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ACES primary care: Alternative cervical screening in primary care

Submission date 08/03/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 09/03/2022	**Overall study status** Completed	
Last Edited 11/04/2023	**Condition category** Cancer	

Plain English summary of protocol

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 by comparing HPV detection rates in urine and cervical samples.

Who can participate?
Women and people with a cervix attending routine cervical screening appointments at participating GP practices or NHS clinics.

What does the study involve?
Individuals will be asked to complete some brief questions about their health and provide a first void urine sample. They will also be asked to complete a short questionnaire to understand views and preferences of current cervical screening attendees. Samples will be tested for high-risk HPV and HPV-positive samples will undergo methylation testing.
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 of taking part.

Where is the study run from?
The University of Manchester (UK)

When is the study starting and how long is it expected to run for?
September 2020 to December 2024

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

Study website
https://sites.manchester.ac.uk/aces/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil Known

IRAS number
309113

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 309113, CPMS 51674

Study information

Scientific Title
Urine HPV testing for cervical screening in primary care

Acronym
ACES Primary Care

Study objectives
Urine HPV testing is an accurate alternative to routine cervical screening in general screening population

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/02/2022, South West - Cornwall & Plymouth Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square, Bristol, BS1 6PN, UK; +44 (0)207 1048071; cornwallandplymouth.rec@hra.nhs.uk), ref 22/SW/0007

Study design
Multicentre observational cross sectional study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
GP practice

Study type(s)
Screening

Participant information sheet
https://sites.manchester.ac.uk/aces/

Health condition(s) or problem(s) studied
Identification of cervical pre cancer in the general screening population using urine HPV testing

Interventions
Current intervention as of 11/04/2023:
This study will see if a urine test can accurately identify individuals with cervical pre-cancer and those who continue to be HPV positive after treatment by comparing HPV detection rates in matched urine and cervical samples. Samples will be tested for high-risk HPV. HPV-positive samples will undergo methylation testing.

Prior to routine clinical procedures, we will collect a voided urine sample. Urine samples will be self-collected at the GP practice or other NHS clinic, in the privacy of the clinic bathroom. Urine will be collected with a Colli-Pee device, which reliably collects a standardised volume of first void urine. 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. A routine cervical screening ('Pap' smear) will then be taken as part of the participant's routine clinical cervical screening care.

We will directly compare HPV detection rates, concordance between urine and matched cervical samples and CIN2+ detection rates in urine samples.

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 acceptability questionnaire to gauge their 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.

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Previous intervention:
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 matched urine and cervical samples. Samples will be tested for high risk HPV. HPV positive samples will undergo methylation testing.

Prior to routine clinical procedures, we will collect a voided urine sample. Urine samples will be self collected at the GP practice, in the privacy of the clinic bathroom. Urine will be collected with a Colli-Pee device, which reliably collects a standardised volume of first void urine. 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. A routine cervical screening ('Pap' smear) will then be taken as part of the participant's routine clinical cervical screening care.

We will directly compare HPV detection rates, concordance between urine and matched cervical samples and CIN2+ detection rates in urine samples.

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 acceptability questionnaire to gauge their 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.

Intervention Type
Other

Primary outcome measure
1. High risk HPV detection rate in matched urine and cervical samples at baseline
2. CIN2+ detection rates according to routine cervical screening outcomes
The above measures will be used to calculate sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of the urine HPV test for CIN2+ detection compared to routine cervical screening

Secondary outcome measures
1. Concordance of HR-HPV+ test results in matched urine and cervical samples measured as in the primary outcome measure at baseline
2. Presence of CIN2+ measured using urine HPV+ test combined with a methylation+ test at baseline (used to calculate diagnostic test accuracy (sensitivity, specificity, NPV and PPV)
3. Preference for urine compared to routine sampling for cervical screening assessed by participant questionnaire at baseline
4. Reasons for declining to take part in the study assessed by participant questionnaire at the time of declining

Overall study start date
01/09/2020

Completion date
31/12/2024

Eligibility

Key inclusion criteria

1. Age 24-70 years
2. Written, informed consent to participate
3. Undergoing routine NHS cervical screening or management of abnormal cervical screening

Participant type(s)
Patient

Age group
Adult

Lower age limit
24 Years

Upper age limit
70 Years

Sex
Female

Target number of participants
1,500 - 2,000

Key exclusion criteria
1. Pregnant
2. Previous hysterectomy
3. Unable to provide a urine sample
4. Unable to understand the Participant Information Sheet and consent form
5. Any condition that would compromise participant safety or data integrity

Date of first enrolment
14/03/2022

Date of final enrolment
01/09/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Bowland Medical Practice
52 Bowland Road
Baguley

Manchester
United Kingdom
M23 1JX

Study participating centre
Didsbury Medical Centre - Dr Whitaker
645 Wilmslow Road
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Manchester
United Kingdom
M20 6BA

Study participating centre
Surrey Lodge Practice
11 Anson Road
Victoria Park
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M14 5BY

Study participating centre
The Maples Medical Centre
2 Scout Drive
Newall Green
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M23 2SY

Study participating centre
Ancoats Urban Village Medical Practice
Old Mill Street
Manchester
United Kingdom
M4 6EE

Study participating centre
Hawthorn Medical Centre
Unit K, Fallowfield Shopping Centre
Birchfields Road
Fallowfield
Manchester

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M14 6FS

Study participating centre
Central Manchester University Hospitals NHS Foundation Trust
Trust Headquarters, Cobbett House
Manchester Royal Infirmary
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M13 9WL

Sponsor information

Organisation
University of Manchester

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Sponsor type
University/education

Website
www.manchester.ac.uk

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

Publication and dissemination plan
Planned publication in a high impact peer-reviewed journal.

Intention to publish date
01/09/2025

Individual participant data (IPD) sharing plan
At the end of the project we will deposit a fully anonymised dataset in an open data repository where it will be permanently stored. Researchers at other institutions can access the anonymised data directly from the repository and use it for further research or to check our analysis and results
The data will be completely anonymised and stored on Figshare (https://figshare.manchester.ac.uk/). Researchers at other institutions can access the anonymised data directly from the repository. We are seeking consent from participants for this.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Plain English results			08/08/2022	No	Yes
HRA research summary			28/06/2023	No	No