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Lynch syndrome research registry pilot study

Submission date
05/04/2022

Recruitment status
No longer recruiting

Registration date
08/04/2022

Overall study status
Completed

Last Edited
07/03/2025

Condition category
Cancer

[X] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Lynch Syndrome (LS) is an inherited disorder that is associated with an increased risk of several cancers, particularly bowel cancer, as well as cancer of the womb. In the UK, there are only 6,000 known LS patients, however, it is estimated that there are about 176,000 undiagnosed cases. Given their high risk of bowel cancer, these patients require close monitoring, also known as 'surveillance', by colonoscopy - a thin tube with a camera on one end which is used to examine the bowel lining.
Despite national guidelines, the management of LS patients is not well-organised and varies significantly throughout the UK, so many of these patients are not getting the surveillance they need to protect against bowel cancer. To address this variability and to support the national guidelines, several experts in the field have called for a national registry to ensure that all LS patients have access to the timely surveillance they need.
In this study the researchers will develop an LS registry with multiple aims. It will be used to review and improve how LS patients are managed; it will provide data to better support the national screening programme's upcoming role in taking on and managing LS surveillance; and it will provide a unique resource to conduct and support future research into LS.

Who can participate:
LS patients who have previously taken part in the Cancer Prevention Project 3 (CaPP3) trial will be recruited from five sites in England over 9 months.

What does the study involve:
This small-scale initial study, known as a pilot study, will help to answer several important research questions around how LS patients are currently managed, as well as assisting with optimising the data collection process and functionality of the registry for both users and researchers.
Participation will involve completing and returning a baseline health questionnaire, followed by collecting surveillance data at the local hospital with additional data provided by NHS Digital. Data will be held on a secure and confidential database and in accordance with GDPR and Data Protection legislation. Further information will be available at the study website (https://lynchregistry.org.uk/) once the study is open to recruitment.

What are the possible risks and benefits of participating?
There are no risks of physical harm associated with taking part in this study. However, as the

registry will be storing some personal information, there is a risk of a breach of confidentiality. The risks stemming from a data breach include; patient distress or loss of patient confidence and fraud by way of identity theft. To minimise the possibility of this occurring, several policies and procedures are in place to help protect participant information and to ensure that any personal information that could identify individuals remains strictly confidential. A data security policy is in place detailing precautions for safe operation such as encryption, access restrictions, security audits and secure software development practices. In the event that there is a breach of confidentiality, all participants will be notified.
There may not be an immediate direct benefit from joining the registry pilot study, but the information we get might help improve the treatment of people with Lynch Syndrome. As the national registry eventually becomes more established Lynch syndrome patients will benefit by being offered regular screening examinations, in line with the national guidelines. Additionally, the national registry will help to raise awareness of Lynch syndrome amongst clinical teams and promote future research projects and collaborations.

Where is the study run from?
Imperial College London (UK)

When is the study starting and how long is it expected to run for?
April 2020 to March 2026

Who is funding the study?
1. Cancer Research UK
2. 40tude (UK)

Who is the main contact?
Prof. Amanda Cross
amanda.cross@imperial.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Prof Amanda Cross

ORCID ID
https://orcid.org/0000-0002-0893-2377

Contact details
Room 505
Imperial College London
St Mary's Campus
Norfolk Place
London
United Kingdom
W2 1PG
+44 (0)20 7594 3401
amanda.cross@imperial.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
295605

Central Portfolio Management System (CPMS)
52834

Protocol serial number
22IC7518

Study information

Scientific Title
Surveillance for individuals at high-risk of colorectal cancer – using Lynch Syndrome patients as a model

Study objectives
Lynch Syndrome (LS) is a hereditary cancer syndrome with a population prevalence of between 1 in 125 and 1i n 400 people. LS is especially associated with an elevated colorectal cancer (CRC) and endometrial cancer risk, but also an increased risk of others such as ovarian, gastric and hepatobiliary cancers. LS arises from germline mutations in mismatch repair genes MLH1, MSH2, MSH6 and PMS2, or also EPCAM, deletions within which result in aberrant expression of MSH2.

The lifetime CRC risk associated with LS is as high as 80% without surveillance. LS is, however, ‘under-recognised, under-diagnosed and under-managed’, as highlighted in a letter to the British Medical Journal from numerous experts in the field. In the United Kingdom (UK), there are only 6000 known LS patients, however, it is estimated that there are ~176,000 undiagnosed cases. To address this, the National Institute for Health and Care Excellence (NICE) issued new guidelines in 2017 recommending universal testing for LS in all newly diagnosed CRCs. Although this will improve LS diagnosis, urgent improvements are needed in other aspects of LS patient care. NICE guidelines have also highlighted that testing for LS in people diagnosed with endometrial cancer is currently not often done or may only be done for people with an identified risk factor for LS; this could be age at diagnosis or a family history of LS-related cancers. The guidelines recommend undertaking IHC of MMR proteins in all cases of endometrial cancer.

Given their high lifetime CRC risk, LS patients should undergo colonoscopy surveillance, which has been associated with a 72% reduction in CRC mortality and a 10-year survival of 90% in those diagnosed with CRC. National guidelines recommend that LS patients undergo colonoscopy surveillance every two years. The responsibility for surveillance of LS patients currently lies with local healthcare providers and, despite these national guidelines, the management of these patients varies significantly across the UK. A national survey reported a widespread perception amongst gastroenterologists, surgeons and oncologists that LS patients were being managed by ‘somebody else’. There is also concern about the robustness and timeliness of the surveillance recall system; few hospitals, for example, have an organised method of providing LS patients with the recommended surveillance. The recent NICE guidelines for CRC tumour testing will increase the number of LS patients identified, which will further exacerbate the need for efficient and well-organised surveillance procedures. It has recently been agreed that the national Bowel Cancer Screening Programme (BCSP) will eventually be taking on the management of LS patient colonoscopy surveillance in England, although this is still likely to

take several years before it is fully implemented. Similarly for endometrial cancer, as more LS patients are identified, there may be a growing need for surveillance for this cancer; however, there is a lack of data on the best management of these patients and indeed whether surveillance in these patients is effective.

A national registry of LS patients is essential to ensure that LS patients have nationally coordinated care, which will begin to reduce the variation in access to colonoscopy services across the country. The registry will allow healthcare providers access to coordinated assistance to adequately monitor and standardise the frequency of check-ups in line with the national guidelines for all LS patients. Appropriate surveillance consistent with the national guidelines is beneficial for this group of high-risk individuals as surveillance is associated with reduced CRC mortality.

The registry will ultimately create a unique resource to conduct and support future research into LS and the associated risk of cancer, including CRC, endometrial and other LS-related cancers, and can also be used as a model for the management of other high-risk conditions.

Research questions:
1. How can we optimise the data collection process and functionality of the registry database for both users and researchers?
2. What would be required to better support the national BCSP and their upcoming role in taking on and managing LS surveillance?
3. What proportion of the registry pilot data collected directly from participants and local sites can be provided by the National Disease Registration Service (NDRS) and NHS Digital on a national scale?
4. Can we capture colonoscopy quality assurance data and ascertain disease-specific colonoscopic quality indicators in LS patients?
5. What proportion of LS patients attend colonoscopy surveillance every 2 years?
6. What proportion of LS patients have been tested for Helicobacter pylori (HP) - an important risk factor in the development of gastrointestinal cancers?
7. What options are appropriate for the gynaecological management of female LS patients, particularly when considering patients with PMS2 pathogenic variants?
8. What proportion of LS patients have had a cancer diagnosis?
9. What proportion of LS patients are taking aspirin, why are they taking it and at what dosage or frequency?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/05/2022, Newcastle & North Tyneside Research Ethics Committee (NHS BT Blood Donor Centre, Holland Drive, Newcastle upon Tyne, Tyne and Wear, NE2 4NQ; +44 (0)207 104 8171; newcastlenorthtyneside2.rec@hra.nhs.uk), ref: 22/NE/0087

Primary study design
Observational

Study design
Multicentre observational questionnaire-based pilot study

Study type(s)

Other

Health condition(s) or problem(s) studied
Cancer in patients with a confirmed Lynch Syndrome diagnosis

Interventions
A baseline health questionnaire and surveillance data will be collected, with additional data provided by NHS Digital.

Intervention Type
Other

Primary outcome(s)
Successful collection of baseline and surveillance data for consented participants and linkage with NDRS data at 9 months

Key secondary outcome(s)
Frequencies and proportions assessed from data successfully collected under the primary outcome measure at 9 months, including data on those attending colonoscopy or gynaecological surveillance, tested for Helicobacter pylori, presymptomatic and those taking aspirin and at what dose/frequency (see research questions)

Completion date
01/03/2026

Eligibility

Key inclusion criteria
1. English participants with a confirmed genetic Lynch Syndrome diagnosis
2. Previously taken part in the CaPP3 trial
3. Consented to be contacted about participation in a national Lynch Syndrome Registry

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
257

Key exclusion criteria
CaPP3 participants who have not agreed to be contacted about registry participation

Date of first enrolment
18/11/2022

Date of final enrolment
07/12/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
North West London Hospitals NHS Trust
Northwick Park Hospital
Watford Road
Harrow
United Kingdom
HA1 3UJ

Study participating centre
The Newcastle upon Tyne Hospitals NHS Foundation Trust
Freeman Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Manchester University NHS Foundation Trust
Cobbett House
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Birmingham Women's and Children's NHS Foundation Trust
Steelhouse Lane

Birmingham
United Kingdom
B4 6NH

Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
40tude

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Individual registry participants will not be identifiable from any reports or publications placed in the public domain.
In the future, anonymised information from the Lynch syndrome registry pilot study may also be used to support other studies in the UK, Europe and outside of the European Economic Area, that aim to conduct further research to improve care for Lynch syndrome patients, but only if participants give specific consent for this.
The use of any information in future studies will require participant consent and the approval of the Lynch syndrome registry pilot study steering committee. Further information about approved research studies will be available at https://www.lynchregistry.org.uk. Participants can choose on the consent form if they would like their information to be used to support future research studies and if they would like to be contacted about taking part in any future research studies. If participants choose to later take part in a national registry or other studies, they will be asked to consent separately for these.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes