Colorectal: Lynch & Inherited Colorectal Ca

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Mainstreaming Criteria
Patient Pathways
Clinical Documents
Patient Support
Educational Resources for Healthcare Professionals
GMSA

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Mainstreaming Criteria: Lynch

These are the R210 panel inclusion criteria for Inherited MMR deficiency.

All new diagnoses of colorectal and endometrial cancers should have tumour MSI/IHC testing completed.

This may include BRAF testing in MLH1 deficient colorectal cancers and MLH1 hypermethylation testing in BRAF negative colorectal cancers and all MLH1 deficient uterine cancers. MLH1 hypermethylation testing is included on the Cancer Test Directory under **M1.5**.

Testing of unaffected individuals can only be carried out by Clinical Genetics Services.

Please refer to the National Genomic Test Directory for other tests related to Colorectal Cancer.

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National Genomic Test Directory: latest version

1. Criteria for germline testing an affected individual:
- A dMMR tumour where additional testing results suggest Lynch Syndrome:
  - BRAF testing in MLH1 deficient colorectal cancers.
  - MLH1 hypermethylation testing in BRAF negative colorectal cancers.
  - ALL MLH1 deficient uterine cancers.
- A positive family history of modified Amsterdam Criteria (regardless of dMMR tumour status).
- **Personal or family history** suggestive of CMMRD (Constitutional Mismatch Repair Deficiency) with Wimmer score of **3 or more.**

2. Criteria for MSI/IHC testing on a stored tumour sample prior to germline testing:
- Personal/family history of colorectal cancers reaching Modified Amsterdam Criteria (≥ 3 cases of Lynch related cancer over ≥2 generations with ≥1 case diagnosed under 50yrs.
- Any lynch-related cancer* **under 50 years** (excluding isolated pancreas, prostate or gastric cancers)
- Two Lynch-related cancers (**any age**, if one is colorectal or endometrial)
- Lynch-related cancer and **1 or more** first degree relative has Lynch-related cancer (both occurred **60 years or less**, one is colorectal or endometrial)
- Lynch-related cancer and **2 or more** relatives (first / second / third degree relatives) have Lynch-related cancer (all occurring ≤75years, one is colorectal or endometrial)
- Lynch-related cancer and **3 or more** relatives (first / second / third degree relatives) have Lynch-related
- cancer (occurring any age, one is colorectal or endometrial)

3. Criteria for somatic (tumour) Lynch syndrome panel testing:
- Individual has colorectal or endometrial cancer with a dMMR tumour with normal BRAF and MLH1 hypermethylation analysis **AND** germline testing did not reveal a pathogenic mutation.
- Personal/family pattern of disease whereby demonstration of acquired MMR mutations (and therefore exclusion of constitutional MMR abnormality) enables downscaling of surveillance
- Deceased affected individual with colorectal or endometrial cancer ≤60 years AND tumour featuring high/intermediate MSI or loss of staining of MMR protein(s) on IHC, AND one first degree relative with Lynch-related cancer ≤60 AND no living affected individual is available for genetic testing.

4. Clinical Criteria for germline testing in an unaffected individual: (see note on testing)
- First degree relative affected with Lynch-related cancer, AND
- Family history of colorectal cancer/Lynch-related cancers reaches Amsterdam Criteria (≥3 cases over ≥2 generations with ≥1 case affected <50 years) AND
- Tumour sample analysis from affected family member has been attempted and is not possible, failed, indeterminate or indicates MMR deficiency (via IHC or MSI), AND
- Somatic sequencing is not possible, or failed, AND
- No living affected individual is available for genetic testing

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*Lynch related cancers include:

1. Colorectal cancer
2. Endometrial cancer
3. Epithelial ovarian cancer
4. Ureteric cancer
5. Transitional cell cancer of renal pelvis
6. Cholangiocarcinoma
7. Small bowel cancer
8. Glioblastoma
9. Endocervical cancer
10. Multiple sebaceous tumours
11. Prostate
12. Gastric
13. Pancreas

Mainstreaming Criteria: inherited polyposis and early onset CRC

These are the R211 panel inclusion criteria. The individual has colorectal polyps and meets one or more of the following criteria:

Please refer to the National Genomic Test Directory for other tests related to Colorectal Cancer.

PLEASE NOTE:

- Inherited polyposis – somatic test should be used if no living affected individual is available for germline testing, no germline DNA sample has been stored from a deceased affected individual, and a molecular diagnosis is required to advise living relatives
- **M1 Colorectal carcinoma test** should be used for somatic testing

- Any colorectal cancer diagnosis **under 40yrs.**
- **5 or more** adenomatous polyps and colorectal cancer.
- **5 or more** adenomatous polyps **under 40yrs.**
- **10 or more** adenomatous polyps **under 60yrs.**
- **20 or more** adenomatous polyps aged **60yrs or over.**
- **5 or more** adenomatous polyps (**under 60yrs)** AND first degree relative with **5 or more** adenomatous polyps or colorectal cancer (**under 60yrs).**

- Serrated polyposis:
  - **5 or more** serrated lesions/polyps near the rectum, 5mm+ in size with at least two being 10mm in size.
  - **20 or more** serrated lesions/polyps of any size in any part of the large bowel with at least 5 being proximal to the rectum.

- Hamartomatous polyposis syndromes:
  - **5 or more** harmartomatous polyps in the colorectum
  - **2 or more** harmartomatous polyps throughout the GI tract
  - **1 or more** harmartomatous polyp and a first/second degree relative with harmartomatous polyps.

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National Genomic Test Directory: latest version

Preimplantation Genetics

- Preimplantation genetic testing is available to potential parents who are at risk of passing an inherited genetic condition down to their children. It is an IVF treatment that identifies the associated genetic change in embryos so that only the embryos that are clear of these pathogenic changes may be implanted. The process can take up to a year following initial consultation with a genetic counsellor. Couples are eligible for treatment via the NHS if they meet certain criteria, please see the following link for more information: How can I access preimplantation genetic diagnosis? | Genetic Alliance UK
- Please see the list of all inherited conditions that have been approved by the Human Fertilisation & Embryology Authority: PGT-M conditions - page 1 of 83 | HFEA
- For more detailed information on Preimplantation Genetic Testing for healthcare professionals: Preimplantation genetic testing — Knowledge Hub (hee.nhs.uk)

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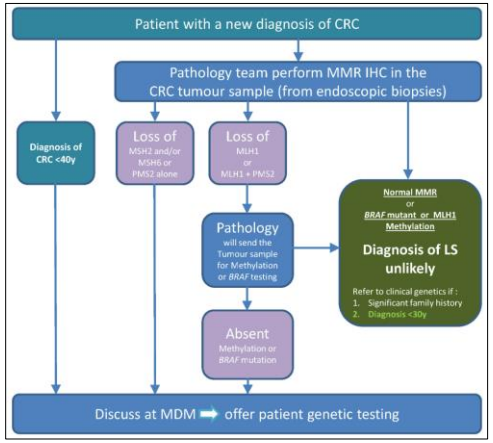
Patient Pathways

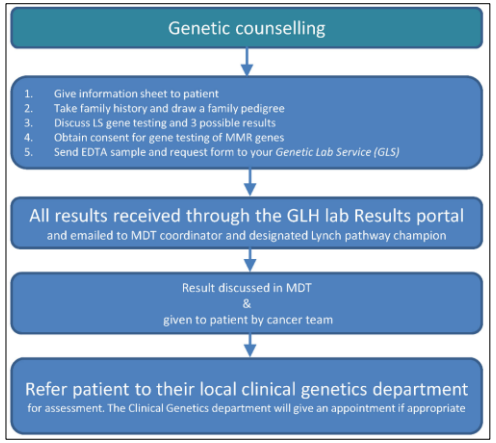
Secondary Care

RM Partners
West London Cancer Alliance
Hosted by The Royal Marsden NHS Foundation Trust

Lynch syndrome quality improvement project flowcharts

Tumour testing: Identifying patients eligible for genetic testing

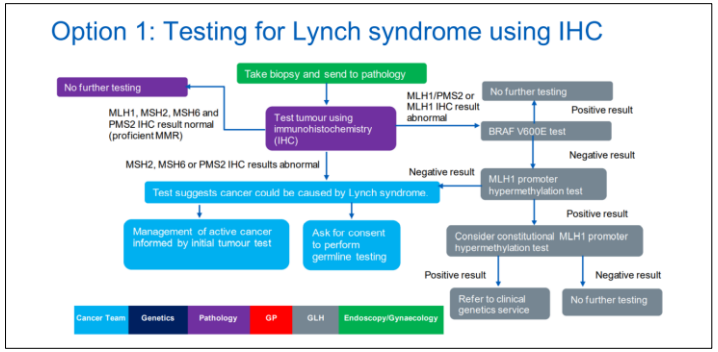


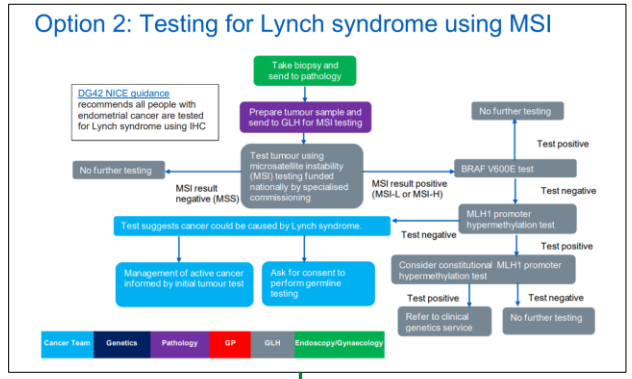


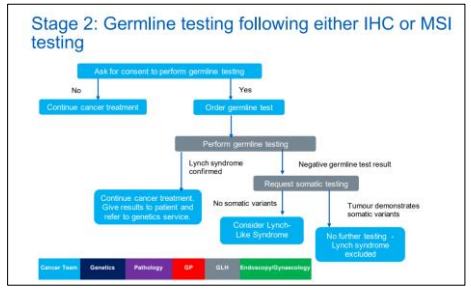
Tumour tissue testing

Option 1: Immunohistochemistry

Option 2: Microsatellite Instability







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Types of Testing for Lynch Syndrome:

Predictive:

- Testing an asymptomatic adult who is related to a person with a diagnosed Lynch Syndrome pathogenic variant.
- Not available to children, due to adult-onset disease associated with LS.

Diagnostic:

- Testing of a patient's germline to identify a pathogenic variant in one of the mismatch repair genes.
- For all colorectal and endometrial cancer patients.
- Follows an abnormal result from the test on tissue sample (abnormal MMR shown on IHC or MSI).
- Offered to people with a history of LS tumours and a confirmed pathogenic variant in the family.

Cascade:

- Aims to find relatives who carry a pathogenic variant for Lynch Syndrome before they develop a cancer.
- In the UK, patients are relied upon to contact possibly affected relatives.
- Georgiou et al, suggest a more novel approach of utilising healthcare providers, with patient consent to lead cascade testing.

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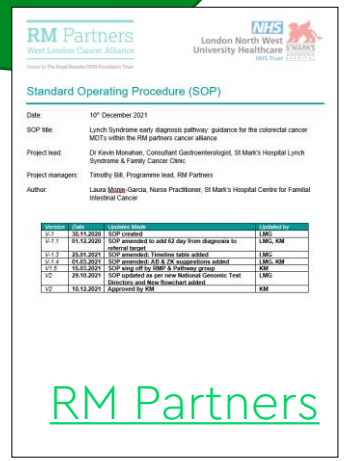
Clinical Documents

Standard Operating Procedure example


RM Partners
West London Cancer Alliance
NHS London North West University Healthcare
Standard Operating Procedure (SOP)
Date: 10th December 2021
SOP title: Lynch Syndrome early diagnosis pathway: guidance for the colorectal cancer MDTs within the RM partners cancer alliance
Project lead: Dr Kevin Monahan, Consultant Gastroenterologist, St Mark's Hospital Lynch Syndrome & Family Cancer Clinic
Project managers: Timothy Bill, Programme lead, RM Partners
Author: Laura Mone-Garcia, Nurse Practitioner, St Mark's Hospital Centre for Familial Intestinal Cancer

Version	Date	Updates Made	Updated by
V.1	30.11.2020	SOP created	LMG
V.1.1	01.12.2020	SOP amended to add 62 day from diagnosis to referral target	LMG, KM
V.1.3	25.01.2021	SOP amended: Timeline table added	LMG
V.1.4	01.03.2021	SOP amended: ASI & ZK suggestions added	LMG, KM
V1.5	15.03.2021	SOP sing off by WMP & Pathway group	KM
V2	29.10.2021	SOP updated as per new National Genomic Test Directory and New flowchart added	LMG
V2	10.12.2021	Approved by KM	KM

RM Partners

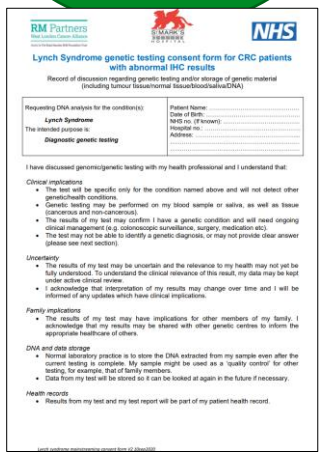
How to complete a RoD form:

Click here

Genomics Education Programme

Record of Discussion & Consent forms:


NHS
Record of Discussion Regarding Genomic Testing
This form relates to the person being tested. One form is required for each person.
All of the statements below remain relevant even if the test relates to someone other than yourself, for example your child.
I have discussed genomic testing with my health professional and understand the following
Family and wider implications
1. The results of my test may have implications for me and members of my family. I understand that my results may also be used to help the healthcare of members of my family and others nationally and internationally. This could be done in discussion with me or through a process that will not personally identify me.
Uncertainty
2. The results of my test may have findings that are uncertain and not yet fully understood. To decide whether findings are significant for myself or others, my data may be compared to other patients' results across the country and internationally. I understand that this could change what my results mean for me and my treatment over time.
Unexpected information
3. The results of my test may also reveal unexpected results that are not related to why I am having this test. These may be found by chance and I may need further tests or investigations to understand their significance.
DNA storage
4. Normal NHS laboratory practice is to store the DNA extracted from my sample even after my current testing is complete. My DNA might be used for future analysis and/or to ensure that other testing (for example that of family members) is of high quality.
Data storage
5. The data from my genomic test will be securely stored so that it can be looked at again in the future if necessary.
Health records
6. Results from my genomic test will be part of my patient record, a copy of which is held in a national system only available to healthcare professionals.
Research
7. I understand that I have the opportunity to take part in research which may benefit myself or others, now or in the future. An offer to join a national research opportunity is available on the following page.
For any further questions, my healthcare professional can provide information. More information regarding genomic testing and how my data is protected can be found at www.nhs.uk/conditions/genetics
Please sign on page three to confirm your agreement to the genomic test.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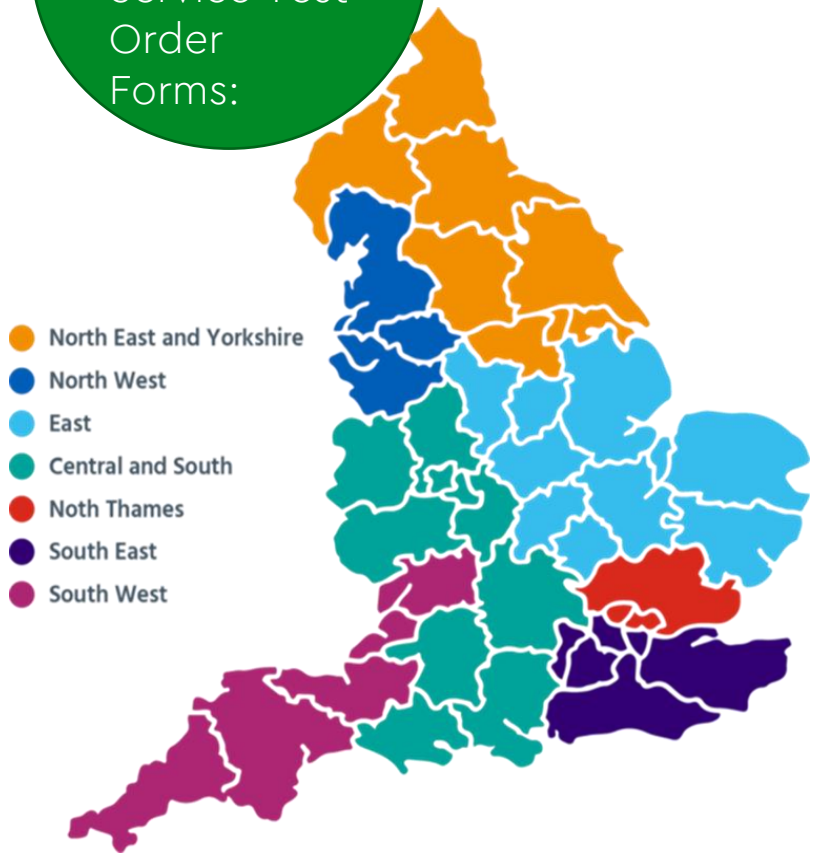
NHS
Lynch Syndrome genetic testing consent form for CRC patients with abnormal IHC results
Record of discussion regarding genetic testing and/or storage of genetic material (including tumour tissue/normal tissue/blood/saliva/DNA)
Requesting DNA analysis for the condition(s):
Lynch Syndrome
The intended purpose is:
Diagnostic genetic testing
Patient Name:
Date of Birth:
NHS no. (if known):
Hospital no.:
Address:
I have discussed genomic/genetic testing with my health professional and I understand that:
Clinical implications
- The test will be specific only for the condition named above and will not detect other genetic/health conditions.
- Genetic testing may be performed on my blood sample or saliva, as well as tissue (cancerous and non-cancerous).
- The results of my test may confirm I have a genetic condition and will need ongoing clinical management (e.g. colonoscopic surveillance, surgery, medication etc).
- The test may not be able to identify a genetic diagnosis, or may not provide clear answer (please see next section).
Uncertainty
- The results of my test may be uncertain and the relevance to my health may not yet be fully understood. To understand the clinical relevance of this result, my data may be kept under active clinical review.
- I acknowledge that interpretation of my results may change over time and I will be informed of any updates which have clinical implications.
Family implications
- The results of my test may have implications for other members of my family. I acknowledge that my results may be shared with other genetic centres to inform the appropriate healthcare of others.
DNA and data storage
- Normal laboratory practice is to store the DNA extracted from my sample even after the current testing is complete. My sample might be used as a 'quality control' for other testing, for example, that of family members.
- Data from my test will be stored so it can be looked at again in the future if necessary.
Health records
- Results from my test and my test report will be part of my patient health record.

NHS Genomic Medicine Service Test Order Forms:



Click on your region for local Non-Whole Genome Sequencing (WGS) form

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Clinical Documents

Letters of results: Examples via RM Partners

Positive: Pathogenic Variant Identified

The result of your genetic test for Lynch syndrome is now available. A genetic change was identified in a gene called ***MLH1***. This genetic change is considered pathogenic (disease-causing). This confirms your diagnosis of Lynch syndrome, and gives us an explanation of why you developed bowel cancer. Your medical team will use this information in their medical management decisions, it give you access to personalised therapies, and a personalised surveillance programme.

This also help us to be able to offer your first degree relatives (parents, siblings, and children) a genetic blood test as they have a 50% chance of having this genetic change, and therefore, a higher risk of developing bowel or other cancers.

For this reason, we have referred you to your local clinical genetics department who will give you an appointment to discuss your result in more detail with you, and facilitate genetic testing and surveillance for your first degree relatives. You should receive an appointment with them over the post in few weeks' time.

Please continue your follow-up with Dr…….. (Oncologist). Please do not hesitate to contact me should you have any clinical questions, or any queries about this result.

Negative: Pathogenic Variant not identified

The results of your genetic testing to see if you have any genetic changes in the genes associated with Lynch syndrome is now available. Analysis shows that you do not have any genetic changes in these genes. A negative result does not change your diagnosis, nor does it rule out an inherited condition and we may need to look at other genes.

We have now referred you to your local clinical genetics department so they can 'virtually' assess if any further testing is available. They may give you an appointment if they can offer you further testing, or surveillance recommendations for your family.

Please continue your follow-up with Dr…….. (Oncologist) . Please do not hesitate to contact me should you have any clinical questions.

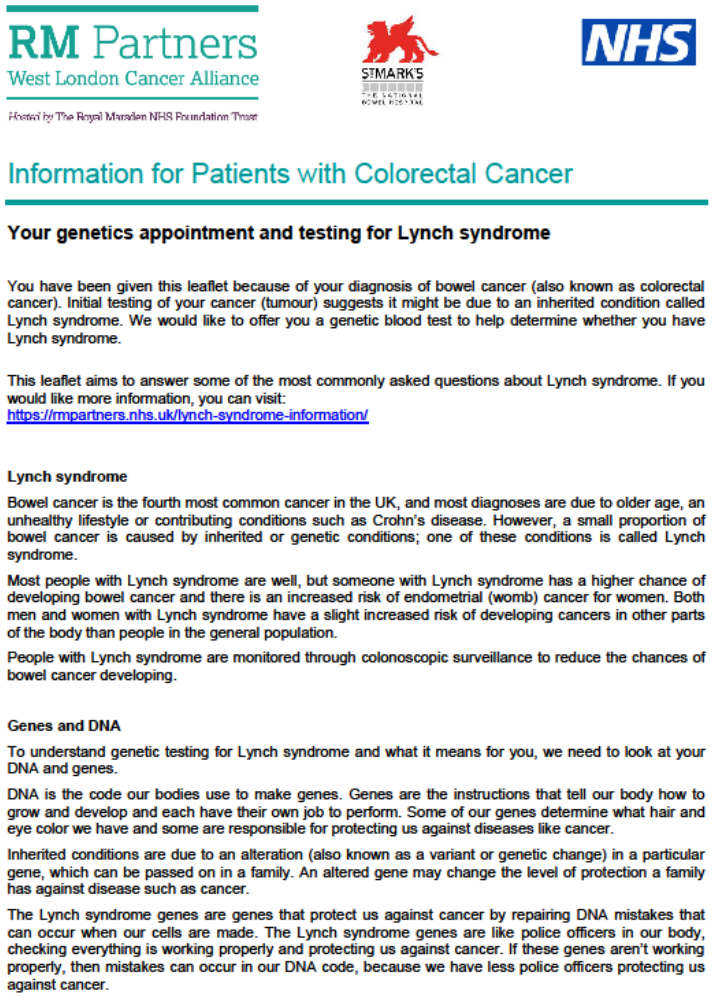
Uncertain result: Variant of Unknown Significance

The results of your genetic test to see if you have any genetic changes in the genes associated with Lynch syndrome are now available. Analysis has revealed a ***variant of unknown clinical significance*** in the ***MLH1*** gene. What this means is that we are not sure whether this genetic change is disease-causing (pathogenic), or part of your normal DNA variability that do not cause disease. For this reason, we are **unsure** that this could explain why you developed colorectal cancer, and we cannot use it to offer genetic testing to your family members.

We have now referred you to your local clinical genetics department so they can 'virtually' assess if any further testing is available. They may give you an appointment if they can offer you further testing, or surveillance recommendations for your family.

Patient Information and Support: Lynch Syndrome

- Genetic testing for Lynch syndrome Leaflet - RM Partners
- Lynch syndrome website – RM Partners
- Bowel Cancer | Lynch Syndrome UK (lynch-syndrome-uk.org)
- Lynch syndrome (LS) | Macmillan Cancer Support
- The Royal Marsden's 'A Beginner's Guide to Lynch Syndrome'
- Eve Appeal patient information on Lynch Syndrome
- Lynch Syndrome UK website
- Genetic Alliance UK | Information about insurance and genetic conditions



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NHS

Information for Patients with Colorectal Cancer

Your genetics appointment and testing for Lynch syndrome

You have been given this leaflet because of your diagnosis of bowel cancer (also known as colorectal cancer). Initial testing of your cancer (tumour) suggests it might be due to an inherited condition called Lynch syndrome. We would like to offer you a genetic blood test to help determine whether you have Lynch syndrome.

This leaflet aims to answer some of the most commonly asked questions about Lynch syndrome. If you would like more information, you can visit:
https://rmpartners.nhs.uk/lynch-syndrome-information/

Lynch syndrome

Bowel cancer is the fourth most common cancer in the UK, and most diagnoses are due to older age, an unhealthy lifestyle or contributing conditions such as Crohn's disease. However, a small proportion of bowel cancer is caused by inherited or genetic conditions; one of these conditions is called Lynch syndrome.

Most people with Lynch syndrome are well, but someone with Lynch syndrome has a higher chance of developing bowel cancer and there is an increased risk of endometrial (womb) cancer for women. Both men and women with Lynch syndrome have a slight increased risk of developing cancers in other parts of the body than people in the general population.

People with Lynch syndrome are monitored through colonoscopic surveillance to reduce the chances of bowel cancer developing.

Genes and DNA

To understand genetic testing for Lynch syndrome and what it means for you, we need to look at your DNA and genes.

DNA is the code our bodies use to make genes. Genes are the instructions that tell our body how to grow and develop and each have their own job to perform. Some of our genes determine what hair and eye color we have and some are responsible for protecting us against diseases like cancer.

Inherited conditions are due to an alteration (also known as a variant or genetic change) in a particular gene, which can be passed on in a family. An altered gene may change the level of protection a family has against disease such as cancer.

The Lynch syndrome genes are genes that protect us against cancer by repairing DNA mistakes that can occur when our cells are made. The Lynch syndrome genes are like police officers in our body, checking everything is working properly and protecting us against cancer. If these genes aren't working properly, then mistakes can occur in our DNA code, because we have less police officers protecting us against cancer.

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Patient Information and Support: Inherited Polyposis and Early Onset CRC

- A support group for those affected by Polyposis Syndromes (polyposispatient.support)
- Bowel Cancer | Bowel Cancer UK
- Genetic Alliance UK | Information about insurance and genetic conditions
- Polyposis and Lynch App

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Key Risk Factors for Hereditary Bowel Cancer:

- Diagnosed with bowel cancer before the age of 50 yrs.
- Bowel cancer that has been screened and tested positive for Lynch Syndrome (an abnormal IHC/MSI)
- Multiple bowel polyps.
- Two or more close relatives diagnosed with bowel or associated cancers (ie endometrial).
- A close relative diagnosed with bowel cancer before the age of 50yrs.
- More than one primary cancer (related) ie Bowel and womb in an individual.

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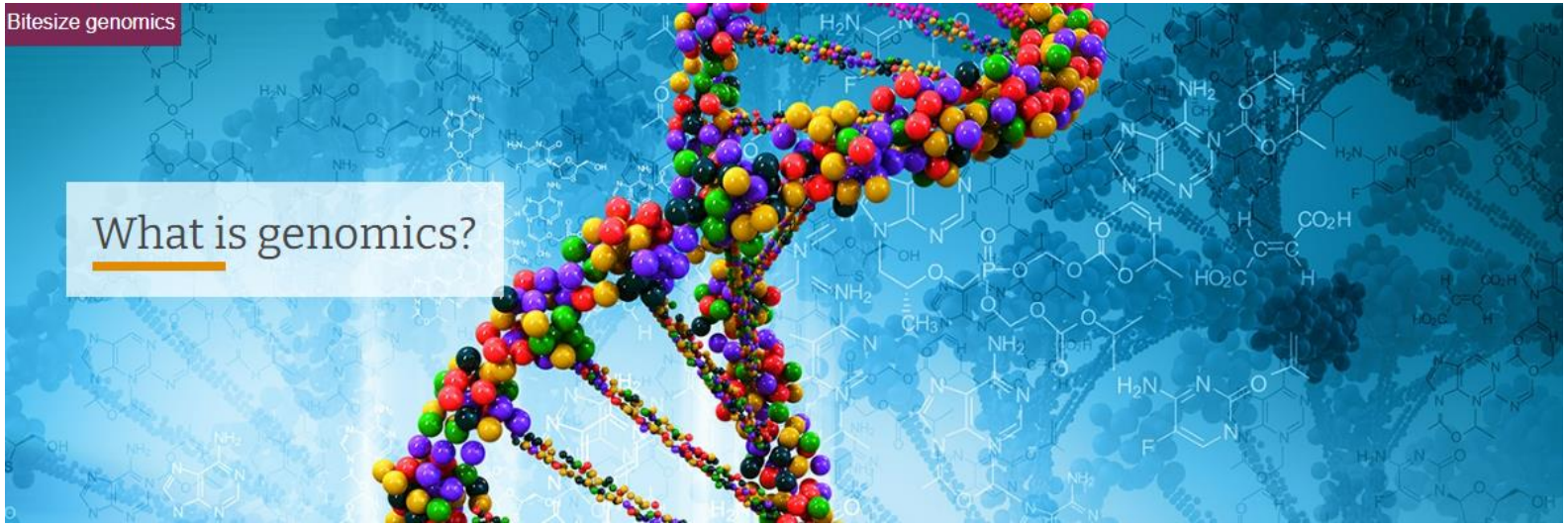
Educational/Training Resources

What is Genomics?

Genomics Education Programme

Click to play



www.genomicseducation.hee.nhs.uk/education/core-concepts/what-is-genomics/

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Educational/Training Resources

Genomics Education Programme

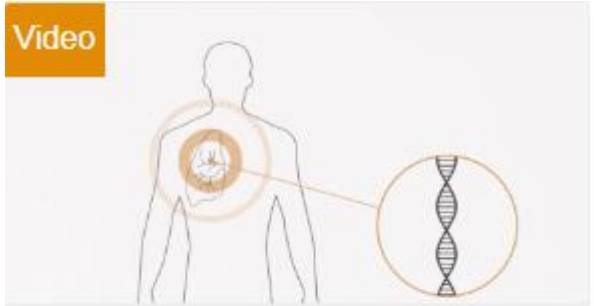
www.genomicseducation.hee.nhs.uk/education/

Genomics 101: Genomics in Healthcare

30 minutes
Certificate of completion
Part Time
Online

Genomics 101: Taking and Drawing a Genetic Family History

40 minutes
Certificate of completion
Part Time
Online



How is genomics used in cancer care?

2 minutes
Online

Genomics 101: Talking Genomics

30 minutes
Certificate of completion
Part Time
Online

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Educational/Training Resources

NHS North Thames Genomic Laboratory Hub

BRCA-DIRECT: Digital pathways to expand capacity for genetic testing

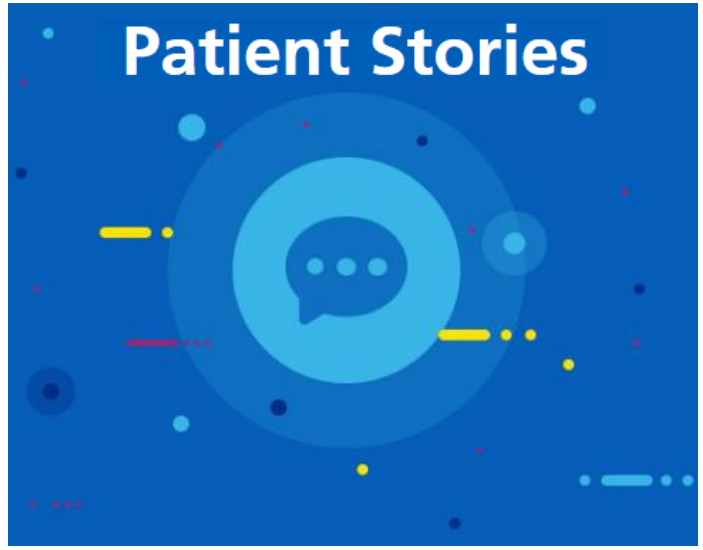
On 14 July 2022 the North Thames Genomic Medicine Service (GMS) held an event showcasing how genomic medicine is...

19 minutes

RM Partners Future Focus Webinar Recordings: Bitesize learning for cancer nurses and AHPs

Between 2021-2022 RM Partners, a collaborative of providers forming the West London Cancer Alliance hosted by The Royal Marsden,...

https://www.norththamesglh.nhs.uk/resources/



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Educational/Training Resources

www.southeastgenomics.nhs.uk/education-and-resources/#educational-resources

NHS South East Genomic Medicine Service Alliance

ONCOLOGY/CANCER GENOMICS

- Genetic testing in ovarian cancer — DOWNLOAD
- Introduction to hereditary breast and ovarian cancer — DOWNLOAD
- Overview of BRCA1 BRCA2 – What we know so far — DOWNLOAD
- Somatic WGS in Breast Ovarian Cancer — DOWNLOAD

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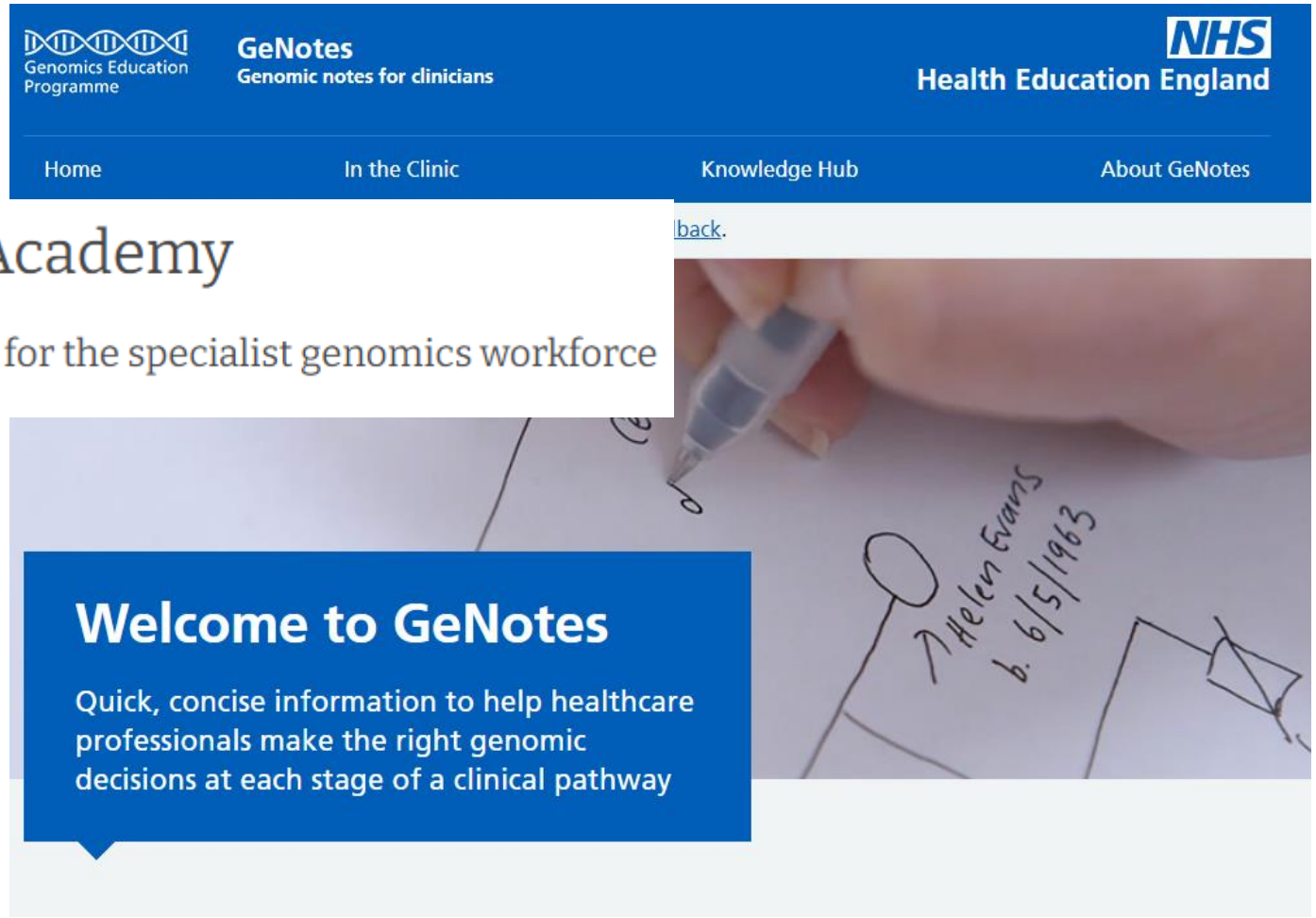
Educational/Training Resources

www.genomicseducation.hee.nhs.uk/genotes/



GTAC: Genomics Training Academy

A national training and education initiative for the specialist genomics workforce

www.genomicseducation.hee.nhs.uk/about-us/gtac-genomics-training-academy

AGNC

Genetic Counselling resources for genetic nurses and counsellors

Includes useful documents, videos and links to other websites recommended by the AGNC for genetic nurses and counsellors.

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Educational/Training Resources: Learning & Development Hub

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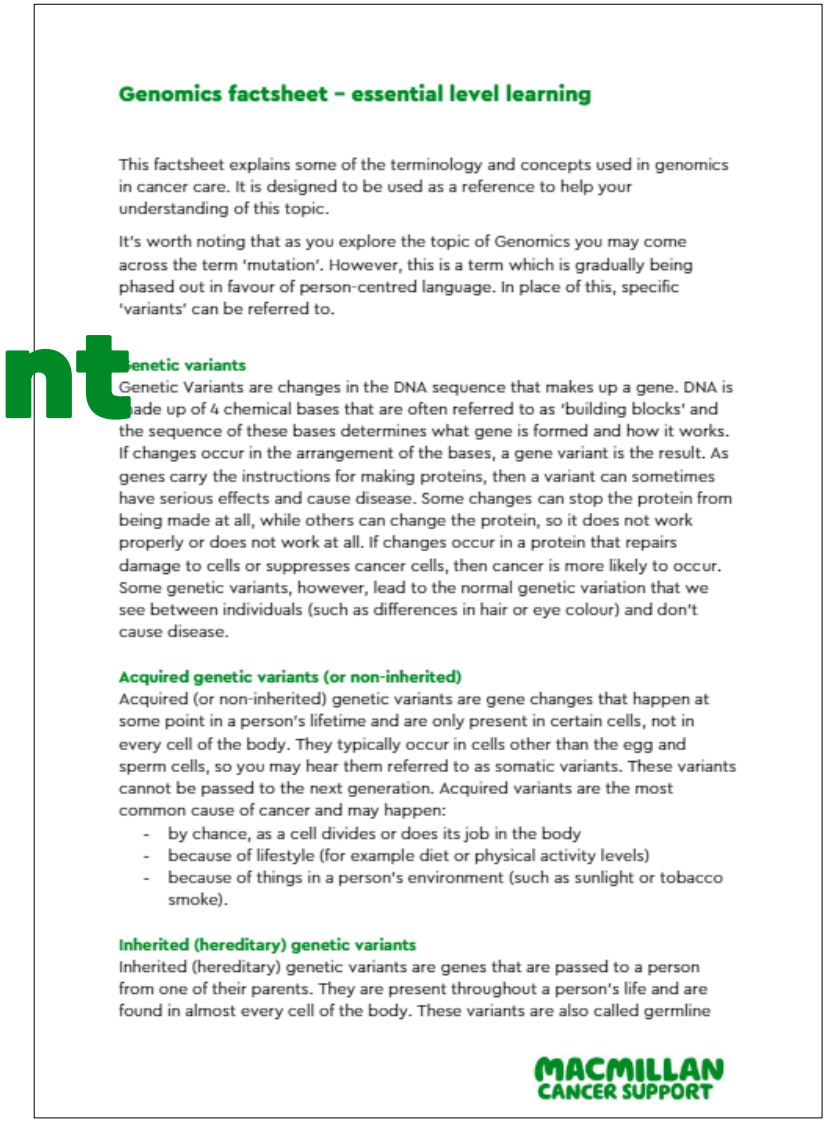
www.macmillan.fuseuniversal.com



Genomics factsheet – essential level learning

This factsheet explains some of the terminology and concepts used in genomics in cancer care. It is designed to be used as a reference to help your understanding of this topic.

It's worth noting that as you explore the topic of Genomics you may come across the term 'mutation'. However, this is a term which is gradually being phased out in favour of person-centred language. In place of this, specific 'variants' can be referred to.

Genetic variants

Genetic Variants are changes in the DNA sequence that makes up a gene. DNA is made up of 4 chemical bases that are often referred to as 'building blocks' and the sequence of these bases determines what gene is formed and how it works. If changes occur in the arrangement of the bases, a gene variant is the result. As genes carry the instructions for making proteins, then a variant can sometimes have serious effects and cause disease. Some changes can stop the protein from being made at all, while others can change the protein, so it does not work properly or does not work at all. If changes occur in a protein that repairs damage to cells or suppresses cancer cells, then cancer is more likely to occur. Some genetic variants, however, lead to the normal genetic variation that we see between individuals (such as differences in hair or eye colour) and don't cause disease.

Acquired genetic variants (or non-inherited)

Acquired (or non-inherited) genetic variants are gene changes that happen at some point in a person's lifetime and are only present in certain cells, not in every cell of the body. They typically occur in cells other than the egg and sperm cells, so you may hear them referred to as somatic variants. These variants cannot be passed to the next generation. Acquired variants are the most common cause of cancer and may happen:

- by chance, as a cell divides or does its job in the body
- because of lifestyle (for example diet or physical activity levels)
- because of things in a person's environment (such as sunlight or tobacco smoke).

Inherited (hereditary) genetic variants

Inherited (hereditary) genetic variants are genes that are passed to a person from one of their parents. They are present throughout a person's life and are found in almost every cell of the body. These variants are also called germline

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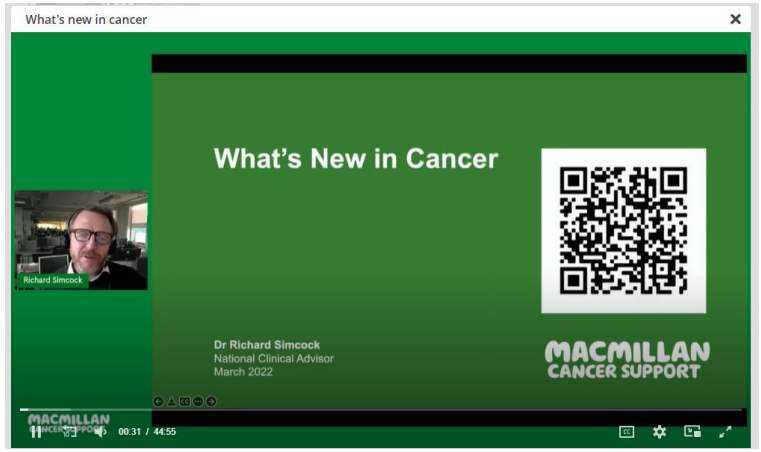

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5 Educational/Training Resources

Counselling & Consent Checklist: key points to cover

- ❑ Has the patient had enough information and time to consider testing and its consequences?
- ❑ Have the conversation and consent form been documented, recorded and stored according to local policy?
- ❑ Always document consultation as a written letter to the patient and sharing correspondence with the GP.
- ❑ Has the patient been provided with:
  - ❑ Record of Discussion Form to sign (**this is the consent form: one copy for patient, one for notes)**
  - ❑ Patient information leaflets
  - ❑ Contact details of the clinical team
  - ❑ GMS test request form (if using phlebotomy services for blood sampling)
- ❑ Has the patient been informed of logistical procedures including:
  - ❑ How the test will be conducted?
  - ❑ When and how to expect results?
  - ❑ How to access support whilst waiting for results?

MACMILLAN CANCER SUPPORT

Educational/Training Resources

FAQs

What is 'Mainstreaming'?

Mainstreaming Genomic testing means delivering a genetic test for patients diagnosed with a colorectal cancer who meet the standardised criteria set out in the National Genomic Test Directory. This is a simple blood test that can be ordered by the Colorectal Cancer Team instead of being outsourced/referred onto an external clinical genetics team. The results of the test are 'actioned' by the Colorectal Multidisciplinary Team, which include referring the patient to clinical genetics if it is necessary (see 'When and How do I refer to Clinical Genetics?' FAQ).

Why do we need 'Mainstreaming'?

Testing within the cancer team speeds up results, reduces the number of healthcare professionals the patient has to interact with and reduces the hospital appointments they have to navigate during a stressful time. It ensures the patient can access relevant treatment in a timely manner based on their results. The patient will be offered counselling and consent for this blood test in the days after their diagnosis (vs seeing genetics—in many places this is a waiting list of more than 3 months).

Educational/Training Resources

FAQs

What is the difference between a Germline and a Somatic Change?

Germline mutations are inherited genetic changes that are present in the DNA of every cell in the body, including sperm and egg cells. These mutations can be passed down from generation to generation and can increase the risk of developing certain diseases, including cancer.

Somatic mutations, on the other hand, are genetic changes that occur in non-germline cells during a person's lifetime. These mutations are not present in every cell of the body and cannot be passed down to offspring. Somatic mutations can occur due to a variety of factors, including exposure to environmental toxins, aging, and errors that occur during DNA replication.

Educational/Training Resources

FAQs How will the results of a positive test for Lynch Syndrome affect treatment?

- Targeted therapies & chemoprophylaxis:
  - Aspirin: (NICE guidelines 2020) between the ages of 25- 65 years. Aspirin has been shown to reduce the long term risk of cancer in Lynch syndrome by around 50%. Trials to determine the best dose of aspirin for cancer prevention are still ongoing. Patients need to discuss with their GP whether you have any contraindications to taking aspirin. Patients younger than 25 who wish to start taking aspirin should with their medical team. [Lynch syndrome: should I take aspirin to reduce my risk of getting bowel cancer. Patient decision aid, NICE, 2020] **To find out the latest information and recommendations in aspirin, you can visit the** CAPP3 trial website
  - Immunotherapy
- Risk reducing surgeries:
  - Bowel Resection
  - Hysterectomy & Bilateral Salpingo-Oophorectomy: Women who have completed their family may consider risk-reducing surgery to remove the uterus, fallopian tubes +/- ovaries, after the age of 35. Hormone replacement therapy is usually recommended after risk-reducing bilateral salpingo-oophorectomy to offset negative impact of premature menopause, up until the time at which natural menopause would be expected to occur.
- Surveillance:
  - 2 yearly colonoscopy:
    - *MLH1* and *MSH2* gene carriers: start at 25 years old
    - *MSH6* and *PMS2* gene carriers: start at 35 years old (BSG Guidelines 2019)
- Lifestyle advice to reduce the risk of colorectal cancer:
  - Losing weight can reduce the risk of early onset colorectal cancer by half.
  - Stopping smoking.
  - Dietary advice: High fibre, low fat, with plenty of fruit and vegetables. Try to eat less red and processed meat. It is also good for your general health that you include starchy foods in your diet such as plantains and green bananas [CAPP2 evidence on resistant starch]
- One-off screening for Helicobacter pylori: H. pylori is a bacteria that 30% of the population have in the stomach. Eradication of these bacteria may reduce the lifetime risk of gastric cancer by up to half. To arrange testing for this contact your GP. This is recommended before commencing aspirin chemoprophylaxis.
- Symptom Awareness: Prompt investigation of any symptoms (gynaecological, urinary, gastrointestinal, dermatological and so on). [HEE, Knowledge Hub: Lynch, 2022]

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Educational/Training Resources

FAQs

How will the results of a positive test for FAP Syndrome affect treatment?

- Surgeries:
  - colectomy with ileo-rectal/distal sigmoid anastomosis
  - restorative proctocolectomy (St Mark's Polyposis Guidelines, 2022)

- Surveillance:
  - Dependent on risk reducing surgeries undertaken.
  - 1-3 yearly colonoscopy: commencing 12-14 years old (BSG Guidelines 2019)

https://bestpractice.bmj.com/topics/en-gb/652

MACMILLAN CANCER SUPPORT

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Educational/Training Resources

FAQs

Lynch Syndrome: How do I and when do I need to refer to Genetics Services?

- Always following results: Discuss your results in the result forum allocated to you by your Lynch syndrome nurse for safety netting to discuss recommendations for your patients, which will include: cancer prevention programme and surveillance recommendations if VUS or negative
- You can use the quick referral letter  Quick referral CRC 1Mar22 - No header
- Refer to local clinical genetics team, usually using a standardised form via email that will be accessible via your nearest Genomics Laboratory Hub website. Enclose the following in your referral.

  Checklist
  1. Attach histopathology reports
  2. Attach minutes from cancer MDT meeting
  3. Attach family pedigree
  3. Call and inform patient they will receive an appointment for genetic referral

- If the result is Negative or VUS the case might be virtually reviewed and your patient might not receive an appointment. You will find out when you discuss your result in your results forum

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Educational/Training Resources

FAQs

How do I and when do I need to refer to Genetics Services?

- When patient has a **positively identified pathogenic variant**
- When a patient has a **variant of uncertain significance** (VUS)
- When a patient has a negative result, but a **significant family history.**
- When the patient has a negative result, but presents with cancer at **a young age (less than 50yrs)**
- When you are not sure!

- Refer to local clinical genetics team, usually using a standardised form via email that will be accessible via your nearest Genomics Laboratory Hub website.

How do I calculate a patient's Risk?

- Consider using validated tools recommended and developed by Genetics services such as:
  - QGenome: Qgenome
  - Modified Amsterdam Criteria

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Educational/Training Resources

FAQs How do I counsel a patient?

Document attached to email/in brief

5

Educational/Training Resources

What are the High Penetrance Cancer Susceptibility Genes for Colorectal Cancers?

- Adenomatous Polyposis Syndrome:
  - *APC* (dominant inheritance)
  - *MUTYH* (recessive inheritance)

- Lynch Syndrome:
  - *MLH1*
  - *MSH2*
  - *MSH6*
  - *PMS2*

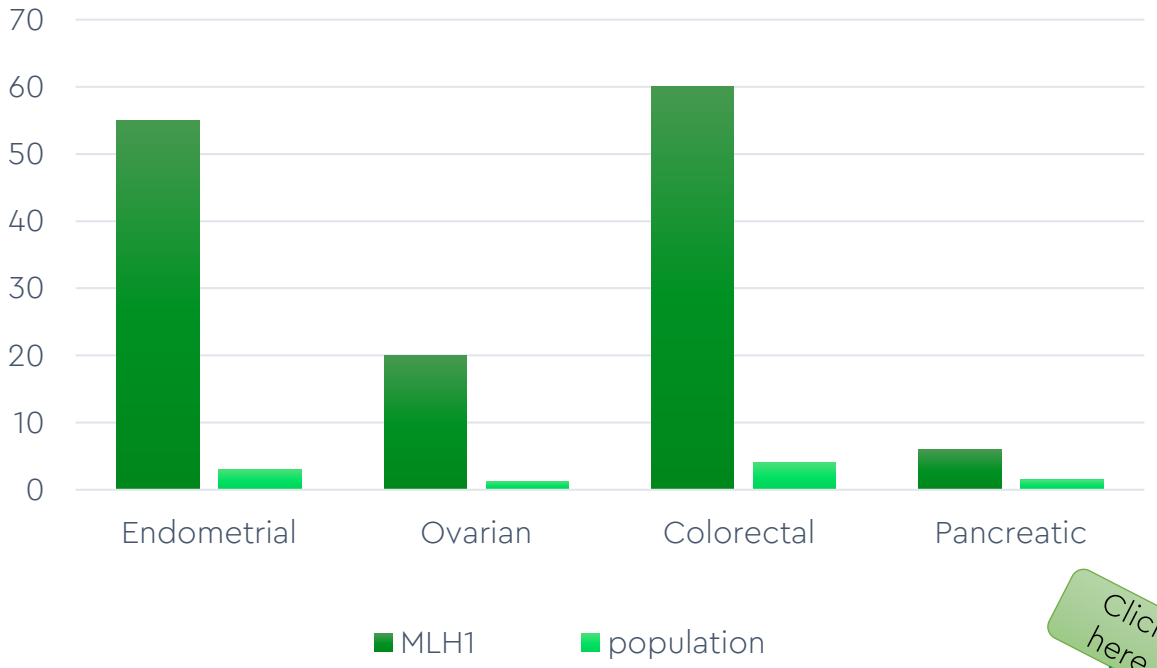
- Hamartomatous Polyposis Syndrome:
  - *SMAD4*
  - *BMPR1A*
  - *STK11*
  - *PTEN*

We all have two copies of every gene in our body, inherited from each of our parents. Genes have different functions and instruct our cells to do different things. High penetrance cancer susceptibility genes are a group of genes that protect the body from developing a cancer, usually through correcting DNA mistakes and repairing DNA copies. If there's a pathogenic change in one of these genes, it means they won't be able to function properly. With a gene not working properly some of that protection against cancer is lost. Over time, DNA mistakes can accumulate which puts someone with a change in one of these genes at risk of developing colorectal, endometrial and other related cancers over their lifetime. Below is more information about individual genes and their associated risks if there is a pathogenic change in them.

MACMILLAN CANCER SUPPORT

MLH1

Estimated lifetime cancer risk for carriers of germline pathogenic variants in *MLH1*



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[Cancer risks for MLH1 and MSH2 mutation carriers - PMC (nih.gov)]
[Cancer risk and MLH1 gene mutations (facingourrisk.org)]

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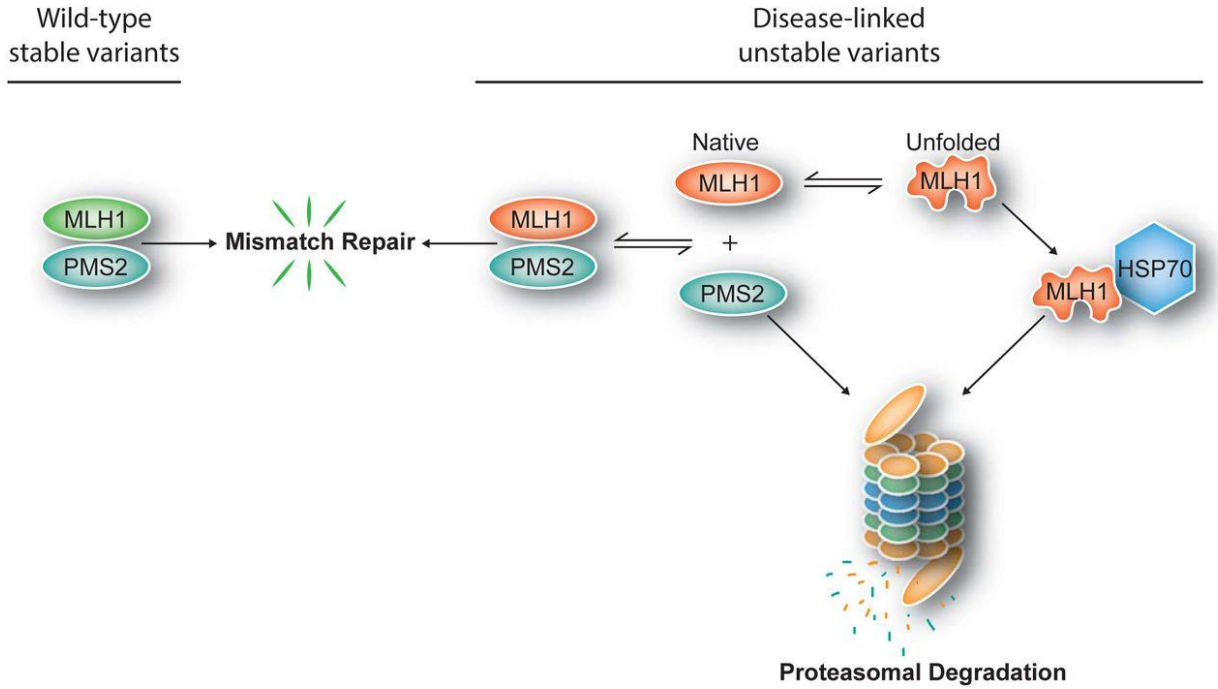


[Structural destabilization and chaperone-assisted proteasomal degradation of MLH1 as a mechanism for Lynch syndrome | bioRxiv]

Management recommendations for PV in *MLH1*: UKCGG

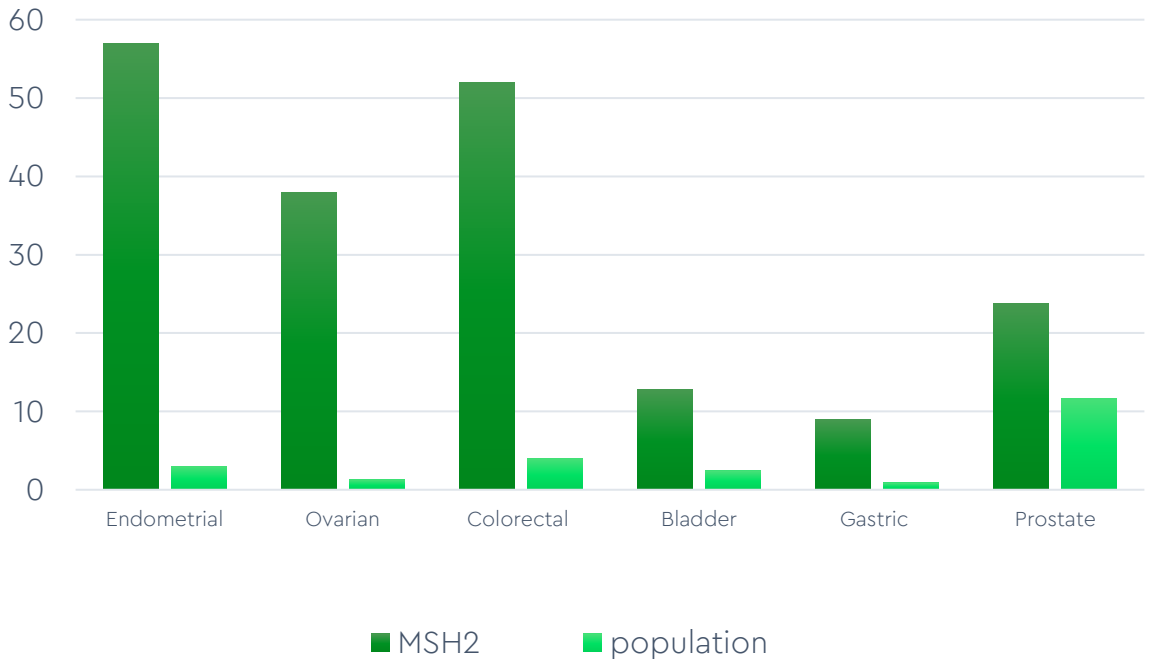
Management recommendations*	
1 Screening	• **Colorectal screening**: 2-yrly colonoscopy from age 25 to 75—review at 75 • **Gastric screening**: Helicobacter pylori one-off screening • **Cervical screening:** As part of the NHS cervical screening programme • No additional cancer screening is currently recommended outside of a research setting; **symptom awareness** to be advised
2 Risk-reducing surgery	• Offer risk-reducing **hysterectomy with BSO**, once childbearing is complete, no earlier than age of 35- 40 (risks and benefits to be discussed) • HRT should be offered until age 51 in women who have not had a ER positive breast cancer
3 Chemoprevention	• Discuss pros and cons of **aspirin chemoprevention** from age 25 to 65 (GP to prescribe): 150mg OD if ≤70kg or 300mg OD if >70kg **(expert opinion)**
4 Research	• **Research studies:** e.g. **IMPACT** (prostate cancer screening study) and **EUROPAC** (pancreatic cancer screening study)
5 Cancer management	• **Targeted therapies** may be available as a treatment option for certain cancer types (immune checkpoint inhibitors e.g. pembrolizumab) • **Surgical management of colon cancer:** discussion regarding pros and cons of segmental vs. extensive resection may be appropriate • **Adjuvant 5-FU chemotherapy** may not be appropriate for patients with Dukes' B colorectal cancers*
6 Family matters	• Facilitate **cascade testing** in at-risk family members • Discuss **reproductive options**

MACMILLAN CANCER SUPPORT

MSH2

Click here

Estimated lifetime cancer risk for carriers of germline pathogenic variants in *MSH2*



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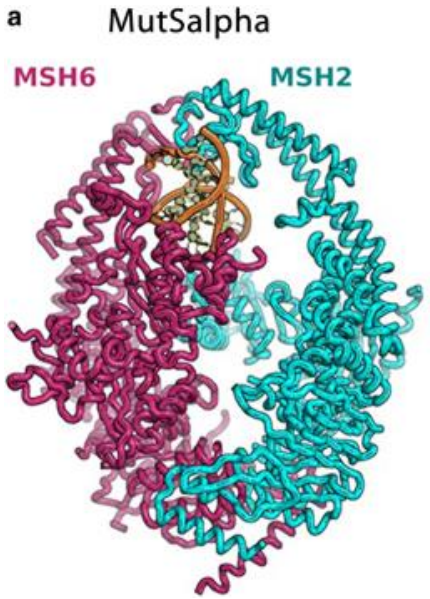
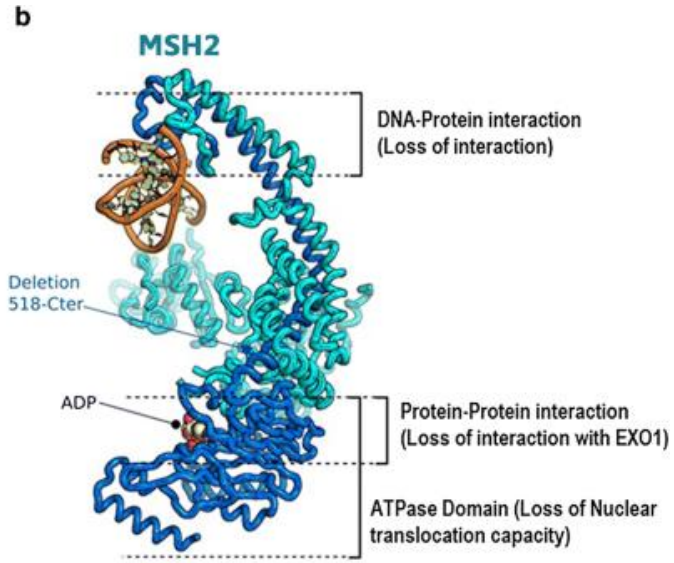
[Cancer risk and MSH2 gene mutations (facingourrisk.org)]





[Identification of novel pathogenic MSH2 mutation and new DNA repair genes variants: investigation of a Tunisian Lynch syndrome family with discordant twins | Journal of Translational Medicine | Full Text (biomedcentral.com)]

Management recommendations for PV in *MSH2*: UKCGG

Management recommendations*	
1 Screening	• **Colorectal screening**: 2-yrly colonoscopy from age 25 to 75– review at 75 • **Gastric screening**: Helicobacter pylori one-off screening • **Cervical screening:** As part of the NHS cervical screening programme • No additional cancer screening is currently recommended outside of a research setting; **symptom awareness** to be advised
2 Risk-reducing surgery	• Offer risk-reducing **hysterectomy with BSO**, once childbearing is complete, no earlier than age 35- 40 (risks and benefits to be discussed) • HRT should be offered until age 51 in women who have not had a ER positive breast cancer
3 Chemoprevention	• Discuss pros and cons of **aspirin chemoprevention** from age 25 to 65 (GP to prescribe): 150mg OD if ≤70kg or 300mg OD if >70kg **(expert opinion)**
4 Research	• **Research studies:** e.g. **IMPACT** (prostate cancer screening study) and **EUROPAC** (pancreatic cancer screening study)
5 Cancer management	• **Targeted therapies** may be available as a treatment option for certain cancer types (immune checkpoint inhibitors e.g. pembrolizumab) • **Surgical management of colon cancer:** discussion regarding pros and cons of segmental vs. extensive resection may be appropriate • **Adjuvant 5-FU chemotherapy** may not be appropriate for patients with Dukes' B colorectal cancers
6 Family matters	• Facilitate **cascade testing** in at-risk family members • Discuss **reproductive options**

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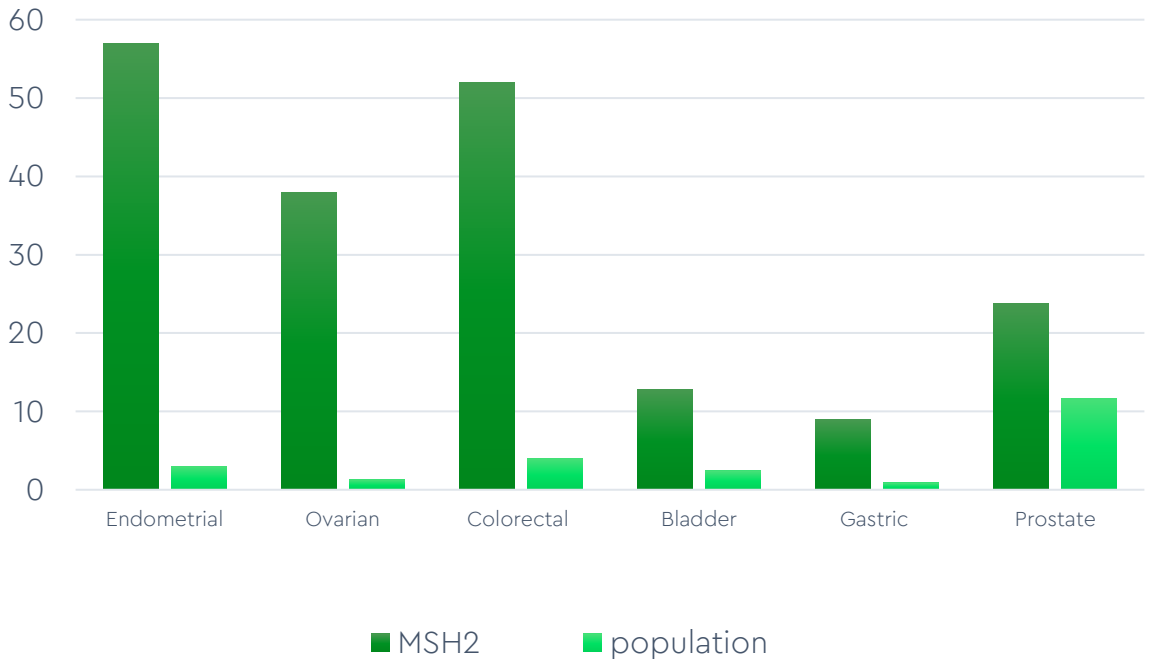
MSH6

Click here

Estimated lifetime cancer risk for carriers of germline pathogenic variants in *MSH2*



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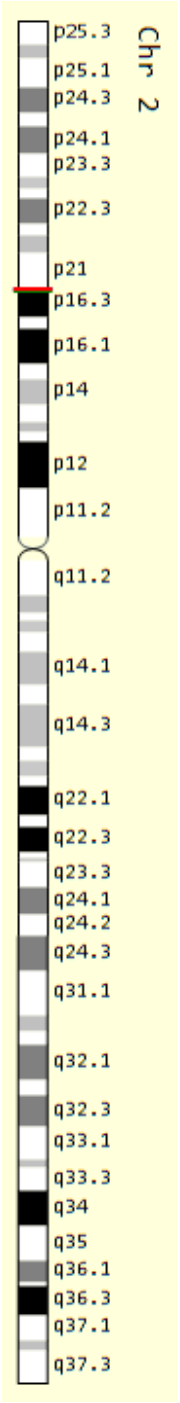


MSH6 is a human gene that provides instructions for making the DNA mismatch repair protein MSH6. This protein is involved in the recognition and repair of errors that occur during DNA replication, including mismatches and small insertion-deletion loops. MSH6 forms a complex with another protein, MSH2, to detect and bind to DNA mismatches. This complex then recruits other proteins to repair the mismatch, ultimately preventing mutations that can lead to cancer and other genetic diseases.

Mutations in the MSH6 gene have been linked to Lynch syndrome, a hereditary form of colon cancer, as well as other cancers such as endometrial and ovarian cancers. Individuals with MSH6 mutations may have an increased risk of developing Lynch syndrome-associated cancers at an earlier age compared to individuals with mutations in other DNA mismatch repair genes. In addition, some studies suggest that MSH6 mutations may be associated with an increased risk of other types of cancer, such as pancreatic and prostate cancer.

Management recommendations for PV in *MSH6* UKCGG

1. Surveillance: Colorectal, Gastric, Cervical, symptom awareness
2. Risk reducing surgery: hysterectomy + BSO once childbearing complete (recommended age: >35-40yrs)
3. Chemoprevention- Aspirin: (NICE guidelines 2020) between the ages of 25- 65 years. Aspirin has been shown to reduce the long term risk of cancer in Lynch syndrome by around 50%. [Lynch syndrome: should I take aspirin to reduce my risk of getting bowel cancer. Patient decision aid, NICE, 2020]
4. Targeted therapy: immune checkpoint inhibitors ie pembrolizumab

Management recommendations*

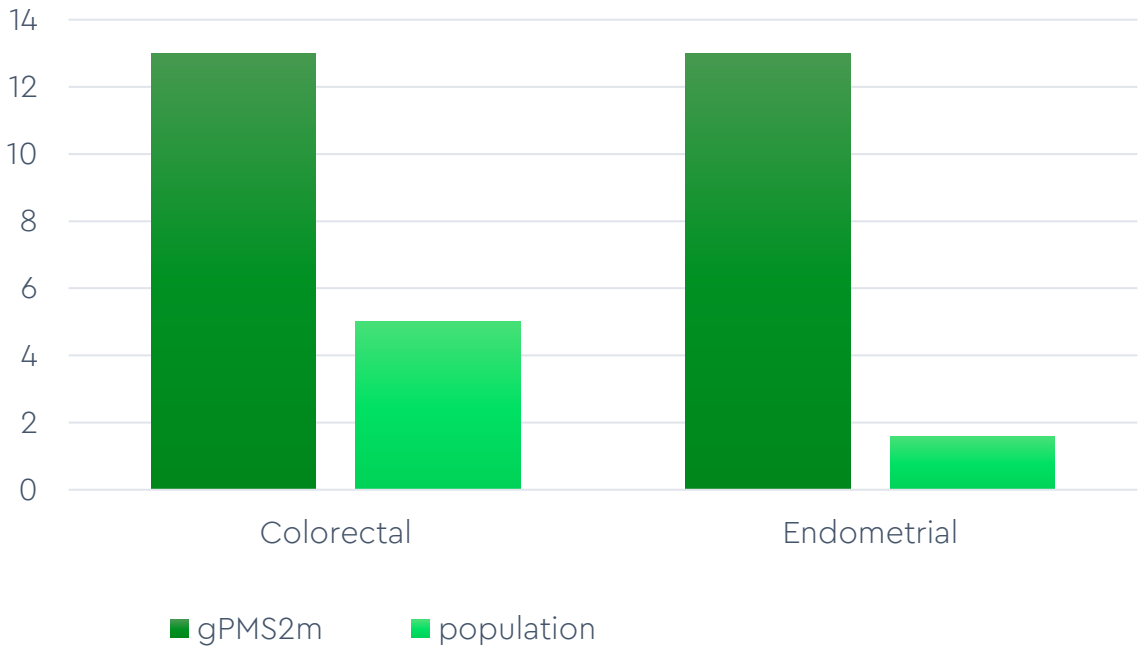
1	Screening	• **Colorectal screening**: 2-yrly colonoscopy from age 35 to 75 - review at 75 • **Gastric screening**: Helicobacter pylori one-off screening • **Cervical screening:** As part of the NHS cervical screening programme • No additional cancer screening is currently recommended outside of a research setting; **symptom awareness** to be advised
2	Risk-reducing surgery	• Offer risk-reducing **hysterectomy with BSO**, once childbearing is complete, no earlier than age of 35-40 (risks and benefits to be discussed) • HRT should be offered until age 51 in women who have not had a ER positive breast cancer
3	Chemoprevention	• Discuss pros and cons of **aspirin chemoprevention** from age 25 to 65 (GP to prescribe): 150mg OD if ≤70kg or 300mg OD if >70kg **(expert opinion)**
4	Research	• **Research studies:** e.g. **IMPACT** (prostate cancer screening study) and **EUROPAC** (pancreatic cancer screening study)
5	Cancer management	• **Targeted therapies** may be available as a treatment option for certain cancer types (immune checkpoint inhibitors e.g. pembrolizumab) • **Adjuvant 5-FU chemotherapy** may not be appropriate for patients with Dukes' B colorectal cancers
6	Family matters	• Facilitate **cascade testing** in at-risk family members • Discuss **reproductive options**

MACMILLAN CANCER SUPPORT

PMS2

Click here

Estimated lifetime cancer risk for carriers of germline pathogenic variants in *PMS2*



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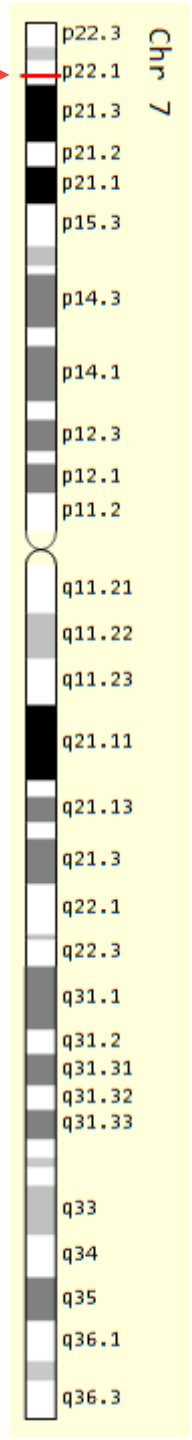
https://ascopubs.org/doi/10.1200/JCO.2018.78.4777

PMS2



The *PMS2* (PMS1 homolog 2, mismatch repair system component) gene is located on chromosome 7. The *PMS2* gene protein plays an important role in repairing DNA damage.

Inherited alterations in *PMS2* are associated with Lynch Syndome. Therefore people with an inherited PV in *PMS2* are potentially at risk of many cancers, but particularly, colorectal and endometrial cancers.

Management recommendations for PV in *PMS2*: UKCGG

Management recommendations*	
1 Screening	• **Colorectal screening**: 2-yrly colonoscopy from age 35 to 75 -review at 75 • **Gastric screening**: Helicobacter pylori one-off screening from age 25 • **Cervical screening**: As part of the NHS cervical screening programme • No additional cancer screening is currently recommended outside of a research setting; **symptom awareness** to be advised
2 Risk-reducing surgery	• Consider risk-reducing **hysterectomy ALONE**, once childbearing is complete, no earlier than age of 45 (risks and benefits to be discussed)
3 Chemoprevention	• Discuss pros and cons of **aspirin chemoprevention** from age 25 to 65 (GP to prescribe): 150mg OD if ≤70kg or 300mg OD if >70kg **(expert opinion)**
4 Research	• **Research studies:** e.g. **EUROPAC** (pancreatic cancer screening study)
5 Cancer management	• **Targeted therapies** may be available as a treatment option for certain cancer types (immune checkpoint inhibitors e.g. pembrolizumab) • **Adjuvant 5-FU chemotherapy** may not be appropriate for patients with Dukes' B colorectal cancers
6 Family matters	• Facilitate **cascade testing** in at-risk family members • Discuss **reproductive options**

MACMILLAN CANCER SUPPORT

Lynch syndrome mainstreaming training programme

Developed by Laura Monje-Garcia, National Lead Nurse for the Lynch syndrome project

Six 2hr Workshops delivered as part of the mainstreaming training for Lynch syndrome

- Programme outline:
  - Worksop 1: taking a family history & drawing a family pedigree
  - Workshop 2: confidentiality and ethics
  - Workshop 3: the consultation
  - Workshop 4: Exercise
  - Workshop 5: Final documents and full consultation practice with regional Lynch syndrome nurse
  - Workshop 6: Clinic set-up – Activities for clinic set-up should start alongside Workshop 1 as it can be tenthly process (3 months on average). Your regional Lynch syndrome nurse and cancer alliance can provide support for this

The Lynch syndrome mainstreaming training programme uses the Health Education England (HEE) Genomic Education Programme (GEP) competency frameworks:

1. "facilitating genomic testing competencies": It covers "informed consent". You will go through all the points during the workshops, but if you are not sure about something, ask your regional Lynch syndrome nurse. This is a reference document and is not intended to be used as an assessment tool
2. "Communicating germline genomics results: A competency framework": This is a reference document and is not intended to be used as an assessment tool

Lynch syndrome mainstreaming training programme

Workshop 1: Drawing a family pedigree

- Make sure that you complete the RM Partners online training OPTION 2

Colorectal cancer MDT:
Link to training
Link to supporting documents

- Other online courses: Taking and Drawing a Genetic Family History
- Use the family history worksheet to practice:

Family-history-work sheet-blank.pdf

- Start your clinic set-up process

1. Start your clinic set-up request now: This can take up to 3 months (sometimes more)
2. Is there a specific system to receive germline genetic results in your region? Do you have to set-up a results portal? Ask your regional Lynch syndrome nurse

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Lynch syndrome mainstreaming training programme

Workshop 2: Confidentiality & Ethics

Confidentiality in Genomics

See "Consent and confidentiality in genomic medicine" document by the Royal of Physicians:
- Most of the confidentiality points discussed in this booklet refer to predictive genetic testing but it is recommended that you read point 4.2 and case studies.
- Save it in a safe place as a reference document

Ethics:

- This will be discussed by the Regional Lynch syndrome Nurses through a presentation
- They will help you identify when ethical situations arise, generally related to "non-disclosure" of information within the family.
- Main message: There are several forums to discuss ethical issues in Genomics. You can start by discussing in MDT, document, and highlight to clinical genetics or specialised services so they can deal with them.

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Lynch syndrome mainstreaming training programme

Workshop 3: The consultation part 1

- As part of your tutorials you will be able to see a full consultation by one of the Regional Lynch syndrome nurses

1. After, discuss the consultation and break it down into sections. This is so its easier for you select an agenda when you have your consultation and know the essentials that need to be covered. The consultation will follow the structure of this flowchart:

2. The information that you need to discuss is covered in the RM Partner's information leaflet for patients with CRC

3. The attached figure will also help you break down the conversation and have an agenda


Figures 3 possible results 10nov22.ppt

4. To find your own way to explain Lynch syndrome, read the RM Partners' patient information webpage as it's easy to understand, and uses a language patients will be able to understand as well (Reviewed carefully by Lynch syndrome UK)

5. **Save all the documents available through this training** in a folder where you can find them easily as you will need them later.
6. *Go to workshop 3 part 2*

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Lynch syndrome mainstreaming training programme

Workshop 3: The consultation part 2

Please, watch these recommended videos that will help you find your own style to have your genetic counselling consultation:

1. To see how others explain the 3 possible results of genetic testing watch these short videos (max. 2.5 minutes). They will give you ideas about how you would like to explain this yourself

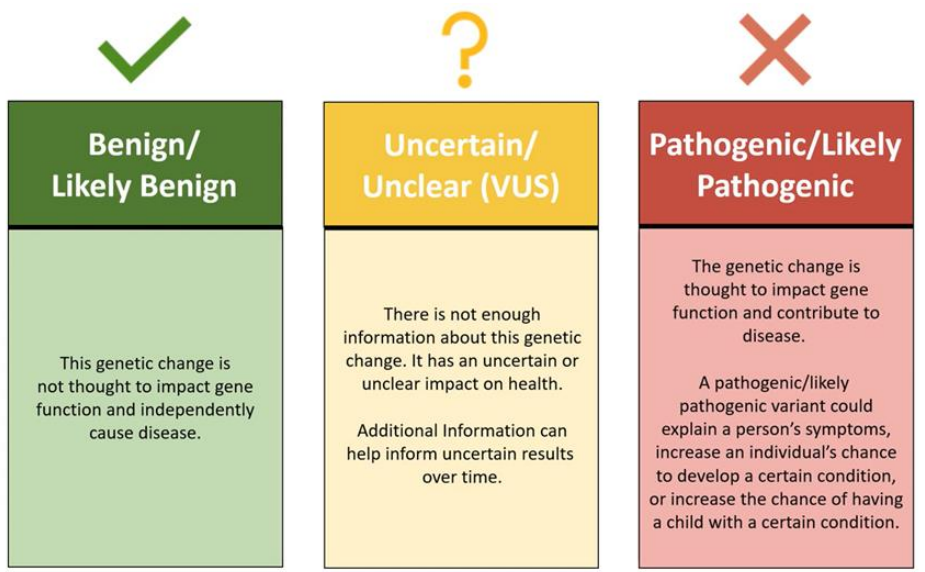
1. Other short related videos available through the genomics education programme

2. To understand how are genetic variants classified

3. What is a genome video

4. Autosomal dominant inheritance

5. How is genomics used in cancer?



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Lynch syndrome mainstreaming training programme

Workshop 4: Consultation in action: finding your style

The consultation in action: finding your own style

Write down how would you like to explain each section of the consultation. Send it over your Lynch syndrome nurse for feedback before or after practising the different sections of the consultation

Exercise: think about what you would cover during your consultation in these 3 scenarios

1st scenario: Maria has been diagnosed with CRC at 42. Her tumour sample IHC result showed loss of PMS2. She had a successful surgery and she is well. She works in genetics so you don't need to teach her about genetics.

- How would you explain Lynch syndrome?
- How would you go through the 3 possible results?

2nd scenario: John has been diagnosed with CRC at the age of 55y. He had surgery but had to have additional chemotherapy which will start in 1 month. He works as a health care assistant in your hospital. His IHC result showed loss of MLH1 & PMS2. MLH1 promoter Hypermethylation was absent. He understands genetics but he is not an expert.

- Would you go through what DNA is?
- How would you explain Lynch syndrome?
- How would you explain the 3 possible results?

3rd scenario: Jennifer has been diagnosed with CRC at the age of 36y. She had surgery but the cancer has metastasized to her liver and kidneys. She is going to have palliative chemo but she hasn't got a start date yet. She hasn't finished school and used to work in McDonalds, but due to her illness she is unemployed now. She would like to go back to work and study to finish her A levels. McDonalds can sponsor her for her A levels course. Her IHC show loss of MSH6. She is not very familiar with what DNA is but some understanding from the mainstream media. She looks depressed.

- Would you go through what DNA is?
- How would you explain Lynch syndrome?
- How would you explain the 3 possible results?
- Do you need to consider her emotional wellbeing?

Lynch syndrome mainstreaming training programme

Workshop 5: Full consultation & final documents

Full consultation: Today you will have the opportunity to practice your full consultation

- You will practice with your regional Lynch syndrome nurse using your own style which you developed and have already written down

Go through these documents:

A couple of documents to save and that you might find helpful before you start your clinic

1. Family history questionnaire (FHQ)

FHQ.doc

2. Example of mainstreaming letter

Lynch syndrome panel template 4mai

Make sure that you have your region's:

1. Record of discussion form
2. Germline genetic testing blood request form
3. Your SOP has been approved by your team, cancer alliance representative, and clinical genetics department

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Clinic Set-up

It's recommended to start set-up when undertaking workshop 1 as it takes around 3 months to make arrangements

Clinic set-up guidance:

- To help you think about what is needed:
See embedded document


Genetics clinic set up PDF 31mar23.pdf

- If you are asked about your new service by clinical and non-clinical managers withing your Hospital:
See embedded document


Lynch Syndrome clinic set-up informa

'TOP TIPS'

- Familiarise yourself with national policy on genomics within the NHS
  - NHS England » NHS Genomic Medicine Service
  - NHS England » Accelerating genomic medicine in the NHS
  - NHS Long Term Plan » The NHS Long Term Plan
- Identify a mentor (this person can be situated outside of your local Trust, for example within the regional GMSA team).
- You may need to develop a business case:
  - Business case toolkit – BHF
  - How to write a robust business case for service development | Nursing Times

Before you start, we recommend that you review the "facilitating genomic testing competencies":

- It covers "informed consent". You would have gone through all the points during the workshops, but if you are not sure about something ask your regional Lynch syndrome nurse
- This is a reference document and is not intended to be used as an assessment tool

Before you give your first genomic result, we recommend that you review the "Communicating germline genomics results: A competency framework"

Resources:

- Mismatch repair deficiency and microsatellite instability — Knowledge Hub (hee.nhs.uk)
- Lynch syndrome — Knowledge Hub (hee.nhs.uk)
- Lynch Syndrome online training for primary care clinicians - RM Partners
- Lynch Syndrome (colorectal cancer) online training for MDTs: Option 1 - RM Partners
- Lynch Syndrome (colorectal cancer) online training for MDTs: Option 2 - RM Partners

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Watch & Listen:

Podcasts:

The G Word, Genomics England

Click here

Genetics Unzipped, The Genetics Society Podcast

Click here

Diagnosis and Management of Lynch Syndrome | FG Podcast (podbean.com)
Dr Kevin Monahan

Webinars & Lectures:

Webinar: Think Patient Care, Think Genomics: Lynch Syndrome
South East GMSA, North Thames GMSA

Click here

Lecture:
DNA Graffiti: The Francis Crick Lecture 2022, Professor Serena Nik-Zainal

Click here

Webinars x3:
Advances in Clinical Genomics

Click here

Royal Society of Medicine Live with Professor Dame Lesley Fallowfield

Click here

Click here

Webinar:

Click here

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Central

Felicity
Starting on the 1st May

North Thames

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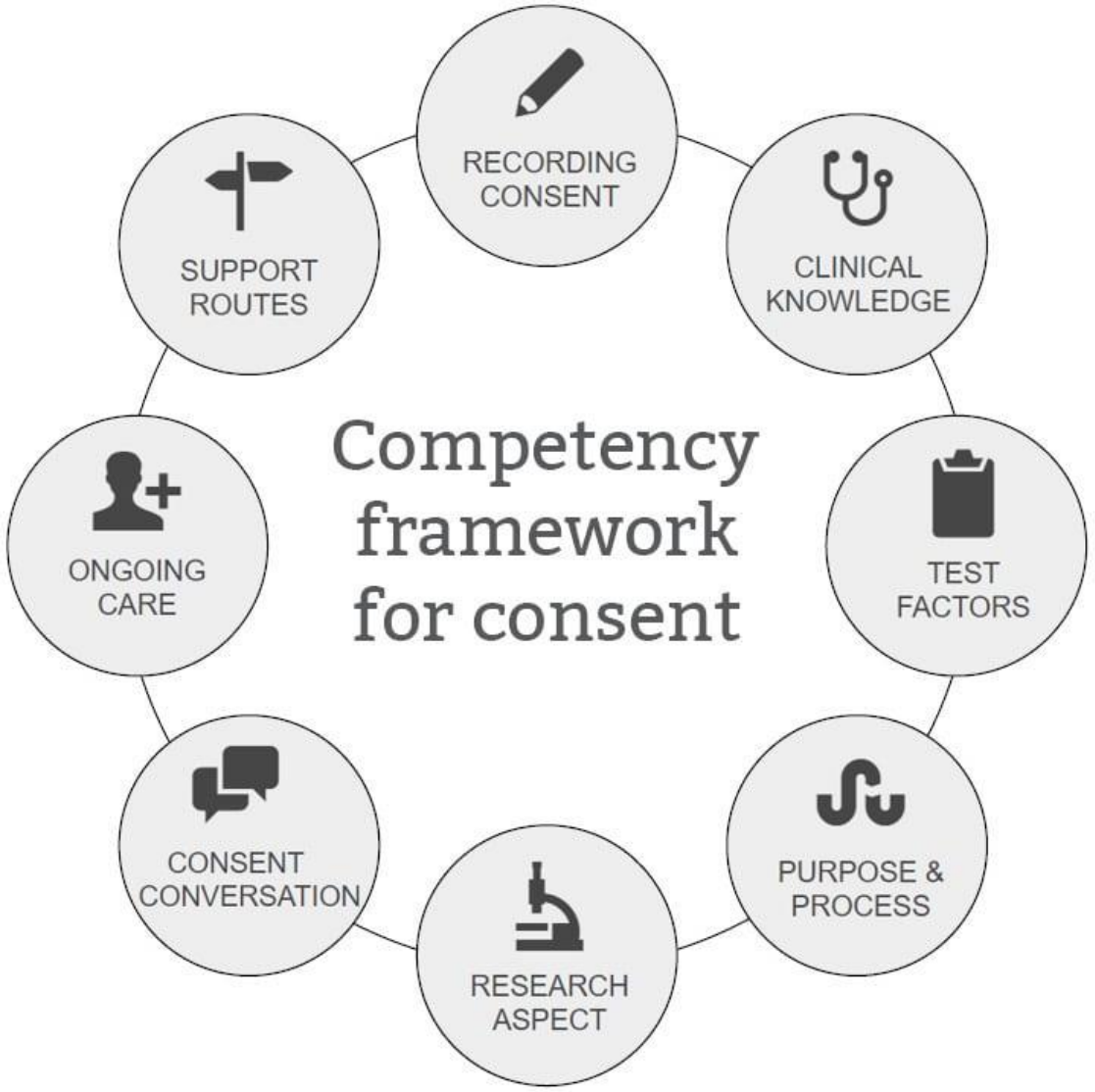

https://www.genomicseducation.hee.nhs.uk/competency-frameworks/consent-a-competency-framework/

Competency training and evidence form: facilitating germline genomic testing

Note: This framework has been designed to be a developmental tool to support individuals and organisations, and is not intended to be used as a grading or assessment tool. This form is an optional resource that may be used to demonstrate evidence of competence for use in clinical practice; it may be useful for individual records, appraisals or CPD records. Further information can be found at www.genomicseducation.hee.nhs.uk/consent-a-competency-framework/

Start date:		Trainee Name:		Position:	
Trainer(s):					
Assessed and signed by:			Date:		
Competency			Tick	Comments	
1 Ensures the process of recording consent for a genomic test follows national and local processes and governance arrangements, and is appropriate for the test being requested					
Demonstrates familiarity with the National Genomic Test Directory and adheres to this guidance when offering genomic testing, including the funding model, sample requirements and local requesting pathways.					
Understands the national and local processes for changes to consent (i.e. at age 16 with capacity, for additional tests, when a patient changes their mind about having the test).					
Demonstrates familiarity with principles of the Human Tissue Act 2004, Data Protection Act 2018 and/or General Data Protection Regulation 2018 as they apply to the use of DNA and genomic data.					
Date discussed with trainer:			E-signature/initials of trainer:		
2 Demonstrates up-to-date knowledge of the conditions occurring within their specialist area for which genetic or genomic testing may be offered					

Reading List

Calzone, K. A., Kirk, M., Tonkin, E., Badzek, L., Benjamin, C., & Middleton, A. (2018). The global landscape of nursing and genomics. Journal of Nursing Scholarship, 50(3), 249– 256 https://doi.org/10.1111/jnu.12380

Coulson J. (2022). 'Understanding the role of genomics in nursing practice.' *Nursing standard (Royal College of Nursing (Great Britain)*, 10.7748/ns.2022.e12053. Advance online publication. https://doi.org/10.7748/ns.2022.e12053

Chen L, Ye L, Hu B. Hereditary Colorectal Cancer Syndromes: Molecular Genetics and Precision Medicine. Biomedicines. 2022 Dec 10;10(12):3207. doi: 10.3390/biomedicines10123207. PMID: 36551963; PMCID: PMC9776295.

Cuthill, V. (2023), 'Demystifying Genomics in Cancer Care', *Macmillan Cancer Support.* Available at: Demystifying genomics in cancer care | Macmillan Cancer Support

Georgiou, D., Monje-Garcia, L., Miles, T., Monahan, K., Ryan, N. (2023) 'A Focused Clinical Review of Lynch Syndrome', *Cancer Management and Research*, 15 (67-85), doi: 10.2147/CMAR.S283668

Launer, J. (2021)'Effective Clinical Conversations: The Art of Curiosity' *Postgrad Med J* , 97, pp 339–340. DOI: Effective clinical conversations: the art of curiosity (bmj.com)

NHS England, (2022) 'Accelerating genomic medicine in the NHS', *NHS England.* Available at: NHS England » Accelerating genomic medicine in the NHS

Patch, C. & Middleton, A. (2018) 'Genetic counselling in the era of genomic medicine', *British Medical Bulletin*, 126(1), 27–36. DOI: https://doi.org/10.1093/bmb/ldy008

Pichini, A & Bishop, M. (2022) 'A nationally agreed cross-professional competency framework to facilitate genomic testing' *Genetics in Medicine.* 24(8), 1743-1752. DOI: https://doi.org/10.1016/j.gim.2022.04.023

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Discussion Tool

Let's Talk About... Genomic Testing on Vimeo Genomics Education Programme

"The key to providing patient education is not to make them experts, but rather to inform and empower them to make decisions."

Things to think about before talking to patients about Genomics:

The Genomics Conversation: What matters to patients - Genomics Education Programme (hee.nhs.uk)

1. Avoid technical terms and use 'plain English'.
2. Give the patient regular opportunities to ask questions, during and after the consultation.
3. Signpost to information for the patient.
4. Clear, open communication is important.
5. Explain the possible outcomes of the test, including uncertainties.

From ONS 'Glad you Asked' series: How do I talk to patients about genomics? | ONS

1. Give the most important information first.
2. Limit the number of messages.
3. What do they *need* to know and why?
4. Limit jargon.
5. Refer to Genetic Counsellors for complex conversations/situations.
6. Resources: patient information/reliable resources to signpost to.

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Discussion Tool: FAQs

What is Genomic Testing?

A genomic test looks at part or all of an individual's genetic material to look for signs that might explain a clinical condition. These may include:

- Differences in the unique sequence of DNA letters
- Missing chunks of DNA
- Additional chunks of DNA
- DNA sequences that are not in the correct order

What is involved in the test and how is it carried out?

Depending on the tumour site, most tests will be carried out by taking a blood sample or a saliva sample. Before this can happen, it is important for the person consenting to testing understands the possible results and the impact on both them and their relatives. This should mean that a person who is taking a genomic test has the opportunity to have an in-depth conversation with a trained professional, their questions answered and uncertainties addressed.
It is important to provide an overview of the possible results that might be returned from a diagnostic test: is it looking at a few genes, is it looking at lots of genes or all of the DNA? Then explain what the implications of the result will be.

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How Will I Access my Results?

Results are usually fed back directly to the clinical team who have ordered the test, usually via end-to-end encrypted email sent directly from the laboratory. This result will then be communicated to you, either in a face-to-face or a virtual/telephone appointment. A copy of the report can be made available to you if you request it.

What do my results tell me?

It is helpful to explain that there are usually three possible results from this test:

1. **Negative:** no pathogenic variant has been found in the DNA looked at during the test. This result can feel like a relief, or for some people, can feel quite frustrating or even disappointing.
2. **Positive:** this means a pathogenic variant has been identified. Depending on the variant and type of cancer you have, it will likely impact on your treatment options, your treatment order and on your family.
3. **VUS: Variant of Unknown Significance.** This result means that a variant has been found but there isn't enough data to conclude that it is definitely linked with the cancer you have been diagnosed with.

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How will this impact my family?

If it is confirmed that you have a 'pathogenic variant' it is likely that this will affect your family. Most pathogenic variants that are linked to cancer are passed on in an 'autosomal dominant' pattern, which essentially means each first degree relative has a 50% (1 in 2) chance of sharing the same variant with you.

Genetic counsellors at your local Clinical Genetics Centre will be able to help you share this information with your family. Each relative should contact their GP if they wish to in order to pursue what is called *predictive* testing. The GP will arrange for the relatives to meet with their nearest clinical genetics team and have a blood sample taken to compare their DNA to yours and see if they share the same pathogenic variant (/gene alteration).

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Will having this test affect my insurance?

In most instances, having a genomic test will not affect the personal health insurance someone has. You do not usually have to tell insurers that you are having a genomic test. You may have to disclose this information on an application form if you are applying for new insurance.

If you already have insurance cover in place, you do not have to disclose any further information to your insurer. More information is available on the Genomics England and Association of British Insurers (ABI) websites. Insurance | Genomics England

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What about my data?

All data used for genomic analysis is kept secure and confidential. More information is available on the NHS England website.

The results of a patient's genomic test will be added to their patient record.

It is normal practice in the NHS to store the DNA and/or RNA extracted from a sample even after the current testing is complete, as it may be used for future analysis and/or to ensure other testing (for example that of family members) is of high quality.

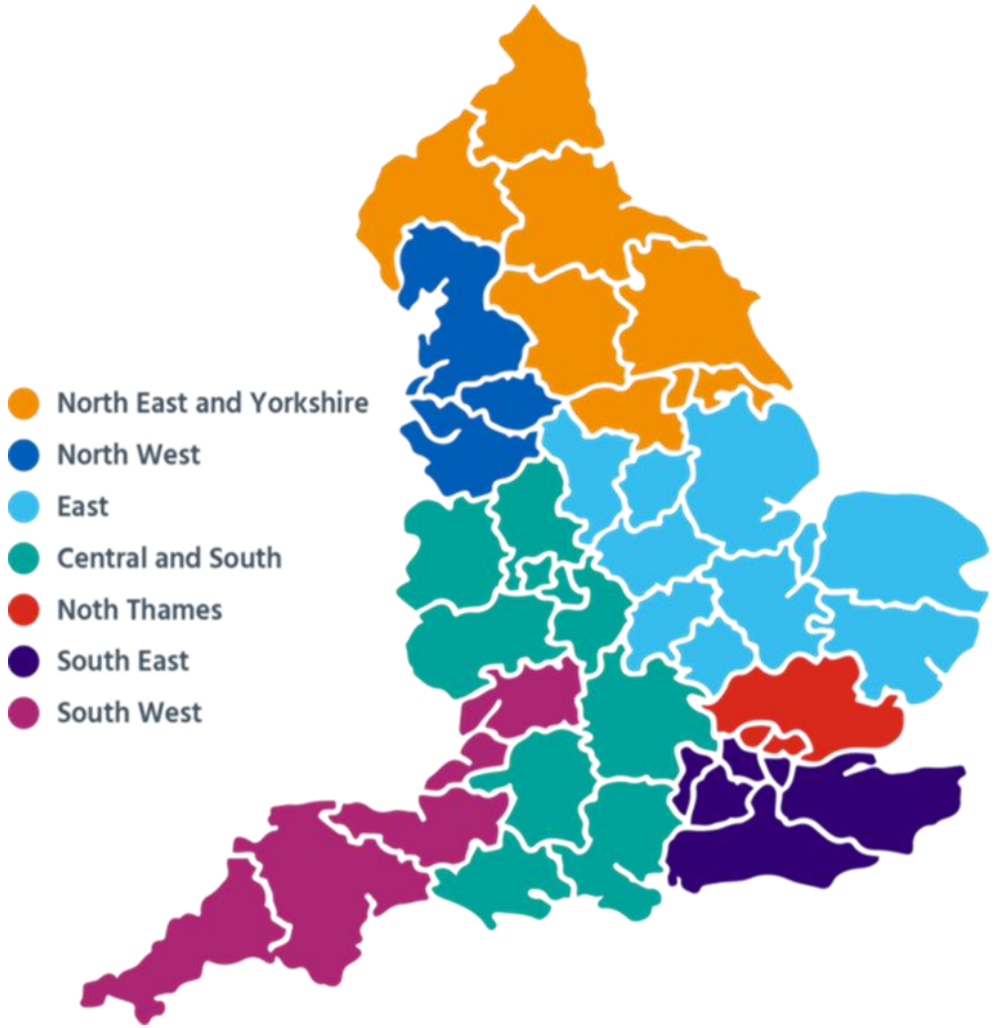
For Whole Genome Sequencing, the data from genomic tests is entered into a secure national database for the NHS Genomic Medicine Service. This system will store data about the test and results. Only staff with approved access can see this data.

As part of the NHS Genomic Medicine Service all patients undergoing whole genome sequencing will be given the option to contribute their genomic data to a secure library so that approved researchers may access that data in a form that does not identify them. If patients choose to do this then your data will be helping researchers and scientists to develop the treatments of tomorrow.

Managing genomic information, informatics and governance will be increasingly challenging. Data needs to be appropriately integrated into NHS IT systems. Genomes produce huge amounts of data ('petabytes'):

- Where is this data stored?
- How is it coded?
- Who owns this information? Individual's or whole family's?

GMSA: Genomic Medicine Service Alliance



"Click on your region" to go to your regional GMSA website.

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