ISRCTN13132810 https://doi.org/10.1186/ISRCTN13132810

Urine human papillomavirus (HPV) testing for cervical pre-cancer screening

Submission date
27/01/2021

Recruitment status
No longer recruiting

Registration date
18/02/2021

Overall study status
Ongoing

Last Edited
17/01/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Current plain English summary as of 18/01/2022:

Background and study aims
Cervical screening can save lives from cervical cancer, yet only 7 in 10 women in the UK attend screening, the lowest rate in 20 years. Reasons include embarrassment, fear of examination and inconvenience. Cervical screening is carried out by collecting cells from the cervix (neck of the womb) with a soft brush. These cells are tested for a virus known to cause cancer called human papillomavirus (HPV). If HPV is detected, the cells are examined under the microscope. If they look abnormal, the woman is referred to colposcopy clinic, where cells that are found to be 'pre-cancerous' (cells with the potential to become cancer cells) are identified and treated. To increase screening rates, vaginal 'self-sampling' has been tried, where a woman collects cells from her vagina at home and returns the sample by post, however only 1 in 10 women return the sample. There is therefore an urgent need for new ways to reverse declining rates of cervical screening.

We have developed a urine test that can detect HPV. This test has the potential to remove many of the current barriers to screening and could substantially increase the number of women attending. This study will see if a urine test can accurately identify women with cervical pre-cancer and those who continue to be HPV positive after treatment by comparing HPV detection rates in urine and cervical samples.

Who can participate?
Women, or people with a cervix attending gynaecology and colposcopy clinics at Manchester University NHS Foundation Trust for cervical screening or management of abnormal cervical screening

What does the study involve?
Participants will be asked to provide a first void urine sample prior to a routine cervical screening test. Individuals requiring test of cure cervical screening will also be asked to self-collect a vaginal sample. Samples will be tested for high-risk HPV and urine/cervical HPV-positive samples will undergo methylation testing. Women will be asked to complete a short questionnaire to understand views and preferences of current cervical screening attendees. This study will help

establish whether the clinical performance of urine testing is sufficient to recommend its use as an NHS cervical screening test.

What are the possible benefits and risks of participating?
There are no immediate benefits to the individual taking part in this study. We will use the results to help us know whether urine HPV testing could be a reasonable alternative to routine cervical screening. This could encourage more women to participate in cervical screening in the future.
We do not expect there to be any side effects by taking part. Some participants may find a smear test uncomfortable, painful or embarrassing. For some women the smear test will be taken as part of their routine care investigations anyway.

Where is the study run from?
Manchester University NHS Foundation Trust (UK)

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

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Suzanne Carter (public), suzanne.carter@manchester.ac.uk
Prof. Emma Crosbie (scientific), emma.crosbie@manchester.ac.uk

Contact information

Type(s)
Public

Contact name
Miss Suzanne Carter

Contact details
The University of Manchester
Division of Cancer Sciences
School of Medical Sciences
Faculty of Biology, Medicine and Health
St Mary's Hospital
Manchester
United Kingdom
M13 9WL
+44 (0)161 701 6941
suzanne.carter@manchester.ac.uk

Type(s)
Scientific

Contact name
Prof Emma Crosbie

ORCID ID
https://orcid.org/0000-0003-0284-8630

Contact details
The University of Manchester
Division of Cancer Sciences
School of Medical Sciences
Faculty of Biology, Medicine and Health
St Mary's Hospital
Manchester
United Kingdom
M13 9WL
+44 (0)161 701 6942
emma.crosbie@manchester.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
286415

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 286415, CMPS 47016

Study information

Scientific Title
Urine HPV testing for cervical screening in women: Alternative CErvical Screening (ACES)

Acronym
ACES

Study objectives
The aims of this study are to optimise urine HPV testing, assess urinary HPV +/- methylation testing for the detection of CIN2+ in a colposcopy referral population, and establish the acceptability of urine HPV testing as an alternative to routine cervical screening.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/11/2020, North West Great Manchester West Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8068; gmwest.rec@hra.nhs.uk), ref: 20/NW/0389

Study design
Observational cross-sectional study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Diagnostic accuracy of urine HPV testing for cervical screening

Interventions
Current intervention as of 11/04/2023:
This study will see if a urine test can accurately identify women with cervical pre-cancer and those who continue to be HPV-positive after treatment by comparing HPV detection rates in urine and cervical samples. Matched urine and cervical samples will be tested for high-risk HPV. HPV-positive samples will undergo methylation testing. Vaginal self-samples will also be taken in a sub-set of participants undergoing Test of Cure.

Prior to routine clinic procedures, we will collect a voided urine sample and an optional self-collected vaginal sample. Samples will be self collected at hospital, in the privacy of the clinic bathroom, or by the participant in their own home. Collection must be done before routine procedures to mirror what would happen in 'real life' if a urine test were to replace routine screening. It must also be done on the same day as the cervical sample, to preclude changes in viral status between sampling time points affecting the validity of the results. We will then take a routine cervical screening ('Pap' smear) sample if one is not taken as part of the participant's routine care.

We will directly compare HPV detection rates at standard concentration thresholds, concordance between urine and matched cervical samples and CIN2+ detection rates in urine samples collected with and without Colli-Pee™ or other CE marked urine collection device. We will also compare HPV detection rates for vaginal self sampling, in those have provided a sample.

If the participant attends for a follow up visit (e.g. for treatment after initial assessment), we may ask them to provide a second or third set of samples, if they consent. This will help us understand more about how well the urine test could work during the natural history of HPV infection and the management of abnormal smears.

Participants will answer a short cross-sectional acceptability questionnaire to gauge views on urine and vaginal testing for cervical screening. Those who decline participation will be asked to record their reasons on a short questionnaire. This is entirely optional.

First the researchers will optimise urine collection and processing using various collection devices and preservative solutions. Next, they will carry out a randomised controlled trial of urine collection using a sterile pot or a 10ml Colli-Pee™ urine collection device + Preservative. A selection of participant samples may also be tested using a variety of NHSCSP-approved HPV tests without the need for randomisation and/or asked to provide a vaginal self sample.

Previous intervention as of 18/01/2022:
This study will see if a urine test can accurately identify women with cervical pre-cancer and those who continue to be HPV positive after treatment by comparing HPV detection rates in urine and cervical samples. Matched urine and cervical samples will be tested for high risk HPV. HPV positive samples will undergo methylation testing.

Prior to routine clinic procedures, we will collect a voided urine sample. Urine samples will be self collected at hospital, in the privacy of the clinic bathroom, or by the participant in their own home. Urine collection must be done before routine procedures to mirror what would happen in 'real life' if a urine test were to replace routine screening. It must also be done on the same day as the cervical sample, to preclude changes in viral status between sampling time points affecting the validity of the results. We will then take a routine cervical screening ('Pap' smear) sample if one is not taken as part of the participant's routine care.

We will directly compare HPV detection rates at standard concentration thresholds, concordance between urine and matched cervical samples and CIN2+ detection rates in urine samples collected with and without Colli-Pee™ or other CE marked urine collection device.

If the participant attends for a follow up visit (e.g. for treatment after initial assessment), we may ask them to provide a second or third set of samples, if they consent. This will help us understand more about how well the urine test could work during the natural history of HPV infection and the management of abnormal smears.

Participants will answer a short cross sectional acceptability questionnaire to gauge views on urine testing for cervical screening. Those who decline participation will be asked to record their reasons on a short questionnaire. This is entirely optional.

First the researchers will optimise urine collection and processing using various collection devices and preservative solutions. Next, they will carry out a randomised controlled trial of urine collection using a sterile pot or a 10ml Colli-Pee™ urine collection device + Preservative. A selection of participant samples may also be tested using a variety of NHSCSP-approved HPV tests without the need for randomisation.

———

Previous intervention:

This study will see if a urine test can accurately identify cervical pre-cancer by comparing HPV detection rates in urine and cervical samples. Matched urine and cervical samples will be tested for high risk HPV. HPV positive samples will undergo methylation testing.

Prior to routine clinic procedures, we will collect a voided urine sample. Urine samples will be self collected at hospital, in the privacy of the clinic bathroom. Urine collection must be done before routine procedures to mirror what would happen in 'real life' if a urine test were to replace routine screening. It must also be done on the same day as the cervical sample, to preclude changes in viral status between sampling time points affecting the validity of the results. We will then take a routine cervical screening ('Pap' smear) sample if one is not taken as part of the participant's routine care.

We will directly compare HPV detection rates at standard concentration thresholds, concordance between urine and matched cervical samples and CIN2+ detection rates in urine samples collected with and without Colli-Pee™ or other CE marked urine collection device.

If the participant attends for a follow up visit (e.g. for treatment after initial assessment), we may ask them to provide a second or third set of samples, if they consent. This will help us understand more about how well the urine test could work during the natural history of HPV infection and the management of abnormal smears.

Participants will answer a short cross sectional acceptability questionnaire to gauge views on urine testing for cervical screening. Those who decline participation will be asked to record their reasons on a short questionnaire. This is entirely optional.

Added 28/09/2021:
First the researchers will optimise urine collection and processing using various collection devices and preservative solutions. Next, they will carry out a randomised controlled trial of urine collection using a sterile pot or a 10ml Colli-Pee™ urine collection device + Preservative. A selection of participant samples may also be tested using a variety of NHSCSP-approved HPV tests without the need for randomisation.

Intervention Type
Other

Primary outcome(s)
1. HR HPV measured in urine sample at baseline
2. CIN2+ via routine cervical screening obtained from clinical test results
The above measures will be used to calculate sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of the urine HPV test

Key secondary outcome(s))
Current secondary outcome measures as of 11/04/2023:
1. Presence of clinically important HPV infection measured using urine HPV / methylation test at baseline (used to calculate diagnostic test accuracy (sensitivity, specificity, NPV and PPV))
2. HPV results from urine collected via a plain sterile urine pot and urine collected via Colli-Pee or alternative sampling device at baseline
3. Preference for urine or vaginal sampling compared to routine sampling for cervical screening assessed by participant questionnaire at baseline
4. To measure the concordance of urinary, vaginal and cervical HPV test results

———

Previous secondary outcome measures:
1. Presence of clinically important HPV infection measured using urine HPV / methylation test at baseline (used to calculate diagnostic test accuracy (sensitivity, specificity, NPV and PPV))
2. HPV results from urine collected via a plain sterile urine pot and urine collected via Colli-Pee or alternative sampling device at baseline
3. Preference for urine compared to routine sampling for cervical screening assessed by participant questionnaire at baseline

Completion date
31/12/2026

Eligibility

Key inclusion criteria

Current inclusion criteria as of 18/01/2022:
1. Age 24 -70 years
2. Written, informed consent to participate
3. Attended or attending gynaecology or colposcopy clinic at Manchester University NHS Foundation Trust
4. Undergoing cervical screening, management of abnormal cervical screening or assessment of gynaecological symptoms

Previous inclusion criteria as of 28/09/2021:
1. Age 24 -70 years
2. Written, informed consent to participate
3. Attending gynaecology or colposcopy clinic at Manchester University NHS Foundation Trust
4. Undergoing cervical screening, management of abnormal cervical screening or assessment of gynaecological symptoms

Previous inclusion criteria:
1. Age 25 - 70 years
2. Written, informed consent to participate
3. Attending gynaecology or colposcopy clinic at Manchester University NHS Foundation Trust
4. Undergoing cervical screening, management of abnormal cervical screening or assessment of gynaecological symptoms

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
24 years

Upper age limit
70 years

Sex
Female

Key exclusion criteria
Current exclusion criteria as of 11/04/2023:
1. Pregnant
2. Previous hysterectomy
3. Unable to produce a urine sample and/or vaginal sample
4. Unable to comprehend the Patient Information Sheet and consent form
5. Any condition that would compromise participant safety or data integrity

———

Previous exclusion criteria:
1. Pregnant

2. Previous hysterectomy
3. Unable to produce a urine sample
4. Unable to comprehend the Patient Information Sheet and consent form
5. Any condition that would compromise participant safety or data integrity

Date of first enrolment
22/02/2021

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St Mary's Hospital
Manchester University NHS Foundation Trust
Oxford Road
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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
We plan to share anonymised, non editable, participant level data with other researchers upon reasonable request. No identifiable confidential information will be shared. Participants will consent to this via the study consent form.

IPD sharing plan summary
Available on request

Study outputs

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