NHS
South East
Genomic Medicine Service Alliance

NHS
North Thames
NHS Genomic Medicine Service Alliance

Delivery of a comprehensive service for the detection of Lynch Syndrome

A national Lynch Syndrome project

Frequently Asked Questions V1.0

Developed by the National Lynch Syndrome Project Oversight Group

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Purpose

This FAQ document has been developed to support implementation of the NHS National Genomic Medicine Service (GMS) Lynch Syndrome (LS) project. It is intended to reach healthcare professionals, commissioners and other system leads with the aim of developing a shared understanding of the project and fostering support and collaboration.

The document is iterative and will be updated periodically. Updates to the document will be shared via Genomic Medicine Service Alliances (GMSAs). If you have questions that are not covered here, please direct them to the relevant lead from the list of contacts set out in Appendix A.

Contents

Background

1. What is Lynch Syndrome?

Lynch Syndrome (LS) is an inherited condition caused by an inherited DNA repair pathway defect which results in an increased risk of colorectal, endometrial, and other cancers.[1] People with LS have up to an 80% risk of developing colorectal cancer in their lifetime and, in women, up to a 60% risk of developing endometrial cancer.[2]

LS was previously called hereditary non-polyposis colorectal cancer (HNPCC), a term relating to some relevant clinical features, but LS is now genetically defined. Most LS cases are caused by an inherited pathogenic variant in one of four genes of the DNA Mismatch Repair (MMR) pathway, *MLH1*, *MSH2*, *MSH6* and *PMS2.* LS may also be caused by pathogenic variants in a non-MMR gene known as *EPCAM*, and less frequently, by sporadic (non-inherited) constitutional epigenetic inactivation of the *MLH1* gene.[1,3,4]

The cancer risk profile of each LS gene is different – for example, for people with pathogenic variants of the *MLH1*, *MSH2* and *MSH6* genes, the cumulative incidence of developing any cancer at 75 years of age is 76%, 80% and 61% respectively.[5] The gene affected also impacts the likelihood of developing specific cancers; the *MLH1* variant is correlated with the highest risk of colorectal cancer, while the *MSH2* variant is correlated with the highest risk of other cancers.[5] Understanding the specific genetic profile of LS patients can support better management and support of these individuals.

2. Why is it important to focus on improving identification of Lynch Syndrome?

In total LS affects approximately 1 in 350 to 1 in 400 people, with 200,000-300,000 people likely to have this condition in the UK. However, it is estimated that only 5% of people with LS in the UK have been diagnosed.[6]

Increasing identification of LS provides the opportunity to detect cancers at an earlier stage through enrolment into screening programmes, and prevent cancers through risk reduction techniques including colonoscopy, prophylactic surgery and chemoprophylaxis with aspirin.[3]

A diagnosis of LS can also influence management plans for people who develop cancer, including impacting the surgical approaches chosen and the use of specific immunotherapy and chemotherapy treatments. In addition, a diagnosis may impact access to emerging therapies.[3]

In addition to preventing cancer and maintaining the health and quality of life of patients and families with LS, there is consistent evidence of the cost-effectiveness of a structured diagnostic pathway in patients with LS following a diagnosis of cancer, linked to cascade testing in families.[3]

3. What has already been done within the NHS to improve the identification and treatment of Lynch Syndrome?

To improve the identification and treatment of LS, guidance has been put in place across the NHS, including several NICE guidelines. These include recommendations for universal screening for LS in people with colorectal and endometrial cancer, use of daily aspirin to reduce the risk of colorectal cancer in LS patients, and recommendations for specific immunotherapy treatments for those with LS who develop colorectal cancer.[7,8,9,10,11]

NHS England and NHS Improvement have also recently published a handbook for Cancer Alliances to support implementation of national LS pathways. This handbook recommends that cancer multidisciplinary teams (MDTs) take responsibility for initiating

and completing LS testing pathways in cancer patients via mainstreaming and liaison with regional expert centres.[3] In addition, multi-society UK guidance for the management of hereditary colorectal cancer has been created.[12]

To reduce geographic disparities in LS diagnosis, genetic testing for LS is now commissioned at a national level through the NHS National Genomic Test Directory and tests can be ordered by any clinician if indicated.[13]

Through use of these existing guidelines and pathways, examples of good practice in LS identification and management are now emerging across the country. However, there remains a need to ensure consistency and equity of access to effective diagnostic pathways for LS, and there is still work to be done. Each year, around 35,000 colorectal and 8,000 endometrial cancer patients are diagnosed in England, of which around 1 in 30 will have Lynch Syndrome.[14,15,16] Ensuring LS testing pathways are implemented successfully for these patients could personalise the care of up to 25% of these individuals, with management decisions being influenced by the outcomes of these tests.[17] Implementing universal screening for these patients will further improve identification of LS through cascade testing in families.

The NHS Genomic Medicine Service (GMS) National Lynch Syndrome Project

4. What is the NHS GMS National Lynch Syndrome project?

The NHS GMS National Lynch Syndrome project is a program working to improve the identification and management of Lynch syndrome.

The project aims to align pathways and processes across the country to drive standardisation and equity of access to LS testing, with an initial focus on colorectal and endometrial cancer patients. It will develop and embed infrastructure to support pathway transformation and quality improvement in patient care working towards regional LS networks that link primary, secondary and tertiary care. Over time the programme will aim to extend LS screening across relevant tumour types.

Through this work, the project will improve access for people with LS to life-saving interventions, such as colonoscopy, preventative medications or surgery, and personalised therapy for cancer. This project builds on a 2019 quality improvement project undertaken by Royal Marsden Partners, across 9 colorectal cancer MDTs in the region.[18]

The focus areas of the project are to;

1. **Determine geographical variation and barriers to access to screening.**
   The project will collaborate closely with the Cancer Alliances, National Disease Registry Service (NDRS), National Cancer Registration and Analysis Service (NCRAS), and the NHS England and NHS Improvement Cancer Programme, to collect data using surveys, NDRS data, a national bowel cancer audit and local MDT audits using a standardised project tool.

2. **Develop mainstreaming pathways through cancer MDTs, supported by Cancer Alliances and the Genomic Medicine Service Alliances (GMSAs).**
   The project will help establish local colorectal and endometrial cancer MDT leadership (supported by cancer alliances) with clearly defined individual clinician roles and responsibilities to ensure testing for LS following a diagnosis of cancer.

   The project will deliver education programmes to support members of cancer MDTs in mainstreaming testing, whilst ensuring support by regional expert centres and genetic services through the GMSAs.

3. **Support the development of a national tiered LS network of cancer teams, linked to regional multidisciplinary expert centres and referral pathways.** Regional expert MDTs will be established including gastroenterologists, surgeons, oncologists, specialist nurses working in concert with genetic counsellors, geneticists and GLHs, enabling discussion of complex cases, monitoring and governance of diagnostic and treatment pathways and the development of patient registries.

5. What are the anticipated outcomes of the project?

The NHS GMS National LS project aims to deliver;

- Improved and standardised diagnostic pathways and clinical management of colorectal and endometrial cancer patients who are at risk of LS
- Visibility and insight into geographic variations in LS screening in accordance with NICE guidelines and GLH/NHS GMSA standard of care
- Evidence of improved access to personalised care and tumour agnostic therapies based on MMR status
- Upskilled mainstream oncology teams, serving as a foundation for mainstreaming of germline testing across relevant tumour pathways
- Established and functioning multi-regional Lynch syndrome Network with local, regional and national leadership.
- Support the development of a national Lynch syndrome registry.

6. How will this project affect patient care?

The project will improve access to screening and genetic testing for LS, increasing identification of patients with LS and ensuring consistent delivery of NICE guidelines. For patients, this will mean that no matter where they are based in England, they should receive equity of access to, and clinical benefit because of, this diagnostic pathway. It has been estimated that universal screening for LS in colorectal cancer patients alone will save 300 lives annually in England.[19]

7. How is this project relevant to different healthcare disciplines?

The NHS GMS National Lynch Syndrome project is relevant to many different disciplines and requires MDT input from gastroenterologists, surgeons, oncologists, gynaecologists, specialist nurses, genetic counsellors, clinical geneticists and those working with genomic laboratory hubs (GLHs).

Through collaboration between these disciplines, local networks will ensure that LS patients are able to access relevant screening and personalised care within existing regional structures, and that this pathway is integrated into day-to-day practice. Through establishment of regional expert centres, this project will also support the delivery and management of diagnosis and care for people with LS by their local cancer teams in a hub and spoke model.

8. Why have colorectal and endometrial cancers been prioritised? Will tumour types be extended over time?

Current evidence suggests LS increases the risk of developing colorectal cancer and endometrial cancer to a larger extent than other cancers; the estimated lifetime risk of developing colorectal cancer in people with LS is approximately 80%, and for women with LS the lifetime endometrial cancer risk up to a 60%.2

Due to this strong correlation, the NHS GMS National LS project will initially focus on delivering the NICE recommendations for universal LS screening in colorectal and endometrial cancer, with the aim that this will deliver improvements in diagnosis and care for a large proportion of LS patients.7,8

Screening pathways for further tumour types will be discussed and designed with key stakeholders moving forwards, building on learnings from the implementation of the colorectal and endometrial pathways. This may include introducing new pathways in urinary tract, prostate, upper gastrointestinal and pancreatobiliary cancers and may also feed into the development of future NICE guidelines for these cancers. Currently, the pathways for diagnosis of LS in these cancers are not well structured, although MMR screening in some tumour types, such as ovarian and upper gastrointestinal, may be performed in some cases.

9. How is the project being funded? How long is the project funded for?

Identification of LS in colorectal and endometrial cancer patients should be delivered by all NHS Trusts, as reflected in NICE clinical guidelines.[7,8] NHS England and NHS Improvement are initially funding this transformation project for 1 year (April 2021 – March 2022) to enable establishment of the local MDT networks and provide training to address any variations in local delivery.

The expectation is that commissioners will cover any annual costs to maintain the newly embedded clinical practice and pathways following the completion of this transformation project.

10. Who is leading the project?

The North Thames and South East Genomic Medicine Service Alliances (GMSAs) are co-leading the development of the project at a national level. For contact details, please see Appendix A.

All 7 regional GMSAs will be supporting delivery of this project at a local level. For a list of the leads within each region, please see Appendix B.

Trust Level Lynch Syndrome Leads

11. What is the ask of hospital trusts?

Each trust is being asked to nominate and support a LS champion within each of their existing colorectal and endometrial cancer MDTs, who will be responsible for ensuring delivery of NICE DG27 or DG42 i.e. universal screening for Lynch syndrome for newly diagnosed patients.

The Trusts will also be asked to respond to requests for information regarding current practice through a national survey.

12. What is the ask of Lynch Syndrome Champions within the Trust Cancer Teams?

The dedicated clinical champion for LS within each multi-disciplinary cancer team will be responsible for allocating specific responsibilities within their team, linking with regional networks via the Genomic Medicine Service and Cancer Alliances, and delivering the pathway locally. For more information on the role of the Lynch champion, please see Appendix C.

The Champion will be provided with a selection of short training modules to complete, anticipated to take no more than 2 hours, and to complete 2-yearly focused CPD delivered by a regional expert centre. Information regarding the initial training modules can be viewed here.

13. How does this fit with other national and local initiatives?

The NHS GMS National LS project aims to support the existing national LS initiatives, helping Trusts to deliver the NICE guidelines DG27 and DG42.

In addition, the project will support delivery of key national strategies, including the UK Government Life Sciences Vision, the national genomics strategy, Genome UK: The Future of Healthcare, and the NHS Long Term plan.

14. What are the reporting requirements for this project?

This project has asked all MDT leads to complete a national survey to identify accessibility barriers and gaps.

The project also asks that all regional genetics services establish a local list of patients diagnosed with Lynch Syndrome, although this list will not need to be shared externally at the present time. For more information about maintaining a local list of patients diagnosed with Lynch Syndrome, please contact Dr Kevin Monahan on k.monahan@nhs.net

15. Is there additional funding available for Trusts?

NHS England are initially funding this transformation project for 1 year to enable establishment of the service. There is no funding available for individual trusts, however Cancer Alliances have been allocated some additional funding for this financial year to support delivery of LS initiatives, including one off funding to support the establishment of IHC MMR testing.

The expectation is that commissioners will cover any annual costs to maintain the newly embedded clinical practice and pathways following the completion of this transformation project.

Finding further information

16. How do I get in touch with project leads?

The North Thames and South East Genomic Medicine Service Alliances (GMSAs) are co-leading the development of the project at a national level. For contact details, please see Appendix A.

All 7 regional GMSAs will be supporting delivery of this project at a local level. For a list of the leads within each region, please see Appendix B.

17. Where can I find further information about this initiative?

The NICE guidelines can be accessed by following the below links:

- Molecular testing strategies for Lynch syndrome in people with **colorectal cancer**. Diagnostic guidance [DG27]. Published February 2017. Available at: https://www.nice.org.uk/guidance/dg27/resources/molecular-testing-strategies-for-lynch-syndrome-in-people-with-colorectal-cancer-pdf-1053695294917. Last accessed Sept 2021.
- Testing strategies for Lynch syndrome in people with **endometrial cancer**. Diagnostic guidance [DG42]. Published October 2020. Available at: https://www.nice.org.uk/guidance/dg42/resources/testing-strategies-for-lynch-syndrome-in-people-with-endometrial-cancer-pdf-1053807829189. Last accessed Sept 2021.

To access the training resources developed for the Lynch Syndrome Champions, please visit https://rmpartners.nhs.uk/lynch-syndrome-early-diagnosis-pathway/

For more information, please contact the project leads as included in Appendix A.

18. Where can I find information appropriate for Lynch Syndrome patients?

There are several existing resources that may be helpful when explaining Lynch Syndrome to patients, including;

- McMillan Cancer Support: https://www.macmillan.org.uk/cancer-information-and-support/worried-about-cancer/causes-and-risk-factors/lynch-syndrome-ls
- Lynch Syndrome UK: https://www.lynch-syndrome-uk.org/

The Royal Marsden Partners team have also developed information for patients with colorectal and endometrial cancer who have been invited for a genetic assessment and possible genetic testing for Lynch syndrome. This can be accessed here: https://rmpartners.nhs.uk/lynch-syndrome-information/

Genomic Medicine Service Alliances (GMSAs)

19. What are the GMSAs?

7 GMSAs were established in February 2021 by the NHS Genomics Programme to oversee and coordinate the embedding of genomics into mainstream clinical care.

They deliver a range of national and local transformation programmes across the country, of which Lynch syndrome is one. Each programme has assigned lead GMS Alliances, for Lynch Syndrome this is South East and North Thames.

Each of the 7 GMSAs have received funding for a lead for Lynch syndrome. A map showing GMSA footprints is attached at Appendix B.

20. What is the role of the GMSAs?

In the LS project, the GMSA role includes:

- Providing support through clinical leadership in each geography and engagement through the senior medical and nursing leadership to help raise the profile of LS
- Ensuring the local networks are appropriately linked, with joint work to support workforce awareness and training, pathway development and reduction of unwarranted variation
- Reviewing equity of access to genomic testing for LS, as a test listed within the National Genomic Test Directory
- Supporting the establishment of testing pathways in Trusts
- Supporting the development of new models of care for easy access to genomic testing
- Dissemination of materials / communications to support awareness across trusts and systems
- Webinars / engagement initiatives
- Reporting on progress through the GMSA Boards

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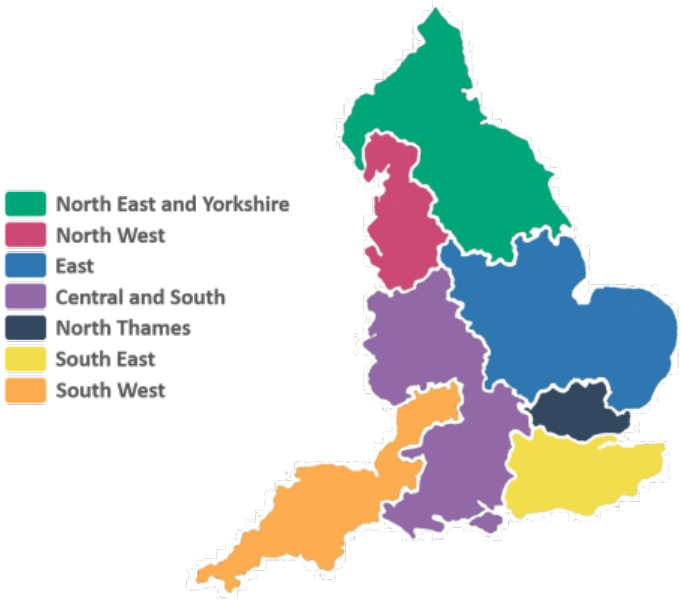
Appendix A: Contact Details – National Lynch Syndrome Project

Role	Contact
National Lynch Syndrome project leads	**Dr Kevin Monahan, *North Thames GMSA*** Consultant Gastroenterologist, Lynch Syndrome and Family Cancer Clinic, St Mark's Hospital k.monahan@nhs.net And/or **Dr Adam Shaw, *South East GMSA*** Consultant in Clinical Genetics Guy's and St Thomas' NHS Foundation Trust Adam.Shaw@gstt.nhs.uk And/or **Anna Kim** Project Manager, South East Genomic Medicine Service Alliance anna.kim@gstt.nhs.uk
National Genomics Programme	**Laurence Russell** Senior Genomics Policy & Strategy Manager NHS England and NHS Improvement laurence.russell@nhs.net
National Cancer Programme	**Susana Lukic** Programme Manager – Early Diagnosis NHS Cancer Programme NHS England and NHS Improvement susana.lukic@nhs.net

Appendix B: NHS Genomic Medicine Service Alliances Contacts

NHS GMS Alliances map



GMS Alliance	Regional Lynch Syndrome Lead(s)	Contact
North East	Jackie Cook Sally Lane	jackie.cook8@nhs.net sallylane@nhs.net
North West	Fiona Lalloo	Fiona.Lalloo@mft.nhs.uk
Central	Andrew Beggs	a.beggs@bham.ac.uk
Eastern	Ruth Armstrong	ruth.armstrong@addenbrookes.nhs.uk
South West	Neil Ryan	neilryan@nhs.net
North Thames	**Dr Kevin Monahan** Consultant Gastroenterologist, Lynch Syndrome and Family Cancer Clinic, St Mark's Hospital	k.monahan@nhs.net
South East	**Dr Adam Shaw** Consultant in Clinical Genetics Guy's and St Thomas' NHS Foundation Trust	Adam.Shaw@gstt.nhs.uk

Appendix C: Local Cancer MDT Lynch Champion Description

Who they should be?

- A cancer MDT clinician e.g. gastroenterologist, surgeon, CNS, pathologist, oncologist
- A responsible individual within each colorectal cancer and endometrial cancer MDT

Where they should be?

- Within every local colorectal and endometrial MDT
- The exception would be if all new cancer cases (without exception) are managed by a regional MDT, in which case the champion may be located there
- They will be linked to a regional expert service, but should not be expected to deliver a regional service themselves (i.e., they are managing their own patients only)

Roles and responsibilities

- Ensure delivery of NICE DG27 or DG42 i.e. universal testing for Lynch syndrome for newly diagnosed patients
    - Allocate specific responsibilities within their team
    - Eligible patients are referred for genetic testing OR offered genetic testing locally via 'mainstreaming' pathway
- Link to regional network via cancer/genomic alliance
    - Streamline referrals i.e. ensure a robust mechanism for referrals is implemented
    - Refer new Lynch syndrome patients for colonoscopic and/or endometrial surveillance
    - Complex case management: can be discussed with regional centre
- Complete the brief national survey: To assess current state of service within their MDT and identify support required https://www.surveymonkey.co.uk/r/lynch_survey
- Training
    - Complete short online training modules: https://rmpartners.nhs.uk/lynch-syndrome-early-diagnosis-pathway/
    - 2-yearly focused CPD delivered by regional expert centre

General Principles

- All newly diagnosed colorectal and endometrial patients who are identified as likely to have Lynch Syndrome should be referred for genetic testing (either locally or specialised genetics centre) in line with NICE guidelines DG27 and DG42.
- Each cancer MDT should identify a responsible local lead for the Lynch diagnostic pathway (a 'Lynch champion'), who may identify specific tasks for others within the MDT.
- Each cancer MDT is responsible for the delivery of the pathway locally. To deliver this pathway each cancer MDT should work with regional genetics expert centres/GMSAs.
- Each MDT should choose to offer either genetic testing via 'mainstreaming' (Cancer MDT clinician designated by the national testing directory) or referring patients to their linked genetics centre. Thus, local cancer MDTs should aim to achieve either
    - Timely referral of patients for genetic testing only after completion of IHC +/- methylation testing, or
    - Mainstreaming of genetic testing 'in-house'

Other Resource: Pathway model from NSHE for cancer MDTs

- https://www.england.nhs.uk/publication/implementing-lynch-syndrome-testing-and-surveillance-pathways/

This handbook sets out guidance to support local systems to implement Lynch syndrome pathways nationally for both colorectal and endometrial cancer. It is intended to be helpful and set out best practice, but of course will need to be adapted to local circumstances.

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