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Can the addition of a stool and urine test rule out significant bowel disease and by doing so, reduce unnecessary invasive colonoscopies – the right test for the right patient?

Submission date
17/08/2020

Recruitment status
No longer recruiting

Registration date
28/09/2020

Overall study status
Completed

Last Edited
06/06/2025

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Investigating people with bowel symptoms uses a test that detects traces of blood in the stools, the Faecal Immunochemical Testing (FIT) test. There are many possible reasons for positive tests. A few people have cancer, but most patients with symptoms don't have any serious bowel disease, rather they have benign problems such as piles or irritable bowel syndrome (IBS). It is very difficult to diagnose on FIT alone, those patients who have serious bowel disease and those who do not.
After a test, people are invited for colonoscopy – a sort of camera examination of the large bowel. Most people invited for colonoscopy don't have cancer. Only about 5% of those with positive FIT tests have cancer. About 25% have other significant bowel diseases, but most have nothing seriously wrong at all. So, they have the inconvenience and discomfort of a colonoscopy but don't get any benefit from it, plus the NHS incurs costs and resources which could be avoided.
Researchers want to try adding another test, the Volatile Organic Compound (VOC) test (from a urine sample), to see if they can separate those with positive FIT tests who do have something wrong from those who don't. Using both tests might be better for detecting cancer as FIT alone misses about 20% of cancers. The researchers think that using both tests might not only be better for detecting cancer, but also might mean that a lot of people will avoid having to have a colonoscopy.

Who can participate?
Patients aged 18 or older with bowel symptoms

What does the study involve?
Participants will provide stool samples for FIT and urine samples for VOC analysis. They will all have a colonoscopy to get a definite diagnosis. Then the researchers will look at their FIT and VOC results to see if a serious bowel disease diagnosis can be made from these tests alone.

What are the possible benefits and risks of participating?
No benefits are envisaged for the patient aside from contributing to the development of future improved medical diagnostic devices. No risks anticipated with this study.

Where is the study run from?
University Hospital Coventry and Warwickshire (UK)

When is the study starting and how long is it expected to run for?
May 2020 to October 2023 (updated 15/09/2021, previously: October 2022)

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

Who is the main contact?
recedestudyoffice@uhcw.nhs.uk

Study website
https://www.uhcw.nhs.uk/leading-research/about-us/our-research/recede/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
282247

ClinicalTrials.gov number
NCT04516785

Secondary identifying numbers

CPMS 45601, IRAS 282247

Study information

Scientific Title
Reducing colonoscopies in patients without significant bowel disease

Acronym
RECEDE

Study objectives
Dual testing of stool Faecal Immunochemical Testing (FIT) and urine Volatile Organic Compound (VOC) analysis is more sensitive in detecting significant bowel disease than FIT alone when compared with colonoscopy.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/08/2020, Liverpool Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)2071048016; liverpoolcentral.rec@hra.nhs.uk), REC ref: 20/NW/0346

Study design
Multicenter observational cross-sectional study

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Oral and gastrointestinal

Interventions
This is a multi-centre, prospective diagnostic accuracy study involving secondary care sites in the UK. PIs or Research/Clinical staff at each site will be responsible for identifying the participants. Participants can be recruited from either gastrointestinal or surgical colorectal clinics who are placed on the referral list either routinely with lower gastrointestinal symptoms or urgently

(fulfilling the national criteria for referral - NICE NG12). The potential list of participants will then be cross-checked against the inclusion criteria. An information pack can be sent out to these participants before a conversation over the phone or face to face at their clinic appointment. Should the overseeing clinician recommend the participant requires a colonoscopy, the participant will be asked if they would like to be involved in the study and they will then undergo the consenting process, which can be completed either verbally over the phone, or face to face in the clinic. The study details will be explained to them and they will be encouraged to ask questions to ensure they fully understand the protocol. They will have the right to refuse to take part in the study without giving any reasons. They will also remain free to withdraw at any time from the study without giving a reason. If a site doesn't have capacity to approach participants on the day of their 1st clinic visit then verbal consent will be obtained over the telephone and documented on the consent form. Upon obtaining consent (verbal or written), participants will be enrolled onto the study. The specimen collection pack will then be given to participants (or posted if consent is obtained over the phone). A pack containing: 1 pre-paid return envelope (for stool sample), 1 pre-labelled return envelope (for urine sample), stool sample collection device, Universal Sterilin sample pots for spot urine and pictorial instructions for sample collection will be given to all of the enrolled participants. If the participant is able, they can provide their urine sample during their first clinic visit, however they will also have the option to collect urine samples at home and post/bring back to the hospital. All stool samples will be collected at the participants home by the participants and posted directly to the Rugby Bowel Cancer Screening Hub for analysis with participant number and date of sample being recorded. All the samples will be collected at least 24 hours prior to the bowel preparation. Both time of collection and time of receipt of the samples at the laboratory will be recorded.

Stool sample collection
A standard FIT picker stool retrieval kit for the HM Jack FIT analyser will be utilised to ensure standardisation of stool sampling. The participants will be asked to collect samples prior to consumption of bowel cleansing preparation. The collected samples will be directly posted to Rugby bowel cancer screening hub by participants in a pre-paid postage envelope (provided). Once contained within the FIT picker, a fixed faecal aliquot is stable from degradation of haemoglobin. Time of collection of samples will be recorded. Quantitative FIT will be undertaken using the automated HM-JACKarc analyser (Kyowa Medex, Tokyo, Japan) as described in our previous publications and in line with the United Kingdom Accreditation Service, UK (UKAS) standard ISO 15189. Samples which are older than 14 days from the time of collection will be excluded from analysis.

Urine sample collection
Each participant will be asked to provide two spot urine samples in universal Sterilin pots. The participants will be asked to collect samples prior to consumption of bowel cleansing preparation. Participants will be requested to collect the urine sample during their 1st clinic appointment once consented. Or, if collecting at home, urine samples must be collected in the morning and either handed over at their GP centres before 10 o'clock the same day to be delivered back to their respective trusts via routine GP courier service OR delivered by the participant back to their trust on the day of their colonoscopy exam. These samples will then be stored at the NHS trusts in a freezer at -80°C. These will then be transported to UHCW in batches via a specialised courier service and stored at the Arden tissue bank until analysis. Both the time of collection and the time of receipt of samples at the site will be recorded. One urine sample will be thawed for analysis and the second one will be kept as a backup (Test for urine VOC will be performed on this sample if it becomes necessary or may be used for future research if the patient consents to this). Thereafter samples will be sent for analysis on dry ice to the Manchester analytical lab (all samples will be sent here) and the UK National Measurement Laboratory (a subset of 100 samples will be sent here) in batches of 30. Once in the lab, they will

be frozen until analysis. Records of the cold chain will be kept by individual and central sites up to storage at -80°C and between storage and analysis.

A subset of 100 samples will be analysed at the National Measurement Laboratory. Urine VOC analysis using established reference methods will be undertaken here which is the national measurement laboratory for chemical and bio-measurement. Gas-chromatography mass spectroscopy system (GCMS) is considered the gold standard for VOC analysis and is commonly used to identify unknown chemicals. It comprises of a GC front-end, which separates complex mixtures of chemical based on their interaction with a retentive layer, resulting in chemical eluding out of the GC at different times (called the retention time). These individual chemicals are then ionised and the mass of the resultant fragments measured. As each chemical always fragments the same way, we can use these to identify specific chemicals. This will be used to validate the headspace sampling methods to be used and to provide an independent analysis of potential volatile biomarkers for the medical conditions of interest in this study. This will feed into subsequent “electronic nose” analysis.

All samples will be analysed for urinary volatiles in Manchester using “electronic nose” techniques using an array of gas sensors coupled with an appropriate polymeric pre-concentrator. This technique provides multivariate data documenting differences in the chemical composition of the urinary volatiles that may contain volatile biomarkers for a condition. This allows screening of populations rapidly using chemometric data analysis, neural networks and receiver operator curves to distinguish one population from another, with receiver operating curves being used to measure the appropriate thresholds to be set to distinguish samples sample as having colon cancer, colorectal adenomas, inflammatory bowel disease or microscopic colitis. Unlike GCMS – this technique does not provide identities of individual biomarkers but considers the data derived from the entire complex mixture of volatile chemicals that are present in urine headspace. A receiver characteristic curve of 0.63 or greater will be applied for the detection of SBD.

If new improved methods of analysis become available during the study, then these will be employed.

Health Economics
An economic analysis will be carried out to determine the costs, benefits and overall cost-effectiveness of FIT + VOC versus FIT in patients with gastrointestinal symptoms referred for further investigation. The analysis will be carried out principally from the perspective of the NHS and Personal Social Services. Calculations will consider all key costs and consequences, including the costs and ‘disutility’ associated with having a colonoscopy.

A smaller sample of participants (n=370, 20% of total) at UHCW will be asked to fill in the EQ-5D-5L questionnaire at 5 points surrounding their colonoscopy if they provide consent for this. This questionnaire measures the disutility associated with having a colonoscopy. The EQ-5D is a widely used validated generic measure of health-related quality of life that enables the calculation of quality-adjusted life years and is recommended for use in economic evaluations in health care. The collected information will enable us to obtain insights into the impact of the procedure (including the preparation) on patients’ quality of life. This questionnaire will be given to participants (either electronically or via post, including a pre-paid return envelope) at five time points: (i) at baseline, defined as upon enrolment (ii) immediately before colonoscopy following bowel cleansing procedure (iii) 24 hours after colonoscopy (iv) 72 hours after colonoscopy and (v) 3 weeks after colonoscopy, once a diagnosis is confirmed. Two non-validated questionnaires will be issued alongside the second and fifth EQ-5D which asks participants whether they have had any consultations or appointments with healthcare officials

for reasons related to their bowel symptoms or colonoscopy procedure outside of their routine care and whether they have incurred any costs relating to their colonoscopy procedure. All information provided on all questionnaires will be anonymous and only delegated research staff at UHCW will have access to this data.

Intervention Type
Other

Primary outcome measure
Diagnostic accuracy (defined as sensitivity, specificity, negative predictive value and positive predictive value) of stool FIT plus urine VOC analysis compared to stool FIT alone in the detection of significant bowel disease. Stool samples will be measured using the automated HM-JACKarc analyser (Kyowa Medex, Tokyo, Japan) for the concentration of blood present, whereas urine samples will be measured for the presence of VOCs using GCMS. Timepoint(s): Samples will be collected before the participant begins their bowel cleansing medication. Results will be available once colonoscopy histology findings are received, normally 6 weeks after colonoscopy.

Secondary outcome measures
1. Diagnostic accuracy of stool FIT plus urine VOC in the detection of SBD: collection of data as for the primary outcome measure. However, the researchers will attempt to develop an optimum threshold for significant bowel disease diagnosis for both FIT and VOC tests.
2. The potential number of colonoscopies avoided in those without SBD: results of FIT and VOC will be compared to colonoscopy histology findings to see how many patients could have avoided a colonoscopy, calculated once histology findings are available
3. Total NHS and personal social services costs: total money spent by NHS on unnecessary colonoscopies which could have been avoided
4. Total quality-adjusted life-years associated with each option, measured using EQ-5D-5L questionnaires at baseline, immediately before colonoscopy, 24 hours, 72 hours and 3 weeks after colonoscopy
5. Resource use measured using questionnaires immediately before colonoscopy and 3 weeks after colonoscopy

Overall study start date
01/05/2020

Completion date
28/10/2023

Eligibility

Key inclusion criteria
1. All patients referred either routinely with lower gastrointestinal symptoms or urgently (fulfilling the national criteria for referral - NICE NG12) for colonoscopy
2. Minimum age of 18
3. Ability to provide informed consent
4. Ability to return both stool and urine samples

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 1,819; UK Sample Size: 1,819

Key exclusion criteria
Pregnant

Date of first enrolment
21/09/2020

Date of final enrolment
30/09/2022

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospital Coventry & Warwickshire
Clifford Bridge Road
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Sponsor information

Organisation
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Sponsor type
Hospital/treatment centre

Website
http://www.uhcw.nhs.uk/

ROR
https://ror.org/025n38288

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC); Grant Codes: NIHR127800

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

Publication and dissemination plan

The protocol will be published in the BMJ Open once recruitment officially opens. The researchers are preparing a health economics plan and statistical analysis plan for the project, but these are not ready yet.

A range of dissemination products to include annual reports, national publications, press releases through UHCW's Communications Department, participant safety collaborations, presentation and talks as well as videos will be included to ensure that all audiences can be updated. The team has close links with the West Midlands Academic Health Science Network (AHSN) and will make use of the Meridian Health Innovation Exchange Platform (https://meridian.wmahsn.org) to disseminate the results of the study. Through this, the wider national network of AHSN's will also be exploited for this purpose together with UHCW Communications and other online stakeholder case study platforms, including MidTECH and NHS Innovation Hub for the West Midlands region.

Intention to publish date
31/10/2024

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current 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?
Protocol article		30/03/2022	20/10/2022	Yes	No
HRA research summary			28/06/2023	No	No