ISRCTN12265297 https://doi.org/10.1186/ISRCTN12265297

Comparing molecular and imaging techniques for the detection of womb cancer in black women

Submission date 23/01/2024	**Recruitment status** Recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 16/02/2024	**Overall study status** Ongoing	
Last Edited 03/07/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims

This study aims to improve the diagnosis of womb (endometrial) cancer amongst black women in the UK. This is the fourth most common cancer in the UK and black women are more likely to be diagnosed at an advanced stage of disease. This worsens their outcomes.

There is currently no screening programme for womb cancer. Most women will present symptomatically with abnormal vaginal bleeding which is considered a red flag. Only a small number of these women will have womb cancer, but clinical assessment is focused on correctly identifying these women for prompt diagnosis and treatment.

In the UK, the gold standard for assessing these women is using transvaginal ultrasound. This approach can sometimes be inaccurate and result in either missed diagnoses, or the need for multiple invasive confirmatory diagnostic tests, in order to detect each case of womb cancer.

The novel WID™-qEC test is a molecular test based on cervical and vaginal swab specimens. It has been shown to be highly sensitive and specific for diagnosing womb cancer, but not adequately studied in black women.

The aim of this study is to assess the performance of the WID™-qEC test in detecting womb cancer in black women. This will be compared with ultrasound triage and the diagnostic accuracy of the two approaches will be compared.

Who can participate?

Women aged 50 years or above who present to rapid access Gynaecology clinics with abnormal vaginal bleeding warranting further investigation. Women should self-identify as belonging to one of the following ethnic groups:

1. Black, African, or Caribbean
2. Mixed/multiple ethnic groups (Black African or Caribbean and other ethnic background)

What does the study involve?

Each participant will require two swabs. One is a self-collected swab from the lower vagina. Instructions for how to collect this will be given to participants. The second is a high vaginal swab from behind the cervix, visualised when the participant undergoes a speculum examination as part of their clinical assessment. Samples will be labelled with an anonymised barcode sticker.

What are the possible benefits and risks of participating?
This study is altruistic, there is no remuneration to take part. Risks include a small amount of bleeding and discomfort from the cervical brush sample. Participants will not personally benefit from taking part in the study.

Where is the study run from?
1. EGA Institute for Women's Health, University College London (UK)
2. European Translational Oncology Prevention and Screening (EUTOPS) Institute, Universität Innsbruck, (Austria)

When is the study starting and how long is it expected to run for?
October 2014 to December 2026

Who is funding the study?
1. The Eve Appeal charity (UK)
2. University Innsbruck (Austria)

Who is the main contact?
Dr Ojone Illah, o.illah@ucl.ac.uk

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
53431

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 53431, CPMS 30876

Study information

Scientific Title
A comparative study of epigenetic analysis and ultrasonography for endometrial cancer detection in black women with abnormal vaginal bleeding

Acronym
EPISURE-B

Study objectives
For most cancers, black individuals are disproportionately affected, often having higher mortality compared to other ethnic groups. Endometrial cancer is not an exception, with black women having higher mortality rates from the disease compared to white women. One key contributing factor to this disparity is an increased likelihood of advanced disease stage at diagnosis in black women.

Current clinical pathways investigate women with abnormal vaginal bleeding using transvaginal ultrasound as a means of assessing the endometrium. This is currently the gold standard test for endometrial cancer triage. For several reasons, including an increased prevalence of fibroids in black women, the sensitivity of transvaginal ultrasound for endometrial cancer detection in black women is much lower than in white women. Additionally, ultrasound does not reliably identify women without endometrial cancer, which results in women with benign disease often undergoing multiple invasive investigations.

A test with a higher specificity than first-line transvaginal ultrasonography would more accurately identify and triage women with and without endometrial cancer. In black women, this may result in earlier diagnosis and improved clinical outcomes. The WID™-qEC is a novel test, developed to test for endometrial cancer on cells collected from cervicovaginal swabs. The test has been shown to detect endometrial cancer with a high sensitivity and specificity, by measuring specific DNA methylation signals at several CpGs across two key genes which are

important for endometrial cancer carcinogenesis. Preliminary studies of the WID™-qEC test have been positive, but with a participant pool consisting of predominantly European, Caucasian women, it is necessary that the test is validated in black women.

The primary objective of this study is to test the diagnostic accuracy (sensitivity, specificity, positive predictive value, and negative predictive value) of the WID™-qEC test in comparison to TVS in the detection of EC in black women presenting with abnormal vaginal bleeding.

The secondary objectives of the study are as follows.
1. To assess the number of additional procedures required in WID™-qEC true-positive and false-negative patients to reach a histological diagnosis.
2. Stage, histology, and grade of disease at diagnosis, and relation to WID™-qEC result
3. Rates of inconclusive results with both WID™-qEC test and TVS.
4. Compare the yield of the WID™-qEC test in self-collected (low) vaginal samples versus in clinician-collected (high) vaginal samples.

It is hypothesised that the WID™-qEC test can diagnose endometrial cancer with a high accuracy in black women presenting with abnormal vaginal bleeding, and thus can reliably be used as a triage test for endometrial cancer in this population.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 27/10/2014, NRES Committee London - Surrey Borders (Skipton House, 80 London Road, London, SE1 6LH, United Kingdom; +44 (0)207 104 8104; nrescommittee.london-surreyborders@nhs.net), ref: 14/LO/1633

Study design
Multi-centre observational prospective cohort study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Endometrial cancer

Interventions
This study will evaluate the accuracy of a novel epigenetic test, the WID™-qEC test, in detecting endometrial cancer in black women. WID™-qEC test performance will be assessed using vaginal and cervicovaginal swabs from 200 black women who present to two tertiary hospitals in London with abnormal vaginal bleeding, with a suspicion of endometrial cancer. The comparator test will be transvaginal ultrasonography, with histology (endometrial biopsy) serving as the gold standard for diagnosis. Using these results, we will calculate the diagnostic accuracy of the WID™-qEC test for the detection of endometrial cancer in black women.

The study procedures will include:

1. Cervicovaginal sampling
The study requires two cervicovaginal samples to be taken using a Copan swab and placed into an eNAT® preservation tube. The first sample is to be self-collected, i.e., by the patient themselves after instructions given. This will be a lower vaginal swab. The second sample will be collected by the clinician prior to any other vaginal manipulation (e.g., transvaginal ultrasound, cervical smear, etc). A standard Cusco speculum will be used for access to visualise the cervix. Water-soluble gel lubricant may be used to reduce any discomfort, but this is not to be applied to the tip of the speculum. The clinician will then take a sample from the posterior vaginal fornix using a Copan swab. Once obtained, this sample will be placed in the eNAT® preservation medium and labelled with a unique participant ID code.
Cervicovaginal samples will be subject to the index test, the WIDTM-qEC test. This test measures the ΣPMR of methylation at three CpGs across two genes. Predefined thresholds will be applied to signify a positive or negative test.

2. Ultrasonography
This represents the comparator test. All women are to undergo a transvaginal ultrasound by a trained clinician. Where a clear sonographic view of the endometrium and uterine cavity is difficult to obtain, additional sonographic techniques will be offered. These may include transabdominal and transrectal sonography. Sonographic assessment must include the following:
1. Measurement of endometrial thickness
2. Doppler ultrasonography
3. Description of any associated anomalies
4. A subjective pattern recognition impression

Ultrasound examiners will classify findings according to the following two criteria:
1. Endometrial thickness (ET): ET <4.0 mm (negative), ET ≥4.0 mm (positive), or uninformative and,
2. Subjective pattern recognition (based on morphological features and colour Doppler findings): likely benign, likely cancer or inconclusive.
Both outcomes will be recorded immediately after the ultrasound procedure and prior to obtaining histology and/or any other procedures.

3. Endometrial sampling
In women with a uniformly thickened endometrium of at least 4 mm, endometrial sampling via pipelle biopsy will be offered in the outpatient setting. If declined or unsuccessful, a hysteroscopic biopsy will be offered. In women with focal pathology warranting histological assessment, such as an endometrial polyp, a hysteroscopy and biopsy and/or polypectomy will be offered. All samples will be histologically assessed, and histology will act as the reference standard for the study. Where other histological samples are used to make a diagnosis, such as a biopsy from a distant organ or a hysterectomy, these will be considered when determining the final diagnosis. The tissue will be examined by the histopathologists who will assign a tissue diagnosis of EC or no EC.

Intervention Type
Other

Primary outcome(s)
The 'real world' diagnostic performance (sensitivity, specificity, positive and negative predictive values) of the WIDTM-qEC test as first-line triage for a cohort of women from the ‘Black’ and ‘Black Mixed’ ethnic groups referred with abnormal vaginal bleeding. WIDTM-qEC test and ultrasound diagnostic performance will be measured when the patient initially presents to the

hospital. Vaginal sample is taken at the time of the initial ultrasound scan. Where endometrial sampling or hysterectomy is required, this will typically occur within 4 weeks.

Key secondary outcome(s))
1. Number of ultrasound and other imaging investigations required in WIDTM-qEC true-positive and false-negative patients to reach a histological diagnosis, measured using ultrasound +/- Pipelle biopsy at initial presentation, and hysteroscopy/endometrial biopsy and/or hysterectomy 1-4 weeks later, respectively.
2. Stage, histology, and grade of disease at diagnosis and relation to WIDTM-qEC and TVUS findings, measured using surgical staging of histopathology specimens after a hysterectomy (+/- other procedures) has been performed, typically within 4 weeks.
3. Rates of inconclusive results with both the WIDTM-qEC test and TVUS, measured using the number of diagnostic procedures carried out throughout the patient's journey to assess the cause of abnormal vaginal bleeding.

Completion date

Eligibility

Key inclusion criteria
1. Women aged 50 years and above
2. Experiencing abnormal vaginal bleeding warranting ultrasound examination
3. Able to give informed consent
4. Fall under one of the following self-defined ethnic categories:
4.1. Black, African, or Caribbean
4.2. Mixed/ multiple ethnic groups (Black African or Caribbean and other ethnic background)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 years

Sex
Female

Key exclusion criteria
1. Current hormone replacement therapy (HRT) use
2. History of hysterectomy

Date of first enrolment
23/01/2024

Date of final enrolment

31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Golden Jubilee Wing Suite 3, King's College Hospital
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Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
The Eve Appeal

Funder Name
Universität Innsbruck

Alternative Name(s)
University of Innsbruck, uibk

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Austria

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be available upon request from the principal investigator Prof. Martin Widschwendter (m.widschwendter@ucl.ac.uk).

IPD sharing plan summary
Available on request