# Current perspectives on Lynch syndrome

## Emma Jenkins and Samantha Seker discuss the implementation of the National Lynch Syndrome Project

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It is estimated that over 175 000 people in the UK have Lynch syndrome (LS); however, less than 5% of these individuals are aware that they have the condition (NHS, 2023). LS is a well-described heritable condition that increases the risk of cancer, but many healthcare practitioners still know little about either the condition or patients' experiences of it. This paper aims to provide an overview of the aetiology of LS and proposed developments in cancer services to ensure that patients with LS are appropriately supported through their healthcare journey. The Association of Coloproctology Nurses (ACPN) short-paper session at the ACPGBI annual meeting in Manchester on 3–5 July will include presentations on this important topic.

## Background

LS, previously known as hereditary non-polyposis colorectal cancer (HNPCC), is an inherited condition which increases the risk of developing certain types of cancer (Li et al, 2021). The condition is named after Henry T. Lynch, an American physician who was instrumental in the identification of HNPCC (Marcus, 2019). The name was changed in the 1980s to highlight that it not only increases the risk of colorectal cancer, but also endometrial, ovarian, small bowel, hepatobiliary, pancreatic, urinary tract, brain, prostate and sebaceous skin cancers (Marcus, 2019). *Figure 1* shows that people with Lynch syndrome are over 80% more likely to develop colorectal cancer and 60% more likely to develop endometrial cancer than the general population. LS is estimated to cause over 3% of bowel cancer in the UK every year, with many affected under the age of 50 (NHS, 2023).

LS is an autosomal dominant genetic disease with pathogenic germline variants (mutations) in MLH1, MSH2, MSH6 or PMS2, the Mismatch Repair (MMR) proteins or an EPCAM deletion (Bateman, 2021). The function of DNA MMR proteins is to maintain genomic stability by recognising and correcting sporadic genetic mutations that occur when DNA is replicated. Mutations can accumulate when there is a deficiency in one of the MMR proteins, increasing the risk of cancer (Bateman, 2021). The MLH1 variant is associated with the highest risk of colorectal cancer and the MSH2 variant with the highest risk of other cancers. The majority of individuals with LS inherited a pathogenic variant from a parent and have a 50% chance of passing this on to the next generation. In understanding the aetiology of LS, it is important to distinguish between somatic and germline variants. Somatic changes arise during an individual's lifetime and only occur in biopsied tissue, so are not heritable. Germline variants, in contrast, occur in all cells of the body and can potentially be passed on to successive generations (*Figure 2*).

## National Lynch Syndrome Project

An aim of the NHS Long Term Plan is for 75% of cancers to be diagnosed at an early stage (stage 1 or stage 2) by 2028 (NHS England, 2021). To increase the diagnosis of LS, the National Institute for Health and Care Excellence (NICE) recommend offering testing to all people with colorectal and endometrial cancer. Consequently, testing and surveillance pathways have been developed and the National Lynch Syndrome Project has been set up to 'mainstream' testing for LS by integrating it into the standardised treatment pathway. The aim of the National Lynch Syndrome Project is for all patients with colorectal and endometrial cancer to have their initial tumour biopsy tested for pathogenic germline variants in one of four DNA MMR genes (MLH1, MSH2, MSH6, or PMS2). Results are then discussed by the Multidisciplinary Team (MDT) and patients with a variant identified for further investigation.

The test for LS should be performed on the diagnosis of colorectal or endometrial cancer, using immunohistochemistry for mismatch repair proteins or microsatellite instability testing to identify tumours with deficient DNA mismatch repair. This can then guide further appropriate testing for LS (NICE, 2017). Immunohistochemistry is a method in which the MMR proteins taken from cancer biopsy or surgical resection are stained and analysed to identify any deficiencies in the MMR proteins and can be performed in most pathology laboratories. Microsatellites are repetitive parts of DNA scattered through the normal human genome; if there are many additional microsatellites from the norm, a tumour can be described as having microsatellite instability (MSI). There are three outcomes from pathology testing: Microsatellite Instability Low

(MSI-L) (abnormal), Microsatellite Stable (MSS) (normal) or Microsatellite Instability High (MSI-H) (abnormal). Patients with LS have a high number of microsatellites due to the faulty 'spellcheck' mechanisms induced by MMR proteins.

Mainstreaming diagnostic testing for LS offers improvement to patient care through timely investigation and diagnosis (Edwards and Monahan, 2022). Early identification and investigation of people with potential LS will enable the MDT to have all the information required to support shared decision-making and consent with the patient based on their individual risk and the potential benefits of curative, prophylactic or risk-reducing surgery and surveillance (Georgiou et al, 2023). *Figure 3* outlines the Cancer Genetics Group (2019) recommendations for surveillance and treatment for people with LS; for those with a cancer diagnosis, adaptive surgery and personalised oncology treatment should be considered (Burn et al, 2020).

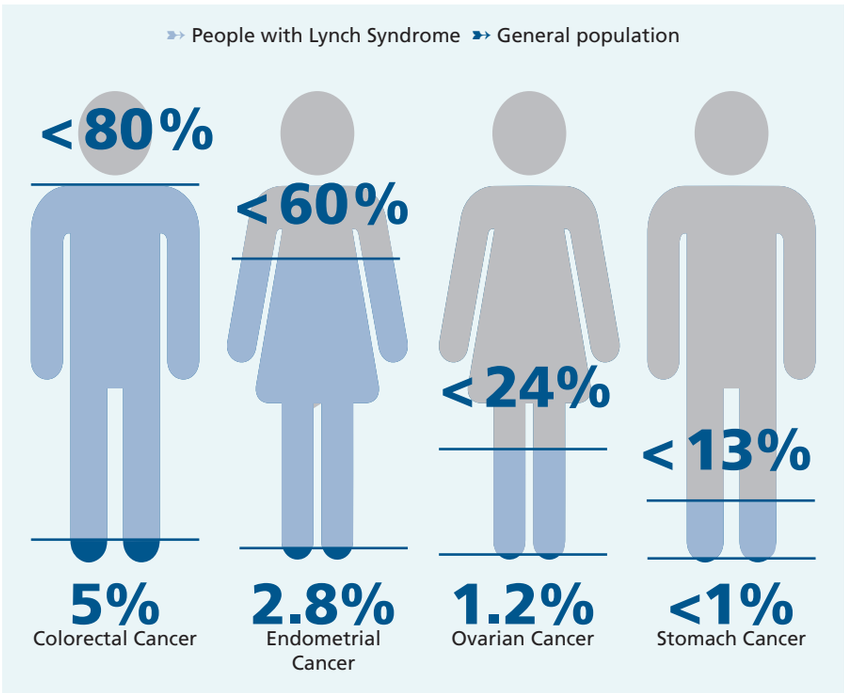


Figure 1. Lifetime cancer risk comparison

## Implementation of the National Lynch Syndrome Project

Education within the MDT is essential to support the identification and management of patients with LS, with an emphasis on improved long-term outcomes. As part of the National Lynch Syndrome Project, all NHS Trusts have appointed a clinical lead or 'champion' for the LS pathway and are beginning to establish regional networks to improve communication with GPs and other specialist teams (Edwards and Monahan, 2022). The traditional pathway is for all patients with suspected LS to be referred to clinical genetics services for counselling and further testing, if appropriate. However, with the service pressures in the NHS and increased referrals for genetic testing, the waiting list for clinical genetics services can exceed 12 months from the time of referral.

The Lynch Syndrome Project proposes developing the role of the clinical nurse

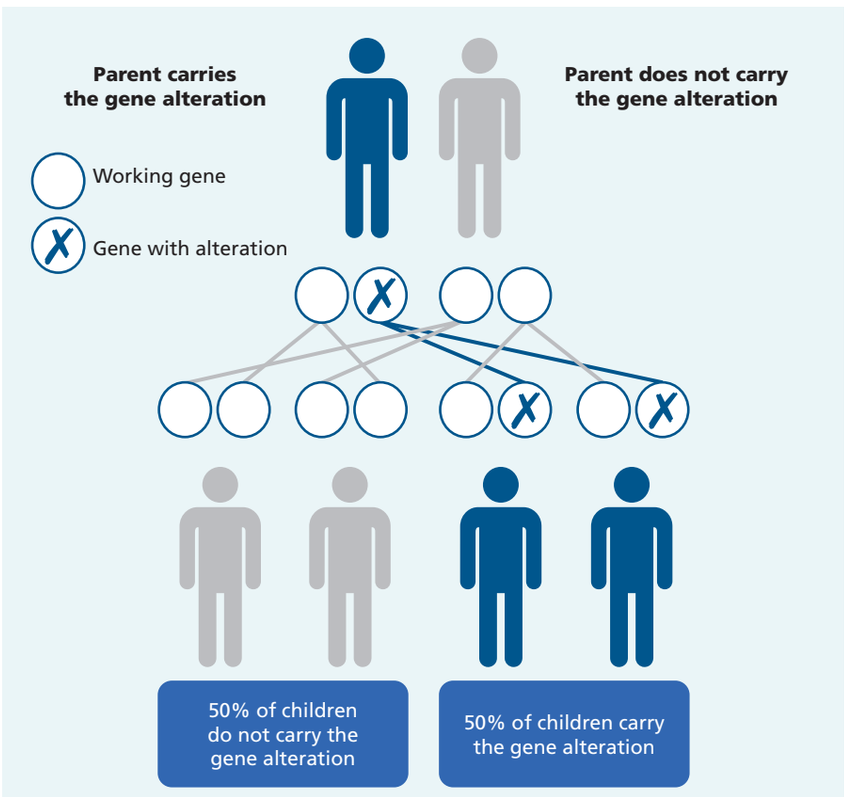


Figure 2. Autosomal dominant inheritance pattern, as evident in germline variants of LS (Cancer Genetics Group, 2019)

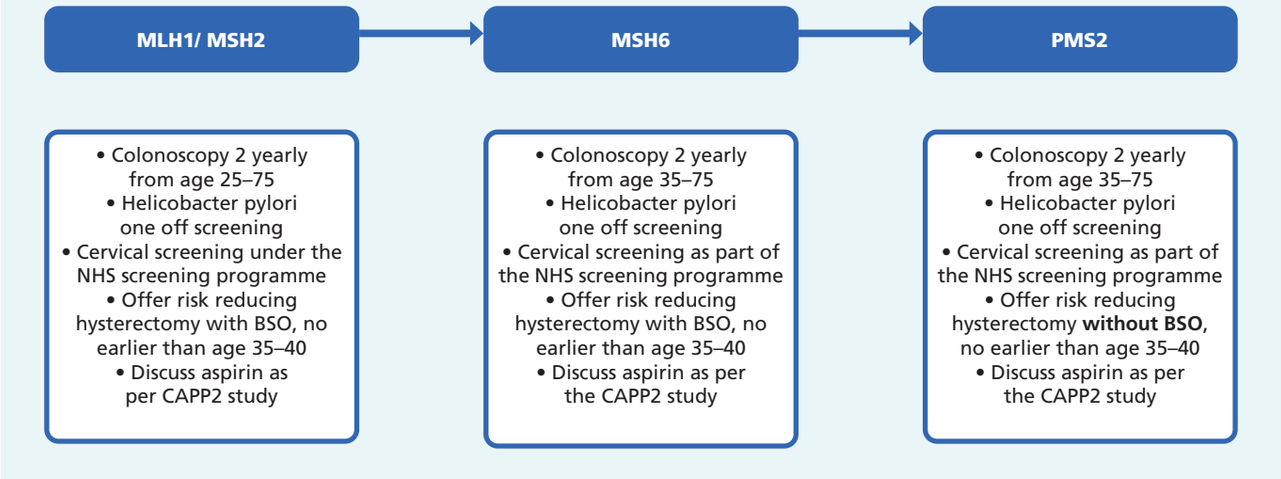


Figure 3. Recommendations for surveillance/ treatment for people with LS (Cancer Genetics Group, no date; Burn et al, 2020)

specialist (CNS) working within colorectal or gynaecological teams to become 'mainstreamers'. This involves taking on an extended role in counselling patients for germline testing. Patients would still be referred to the clinical genetic services when the test results are available, but this initiative is expected to reduce waiting times and improve the cancer pathway through earlier diagnosis to support surveillance and treatment planning. The extension of the role of the CNS to take on this position appears logical as they are a core member of the MDT, coordinate and implement patient care within the cancer pathway and have essential early contact with the patient, building crucial trust and rapport (Edwards, 2011). This initiative recognises the CNS as having a pivotal role in mainstreaming for LS and key to the development of care pathways for people with LS, in collaboration with the clinical lead and wider MDT to support the implementation of the project.

Specialist communication skills are required as part of mainstreaming, including elements of person-centred therapy (Witty, 2007), to ensure that patients are counselled in a timely and sensitive way, achieve shared decision-making and provide fully informed consent for all aspects of care within the treatment pathway (Rego et al, 2020). The CNS has many transferable skills to fulfil this role but may require further training and education to meet the needs of individualised care for people with LS. Counselling for germline testing comes with many complexities, which may influence a patient's decision to have germline testing. Disparities in accepting the offer of genomic testing are well known due to lack of education and sociological background, meaning that the CNS must consider inclusivity and diversity in their communication approach (Miller and Mustapha, 2023) and the potential impact on and implications for family members (Bleiker et al, 2013). The CNS must understand the additional psychological impact of genomic testing, in addition to a new cancer diagnosis, which can influence patient decision-making and coping.

In addition to specialist communication skills, competencies relating to informed consent must also be demonstrated by the specialist nurse, as well as an understanding of what the results mean for the patient (NHS England, 2020) and knowledge of the impact of the results on the future care of the patient and their family (Johnson et al, 2022). Close liaison between the CNS, clinical lead, core members of the MDT and the Clinical Genetics Team is crucial to optimise the pathway of care.

## Conclusion

The National Lynch Syndrome Project highlights the need for greater emphasis on pathways of care to recognise, diagnose and treat patients with LS more effectively and therefore to improve patient outcomes. This involves a wider MDT approach, working locally and nationally to improve pathways of care, including mainstreaming. As a 'mainstreamer,' the CNS plays a key role in ensuring the effectiveness of pathways of care for people with LS, although it is important to emphasise that the Clinical Genetics Team remains an integral part of the pathway, providing specialist knowledge and a safety net for genetics diagnoses. The developments in LS diagnosis and management represent an exciting time in applied genomic science, offering opportunities for nurses to extend their knowledge and scope of practice. Transformation projects within the healthcare system are vital to ensure that all MDT members involved in the care of patients with LS can recognise and address the complex needs of patients through mainstreaming of services.

We welcome all practitioners working in coloproctology to join us at the Annual Meeting of the ACPGBI on 3–5 July 2023 at the Manchester International Convention Centre. The first 50 nursing places are free for ACPN members and

membership is just £25 per year. Please contact Nicole at *ntaub@acpgbi.org.uk* or Gabby Thorpe (ACPN Chair) at *gabrielle.thorpe@uea.ac.uk* for further information about ACPN or to enquire about joining the Association. GN


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