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Evaluating the feasibility of offering HPV self-sampling kits to those who have not attended the NHS cervical screening programme in England

Submission date
24/09/2020

Recruitment status
No longer recruiting

Registration date
28/10/2020

Overall study status
Completed

Last Edited
30/09/2025

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Background and study aims
In England, cervical screening uptake has been falling for 21 years. London consistently has the lowest uptake nationally. Underscreened women are at the highest risk of cervical cancer. A potential solution is to offer self-sampling for HPV (human papillomavirus) testing: women can take their own sample, in private and at a time and place of their choice.

Research has shown that offering self-sampling increases uptake in non-attenders and that self-samples have similar accuracy to conventional (clinician-taken) samples. Uptake has been highly variable between studies and likely to differ between settings.

To date, all UK studies have been done outside of the national cervical screening programme. Self-samples have not been recorded in the national screening database and not counted towards uptake (and GP financial incentives) and therefore had suboptimal uptake.

A challenge with introducing new tests is establishing robust pathways for accurately identifying the relevant population, recording and reporting results. This will be an implementation feasibility project of offering self-sampling to non-attenders in 5 Clinical Commissioning Groups with the lowest uptake in North and East London. All 212 GP practices will be invited to take part.

Kits will be offered in one of two ways: either a systematic offer where women at the 15 month anniversary of their last test due date without being screened will be mailed a kit; or an opportunistic offer in GP primary care where GPs, nurses and healthcare assistants will be asked to offer eligible women kits when they have an appointment for any reason.

The project will serve to test the new pathways for delivery, generate lessons to help ensure a smooth transition to a wider roll-out, and provide the evidence-base for implementing self-sampling at a larger scale.

Who can participate?
People eligible for the NHS cervical screening programme in England who are at least 6 months overdue cervical screening and are registered at a GP practice in North or East London.

What does the study involve?
Participating GP Practices will be invited to offer self-sampling kits to eligible women during a routine consultation. Eligible women will be flagged by the EMIS patient software. GP Practices will be required to complete data entry into the EMIS patient record to collect information about the self-sampling offer.

Cervical screening data for all eligible women will be collected from GP records during the study and for 6 months after the end of recruitment. GP Practices will also agree for women who are registered at their practice who are most overdue their cervical screening to be sent a self-sampling kit in the post.

Women will take their own sample in the privacy of their home or at the GP Practice. Women will also be invited to complete a questionnaire about their views on cervical screening and self-sampling.

Data will be collected from the national cancer registry at 3 and 6 years following the study.

What are the possible benefits and risks of participating?
Some women find it difficult to make an appointment for cervical screening because they are busy or their GP practice is busy. Some women may find it uncomfortable or embarrassing to have a test taken by a doctor or nurse. If women choose to take part in this study, they will be able to take a test for cervical screening themself. They will not need an appointment or examination. In other studies, some women who had not been for routine cervical screening and took a self-sample were found to have abnormal cervical cells and were successfully treated.

There is a very small chance that the swab could break while taking a sample. However, this is very unlikely unless excessive force is applied to the swab. No one has reported this happening in any of our previous studies. Women who have taken self-samples in our previous studies have not reported any problems. They found the test easy and convenient to do.

No screening test is 100% effective. An HPV infection can sometimes be missed (a ‘false negative result’). It is important to understand the possible risks and benefits of cervical screening. Further information here: www.gov.uk/phe/cervical-screening-leaflet.

Where is the study run from?
King’s College London (UK)

When is the study starting and how long is it expected to run for?
From March 2019 to July 2022

Who is funding the study?
North Central and East London Cancer Alliance (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
264776

Protocol serial number
CPMS 41934, IRAS 264776

Study information

Scientific Title
YouScreen: A pragmatic implementation feasibility clinical trial of offering HPV self-sampling to cervical screening non-attenders within the NHS cervical screening programme in England

Acronym
YouScreen

Study objectives
To estimate the uptake and potential increase in coverage associated with offering HPV self-sampling kits to those who have not attended the NHS cervical screening programme in England.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 15/05/2020, West Midlands -South Birmingham Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, UK; southbirmingham.rec@hra.nhs.uk), ref: 20/WM/0120

Study design
A pragmatic implementation feasibility stepped wedge trial with randomly allocated cluster intervention start dates

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
Malignant neoplasms of female genital organs due to Human papillomavirus (HPV) infection

Interventions
The study aims to test a new pathway for the implementation of self-sampling for non-attenders within the NHS cervical screening in England, and to provide the evidence-base that self-sampling can improve cervical screening coverage in England and to increase detection and treatment of high grade CIN (CIN2+).

This is a pragmatic implementation feasibility clinical trial to be carried out in GP practices in 5 CCGs in North Central London and East London (Barnet, Tower Hamlets, Newham, Camden, Islington).

Self-sampling kits will be offered in two different ways:
1. Direct mail-out (systematic offer) of kits in monthly cycles to women who reach the 15 month anniversary of their last test due date without being screened (identified using the national screening database)
2. Opportunistic offer of kits to women ≥6 months overdue cervical screening according to their electronic GP records in GP primary care when they consult for any reason (GPs, nurses, or healthcare assistants/practitioners)

For direct mail out: Eligible women will be identified using the national cervical screening database NHAIS (National Health Application and Infrastructure Services - owned by NHS England and Public Health England).

Each month from the date the practice is included, a list of women who reach the 15 month anniversary of their last test due date without being screened (by self-sample or standard cervical screening (HPV primary testing) will be extracted from NHAIS. This 15 month timepoint has been chosen so as to avoid the usual call/recall screening reminder letters.

NHAIS will send the list of eligible women to the Cervical Screening Administration Service (CSAS) who are responsible for sending invitations and reminders for the call/recall Cervical Screening Programme in England. CSAS will then send the list to a commercial print company (contracted by KCL) with the appropriate level of information governance standards to securely handle NHS data

The print company will send a pre-notification letter to women (on behalf of the GP practices and the Cervical Screening Programme) informing them that they are overdue cervical screening and that a self-sampling kit will be posted to them. Within 1-2 weeks of sending the letter, the print company will send women a self-sampling kit along with a brief invitation letter.

Women will be instructed to write the date sample taken on the tube label and laboratory request/consent form. Women will collect their self-sample at home and post it directly to the laboratory (Royal Mail freepost) for analysis.

Opportunistic offering Women targeted for opportunistic offering will be identified using the GP patient record software system. Eligible women will be automatically flagged during consultation using the electronic patient record software. GPs, nurses and healthcare practitioners will confirm eligibility -briefly explain the study, provide a kit to those willing to take part, and document which women are offered, accept and decline kits in the electronic patient records.

Women have the option of collecting a self-sample in the GP surgery bathroom or at home. However, to ensure optimal uptake women will be encouraged to collect the sample at the GP practice. Samples will be sent to the NHS Cervical Screening laboratory for London for analysis. Women who take their sample at the GP practice will hand it to a member of staff who will put it in their usual NHS cervical screening collection services or send it to the lab via the post (daily) using free envelopes. Samples taken by women at home will be posted to the lab (postage paid envelope).

Consent
This study will be conducted as closely as possible to the likely pathway self-sampling at the national level. The patient information booklet will be provided in each kit. As only women who wish to participate will return a self-sample (i.e. opt-in), consent is implicit.

The laboratory request/consent form and study invitation letter will state that if consent to participate in the study will be assumed if the sample is returned. It will be made clear in the invitation letter and participant information sheet that if women prefer to have their conventional screening test taken doctor or nurse that they are free to do.

Opportunistic offer
GP primary care is a busy and time-pressured environment with an average GP consultation length of just 9 minutes. In our previous studies of the opportunistic offering of self-sampling in GP primary care the consent procedure consisted of a brief (2 min) study explanation and verbal consent. This simplified approach was suggested by the reviewing REC committee and worked well for both studies with no issues raised. Therefore, we intend to use the same verbal consent procedure for this study. Consent to accept a self-sampling kit will be recorded in the women's GP medical record.

Direct mail out
Consent will be implicit by return of a self-sample. Kits will come with a laboratory request /consent form which will contain the women's details (to identify the women) and statements detailing outlining what the study involves and what they are agreeing to by returning a self-sample.

HPV testing and reporting/recording of results Self-samples will be analysed for the presence of high-risk HPV DNA by the Health Services Laboratory who currently analyse all cervical screening samples for the NHS Cervical Screening Programme in the London.

As this study aims to test the new IT pathways for self-sampling, we plan to integrate self-sampling ordering, processing of samples, results recording and reporting as much as possible into the existing systems for cervical screening programme.

Results will be reported back to GP practices using the usual electronic routes. Women should receive their results letter within two weeks of returning a self-sample.

Self-sampling will be recorded in NHAIS and will elicit the relevant changes in the call/recall pathway in NHAIS. This will allow accurate calculation of the impact of self-sampling on coverage and to test the IT pathways.

Women who test HPV negative on a self-sample will not require any further action or tests. They will have their Next Test Due (NTD) date reset within the national cervical screening (call/recall) programme according to age (3 years if aged 25-49y, 5y if aged 50-64, or if aged 60 or above at the time of testing, they will be ceased from the cervical screening programme - in keeping with the usual auto-ceasing rules).

Women who test HPV positive on a self-sample will be advised in their results letter to have a clinician sample, a clinician-taken (doctor/nurse) cervical screening test at their GP practice. These women who subsequently undergo a standard cervical screening test will be managed according to their results as per routine clinical care under the NHS Cervical Screening Programme (CSP). The women's call/recall status will be updated in NHAIS to early recall in 3 months, and her NTD will be set to 3 months from the date the self-sample was taken (as recorded on the sample tube and laboratory request/consent form).

If a follow-up test (standard cervical screening test) is not received in NHAIS within 10 weeks of the reset NTD (3m), the woman will be added to her GP practices Prior Notification List (PNL). The PNL is a list of women at a GP practice who will be invited to be screened within the next 10

weeks. The purpose of the PNL is to allow GPs to remove women from the list who do not need to be invited for screening (e.g. recent hysterectomy or pregnant). We have requested that NHAIS add women who test HPV positive on a self-sample into the PNL so that they will receive two “reminder” letters to attend for a follow-up (clinician) test.

Self-sampling studies have found that most (~82%) women who test HPV positive attend for follow-up. In our previous study of opportunistically offered kits in London, 85% of women who tested HPV positive on a self-sample attended for follow-up investigations. We will collect details of follow up tests for HPV positives from NHAIS (with women’s permission).

As an additional safety-net, at the end of the study women who have not attended for a follow up test after testing HPV positive (on a self-sample) will be highlighted to their GP practices who will make one further attempt to contact the women to come for a follow up test. This will be either telephone call or text message. Relevant women will be identified by the participating GP practices (designated study administrator) using a pre-written search of the GP records or by the laboratory.

Women who return a sample that is not analysable due to insufficient DNA will be asked to repeat the self-sample. A repeat kit will be sent to them separately by the print company within ~1 week after results are sent. If a woman returns two self-samples which have an insufficient DNA result, she will be advised (in the results letter) to attend her GP practice for a standard cervical screening test (collected by a nurse or doctor).

Invalid samples arriving at the laboratory will be rejected and not analysed. The sample details will be recorded on the central laboratory LIMS database but will not be reported back to the NHAIS database. Samples will be considered to be “rejected” for analysis if they fall under one of the following:
1. Arrive >14 days after the date the sample has been taken (as recorded on the sample tube and lab request/consent form
2. Do not meet the minimum required information on the sample tube and/or lab request /consent form to meet NHSCSP requirements for valid samples
3. Returned by women who are ineligible

As rejected samples will not be analysed or reported to NHAIS, a letter cannot be sent by CSAS. Therefore, the print company (CFH Docmail) will send a letter to women who return an invalid (rejected) sample, informing them of this, and advising them that they will either receive a repeat kit or should book for a clinician-taken sample at their GP practice (as appropriate). The central laboratory will securely send (via secure file transfer protocol (SFTP)) the necessary details to issue these letters and repeat kits to CFH Docmail (NHS number, full name, date of birth, postal address, GP practice code, study ID (encrypted NHS number)). Results will be sent to the GP practices in the usual way (electronic lab links). The trial team at King’s will receive the list of encrypted NHS numbers with date of rejected result in order to ensure sufficient oversight for this process.

Samples returned by women who are ineligible (i.e. women who are not ≥6 months overdue cervical screening) may arise if they receive a kit and are screened by conventional screening or self-sample or if they have received a kit in error. The central laboratory will contact the women’s GP practice to inform them that the sample is rejected and will therefore not be analysed or reported to NHAIS. The GP practice will in turn, contact the woman to inform her that her sample was not analysed because she is not eligible. Detailed instructions for the handling of rejected samples by the laboratory will be included in the YouScreen Laboratory Manual, in accordance with current NHSCSP guidelines.

Women will be asked to opt-in to giving permission for retention of their residual samples by providing their initials into a box on their laboratory request/consent form. In the future, as part of a separate ethical application, we plan to carry out HPV DNA methylation studies on these samples - a test which could help improve self-sampling by identifying women who need onward referral or not if they test HPV positive on a sample. Results will not impact clinical management for women in the study.

Intervention Type
Other

Primary outcome(s)
Current primary outcome measure as of 12/05/2023:
1. Uptake of kits at 30 days, 90 days and at the end of the trial
2. Change in coverage at participating GP practices from the start vs the end of the trial
3. Change in the proportion of nonattenders screened each month due to the intervention

Previous primary outcome measure:
Uptake and increase in coverage associated with self-sampling measured at 30 and 90 days after kits are mailed out and at the end of the trial

Key secondary outcome(s))
1. Rates of compliance with follow-up for women who test HPV positive on a self-sample, measured by their attendance for conventional cervical screening within 6 months of testing HPV positive
2. CIN2+ detection rate of self-sampling, measured by the number of women who have CIN2+ detected at 3 and 6 years after the end of the study
3. Impact of self-sampling on colposcopy referral, measured by the number of referrals for women who returned a self-sample at the end of the study
4. Uptake of self-sampling according to the mode of kit offer, measured by the number of women returned self-sample from each pathway, at the end of the study
5. Impact of self-sampling on inequalities, measured by the distribution of women who have a self-sample result according to ethnic group and area of deprivation, at the end of the study
6. Cost effectiveness of this intervention, measured by the cost of self-sampling kits for the number of women who return a self-sample as a percentage of those women who receive a CIN2+diagnosis, at the end of the study
7. Logistics of testing samples, recording results, and giving women their results in a timely manner, measured by the turnaround time for HPV testing samples, by the mean number of days between laboratory timepoints of sample receipt, analysis, and result reporting
8. Acceptability of self-sampling in cervical screening non-attenders, measured from survey sub-study for all women who return a questionnaire, examined at the end of the study

Completion date
31/07/2022

Eligibility

Key inclusion criteria
1. Aged between 25 and 64 years
2. Eligible for cervical screening under the NHS Cervical Screening Programme (NHSCSP) in England

3. ≥6 months overdue cervical screening
4. Registered at a participating GP practice

A subgroup of eligible women will also be eligible for direct mailout of self-sampling kits who reach the 15 month anniversary of their last test due date without being screened.

*Women aged 65 will not be targeted but if included will not be considered a protocol violation. This is because although women aged 65+ are not invited to routine cervical screening they may still be offered a test if they have not been screened since age 50, or if they have not yet met the criteria to be ceased from the programme.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
25 years

Upper age limit
64 years

Sex
Female

Total final enrolment
8286

Key exclusion criteria
1. Unable to provide informed consent.
2. Under the care of colposcopy within the last 36 months and/or due for a test of cure (HPV test to confirm successful treatment following treatment for cervical abnormalities)
3. Documented in NHAIS to have opted out of cervical screening by returning a signed cervical screening disclaimer form will not be sent a self-sampling kit by direct mail-out. By contrast, women who have opted out of cervical screening may be offered a kit opportunistically at their GP practice at the discretion of the health professional consulted.
4. Pregnant individuals will be advised to not take part in the study. There are no safety concerns with pregnant women self-collecting a vaginal swab, however the study will advise against it for two reasons. The first is that the CE-mark for the Copan 552C.80 FLOQ swab does not cover pregnancy because pregnant women were not included in Copan's validation studies. The second is that there are potential issues with ensuring adequate follow up within the study lifetime if they test HPV positive on a self-sample (colposcopy is less inaccurate due to hormone changes and excisional treatment to the cervix for high-grade cervical disease is sometimes deferred until post-partum). The NHSCSP recommend that those who are pregnant defer cervical screening until 12 weeks post-partum.
5. Documented as being HIV positive in the Cervical Screening Programme are recalled annually (as opposed to 3 or 5 yearly). These individuals will only be included in the opportunistic offering

of self-sampling. By definition, they will never reach the 15 month anniversary of last test due date to trigger direct mail out of a kit as their Next Test Due date is reset every 12 months.

Date of first enrolment
13/01/2021

Date of final enrolment
30/11/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR CRN: North Thames
United Kingdom
W1T 7HA

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
North Central and East London Cancer Alliance

Funder Name
National Institute for Health Research (NIHR) (UK)

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
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		16/07/2024	24/10/2024	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Questionnaire results	03/07/2024	03/07/2024	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 7.0	05/01/2022	06/10/2022	No	No
Protocol file	version 8.0	13/10/2022	30/09/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes