

# Urine DNA testing as a non-invasive screen for urothelial cancer in people with Lynch syndrome

|                                        |                                                 |                                                                                                                         |
|----------------------------------------|-------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| <b>Submission date</b><br>27/10/2026   | <b>Recruitment status</b><br>Not yet recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol                       |
| <b>Registration date</b><br>27/10/2026 | <b>Overall study status</b><br>Ongoing          | <input type="checkbox"/> Statistical analysis plan<br><input type="checkbox"/> Results                                  |
| <b>Last Edited</b><br>27/10/2026       | <b>Condition category</b><br>Cancer             | <input type="checkbox"/> Individual participant data<br><input checked="" type="checkbox"/> Record updated in last year |

## Plain English summary of protocol

### Background and study aims

Urothelial cancer is a tumour of the lining of the urinary tract, which includes parts of the kidneys, the ureters, the bladder, and the urethra. People who have Lynch syndrome have up to a 1-in-4 chance of developing urothelial cancer during their lifetime, making it the second or third most common Lynch syndrome cancer. However, there are no suitable surveillance or prevention options.

This study will use a DNA-based test to screen for urothelial cancer DNA in urine samples. Collection of urine is easy and painless and can be done at home with postage of the urine sample to the laboratory. A pilot study has shown that the urine test (the Newcastle MSI-Plus Assay) could be a highly accurate test for urothelial cancer. However, the pilot study included only a few hundred people and so these accuracy estimates are uncertain. We also do not know how well the test detects early-stage tumours and need quality of life and cost data to understand the health economics of offering a urine surveillance programme to people with Lynch syndrome.

### Who can participate?

People aged 40 years or older who have a diagnosis of Lynch syndrome caused by the MLH1, MSH2, or MSH6 gene can take part. This study will primarily recruit people with MSH2-Lynch syndrome as they are at highest risk of developing urothelial cancer.

### What does the study involve?

Potential participants will be contacted by participant identification centres across NHS England, NHS Scotland, and NHS Wales. Potential participants will be sent a study advert, including a brief summary of MUSICaL and contact details for the research team at Newcastle University / Newcastle upon Tyne Hospitals NHS Foundation Trust to be able to get more information and be recruited.

When a potential participant contacts the research team, they will be screened for eligibility and then provided with the participant information sheet and consent form by email if eligible and willing to take part. Once the consent form has been completed, the participant will be sent a short electronic questionnaire to collect personal details needed for contact and sample collection, as well as important health data. If a (potential) participant can't use email, a member of the research team will send information about the study and consent form by post and can

complete questionnaires on their behalf via telephone.

Participants will be sent a sample collection kit to their home address within a few months of consenting to the study. This may be a few months to ensure capacity in the laboratory to process the sample. This kit contains a device called a ColliPee to collect the urine sample. The kit will include clear instructions to follow. There will be a label for time and date of sample collection. The sample will be sent by the participant to the research team via the post using the pre-paid and addressed postage box that is included with the kit. Sample collection is easy and all costs are covered. There will also be two short questionnaires sent by email for the participant to complete on symptoms and quality of life at the time of sample collection. These questionnaires will each take less than 5 minutes to complete. If a participant is unable to use email, a member of the research team can complete questionnaires on their behalf via telephone.

The urine test result will be sent to participants in 2 months or less of sample collection.

Participants will be informed at the time what to do next.

About 2% of urine tests are expected to give a positive result. Participants with a “positive” result (the urine has MSI) will be sent a new sample collection kit and asked to send a second urine sample to confirm the result. If the second sample is also positive, the MUSICaL clinical team will refer the participant to their local hospital for further investigations for urothelial cancer. The urology clinic will likely involve the following, though investigations may vary:

1. CT urogram, a non-invasive imaging test that combines X-rays and computers to create highly detailed, 3D cross-sectional images of the kidneys, ureters, and bladder.

2. Cystoscopy, a minimally invasive test using a camera on a thin tube inserted through the urethra (the tube connecting your bladder to the outside) to view the inside of the urethra and bladder and the openings of the ureters.

If the participant has a womb, they may also be referred to a gynaecology clinic as a womb cancer could cause the positive result. The gynaecology clinic will involve the following, though investigations may vary:

3. Trans vaginal ultrasound scan, a non-invasive imaging test that uses ultrasound to assess the inside of the womb.

4. Hysteroscopy, a minimally invasive test using a camera on a thin tube inserted through the vagina and cervix to examine the inside of the womb. A biopsy (small tissue sample) of the womb lining will likely be taken.

About 98% of urine tests are expected to give a negative result. If a participant’s urine test result is “negative” (the urine does not have MSI), they will not need any further tests or investigations but will be followed for at least 2 years by the research team to see if they develop urothelial cancer despite the negative result.

Rarely, the first urine test will be positive but then the confirmatory test will be negative. This probably means the first result was a “false positive”. In some cases, this could be a small tumour or precancerous lesion that has been destroyed by the immune system. To make sure, another urine test kit can be sent approximately 12 months later.

Regardless of test result, if a participant is found to have a cancer, the research team will establish regular contact with their local clinical team and will send additional urine sample collection kits to their home at key timepoints during treatment (for example before and after surgery). These additional samples will allow changes in the urine MSI signal to be tracked.

Details of the cancer, including its stage and grade, and tumour tissue will be requested from the hospital responsible for treatment. A blood sample may also be collected during treatment appointments. Tumour and blood samples will allow us to confirm that the urine MSI signal originates from the cancer when the urine test is positive, or investigate why the cancer was missed when the urine test is negative. The blood sample is helpful for this analysis but is not needed, so the participant can choose not to give a blood sample.

In some cases, the research team will also access tumour tissue and data from cancer diagnoses that occurred before a participant started on the study. For example, the urine test may detect

recurrence of a cancer that was treated before starting on the study, in which case the pre-study cancer will need to be analysed to see if the tumour MSI signal matches the MSI signal in the urine.

During follow-up, participants will be asked to complete a short electronic questionnaire sent by email every 6 months after the initial urine sample to inform the research team if they have had a cancer diagnosis or symptoms since last contact. There will also be a short electronic questionnaire on health-related quality of life that uses simple scoring systems. These questionnaires will each take less than 5 minutes to complete. On rare occasion, the research team may also contact participants by telephone. If a participant is unable to use email, a member of the research team can complete questionnaires on their behalf via telephone.

What are the possible benefits and risks of participating?

Participants will be contributing to research that may benefit the wider Lynch syndrome community. Although this testing approach needs to be carefully evaluated, participants could benefit from early detection of a cancer that is not showing any symptoms, which may be curable without needing an operation. Urine samples will also be tested after treatment for cancer, which can detect regrowth of the cancer and allow the clinical team to adapt their treatment plan. Participants will have the support of the expert clinical team leading the study, who have decades of experience caring for and running clinical trials for people with Lynch syndrome.

There are minimal risks to participating. The ColliPee device for urine sample collection is safe and easy to use. The data analysis and urine sample testing will be carried out by expert scientists at Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust. The test has quality control metrics to ensure a reliable result. The test was highly accurate during a pilot study, giving a "positive" result in 100% of urothelial cancer patients and giving a "negative" result in 99.5% of people without urothelial cancer. However, these results are based on small numbers and the true accuracy of the test may vary. There is a risk of incorrect test results:

1. "False positive" results, meaning the test indicates a cancer may be present when there is no cancer, can lead to unnecessary anxiety and further clinical investigations.
2. "False negative" results, meaning the test indicates there is no cancer when a cancer is present, can lead to false reassurance. Participants will be advised of symptoms to be aware of regardless of the test result.

There will be additional clinical investigations in a urology or gynaecology clinic after a positive test result, which will occur in about 2% of participants. These are generally safe and are standard clinical procedures when cancer is suspected but do carry some risks. Participants will be informed of these risks in detail in preparation for the clinic.

Screening for cancer can sometimes detect very slow growing tumours that do not cause ill health and so would not have impacted day-to-day life or lifespan if undetected. This is known as over-diagnosis. Therefore, screening for urothelial cancer in this study may lead to over-diagnosis and unnecessary investigations and treatment.

Where is the study run from?

Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?

November 2026 to October 2029

Who is funding the study?

Cancer Research UK

Who is the main contact?

Dr Richard Gallon, richard.gallon@newcastle.ac.uk

## Contact information

### Type(s)

Principal investigator, Scientific, Public

### Contact name

Dr Richard Gallon

### ORCID ID

<https://orcid.org/0000-0002-5395-0099>

### Contact details

Newcastle University, International Centre for Life, Central Parkway

Newcastle upon Tyne

United Kingdom

NE1 3BZ

+44 (0)7530949298

richard.gallon@newcastle.ac.uk

## Additional identifiers

### Integrated Research Application System (IRAS)

375977

### Central Portfolio Management System (CPMS)

76261

### Grant Code

EDDPJT-May26/100028

## Study information

### Scientific Title

MSI urine surveillance to identify cancer in Lynch syndrome

### Study objectives

Primary objective:

Is the Newcastle MSI-Plus Assay of urine a useful screening test for the early detection of Lynch syndrome urothelial cancer?

Secondary objectives:

1. What is the impact of urine screening on participants' quality of life?
2. Would a urothelial cancer surveillance programme for people with Lynch syndrome, using the Newcastle MSI-Plus Assay on urine samples, be cost-effective?

**Ethics approval required**

Ethics approval required

**Ethics approval(s)**

Approved 06/10/2026, East Midlands - Derby Research Ethics Committee (2 Redman Place, Stratford, London, EC20 1JQ, United Kingdom; -; derby.rec@hra.nhs.uk), ref: 26/EM/0221

**Primary study design**

Interventional

**Allocation**

N/A: single arm study

**Masking**

Open (masking not used)

**Control**

Uncontrolled

**Assignment**

Single

**Purpose**

Screening

**Study type(s)****Health condition(s) or problem(s) studied**

Urothelial cancer

**Interventions**

Participants will be asked to collect a urine sample at home to be posted to the research laboratory at Newcastle University where the sample will be tested using the Newcastle MSI-Plus assay, in collaboration with Newcastle upon Tyne Hospitals NHS Foundation Trust. Participants with a "positive" urine (the urine has MSI) will be invited to send a second urine sample to confirm the result. If the second sample is also positive, the MUSICaL clinical team will refer the participant to their local hospital for further tests for urothelial cancer, as well as endometrial cancer if they have a womb. If the urine tests "negative" (the urine does not have MSI), the participant will continue in the study with follow-up by the research team to see if they develop symptoms and/or cancer. All participants will be followed for at least 2 years. Approximately 40 cancers are anticipated. This number will allow the accuracy of urine testing to be determined with confidence.

Any urothelial cancers diagnosed during the study will also be tested by the MSI-Plus assay to see if the MSI signal matches the urine. Other tumour data will be collected to assess if screening finds cancers at an earlier stage. Health-related quality of life data will be collected to evaluate the impact of screening on general well-being and the cost-effectiveness of screening will be assessed.

MUSICaL will establish a stakeholders committee of people with Lynch syndrome, scientists, and healthcare providers to support the study, patient and clinician education, and NHS adoption.

## **Intervention Type**

Other

## **Primary outcome(s)**

1. The diagnostic sensitivity of urine MSI screening for the early detection of Lynch syndrome urothelial cancer, calculated at the end of the study as the percentage of participants diagnosed with urothelial cancer during the study who had a positive urine using the Newcastle MSI-Plus Assay.
2. The proportion of urothelial cancers diagnosed following urine MSI screening that are early stage (clinical stage <pT2), calculated at the end of the study using pathology data available from urothelial cancers diagnosed during the study.

## **Key secondary outcome(s)**

Incremental cost per quality adjusted life year of urine MSI screening for the early detection of Lynch syndrome urothelial cancer with model sensitivity analysis, calculated at the end of the study using a comprehensive health economic model and the test performance, cancer staging, and health-related quality of life data collected during the study.

## **Completion date**

31/10/2029

# **Eligibility**

## **Key inclusion criteria**

1. Constitutional (germline) pathogenic variant in one of the following DNA mismatch repair genes: MLH1, MSH2 or MSH6
2. Age  $\geq 40$  years
3. Fluency in written and spoken English as study materials, questionnaires, assessments, and communications are available in English only

## **Healthy volunteers allowed**

No

## **Age group**

Mixed

## **Lower age limit**

40 Years

## **Upper age limit**

100 Years

## **Sex**

All

**Total final enrolment**

0

**Key exclusion criteria**

1. Incapable of self-collection of a urine sample, for example on renal replacement therapy
2. Unable to provide informed consent to the study protocol
3. Participation in other interventional studies that use any method to screen for urothelial cancer or use a urine sample to screen for any cancer

**Date of first enrolment**

01/11/2026

**Date of final enrolment**

31/10/2027

**Locations****Countries of recruitment**

United Kingdom

England

Scotland

Wales

**Study participating centre**

**The Newcastle upon Tyne Hospitals NHS Foundation Trust**

Freeman Hospital

Freeman Road

High Heaton

Newcastle upon Tyne

England

NE7 7DN

**Study participating centre**

**Birmingham Women's and Children's NHS Foundation Trust**

Steelhouse Lane

Birmingham

England

B4 6NH

**Study participating centre**

**Bristol NHS Foundation Trust**

Trust Headquarters

Marlborough Street  
Bristol  
England  
BS1 3NU

**Study participating centre**  
**Cambridge University Hospitals NHS Foundation Trust**  
Cambridge Biomedical Campus  
Hills Road  
Cambridge  
England  
CB2 0QQ

**Study participating centre**  
**Royal Devon University Healthcare NHS Foundation Trust**  
Royal Devon University NHS Ft  
Barrack Road  
Exeter  
England  
EX2 5DW

**Study participating centre**  
**Great Ormond Street Hospital for Children NHS Foundation Trust**  
Great Ormond Street  
London  
England  
WC1N 3JH

**Study participating centre**  
**Leeds Teaching Hospitals NHS Trust**  
St. James's University Hospital  
Beckett Street  
Leeds  
England  
LS9 7TF

**Study participating centre**  
**University Hospitals of Leicester NHS Trust**  
Leicester Royal Infirmary  
Infirmary Square  
Leicester

England  
LE1 5WW

**Study participating centre**  
**Liverpool Women's NHS Foundation Trust**  
Liverpool Womens Hospital  
Crown Street  
Liverpool  
England  
L8 7SS

**Study participating centre**  
**Guy's and St Thomas' Hospitals**  
Trust Offices  
Guy's Hospital  
Great Maze Pond  
London  
England  
SE1 9RT

**Study participating centre**  
**Manchester University NHS Foundation Trust**  
Cobbett House  
Oxford Road  
Manchester  
England  
M13 9WL

**Study participating centre**  
**Nottingham University Hospitals NHS Trust**  
Trust Headquarters  
Queens Medical Centre  
Derby Road  
Nottingham  
England  
NG7 2UH

**Study participating centre**  
**Oxford University Hospitals NHS Foundation Trust**  
John Radcliffe Hospital  
Headley Way

Headington  
Oxford  
England  
OX3 9DU

**Study participating centre**  
**The Royal Marsden NHS Foundation Trust**  
Fulham Road  
London  
England  
SW3 6JJ

**Study participating centre**  
**St George's Healthcare Nhs**  
Blackshaw Road  
London  
England  
SW17 0QT

**Study participating centre**  
**Sheffield Teaching Hospitals NHS Foundation Trust**  
Northern General Hospital  
Herries Road  
Sheffield  
England  
S5 7AU

**Study participating centre**  
**University Hospital Southampton NHS Foundation Trust**  
Southampton General Hospital  
Tremona Road  
Southampton  
England  
SO16 6YD

**Study participating centre**  
**Wales Genomics Health Centre**  
Longwood Dr  
Cardiff  
Wales  
CF14 7YU

**Study participating centre**  
**London North West University Healthcare NHS Trust**  
Northwick Park Hospital  
Watford Road  
Harrow  
England  
HA1 3UJ

**Study participating centre**  
**Aberdeen Royal Infirmary**  
Foresterhill Road  
Aberdeen  
Scotland  
AB25 2ZN

**Study participating centre**  
**Ninewells Hospital**  
Ninewells Avenue  
Dundee  
Scotland  
DD1 9SY

**Study participating centre**  
**Western General Hospital**  
Crewe Road South  
Edinburgh  
Lothian  
Scotland  
EH4 2XU

**Study participating centre**  
**Queen Elizabeth University Hospital**  
1345 Govan Road  
Glasgow  
Scotland  
G51 4TF

**Study participating centre**

**University Hospitals Birmingham NHS Foundation Trust**  
Queen Elizabeth Hospital  
Mindelsohn Way  
Edgbaston  
Birmingham  
England  
B15 2GW

## Sponsor information

### Organisation

Newcastle upon Tyne Hospitals NHS Foundation Trust

### ROR

<https://ror.org/05p40t847>

## Funder(s)

### Funder type

Government

### 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

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

## **IPD sharing plan summary**

Published as a supplement to the results publication