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Study of novel endometrial cancer diagnostics

Submission date 13/05/2026	**Recruitment status** Recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 16/06/2026	**Overall study status** Ongoing	[ ] Statistical analysis plan [ ] Results
Last Edited 03/07/2026	**Condition category** Cancer	[ ] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
Post menopausal bleeding is the red flag symptom of womb cancer. Urgent investigations may include internal vaginal scan, camera test of the womb and/or biopsy. These tests are invasive and can cause anxiety, pain, bleeding and infection. Only ~5% of people investigated for post menopausal bleeding are diagnosed with womb cancer.

The study team are developing new patient-friendly tools to help doctors identify who really need these tests to rule out womb cancer, and who can be safely reassured without them. These tools could reduce the number of people undergoing unnecessary tests, improve patient experience and help detect cancer earlier. This 5 year programme will see how well the tools work across people from different backgrounds and types of womb cancer and pre-cancer.

Who can participate?
People referred with post-menopausal bleeding from gynaecology clinics across hospitals in England, Wales and Scotland.

What does the study involve?
Participants will be asked to complete questionnaires, and provide medical information, urine, blood and vaginal samples. Most participants will complete the study in one day, some may provide further information or samples at follow on clinical visits.

This study will primarily test a novel diagnostic tool 'PREDICT EC' for the triage of women undergoing investigations for suspected endometrial cancer. PREDICT-EC uses patient demographics and clinical factors, symptoms, scan results and a simple urine test for blood, to produce a risk prediction score for endometrial cancer.

The study will also look at 2 additional tools; Spectroscopy, which predicts whether or not there is an underlying cancer from blood or urine using spectroscopy; and WID®-easy, which tests for methylated genes in DNA collected from the vagina to predict the likelihood of womb cancer in women with symptoms. The study will look at current NHS resources and costs, what patients and experts think of new tools and design a digital clinician-facing calculator to generate PREDICT-EC scores.

What are the possible benefits and risks of participating?
Benefits - There are no direct benefits from taking part in this study. Participation will contribute to research that may, in the future, reduce the burden of unnecessary invasive tests for people with bleeding after the menopause.

Risks - Participants will receive usual NHS care for people experiencing bleeding after the menopause, and their medical care will not be affected in any way. They may feel a scratch and experience bruising if providing a blood sample.

Where is the study run from?
University of Manchester, UK.

When is the study starting and how long is it expected to run for?
May 2026 to May 2030.

Who is funding the study?
National Institute for Health and Care Research (NIHR), UK.

Who is the main contact?
Prof Emma Davidson, emma.davidson@manchester.ac.uk

Contact information

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Public

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Additional identifiers

Integrated Research Application System (IRAS)
361257

Central Portfolio Management System (CPMS)
73395

National Institute for Health and Care Research (NIHR)
304303

Study information

Scientific Title
Prospective observational study of novel diagnostic tools for suspected endometrial cancer

Acronym
SONNET

Study objectives
Primary Question/Objective
To determine the clinical performance of PREDICT-EC, an endometrial cancer risk prediction tool for triaging women with suspected endometrial cancer for invasive diagnostics.

Secondary Question/Objectives
• To determine the clinical performance of the WID®-easy test for triaging women with suspected endometrial cancer for invasive diagnostics;
• To determine the clinical performance of blood and urine spectroscopy for triaging women with suspected endometrial cancer for invasive diagnostics;

• To compare the clinical performance of the tools alone and in combination in postmenopausal women with
(i) pre-malignant disease,
(ii) endometrial cancers of different molecular subtypes: DNA polymerase epsilon-mutated (POLE mutant), mismatch repair (MMR) deficient, p53 abnormal and no specific molecular profile (NSMP),
(iii) above and below age 55 years,
(iv) in those from diverse socioeconomic and ethnic backgrounds.
• Identify where these tools would sit best within standard NHS care pathways;
• To externally validate published endometrial cancer risk prediction models incorporating HE4 and CA125;
• Understand women's experience of accessing healthcare for postmenopausal bleeding; assess patient and clinician views about the acceptability/value of a new tool;
• Describe current secondary care diagnostic and treatment pathways for endometrial cancer and the costs to the NHS;
• Quantify the costs to the NHS of using PREDICT-EC in a secondary care setting at different risk thresholds within a defined diagnostic pathway;
• Develop a clinician-facing digital tool for PREDICT-EC for NHS use.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 28/04/2026, London - Central Research Ethics Committee (3rd Floor 3 Piccadilly Place London Road, Manchester, M1 3BN, United Kingdom; -; londoncentral.rec@hra.nhs.uk), ref: 26 /LO/0259

Primary study design
Observational

Secondary study design
Case-control study

Study type(s)

Health condition(s) or problem(s) studied
Triage for the investigation of endometrial cancer in patients with post-menopausal bleeding

Interventions
Bleeding after menopause can be a sign of womb cancer and people with this symptom typically undergo transvaginal ultrasound scan +/- a hysteroscopy and biopsy to rule out womb cancer. These tests are invasive, may require multiple hospital visits, and can cause discomfort, anxiety, bleeding and infection. Only about 5 in 100 people who experience post-menopausal bleeding have womb cancer. This means that for most people, these tests give negative results.

We are developing new patient-friendly tools to identify who needs these tests and who can be safely reassured without them. The tools could reduce the number of people undergoing unnecessary tests, shorten waiting times, improve patient experience and help detect cancer earlier.

We will recruit 3000 participants undergoing investigations for post-menopausal bleeding across ~10 NHS hospitals in England, Wales and Scotland.

1) The participant will be asked to sign a consent form at their hospital clinical appointment.
2) The participant will be asked some questions about their medical history by a member of the healthcare study team.
3) The participant will be asked to complete EQ-5D-5 level questionnaire.
4) The participant will be asked to self-collect a urine sample in a sterile pot, in privacy, in the clinic bathroom. A dipstick haematuria test will be performed by clinical staff.
5) The participant will be asked if a healthcare study team member can collect a blood sample. This is optional.
6) The participant will be asked if a healthcare study team member can collect a vaginal swab (FLOQSwab®) sample. This is optional.
7) The participant will have a transvaginal scan as part of their routine clinical investigations, from which we will collect data. The scan may occur before, or after recruitment.
8)The participant will be asked to complete a questionnaire regarding how they found the tests and how they feel about the proposed tools.

If a sample is deemed unsatisfactory, a repeat sample may be requested, provided the participant has not yet completed their clinical diagnostic investigations.

Participants will be managed according to routine clinical practice. We will track participants on the standard suspected womb cancer diagnostic pathway recording clinic visits, test results and clinical outcomes.

Using the data and samples collected we will test the clinical performance of three novel diagnostic tools for the investigation of women with postmenopausal bleeding and suspected endometrial cancer. In addition, we will externally validate published risk prediction models that have previously shown clinical utility in this area. We will establish the clinical performance of each tool alone and in combination, and determine where they best fit in the current endometrial cancer diagnostic pathway.

Tool 1) PREDICT -EC
Alongside routine care, we will calculate participant PREDICT-EC scores. The score could be used in future, to help identify women for invasive testing or no testing and will be calculated without knowing their cancer status. We will see how well the tool would work across people from different ethnic and socioeconomic backgrounds and for all types of womb cancer and pre-cancer. We will look at current NHS resource use and the costs of embedding the tool in routine clinical practice. We will ask women and patients (40) from a range of backgrounds, as well as health care professionals (40) from primary and secondary care, what they think of the tool via interviews and focus groups. Finally, we will design a digital clinician-facing calculator to generate PREDICT-EC scores. We will check it is easy to use and clearly indicates which women will benefit most from invasive testing.

Tool 2) WID-EASY
The WID®-easy test will be performed on vaginal samples. The test uses a UKCA marked PCR Kit and tests for methylated genes in DNA collected from the vagina using a swab to predict the likelihood of endometrial cancer in symptomatic women. Sample analysis will be conducted whilst blinded to the clinical outcome.

Tool 3) SPECTROSCOPY
Spectroscopy will be performed on residual urine, and blood samples in real time, using hand

held devices and according to the manufacturer's instructions, and/or after thawing frozen biobanked samples in batches using bench top machines. Spectroscopy predicts whether or not there is an underlying cancer from blood or urine in women with postmenopausal bleeding. Sample analysis will be conducted whilst blinded to the clinical outcome.

Intervention Type
Other

Primary outcome(s)
1. The ability of the PREDICT EC model to predict probabilities that match observed outcomes measured using standard endometrial cancer diagnostic tests including transvaginal ultrasound (at the threshold which would prompt further investigation, defined by national guidelines), hysteroscopy and endometrial biopsy at final clinical outcome

Key secondary outcome(s)
1. Performance of each risk score measured using cancer type and demographics (i) atypical hyperplasia, (ii) endometrial cancers of different molecular subtypes: DNA polymerase epsilon-mutated (POLE mutant), mismatch repair (MMR) deficient, p53 abnormal and no specific molecular profile (NSMP), (iii)FIGO stage, (iv)above and below age 55 years, (v) Indices of Multiple Deprivation (IMD) quintile groups based on postcode, (vi) self-reported ethnicity at final clinical outcome

2. Clinical utility of a risk score measured using a decision curve analysis at final clinical outcome

3. Patient acceptability of PREDICT-EC compared to standard care measured using a non-validated questionnaire at baseline

4. The ability of the WID-easy test to predict probabilities that match observed outcomes measured using standard endometrial cancer diagnostic tests at final outcome

5. The ability of the blood and urine spectroscopy to predict probabilities that match observed outcomes measured using standard endometrial cancer diagnostic tests at final outcome

6. Patient acceptability of WID-easy and spectroscopy sampling methods (urine, blood, vaginal swab) compared to standard care measured using a non-validated questionnaire at baseline

Completion date
31/05/2030

Eligibility

Key inclusion criteria
1. Women referred to secondary care for investigation of postmenopausal bleeding*
2. Written, informed consent to participate
3. Minimum transvaginal ultrasound dataset available**

*Postmenopausal bleeding will be defined as vaginal bleeding more than 12 months after menstruation has stopped due to menopause.
** Applicable only to participants approached for recruitment after transvaginal scan performed as part of their current PMB investigations.

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
110 Years

Sex
Female

Total final enrolment
0

Key exclusion criteria
1. Previous treatment for endometrial cancer
2. Previous hysterectomy
3. Unable to collect a urine sample

Date of first enrolment
01/05/2026

Date of final enrolment
01/05/2028

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Lancashire Teaching Hospitals NHS Foundation Trust
Royal Preston Hospital
Sharoe Green Lane
Fulwood
Preston
England
PR2 9HT

Study participating centre
Ysbyty Gwynedd Day Hospital
Ysbyty Gwynedd
Penrhosgarnedd
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Study participating centre
Manchester University Hospital NHS Ft (hq)
Oxford Road
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M13 9WL

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from emma.davidson@manchester.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website			14/05/2026	No	No