
A beginner's
guide to
Lynch syndrome

Patient Information





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Introduction


What does it mean to have Lynch syndrome?

Lynch syndrome is an inherited condition, which causes an increased risk of certain cancers. It is caused by a mutation (a genetic change) in one of five different genes.

This information booklet provides answers to some of the many questions you may have, following the news that you carry a gene mutation which causes Lynch syndrome. Healthcare professionals working in Cancer Genetics have met many people who have Lynch syndrome and we can share our experience to some extent. We can provide information and make referrals to other healthcare professionals. We can tell you that other people in your situation have had similar feelings and anxieties but we do not truly know what it is like for you and how it may affect your life.

Many people have questions that, for the time being, cannot be answered fully because we are still studying Lynch syndrome and its impact. One of the challenges that people with Lynch syndrome face is coping with the uncertainty of what the future holds, both for you and your family. You may be asked to make life-changing decisions about cancer screening and risk-reducing surgery without the benefit of all the facts you would like. This may be difficult and could cause you to feel quite anxious, frustrated or even angry at times. It may take you some time to feel that you have absorbed enough information to feel confident about your decisions.

Unlike other health-related issues, there is an extra set of challenges for people with Lynch syndrome – the risks for your relatives. If you are the first person in the family to have been diagnosed with Lynch syndrome, you will have to find a way to share this information with your family. Even if you are not the first person in the family to be tested, there may be family pressures to face. Will relationships be affected if one person has a positive gene test and their relative has a negative result? What about starting a new relationship – when do you tell someone and what do you say? What if you have young children or are planning a family?



We hope that this guide will be useful in providing you with some of the information you need and also help you to think about questions you may wish to discuss with your family and the genetics department. We realise that the guide contains some detailed information, which may be new to you. If you have any difficulties in understanding the information, or have any queries about this, please contact your genetics professional. If you have any comments about the guide, do let us know. We would like to make this booklet as useful and accessible as we can to support you and your relatives.

Background information about the Lynch syndrome genes

Is colorectal cancer inherited?

Generally speaking, cancer is not an inherited illness. Colorectal cancer is common, affecting about one in 14 men and one in 19 women at some point during their life, more commonly after the age of 60. It is not unusual to have a relative who has been affected by colorectal cancer. Most colorectal cancer occurs sporadically or out of the blue. However, we know that faulty genes are the underlying cause for about 5–10% (5 to 10 in 100) of colorectal cancers. There are five genes that, if mutated, can cause a high risk of colorectal cancer due to Lynch syndrome. There are also other inherited colorectal cancer syndromes which will not be discussed in this guide. Research to identify new genes that also contribute to a high risk of colorectal cancer or modify the risk associated with a Lynch syndrome gene mutation is ongoing.

What are Lynch syndrome genes?

Genes are pieces of the DNA code that we inherit from our parents. We have two copies of each gene – one copy is inherited from our mother and one from our father. We have about 20,000 genes, each with a specific function that helps our bodies grow and function normally. Some genes work to protect against cancer by correcting damage that can occur in the DNA during cell division. The Lynch syndrome genes are tumour suppressor genes. If an individual has a mutation in a Lynch syndrome gene, they have a greatly increased risk of developing colorectal cancer.

The Lynch syndrome gene mutation does not cause cancer to occur on its own. The individual is at greater risk of developing cancer because their cells' ability to repair DNA damage may be affected by the gene

mutation. It is the build up of DNA damage which causes a cell to change into a cancerous cell. We do not yet understand why mutations in the Lynch syndrome genes primarily give a high risk of colorectal cancer and gynaecological cancers rather than other types of cancer.

There are four main genes which, when mutated, can cause Lynch syndrome. These genes are called *MLH1*, *MSH2*, *MSH6* and *PMS2*. There is also a gene called *EPCAM* which can cause Lynch syndrome, but this is very rare.

Cancer risks are slightly different depending on which gene carries the mutation. You will need to know which gene carries the mutation in your family, so that you can find out about your cancer risks. Ask your Genetics Professional if you are not sure about this. Your cancer risk may also vary depending on other factors, such as your family history of cancer. For instance, some families seem to have a very strong family history of a certain cancer type whilst other families might just have one person who is known to be affected by a cancer related to Lynch syndrome. This may be because other genes could modify the effects of the Lynch syndrome genes and therefore affect a person's cancer risk. However, we don't yet know which genes these are or how cancer risks could vary. At the moment, your estimated cancer risk will be mostly based on the gene mutation that you carry.

There are several factors which will affect your own personal cancer risk:

- Age
- Gender
- Gene mutation
- Family history of cancer
- Previous cancer diagnoses
- Previous surgery (for example, if you have had your womb/ ovaries removed)
- Diet and lifestyle.

We don't yet know how all of the above factors could interact to influence your cancer risk.

Cancer risks

What are the cancer risks associated with *MLH1* gene mutation?

Male <i>MLH1</i> risks		
Cancer type	Male approximate risk (up to 70 years)	
	General population in UK	<i>MLH1</i> mutation carrier
Colorectal	2%	35% to 65%
Endometrial	–	–
Ovarian	–	–
Gastric	<1%	<10%
Urinary Tract	<1%	<5%
Pancreatic	<1%	<5%
Small bowel	<1%	5%
Brain	<1%	<2%
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	3%

Female <i>MLH1</i> risks		
Cancer type	Female approximate risk (up to 70 years)	
	General population in UK	<i>MLH1</i> mutation carrier
Colorectal	<2%	35% to 55%
Endometrial	<2%	20% to 25%
Ovarian	<2%	10% to 15%
Gastric	<1%	<3%
Urinary Tract	<1%	<3%
Pancreatic	<1%	<5%
Small bowel	<1%	<3%
Brain	<1%	<2%
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	3%

<i>MLH1</i> – Risk of developing cancer by age				
Current age	Male colorectal	Female colorectal	Endometrial	Ovarian
30	<3%	<1%	<1%	<1%
40	10%	<5%	<3%	<3%
50	25%	10%	<10%	<5%
60	30%	25%	10%	<10%
70	35%	35%	20%	15%
80	40%	50%	25%	20%



What screening or surgery is recommended for *MLH1* gene mutation carriers?

- Bowel Screening by colonoscopy – every 18 months from 25 years. This screening can be reviewed by your bowel surgeon once you reach the age of 75. More frequent bowel screening may be required, depending on the findings.
- Surgical removal of ovaries, fallopian tubes and womb, once childbearing is complete.

What are the cancer risks associated with *MSH2* and *EPCAM* gene mutation?

Male <i>MSH2</i> risks		
Cancer type	Male approximate risk (up to 70 years)	
	General population in UK	<i>MSH2</i> mutation carrier
Colorectal	2%	45% to 75%
Endometrial	–	–
Ovarian	–	–
Gastric	<1%	<10%
Urinary Tract	<1%	<30%
Pancreatic	<1%	<5%
Small bowel	<1%	5%
Brain	<1%	<3%
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	<1%



Female <i>MSH2</i> risks		
Cancer type	Female approximate risk (up to 70 years)	
	General population in UK	<i>MSH2</i> mutation carrier
Colorectal	<2%	35% to 55%
Endometrial	<2%	30% to 40%
Ovarian	<2%	10%
Gastric	<1%	<10%
Urinary Tract	<1%	10%
Pancreatic	<1%	<5%
Small bowel	<1%	<3%
Brain	<1%	<3%
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	<1%

<i>MSH2</i> – Risk of developing cancer by age				
Current age	Male colorectal	Female colorectal	Endometrial	Ovarian
30	<3%	<3%	<1%	<1%
40	10%	<10%	5%	1%
50	25%	20%	15%	<3%
60	40%	30%	25%	5%
70	50%	40%	30%	10%
80	60%	45%	35%	15%

EPCAM cancer risks

EPCAM gene deletion carriers have approximately 75% lifetime risk of colorectal cancer and female carriers have approximately 15% lifetime risk of endometrial cancer. Risks for other cancers have not been defined. We currently recommend that *EPCAM* deletion carriers have the same screening and management as *MSH2* gene mutation carriers.

What screening or surgery is recommended for *MSH2* and *EPCAM* gene mutation carriers?

- Bowel Screening by colonoscopy – every 18 months from 25 years. This screening can be reviewed by your bowel surgeon once you reach the age of 75. More frequent bowel screening may be required, depending on the findings.
- Surgical removal of ovaries, fallopian tubes and womb, once childbearing is complete.
- Skin examinations by a dermatologist are recommended for *MSH2* gene mutation carriers with a family history of particular types of skin tumours. These skin tumours can be both benign (non-cancerous) and cancerous and are called sebaceous adenomas, sebaceous carcinomas and keratocanthomas.

What are the cancer risks associated with *MSH6* gene mutation?

Male <i>MSH6</i> risks		
Cancer type	Male approximate risk (up to 70 years)	
	General population in UK	<i>MSH6</i> mutation carrier
Colorectal	2%	20% to 70%
Endometrial	–	–
Ovarian	–	–
Gastric	<1%	similar to population
Urinary Tract	<1%	similar to population
Pancreatic	<1%	similar to population
Small bowel	<1%	similar to population
Brain	<1%	similar to population
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	similar to population

Female <i>MSH6</i> risks		
Cancer type	Female approximate risk (up to 70 years)	
	General population in UK	<i>MSH6</i> mutation carrier
Colorectal	<2%	10% to 30%
Endometrial	<2%	25% to 70%
Ovarian	<2%	similar to population
Gastric	<1%	similar to population
Urinary Tract	<1%	similar to population
Pancreatic	<1%	similar to population
Small bowel	<1%	similar to population
Brain	<1%	similar to population
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	similar to population

<i>MSH6</i> – Risk of developing cancer by age			
Current age	Male colorectal	Female colorectal	Endometrial
50	<5%	<3%	<10%
60	10%	5%	15%
70	20%	10%	25%
80	45%	20%	45%



What screening or surgery is recommended for *MSH6* gene mutation carriers?

- Bowel Screening by colonoscopy – every 18 months from 30 years. This screening can be reviewed by your bowel surgeon once you reach the age of 75. More frequent bowel screening may be required, depending on the findings.
- Surgical removal of the womb, once childbearing is complete.
- Surgical removal of ovaries and fallopian tubes could be considered in women who are post-menopausal or those who have a significant family history of ovarian cancer.

What are the cancer risks associated with *PMS2* gene mutation?

Male <i>PMS2</i> risks		
Cancer type	Male approximate risk (up to 70 years)	
	General population in UK	<i>PMS2</i> mutation carrier
Colorectal	2%	20%
Endometrial	–	–
Ovarian	–	–
Gastric	<1%	similar to population
Urinary Tract	<1%	similar to population
Pancreatic	<1%	similar to population
Small bowel	<1%	similar to population
Brain	<1%	similar to population
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	similar to population



Female <i>PMS2</i> risks		
Cancer type	Female approximate risk (up to 70 years)	
	General population in UK	<i>PMS2</i> mutation carrier
Colorectal	<2%	15%
Endometrial	<2%	15%
Ovarian	<2%	similar to population
Gastric	<1%	similar to population
Urinary Tract	<1%	similar to population
Pancreatic	<1%	similar to population
Small bowel	<1%	similar to population
Brain	<1%	similar to population
Hepatobiliary (liver, bile ducts, biliary tract)	<1%	similar to population

<i>PMS2</i> – Risk of developing cancer by age			
Current age	Male colorectal	Female colorectal	Endometrial
50	<3%	<3%	<5%
60	<10%	<10%	10%
70	20%	15%	15%

What screening or surgery is recommended for *PMS2* gene mutation carriers?

- Bowel Screening by colonoscopy – every 18 months from 30 years. This screening can be reviewed by your bowel surgeon once you reach the age of 75. More frequent bowel screening may be required, depending on the findings.
- Surgical removal of the womb, once childbearing is complete.
- Surgical removal of ovaries and fallopian tubes could be considered in women who are post-menopausal or those who have a significant family history of ovarian cancer.

Managing cancer risk

Colorectal cancer risk

People with Lynch syndrome have an increased lifetime risk of colorectal cancer. Lynch syndrome carriers are recommended to have regular bowel screening which is done by a procedure called a colonoscopy. This is an effective form of screening for bowel cancer and can pick up cancers at an early stage, when they may be more easily treated.

What is a colonoscopy?

Colonoscopy is a telescopic examination of the large bowel. This is done using an endoscope, a flexible tube, which is passed through the anus (back passage) and into the large bowel. The endoscope is about the thickness of your little finger and has a camera and light at one end. This is usually performed under sedation, often as an outpatient after what is called bowel preparation. If small outgrowths of the bowel wall (called polyps) are seen, these can often be removed during the procedure. Colonoscopy is performed to try to detect these outgrowths of the bowel wall, so that they can be removed before they turn into cancers. There is a small risk of perforation of the bowel associated with colonoscopy. Your gastroenterologist will discuss this with you prior to the procedure.

What is bowel preparation?

Bowel preparation is a form of laxative. It speeds up bowel movements and clears the bowel which ensures the bowel lining is visible during a colonoscopy. This is usually taken in the form of a drink the day before your procedure. This will cause your bowels to open frequently and is likely to cause diarrhoea. Most people will choose to stay at home the day before their colonoscopy, to ensure that they are close to a toilet.

What happens during the procedure?

You will usually be given a sedative and some painkillers before your colonoscopy. The sedative will make you sleepy, but does not

put you to sleep. Some people choose not to have a sedative. You can discuss this with your doctor prior to the procedure.

You will be asked to lie down on your side with your knees bent. You will usually be able to see a television screen showing the lining of your bowel as the endoscope is passed through. The endoscope will be inserted into your bowel through your back passage. Your bowel is inflated slightly with some gas. This makes it easier to see the bowel lining. Some people can find this uncomfortable, which is why painkillers are used. The bowel itself does not have any nerve endings and so you will not be able to feel anything if the doctors need to remove any polyps. The test itself takes around 30 minutes.

Is it painful?

You should not feel pain during the colonoscopy, but you may have brief periods of discomfort.

What is a bowel polyp?

A bowel polyp is a small growth in the bowel, which can usually be removed at the time of the colonoscopy. Polyps can be benign (not cancerous), or sometimes they can turn into a cancer. Polyps that are removed during the procedure will be sent to the laboratory for testing. One of the advantages of having a colonoscopy is that bowel polyps can be removed before they turn into a cancer.

Bowel screening guidelines

Gene mutation	Age when bowel screening should start	How often
<i>MLH1</i>	25	Every 18 months
<i>MSH2 / EPCAM</i>	25	Every 18 months
<i>MSH6</i>	30	Every 18 months
<i>PMS2</i>	30	Every 18 months



At what age does bowel screening finish?

We would recommend that you have regular bowel screening until the age of 75, unless there are any other medical reasons why you should not have this screening. When you reach 75, your screening should be reviewed by your bowel surgeon to check that you are well enough to continue with the screening. There are some risks associated with bowel screening and you will have to weigh up the risks of having the procedure along with the benefits. Your doctors will be able to discuss this with you.

What can I do if I am worried about having bowel screening?

Having a colonoscopy is usually very straightforward. However, you may still be worried about having bowel screening, particularly if this is your first time. Some people are worried about the procedure being painful or uncomfortable. It may also make you feel embarrassed or concerned about what might be found. It is normal to feel this way and you can discuss any concerns you have with your genetics professional or gastroenterologist.

You may also find it helpful to discuss bowel screening with someone else who has had a colonoscopy. Maybe you could ask another family member about their experience? Lynch syndrome charities may also be able to offer you advice and support. You can find a list of contacts at the end of this guide.

Where will I have my bowel screening?

This will depend on where you live and you do not need to have your screening at The Royal Marsden. You may prefer to have your bowel screening done locally, as it is likely to be uncomfortable if you need to travel too far once you have taken your bowel preparation. The colonoscopy procedure is similar wherever you go for your screening.

If you have your bowel screening done at a different hospital, please contact the genetics team at The Royal Marsden to let us know the date of your last colonoscopy and the results. This will help us to keep your records up to date.

How can I organise future bowel screening?

Some hospitals have an automatic re-call system, which means that you are sent an appointment for a colonoscopy every 18 months – two years without the need for a new referral. Other hospitals do not have this system and you will need to contact the gastroenterology department or your GP to request another colonoscopy at the appropriate time. Regardless of the systems in place at your hospital, you should try to make a note of the date of your last colonoscopy. This will help you to keep track of when your next colonoscopy is due. You should make sure that you have a colonoscopy at least every two years.

If you have any problems with organising your bowel screening, please contact your genetics professional or your GP so that a new referral can be organised.

Where can I find more information about the colonoscopy procedure?

You might find it helpful to watch a video about having a colonoscopy before you have the procedure. There are videos available on the NHS choices website.

What are the symptoms of colorectal cancer?

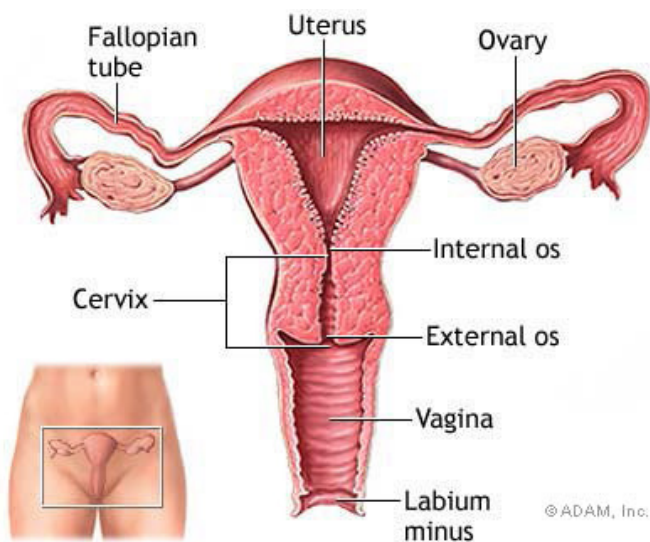
If you have any concerning symptoms, you should report these to your GP even if you have recently had a colonoscopy:

- Bleeding from the back passage
- Blood in your stools
- Change in bowel habit
- Abdominal pain
- Weight loss
- Fatigue.

Endometrial and ovarian cancer risk

Women who have Lynch syndrome may have an increased risk of developing endometrial and/or ovarian cancers during their lifetime. This risk depends on which gene mutation has been identified in your family.

Endometrial cancer develops in the lining of the uterus, which is called the endometrium. Ovarian cancer can start in the ovaries or in the fallopian tubes.



What is my risk compared with other women?

On average, women have about a 2% chance of developing ovarian cancer or endometrial cancer in their lifetime. Women with a close relative affected with ovarian or endometrial cancer may have a slightly increased risk of around 4–5%. Women who have Lynch syndrome may have a much higher risk of ovarian and/or endometrial cancer. The risk of developing ovarian and/or endometrial cancer starts to increase from around the age of 40 years in people with Lynch syndrome.

Am I at risk of endometrial or ovarian cancers?

This will depend on which Lynch syndrome gene carries the mutation in your family. Not all Lynch syndrome genes are associated with an increased risk of ovarian cancer. All of the Lynch syndrome genes are associated with an increased risk of endometrial cancer, although the risks vary depending on which gene has the mutation. You may carry a mutation in the *MLH1*, *MSH2*, *MSH6*, *PMS2* or *EPCAM* gene.

Gene	Endometrial Cancer Risk (lifetime)	Ovarian Cancer Risk (lifetime)	Recommendations for managing risk
<i>MLH1</i>	20–25%	10–15%	Risk-reducing BSO and hysterectomy are recommended.
<i>MSH2</i>	30–40%	10%	Risk-reducing BSO and hysterectomy are recommended.
<i>MSH6</i>	25–70%	Similar to population	Risk-reducing hysterectomy is recommended. BSO can be considered in post-menopausal carriers or those with a significant family history of ovarian cancer.
<i>PMS2</i>	15%	Similar to population	Risk-reducing hysterectomy is recommended. BSO can be considered in post-menopausal carriers or those with a significant family history of ovarian cancer.
<i>EPCAM</i>	15%	Unknown	Risk-reducing BSO and hysterectomy are recommended.

Note: Risk-reducing BSO is removal of the ovaries and fallopian tubes. Hysterectomy is removal of the womb.



How can I manage my risk of endometrial and/or ovarian cancer?

Currently there is no proven form of screening for endometrial (womb) cancer in women. We therefore recommend that women at an increased risk of endometrial cancer consider having surgery to remove their womb once they have completed their family, at around the age of 40–45. This procedure is called a hysterectomy.

There is also no effective form of screening for ovarian cancers in women. Large studies have evaluated the use of trans-vaginal ultrasound scans and CA125 blood tests for ovarian screening. The results showed that screening for ovarian cancer does not help to identify ovarian cancers at an earlier stage which would make a difference to treatment or prognosis.

Women who have an increased lifetime risk of ovarian cancer should consider having their ovaries and fallopian tubes removed. This procedure is called a risk-reducing bilateral salpingo-oophorectomy (BSO). Women with a mutation in *MLH1*, *MSH2* or *EPCAM* should all consider having their ovaries removed, due to the increased risk of ovarian cancer. Women with a mutation in *MSH6* or *PMS2* may wish to consider having their ovaries removed if they are post-menopausal or if they have a significant family history of ovarian cancer.

Risk-reducing BSO can be done at the same time as a hysterectomy, or at a different time. Some women may have both their ovaries and womb removed at the same time. In other cases, women may have their womb removed in their 40's and then have their ovaries removed once they are post-menopausal, usually in their 50's.

What is a risk-reducing bilateral salpingo-oophorectomy (BSO)?

A risk-reducing bilateral salpingo-oophorectomy (BSO, Bilateral (both sides) salpingo- (fallopian tube), oophor- (ovaries), ectomy (excision of)) is the surgical removal of a woman's ovaries and fallopian tubes before an ovarian cancer has occurred. This surgery is carried out to reduce the risk of developing ovarian or fallopian tube cancer. It can be done by keyhole surgery for many

women, which significantly reduces the recovery period. Some women will need to have open surgery, which is associated with a longer recovery period. If a woman is having her ovaries and womb removed at the same time, this will be done by open surgery.

What is a hysterectomy?

This is where the womb is removed by surgery and can be done to reduce a person's risk of endometrial cancer. It is done by open surgery, which means that the surgeon will make an incision in the lower abdomen in order to remove the womb. There is a longer recovery period needed after this surgery.

How does keyhole surgery compare with open surgery?

Keyhole surgery usually involves one overnight stay in hospital. Some keyhole surgery may be carried out as a day case, if this is considered appropriate for the individual. The average hospital stay for open surgery (when keyhole surgery is not considered the appropriate procedure) is increased to about five nights. The average return to normal activity is two to three weeks for keyhole surgery compared with about four to six weeks for open surgery. These figures are averages and this does vary a lot between different people depending on their usual work, family and exercise commitments. Both procedures take about the same operating time. Patients often ask when they can travel after surgery, in particular travel by plane. This does need to be discussed before the procedure due to the variations in patients' age, general health, post-operative recovery and lifestyle commitments.

What are the disadvantages of having a risk-reducing hysterectomy?

When women have their womb removed, this will make them infertile and unable to achieve a pregnancy. This is why we recommend that women have this surgery once they have completed their family.

Having a hysterectomy with preservation of the ovaries should not cause women to immediately go through the menopause, but it may cause menopause to happen earlier than it would have started otherwise.



What are the disadvantages of having a risk-reducing BSO prior to the menopause?

We would not usually recommend that women with Lynch syndrome have their ovaries removed under the age of 40 years, as the ovaries produce important hormones which protect organs such as the heart and brain. These hormones also maintain bone density and therefore help to prevent conditions such as osteoporosis (bone thinning). Please ask your genetics professional if you are unsure whether or not to have your ovaries removed.

When women have their ovaries removed prior to the natural menopause, they will experience a surgery-induced menopause and are likely to have menopausal symptoms.

Can I take Hormone Replacement Therapy if I have my ovaries removed?

Short-term hormone replacement therapy (HRT) may be prescribed to manage or avoid menopausal symptoms for women who choose to have their ovaries removed before the menopause. This can help to protect the heart, bones and brain. In this situation, breast cancer risk does not appear to be increased by the use of HRT. If you have your ovaries removed prior to the age of 50 and have not had breast cancer, we would usually recommend that you take HRT until the age of 50.

Bone density check-ups are advised for women having their ovaries removed before the age of 50. This is so that bone density can be monitored – treatment is recommended if your bone density appears to be reduced.

HRT should be used cautiously in women that have had breast cancer. In particular, we would not usually recommend HRT use for women who have had a breast cancer which responds to oestrogen (ER+ve). You should discuss this with your GP and gynaecologist if you have a history of breast cancer.

What are the symptoms of menopause?

Not all women experience the same type or severity of symptoms. Some of the issues reported by women are listed below. It is important to remember that only a minority of women have very severe symptoms or many symptoms at once. Very few women have many of the problems at the same time.


- Hot flushes and accompanying sweats, often at night (75% of women experience this, more so in the first two years, but 20–50% continue long term)
- Headaches, lack of concentration and memory, low mood, insomnia
- Uncharacteristic tiredness, anxiety and irritability
- Palpitations, panic attacks
- Loss of bone mass or pain in joints
- Vaginal dryness and itching, reduced sex drive
- Dry skin, brittle hair, thinner hair, weight gain
- Stress and urge incontinence, urinary tract infections.

Remember that women who have their ovaries removed prior to the age of 50 and have not had a breast cancer would be advised to take HRT. This will reduce menopausal symptoms.

What if I prefer not to choose any of these options?

After discussion with your doctor you may decide that none of these options are appropriate for you at this time. It may be that you are younger than the recommended age for surgery, or it may be that you wish to stay fertile as you have not completed your family. It is important to make the decision that is right for you and this decision can be discussed with your doctor, nurse or genetic counsellor at any time.

For women who choose not to have surgery, there are certain advantages and disadvantages that need to be considered. The advantages include that you will remain fertile (if you have not yet gone through the menopause) and that there are no side-effects,



such as menopausal symptoms. The disadvantage of not having surgery is that you are more likely to develop an endometrial and/or ovarian cancer. It is not easy to recognise the signs and symptoms of ovarian cancer during the early stages. If ovarian cancer does occur and is only found at an advanced stage, it is much more difficult to treat effectively.

What are the symptoms of ovarian or endometrial cancer?

It is important to be aware of cancer symptoms and discuss them with your GP. Ovarian cancer was once known as a ‘silent’ disease, because its symptoms can be vague. Evidence now shows that any of the following three symptoms, if they occur on most days may suggest ovarian cancer:

- Persistent pelvic and abdominal pain
- Increased abdominal size or persistent bloating (not bloating that comes and goes)
- Difficulty eating, and feeling full quickly.

Occasionally, women may also experience other symptoms, such as urinary symptoms, changes in bowel habit, extreme fatigue or back pain, either on their own or at the same time as those listed above. These symptoms are unlikely to be ovarian cancer, but may be present in some women with the disease. If you regularly experience any of these symptoms and they are not normal for you, see your GP.

There is a further leaflet available on:

www.nhs.uk/conditions/cancer-of-the-ovary/pages/symptoms.aspx

Women who have an increased risk of endometrial cancer should also report any abnormal vaginal bleeding to their GP. This includes post-menopausal bleeding, irregular periods and bleeding between periods.

Gastric cancer and other cancers

People with a mutation in the *MLH1*, *MSH2* or *EPCAM* genes may have an increased risk of gastric cancer and other cancers.

What are the symptoms of gastric (stomach) cancer?

It is important to be aware of gastric cancer symptoms and discuss any concerns with your GP. Symptoms of gastric cancer include:

- Prolonged indigestion
- Feeling full quickly
- Fatigue
- Dark or sticky stools
- Weight loss
- Feeling sick.

Is gastric cancer screening available?

Currently there is no proven test or group of tests that can reliably diagnose gastric cancer at an early stage. Therefore, no routine screening for gastric cancer is currently available.

The problem with having screening for gastric cancer is the risk of a false negative result – people may get results which initially appear normal, but they may have a gastric cancer which was not detected by screening. This is because screening for gastric cancer relies on random biopsies of the stomach lining. It is easy to miss a cancer in this way. We can only offer a screening test if it has a good rate of detecting cancers at an early stage.

What can I do to prevent gastric cancer?

If you are over 25 years and have an increased risk of gastric cancer, we would recommend that you have a H.Pylori screen. H.Pylori is a bacteria which can be found in the stomach and is associated with an increased risk of gastric cancer. Your GP can do a simple test to check for a H.Pylori infection. This test is usually done by stool sampling or a breath test. If you do carry the bacteria, this can be treated by antibiotics.



Is there screening for any other cancers associated with Lynch syndrome?

Some people with Lynch syndrome may have a slightly increased risk of other cancers, such as pancreatic cancer, cancer of the urinary tract or brain tumours. Your risk of other cancers depends on your family history of cancer and the gene mutation in your family.

Currently there is no screening available for any other cancers associated with Lynch syndrome apart from skin cancer which will be explained in the next section of this guide. This can be worrying for some people, but you should remember that the risk of developing any other cancers is low. If any other screening does become available at a later date, we will contact anyone who is on the Lynch syndrome carrier register with The Royal Marsden. You can also contact us if you are concerned about any other cancers that have happened in your family, or if you want to find out more information about screening.

Are there any symptoms I should watch out for?

If you have any of the following symptoms, please seek advice from your GP and make sure that your GP is aware that you have Lynch syndrome. They may not be due to cancer, but it is worth getting checked out by your doctor.

- Blood in your urine
- Abdominal mass (lump)
- Loin pain (pain in your side, back or upper abdomen)
- Fatigue.

Breast cancer risk

Research studies have been done to investigate whether women with Lynch syndrome might have an increased risk of breast cancer. The evidence is varied and further studies are needed to clarify the risks.

Women with Lynch syndrome should take part in the National Health Service Breast Screening Programme which involves three-yearly mammograms from the age of 50. This is the same screening offered to those women in the general population. All women should be aware of any changes to their breast tissue and report any concerns to their GP, in line with general health advice. Additional breast screening is only offered to those women with a significant family history of breast cancer.

Skin abnormalities

Rarely, families with a mutation in the *MSH2* gene may have an increased risk of skin tumours. This is sometimes called Muir Torre Syndrome and is a sub-type of Lynch syndrome. If you have a *MSH2* gene mutation and have a family history of particular skin abnormalities, you may have Muir Torre Syndrome and you should discuss this with your genetics team.

What screening should I have for skin abnormalities?

Screening for skin problems is only necessary if you have a *MSH2* gene mutation and a family history of any of the following skin conditions:

- Sebaceous Adenomas
- Sebaceous Carcinomas
- Keratocanthomas.

Screening consists of a skin examination by a dermatologist. You may be seen every year, or your dermatologist might teach you self-examination. You should also remain aware of any new skin lesions and report these to your GP.



Reducing risk

Aspirin Chemoprevention

Adults who are at an increased risk of developing a bowel cancer can consider taking daily aspirin. A study called CAPP2 has been published showing that 600mg of aspirin taken daily for an average of about two years significantly lowered cancer risk in individuals with Lynch syndrome. This is a large dose of daily aspirin which is not recommended outside of a research study at this time. Further studies are needed to decide the best dose. The CAPP3 study will aim to address this question. You may like to take part in this study. Please ask your Genetics professional if you are interested.

In the meantime, we recommend that adults consider taking a lower dose of aspirin (75mg daily) after discussion with your General Practitioner (GP) to make sure that you do not have any risk factors that mean you should not take aspirin.

Lifestyle and diet

Individuals with Lynch syndrome are recommended to follow the same advice as those in the general population with regards to lifestyle and diet. These measures are known to help reduce the risk of bowel cancer in the general population. It is not known exactly how lifestyle and diet impacts upon cancer risk in people with Lynch syndrome.

- Eat a healthy diet with plenty of fruit and vegetables
- Eat plenty of fibre
- Avoid eating too much cured and processed meat
- Avoid eating too much red meat
- Take regular exercise
- Maintain a healthy weight
- Do not smoke
- Avoid excessive alcohol.

More information regarding these recommendations can be found on the NHS choices website.

Sharing information with your family

Genetic testing for your relatives

Who needs to know that Lynch syndrome has been diagnosed in my family?


During your genetic appointment, the doctor or the genetic counsellor will go through your family tree with you to identify who is at risk of inheriting Lynch syndrome. Lynch syndrome is inherited. Your close relatives (brothers, sisters and your children) will have a 50% chance of inheriting Lynch syndrome. In most families it will be easy to predict if the gene mutation came down through your mother's or your father's family, because of the family history of cancer. The only way to prove this is to test family members to see who has the faulty gene. Only your relatives from that side of the family will be at risk of Lynch syndrome.

What do I tell people?

You will have received quite a lot of information about Lynch syndrome, your risks and your options. It can be daunting to know how to share all this information with someone else. Many people worry that they will be asked questions and they will not know the answers. Your genetics unit will not approach your relatives about your result, so usually it is you who would provide this initial information about the presence of a faulty gene to the family. The geneticists can provide you with a 'to whom it may concern' letter for you to share with your relative(s) which contains all the required information so that they can ask for a referral from their GP to their local genetics unit.

Why do other people in my family need this information?

Genetic information is different from most medical information an individual receives, because it is not only relevant to the individual but also to their family members. Genetic information can provide an explanation as to why someone has a particular health problem, but it can also predict future poor health or the risk of having a child affected with a particular genetic problem. If someone is aware that they have an increased risk of developing



cancer, they have the chance to make choices about genetic testing, cancer surveillance or preventative surgery. They may also decide to make changes to their lifestyle to help decrease their risk of developing cancer, and they may wish to consider the family planning implications and insurance issues. Knowing about the risk gives your relatives a chance to take action to reduce their risk of getting cancer or help ensure that cancer is detected at an early stage so it can be treated more effectively.

When should I share this information?

There is probably no right time to tell people. Sometimes families are aware of the testing process and are waiting to hear the results. Other people choose to wait until they know their results before they mention it to anyone else. There will be a variety of factors that affect your decision to share this news, for example you may need time to get used to the information first, or someone may have been bereaved recently and you may feel it is better to wait a bit. Sometimes people are too young to be told everything or maybe you are waiting until you have the chance to see someone in person rather than telling them over the telephone or by mail.

Bowel screening can start from 25 to 30 years of age, depending on the gene mutation. If your relative is over 25, they could start screening right away if they are at risk of having Lynch syndrome. Anyone in the family who has been affected with cancer should be told as soon as possible, because their doctors may need this information to make appropriate treatment decisions. It is important to highlight that people who are closely related (sister, brother, daughter, parent) to a person with Lynch syndrome can also have bowel screening, without undergoing genetic testing. We realise that not everyone wishes to have the genetic test.

How can I avoid upsetting my relative?

Many people are concerned that sharing this information will cause their relative to feel very anxious or guilty and feel responsible for causing this upset. It is always difficult to share bad news. It might be useful to think of other times that you have had to share bad news, how you did it and what you learned from that experience. It may be useful if you think about this

information in a positive light; that members of your family, with this information, are in a better position to make choices that could reduce their risk of cancer or ensure it is detected as early as possible. It is important to remember that if someone has Lynch syndrome, it is nobody's fault – we cannot control which genes were passed on to our children. It is also important to remember that if someone has a faulty gene, they have always had it since the moment they were conceived, so what is different now is that we can identify it and give people options to manage their risk.

Where can I get help with telling my family?

The genetics team can help you to identify who needs to be informed in your family and provide you with a '**to whom it may concern**' letter. It can be a burden to have this responsibility. Perhaps there is someone else within your family that you could share the information with and who could then help by taking on some of the responsibility of telling other people within the family. In some families, we see the information being passed on to one generation and it is then passed down within family units. The genetics team can discuss strategies for sharing information with you to make it as easy as possible.

Who is at risk of having Lynch syndrome in my family?

If you have Lynch syndrome, your close relatives have a 50/50 risk of having the faulty gene. The faulty gene is highly likely to have been present in your family for many generations. It is only that we are now able to identify who actually carries the faulty gene. You would almost certainly have inherited the mutation from either your mother or your father. It is extremely rare for a person to carry a Lynch syndrome gene mutation which has not been inherited from either of their parents.

Your brothers and sisters

Your brothers and sisters each have a 50/50 risk of having the faulty gene. Each person would need to have genetic testing to determine if they have the faulty gene or not. You cannot predict if someone has the gene on the basis of their brothers' or sisters' genetic test results or if people look alike in the family.



Your children

Your children (or future children) each have a 50/50 risk of having the faulty gene. We do not offer predictive testing to children because screening or risk-reducing treatment is not generally needed or available for children. Once they are older, each of your children could choose to have genetic testing to find out if they have inherited the faulty gene or not.

If you have more than one child, each of your children will have a 50/50 risk of carrying the gene mutation. This is regardless of the way that they look, their personality traits, or whether their siblings carry the gene mutation. Sometimes, a parent with Lynch syndrome won't have passed the gene mutation onto any of their children. In other cases, all or some of their children will have inherited the gene mutation. Even if your children have inherited the gene mutation, they may not ever develop a cancer.

Cancer treatments, screening and risk-reducing strategies do improve over time. Therefore, the options available to your children when they are adults may be different to those options which have been available to you.

Your extended family

The faulty gene would either have come down through your mother's or your father's family. So if you inherited the faulty gene from your mother, for example, then only your aunts, uncles and cousins on your mother's side of the family are at risk of having the faulty gene which causes Lynch syndrome.

Does Lynch syndrome skip a generation?

The faulty gene does not skip a generation. Not all individuals with a mutation in one of the Lynch syndrome genes will develop cancer. For this reason, it may look as if the mutation has skipped, but in reality it was present in the previous generation.

Is the faulty gene only important if you are a woman?

When thinking about who is at risk of having the mutation in the family, it does not matter if you are a man or a woman. Both men and women have the genes which cause Lynch syndrome.

How do I know who to tell about the gene?


When you have your appointment in the genetics clinic, the doctor or genetic counsellor will go through your family tree with you and explain who is at risk of having the faulty gene and who is not at risk. We can provide you with a letter that explains about the gene fault for you to share with your at-risk relatives – they can then decide if they want to have a genetics appointment to find out more information.

Some people will need to consider how to tell any future partners about their diagnosis of Lynch syndrome. This is important to consider and there may be no right time. If you are planning to have children, you will need to tell your partner about the risk of passing on the gene mutation to your children. They may have questions of their own which you are unable to answer. In this case, it might be helpful to request a genetics appointment and invite your spouse to attend, so that they can ask questions of their own. You could also encourage them to read this guide.

What does dominant inheritance mean?

You may have heard the term **dominant inheritance** at your genetics appointment when the doctor or the genetic counsellor was describing how the gene mutation is passed down within the family. When we understand how a gene is passed down in a family, we can then determine who is at risk of having the faulty gene in the family.

We have about 20,000 genes. These genes are the instructions that our bodies need to develop and function normally. All genes come in pairs – we get one copy from our mother and the matching copy from our father.



A dominant condition is one where a person only needs one of the two genes to have a mutation, in order to be affected. Having one faulty (mutated) copy of a Lynch syndrome gene is enough for someone to have the increased risk of developing cancer, even though the other copy of the gene, which they inherited from their other parent, works normally.

Therefore we know that if a person carries a mutation in a Lynch syndrome gene, there is a 1 in 2 or 50% chance they will pass the faulty copy of the gene to their offspring; hence the 50% risk for children of those with Lynch syndrome. We can also work out the risk for extended family members by looking at how they are related to the person in the family who has Lynch syndrome.

Predictive genetic testing

What does predictive genetic testing mean?

This term refers to a genetic test that is offered to someone who is healthy (for example, has not had a diagnosis of a cancer which is associated with Lynch syndrome). The purpose of the test is to determine if the person has inherited the faulty gene that has already been identified in one of their close relatives. It is called a predictive test because if the person has the faulty gene, it means that they have an increased risk of developing these cancers over their lifetime. Not everyone who has Lynch syndrome goes on to develop cancer, but the risk is increased.

Who can have predictive testing?

Close relatives of an individual with Lynch syndrome can ask to be referred to their local genetics service by their GP to discuss the option of genetic testing. Your genetic doctor or genetic counsellor will go through the family tree with you to show you who in your family is at risk of having Lynch syndrome. We do not offer predictive genetic testing to children because this is an adult onset disorder so cancer screening or interventions are not necessary for children.

What happens when someone is referred for genetic testing?

If someone is coming for a predictive genetic test, they may have one or two appointments to discuss the issues around testing, depending on their age and their understanding of the genetic information.

The first step for the genetics department is to confirm that there is a gene mutation in the family and obtain a copy of the relative's mutation report from the genetics centre where they had their test. If the report is not available, then predictive genetic testing may not be possible. At their first appointment, the doctor or counsellor will explain what the faulty gene is, how it is inherited, the associated cancer risks, and their risk of having the faulty gene and options for cancer screening or risk-reducing options. They will also discuss whether or not the individual wants to have a test at this point in their life, who they have for support and who they have told about the test. We also discuss how a positive or negative result will impact on their lives and their relationships within the family. A letter summarising the consultation is sent to the individual after the clinic appointment. If they decide to have the test, results are available within a few weeks and are usually given by letter. If someone is found to carry the gene mutation, they will be invited to attend another clinic appointment. Individuals are welcome to bring a friend or relative with them to the appointment for support.

What if someone does not want genetic testing?

Not everyone who is at risk of having Lynch syndrome wishes to have a predictive genetic test. Even if someone does not want genetic testing, it is still useful to talk to them in the genetics clinic. We can explain the options and give them a chance to ask any questions. If people are at 50% risk of having Lynch syndrome, they are still eligible for extra cancer surveillance, such as bowel screening, even if they do not want testing.



Does predictive genetic testing have a negative impact on insurance?

Sometimes people worry that if they have a genetic test, they will have problems taking out life insurance. There is an agreed code of practice amongst insurance companies that results of predictive testing for high risk cancer genes will not be used by ABI insurers to determine premiums or eligibility for life insurance. This agreement was recently extended. Further information can be found on the website: www.abi.org.uk

Planning to emigrate?

If you are planning to emigrate to a new country, it would be good to check with that country's relevant office to determine if having a predictive genetic test could impact either your emigration application or your ability to obtain health insurance and/or health care provision before undertaking genetic testing.

Talking to children and young people about Lynch syndrome

Many parents find the prospect of talking to their children about the presence of Lynch syndrome within the family difficult and distressing. Studies show that parents' first instinct is to protect their children and they find it difficult to know what and when they should tell their children. Parents are often dealing with their own concerns about their health and future wellbeing, and can feel a sense of guilt that their children may also be at risk.

What helps children and young people?

In most cases, children cope better when the family is more willing to discuss what is happening to different family members. Talking to children helps them feel valued and respected and helps them cope better than when they are left feeling confused and unsure how or what to ask.

Children get information from many places including school, television and friends. They are likely to already have some knowledge about cancer and possibly about hereditary cancer.

By talking to them, you can help them sort out what is accurate and what is inaccurate and clarify things they are not sure about.

Children will probably be most worried about their parent developing cancer, so they will need reassurance and reminders that having Lynch syndrome does not always result in cancer. However, knowing you carry the gene mutation means that you can have regular tests to ensure that if a cancer arises, it can be detected very early on and treated

When is a good time to tell your children?

There is no right age but try not to keep secrets. Children and young people place great emphasis on trust and honesty from parents. Children often observe changes in their parent's behaviour and may try asking questions or may be waiting for you to discuss what is happening. Watch for any changes in your child's behaviour as this may indicate that they are worried or concerned about what they have observed or overheard.

By the age of eight years, children learn not to ask difficult questions unless their parent(s) gives them permission because they fear upsetting their parent(s). Therefore, you may have to prompt your child, and let them know you are willing to talk with them about Lynch syndrome. This applies to older children too.

What information do you tell children?

Try to respond to children's questions using language appropriate to their age. Providing small amounts of information gradually is likely to help children understand and cope best. Check on the question being asked so that you find out what your child actually wants to know.

Explain and provide the name 'Lynch syndrome' – children cope better because knowing the name allows them to discuss it with you, and this knowledge gives them a sense of control. Parents often place a positive emphasis on the importance of knowing about a diagnosis of Lynch syndrome because it means there are improved screening and perhaps treatment options. When children become adults, there may also be even better treatments available, which you can explain to your child.



Communication tips

- Children and young people prefer informal discussion often while doing other things together, for example, driving, cooking or gardening.
- Check their understanding because children worry about upsetting their parents and so may not always ask.
- Talking about Lynch syndrome is an ongoing discussion rather than a one-off conversation. Like adults, children probably need information given to them more than once. They may need time to digest information and then want to come back and discuss it with you.
- Discuss information young people find on the internet or in newspapers.
- Discuss emotions and provide reassurance they are not alone.
- Explain parents' behaviour if they are anxious or upset.
- Being with peers, for example cousins, in similar circumstances might be helpful.
- Support and guide decision-making, especially with young people, who usually like to make their own decisions but with advice from parents.
- If you do not know the answer, explain some questions do not have answers or that you will try to find out for your child.
- Agree appropriate times to discuss Lynch syndrome and cancer if your child asks questions at difficult or awkward moments.

What are children likely to know about genes and inheritance?

8–11 years: They have a very basic understanding of heredity and that they share characteristics with parents. They may talk about genes but not fully understand what they are. Often children of this age cope with simple explanations in response to their questions and are not easily upset, although you may have to reassure them that having Lynch syndrome is not the same as having cancer. Children and young people can easily confuse this, so it often needs repeating throughout development into adulthood.

12–14 years: Children are beginning to develop more insight about hereditary. They will begin to recognise that you having the gene mutation may have implications for them but will usually cope well if you explain there is only 50% chance of them having Lynch syndrome.

15–17 years: Children recognise the risks to their parent, themselves and often their future children and can begin to consider genetic testing. By this age, young people will be learning about hereditary diseases in school curricula.

Most children are quite pragmatic in response to genetic risk in families affected by inherited genetic conditions. Children and young people are often focused on developing friendships, school and their personal interests, so do not dwell on the risk.

What helps parents talk to their children?

It has been observed that the following points have helped parents talk to their children:

- Younger children do not have the experience to recognise and anticipate the fuller implications so there is a gradual realisation.
- Not feeling under pressure to talk before an impending event, for example, a school science lesson.
- Talking was a relief for parents and ultimately easier than keeping the secret.
- Parents can be the role models for young people – giving them insight into how to cope with the risk.
- Recognising siblings may all have different needs and trying to find out what each understands at different times in their development.
- Ensuring children and young people understand a positive genetic test is not a cancer diagnosis – some get quite confused about this.
- Belief in a child's right to know.
- Support of other family members, friends and health professionals.
- Attendance at support groups gave focus to regular discussion with children and young people, with parents discussing where they were going and what had been discussed when they returned.

Preparing to talk to your children

It might be worth considering the following benefits and drawbacks in preparing to talk to your child but try to take naturally occurring opportunities where possible.

Benefits	Drawbacks
<ul style="list-style-type: none">• Makes the family closer.• Provides support for children.• Gives insight and helps them realise that parents being upset about Lynch syndrome is not down to them or their behaviour – it is no fault of theirs.• Gives children confidence to talk to close friends.• Children and young people feel valued by parent(s).• Allows discussion of Lynch syndrome and cancer risk without centralising it to life.• A shared reality and understanding helps children and young people cope.• Reduces risk of children getting inaccurate information from elsewhere.	<ul style="list-style-type: none">• It can be emotionally taxing dealing with questions.• Children and young people can remind you about Lynch syndrome when you do not want to be reminded.• Questions can arise at difficult or awkward moments – explain when it is appropriate to discuss it.• Children may want to talk to peers but networks can be limited.• Can affect schoolwork for a short time (but so can worrying about what is happening in their family if there is secrecy).

[Alison Metcalfe & Gill Plumridge (June 2010 Version 2)]


Did you know?

Family planning

If you are found to have Lynch syndrome before you have your family, you may have some questions about risk for your future children and you may wish to know if anything can be done to minimise this risk. Anyone with an inherited condition has a risk of passing it on to their children. The risk depends on the specific genetic condition, as there are several ways an inherited condition can be passed on in a family.

If you have Lynch syndrome, it is a dominant condition. Therefore there is a 50/50 or one in two chance that each of your children could inherit the gene mutation. This risk is the same for each pregnancy. The concept of dominant inheritance is explained in more detail in an earlier section of this booklet. Everyone who has a genetic condition can choose from a variety of family planning options and each option has pros and cons. It is a highly personal decision for you and your partner, and many factors may influence your choice. There is no right or wrong decision – you have to make the choice that best suits your circumstances, feelings and beliefs. In summary the options are:

1. Have your children without any intervention. Each child would have a 50% chance of inheriting the gene mutation and if they inherited the mutation, they would be at an increased risk of developing cancer as an adult.
2. Some couples decide not to have a family at all because they are very concerned by the risk of passing on the gene mutation.
3. Adoption – some couples choose to adopt a baby to avoid the risk of passing the gene mutation to the next generation.
4. Egg or sperm donation – by using donor eggs (if the mother carries the gene mutation) or donor sperm (if the father carries the gene mutation) couples can avoid passing Lynch syndrome to the next generation.

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5. Prenatal testing – some couples may choose to become pregnant naturally and have a test during the pregnancy to see if the baby has inherited the gene mutation. The couple would plan to continue the pregnancy if the baby has not inherited the mutation. However, if the baby has inherited the mutation, they may choose to terminate the pregnancy.
 6. Pre-implantation genetic diagnosis (PGD) – some couples choose this option to avoid passing Lynch syndrome to their offspring and avoid prenatal testing and possibly termination. There is no guarantee this technique will result in a successful pregnancy and funding for it on the NHS may not be available to all patients (for further information, see below).

Some of these options may seem drastic at first glance. Bear in mind that these are the options for couples at risk of passing any genetic condition to their children. Some genetic conditions cause severe learning or physical disabilities, or often both, and some genetic conditions may be life-limiting, meaning that the child would not survive into adulthood due to the condition. For most genetic conditions, there is no cure and limited options to treat the symptoms.

In our experience of talking to couples about family planning, most choose to have their family without any intervention. If anyone expresses an interest in finding out more about any of the other options, we can help make referrals or direct people to the appropriate services. We are happy to talk about these options in more detail at a genetic counselling appointment, if you would find that helpful.

We are often asked about PGD. Below is a brief overview of PGD as well as websites for more detailed information.

Pre-implantation Genetic Diagnosis (PGD)

What is it?

It is a technique used to select embryos that have not inherited the gene mutation which causes the genetic illness or cancer predisposition in a family.

Why would people consider having PGD?

Some couples wish to ensure that they avoid passing on a gene mutation to their children. They want to be confident that their children will not be affected with the genetic illness or cancer predisposition (although it is important to point out that a risk of cancer would still be present in a child without the genetic mutation, just like for everyone else). Alternatives to PGD could include prenatal testing and termination of affected pregnancies, using donor sperm or eggs, adoption or deciding not to have children.

How is it done?

PGD is carried out in conjunction with an IVF (in vitro fertilisation) procedure. The egg and sperm cells are collected from each parent and the embryos are created outside the woman's body. The embryos are then tested for the genetic mutation in the family. Only embryos that have not inherited the genetic mutation are selected to be implanted.

Who can have PGD?

If an individual has a specific gene mutation that is known to cause a predisposition to cancer, they may be able to have PGD. If there is a strong family history of cancer, but no gene mutations have been identified or genetic testing is not possible in your family, then PGD is not an option.

If you have had cancer and stored embryos prior to treatment and your treatment has left you unable to have children naturally, you would need to have an in depth discussion about the pros and cons of using PGD technology with the PGD team.

Where can I find out more about PGD?

If you are interested in considering this option, please ask to be referred to a PGD centre. There is one NHS PGD centre in London which offers testing for inherited cancer syndromes. At your first appointment they will discuss all aspects of PGD, including fertility assessment, funding applications, licence applications, time frame, risks and success rates. It can take many months from the first appointment to starting treatment, so you may wish to ask



for an initial consultation long before you actually want to start your family.

Please refer to the centre's website for more detailed information. The Centre for Pre-Implantation Genetic Diagnosis:

www.pgd.org.uk/home

Current studies and trials

Individuals attending the cancer genetics clinic may be offered an opportunity to take part in appropriate research trials. Specific details about research projects that are currently open can be obtained from the genetics team.

Taking part in research

Taking part in research studies is voluntary, and if you prefer not to take part in research that is not a problem at all. We invite everyone we meet in the clinics, who is eligible, to take part in research. If you would prefer that we did not ask you, then please let one of the clinicians know so that we can make a note of your preference. We have many research projects running at one time, and it is likely that you will be invited to take part in several studies. You will be given an information sheet about each study and given as much time as you need to think about whether you would like to take part in the study. You will also be given the opportunity to ask any questions about the research project, including any benefits or disadvantages of taking part. With all research, if you decide to take part, you are free to withdraw at any time, without giving a reason and this would not affect the standard of care you receive.

Confidentiality

If you decide to take part in a research project, any information you give us for the purposes of the study will be treated like all medical information. It will be kept strictly confidential and will be accessible only to the immediate study team. Information is stored on databases adhering to guidelines set out in the Data Protection Act. If specimens (for example, blood or urine) are obtained from

you as part of the study, they will be stored using identifying codes that will be known only by the research team. If you decide to withdraw from a study and you would like us to destroy any samples that you have provided for research, we will be happy to do so.

Types of research project

Epidemiological studies: studies looking at the interaction of environmental, lifestyle and genetic factors in the development of cancer.

Screening studies: studies looking at new methods of screening for cancer.

Psychosocial studies: studies looking at the emotional and societal impact of disease.

Drug trials: studies looking at the use of new drugs for treatment or prevention of cancer.


Tissue bank: the storage of samples in a sample bank for future research.

Current research studies

CAPP3

This study will focus on finding the right dose of aspirin for cancer prevention in people with a mismatch repair (MMR) gene defect, the underlying cause of Lynch syndrome, also known as HNPCC (Hereditary Non-Polyposis Colon Cancer). The previous study, CAPP2, showed that aspirin (600mg) reduces the risk of cancer in people with Lynch syndrome and in CAPP3 we would like to determine which dose is best at doing this. Aspirin sometimes causes side effects. About one person in every 1000 develops an ulcer which can cause bleeding in the stomach. This side effect occurs more often when people take bigger doses of aspirin. We want to give as little as possible but we need to be sure if the smaller dose still works.

If you take part, you will be given a daily dose of aspirin as three tablets.

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- Some people will be on **600mg** each day
 - Some people will be on **300mg** each day
 - Some people will be on **100mg** each day.

There is **no** placebo group – everyone will be on active aspirin.

After two years on treatment, everyone will be asked to take a 100mg daily dose of aspirin until the end of the study. We expect to finish the study in 2021.

If you would like to consider taking part in the CAPP3 trial, we are currently recruiting to this study. You can ask your genetics team for more information.

IMPACT

The IMPACT trial is investigating prostate cancer screening for men who may be at an increased risk of prostate cancer. At the moment, there is no good evidence to show whether or not men with Lynch syndrome have an increased risk of prostate cancer. The results of this study may answer this question and provide us with guidance as to how men should be screened.

If you are a man and have been found to carry a Lynch syndrome gene mutation, you may be eligible to take part. Please ask your genetics team for more information.

New cancer treatment options for people with Lynch syndrome

It is useful for the oncology team to know when patients have Lynch syndrome to help guide their choice of treatment. Treatment choices may be between established chemotherapy drugs or may include entry into clinical trials.

Your oncologist may discuss a clinical trial with you. These trials help to establish the best treatment for a particular type of cancer and sometimes will include the use of new drugs.

If you are seeking information on cancer trials you should discuss this with your oncology team and you can also refer to the following websites:

www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/what-you-should-be-told-about-a-clinical-trial

www.cancer.gov/about-cancer/treatment/clinical-trials

Sometimes a clinical trial may be available at your own hospital or you may need to go to a different hospital. It is important to know that trials for a particular drug may not be open to new patients at the time you are discussing treatment options with your oncologist.


Insurance

Insurance implications of genetic testing for individuals who have had cancer

If you have been diagnosed with cancer and have been offered a genetic test because of your cancer diagnosis, you are having a diagnostic genetic test. This includes cancer diagnoses that occurred in the past, even if treatment has been completed. The diagnostic genetic test may either be a full test of one or more genes associated with developing cancer (such as testing for all of the Lynch syndrome genes), or a specific test for a gene mutation that has been identified in your relative.

For Life, Income Protection and Critical Illness insurance policies, insurers can ask for information about your diagnostic genetic test to set the level of cover and cost of your premiums, in the same way as they ask about the rest of your medical history. For example, if you have been diagnosed with colorectal cancer that is due to Lynch syndrome, that genetic information is part of your personal medical history. However, insurers cannot ask you to take a genetic test and can only ask for the results of a genetic test you have already had.

If you are offered a diagnostic genetic test after your insurance policy is in place, then you do not have to disclose that you have had a genetic test or the results of the test. If you are taking out a



new insurance policy after you have had a genetic test, you will need to disclose that you have had the test along with the results. Genetic test results do not have to be disclosed for health or travel insurance policies, but associated medical conditions such as cancer diagnoses do need to be disclosed.

If close relatives without cancer are taking out a new insurance policy (Life, Income Protection or Critical Illness) they would need to tell the insurance company about both the cancer diagnoses in the family and if any are due to a genetic diagnosis, if they are aware of this information. Relatives without cancer do not have to disclose the results of their own predictive genetic testing to insurance companies, but may choose to do so, particularly if their test result is negative.

Insurance implications of genetic testing for individuals without cancer

If you have not had cancer and have been offered a genetic test because there is a known mutation in the family or because no family members with cancer can be offered a genetic test, you are having a predictive genetic test.

There is an agreed Code of Practice amongst members of the Association for British Insurers (ABI) that information about predictive genetic tests for cancer predisposition gene mutations is not used by insurance companies to determine if a policy is offered, or to determine the cost of the policy. The agreement relates specifically to Life, Income Protection and Critical Illness insurance products only. The agreement will be reviewed in 2019. Health insurance and travel insurance policies are not specifically covered by the agreement, but also do not require disclosure.

It is important to note that insurance companies will assess risk based on family history information, as they have always done.

If any of your relatives have had cancer due to a cancer predisposition gene mutation, both the cancer diagnoses and the genetic test results are part of your family history information that should be disclosed. You are only required to provide the requested

information that you are aware of at the time of taking out a new policy. If a relative has had cancer and/or genetic testing but you were not aware of it when you took out the policy, this will not subsequently be used to alter the policy.

You can choose to disclose your genetic test result. For example, if your test shows you do not have the gene mutation that caused cancer in your relatives this may have a favourable impact on your premiums as it reduces the impact of family history on your risk of cancer.

Further information can be found on this website:

www.abi.org.uk/Insurance-and-savings/Topics-and-issues/Genetics

Insurance implications for those living abroad

The implications of genetic testing on insurance for those patients living abroad depends on the country of their residence. The rules and regulations regarding this topic can change over time.


In the Republic of Ireland, for example, it has been illegal since 2005 to consider the results of a genetic test, whether positive or negative, in relation to insurance, mortgages or employment. Insurance companies can, however, still ask questions regarding a person's family medical history and it is a legal requirement that the questions be answered truthfully and comprehensively.

It is important for individuals in other countries to ask genetics professionals in their local genetics department about the specific laws regarding genetic testing in their country of residence. Some people may wish to get formal legal advice before going through genetic testing.

Organ donation

Can I still be on an organ donor?

People with Lynch syndrome have asked if they can still register to be an organ donor, given that they carry a gene mutation and/or personal history of cancer. The NHS Organ Donation information team provided the following information:



There are only two conditions where organ donation is ruled out completely. A person cannot become an organ or tissue donor if they have been diagnosed with HIV or have, or are suspected of having, Creutzfeld-Jakob disease (CJD). Cancer is one of the diseases that can be passed from donor to the recipient. However the risk that this will happen depends to some extent on the type of cancer, the treatment received and the length of time since the disease was diagnosed and treated. Corneas can always be used. At the time that donation is being considered:

- The family would be asked about any history of cancer
- The medical records would be reviewed
- A report would be obtained from the GP, although this is not always available pre-transplantation.

So if the potential donor had been confirmed as having a genetic predisposition to cancer, this would be reported as part of the assessment process pre-donation and would be included as part of the information provided to the transplant surgeon. A decision will then be made by a healthcare professional, at the time of death, about whether or not the organs can be used.

How can I register to be an organ donor?

If you do decide to register please make sure that you have informed your family, both so that they are aware of your wishes and to ensure the information about your genetic status is available for the assessment. People can sign up to the register at the following web page:

www.organdonation.nhs.uk/register-to-donate/

Where can I get more information?

This list of resources is intended to help you find further information or additional sources of support. Some patients may find these websites, books and charities helpful, but not all information will be relevant to all individuals.

Please consider the source of the material, for example clinical practice in the US may differ to clinical practice in the UK. Responsibility for the content of the information remains with the organisation that publishes it.

Books

Singing the Life: The Story of a Family Living in the Shadow of Cancer by Elizabeth Bryan Vermilion (2008)
ISBN-13: 978-0091917166

The C List: How I Survived Bowel Cancer by Rachel Bown (2014)
ISBN-13: 978-1780286792

Websites for further information

Association of British Insurers (ABI)

Website: www.abi.org.uk

Telephone: 020 7600 3333

Genetic Alliance UK

Website: www.geneticalliance.org.uk

National Cancer Institute (US)

Website: www.cancer.gov/cancertopics/types/breast

Genetics Home Reference (US)

Website: www.ghr.nlm.nih.gov/condition-breastcancer

National Institute for Health and Clinical Excellence

NICE guidelines for familial breast cancer

Website: www.nice.org.uk/Guidance/CG41



Cancer Research UK (CRUK)

Website: *www.cancerresearchuk.org*

Charities and support groups

Macmillan Cancer Support

Website: *www.macmillan.org.uk*

Freephone information line: 0808 808 0000

Lynch Syndrome UK

Website: *www.lynch-syndrome-uk.org*

Lynch Syndrome International

Website: *www.lynchcancers.com*

Beating Bowel Cancer

Website: *www.beatingbowelcancer.org*

Cancer Research UK

Website: *www.cancerresearchuk.org/about-cancer/type/bowel-cancer*

Bowel Cancer UK

Website: *www.bowelcanceruk.org.uk*

Bowel Cancer Information

Website: *www.bowelcancer.tv*

International Society for Gastrointestinal Hereditary Tumours (InSiGHT)

Website: *www.insight-group.org*

Ovacome

The Ovarian Cancer Support Network

Website: *www.ovacome.org.uk*

Freephone: 0800 008 7054

Ovarian Cancer Action

Website: *www.ovarian.org.uk*

Information line: 020 8238 7605

The Eve Appeal

Website: *www.eveappeal.org.uk*

Target Ovarian Cancer

Website: *www.targetovariancancer.org.uk*

Womb Cancer Support UK

Website: *www.wombcancersupportuk.weebly.com*

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This booklet is evidence based wherever the appropriate evidence is available, and represents an accumulation of expert opinion and professional interpretation.

Details of the references used in writing this booklet are available on request from: The Royal Marsden Help Centre

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Email: patientcentre@rmh.nhs.uk

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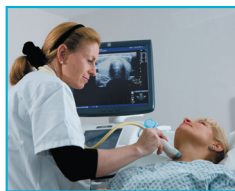
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The Royal Marsden publishes a number of booklets and leaflets about cancer care. Here is a list of information available to you.



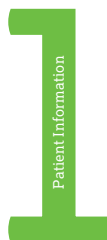
Diagnosis

- A beginner's guide to the BRCA1 and BRCA2 genes (*available to download from www.royalmarsden.nhs.uk/brca*)
- CT scan
- MRI scan
- Ultrasound scan
- Lynch Syndrome



Treatment

- Central venous access devices
- Chemotherapy
- Clinical trials
- Radiotherapy
- Radionuclide therapy
- Your operation and anaesthetic



Supportive Care

- Coping with nausea and vomiting
- Eating well when you have cancer
- Lymphoedema
- Reducing the risk of healthcare associated infection
- Support at home
- Your guide to support, practical help and complimentary therapies



Your hospital experience

- Help Centre for PALS and patient information
- How to raise a concern or make a complaint
- Your health information, your confidentiality



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