Polyps are usually benign but can turn cancerous.

### Rectum

The last 12–15 centimetres of the large bowel, which opens to the outside of the anus. The faeces collect in the rectum before they are passed as a bowel motion.

### Sigmoid colon

The last 20–25 centimetres of the colon, which leads into the rectum.

### Small bowel

The first part of the gut made up of the duodenum, jejunum and ileum.

This guide is based on the booklet *Understanding Hereditary Non-Polyposis Colorectal Cancer (HNPCC) Syndrome*, published by the Cancer Council NSW in June 2004.