ISRCTN85044808 https://doi.org/10.1186/ISRCTN85044808

Assessing the use of a capsule sponge device as a screening tool to identify signs of the precancerous condition Barret's oesophagus in patients with heartburn, acid reflux and indigestion symptoms

Submission date 26/06/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 12/09/2024	**Overall study status** Ongoing	
Last Edited 12/09/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Oesophageal cancer is a poor prognosis cancer, and the current clinical pathways are ineffective for early diagnosis. The capsule sponge test provides a quick, less invasive method to test for signs of Barrett's Oesophagus and early cancer and we now need to understand the impact of the capsule sponge test on mortality before adopting this test into a national population-based targeted screening programme.
This study aims to:
1. Conduct a trial of targeted screening using the capsule sponge test to evaluate the effect on oesophageal adenocarcinoma-associated illness and death
2. Establish a biobank of samples and data with gastro-oesophageal reflux disease for use in other research studies
3. Establish a cohort of patients with gastro-oesophageal reflux disease who are willing to be contacted regarding further research studies such as behavioural studies, lifestyle interventions, and chemopreventive medications to reduce the risk of progression of the disease.

Who can participate?
Men aged 55-79 years and women aged 65-79 years

What does the study involve? (for participants)
Participants will join the Heartburn health programme and will receive regular newsletters and be invited to join future research studies. Some participants will also be invited to join the BEST4 Screening Trial and offered a capsule sponge test in their local area.

What are the possible benefits and risks of participating?
Participants will have access to the Heartburn Health programme, a platform which will provide resources to support participants with heartburn, acid reflux and indigestion symptoms. This will

include educational information on how to best manage symptoms and offer opportunities to participate in research studies. Some participants will also be enrolled on the BEST4 Screening trial and could have a capsule sponge test.

Where is the study run from?
Cancer Research UK Clinical Trials Unit and Queen Mary's University of London (UK)

When is the study starting and how long is it expected to run for?
October 2022 to June 2036

Who is funding the study?
1. Cancer Research UK
2. National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
best4-management@qmul.ac.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
332589

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 57984, NIHR135565, IRAS 332589

Study information

Scientific Title
Barrett’s oESophagus Trial 4 (BEST4): a randomised control trial comparing capsule sponge test screening to usual care

Acronym
BEST4 Screening Trial

Study objectives
The aim of the trial is to assess the use of the capsule sponge device as a screening tool to identify signs of the premalignant condition Barret's oesophagus (BO), which can often be a precursor for oesophageal adenocarcinoma (OAC).

The other aim of the trial is to build a cohort of participants with gastro-oesophageal reflux disease (GORD), who have consented to health-related data collection and to be contacted further regarding research opportunities.

It is hypothesised that the capsule sponge test can be used to screen and lead to early detection of early-stage BO-related neoplasia which could lead to a decrease in OAC-associated mortality.

It is hypothesised that establishing a cohort of people with gastro-oesophageal reflux disease (including many with BO) who are willing to participate in research, have consented to allow researchers to access their medical records and are willing to provide longitudinal clinical samples (including blood, saliva and capsule sponge) will accelerate progress towards the understanding of the neoplastic process in OAC and lead to advances in prevention, early detection, and management of these patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/03/2024, West Midlands – South Birmingham REC (Health Research Authority, 2 Redman Place, Stratford, E20 1JQ, UK; +44 (0)2071048121, +44 (0)207 104 8019; southbirmingham.rec@hra.nhs.uk), ref: 24/WM/0017

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Barret's oesophagus

Interventions
The BEST4 Screening study aims to recruit 120,000 people (men aged 55-79 years and women aged 65-79 years) with heartburn over a two-and-a-half-year period. This recruitment will take place across four different Regional Research Delivery Networks (RRDNs), these being Yorkshire & Humber, East Midlands, East of England and South East Central. Identification of suitable patients for inclusion will be handled by NHS Digitrials and iPLATO, a trusted NHS primary care digital patient engagement provider. NHS Digitrials will employ the specified inclusion and exclusion criteria via in their search of the NHSE Patient Demographic Service for data extracts for the invitation process. Patients will be initially invited to join the 'Heartburn Health Programme'. The programme will establish the Bioresource and also act as the first stage of participant identification. Participants will be invited to join the programme, by iPLATO, via one of two routes:
1. SMS text messages
2. Advertisement through the iPlato myGP app

Upon consenting to join the programme, participants will be asked if they would be interested in a capsule sponge test if it was available locally. Those that express interest will be randomised at a 2:1 ratio, control and intervention arm, respectively. Those in the control arm (n = 80,000) will not be contacted again nor consented to the Screening trial (Zelen design). Those in the investigational arm (n = 40,000) will then be invited to book an appointment on a local mobile unit in order to have the capsule sponge test. The qualified nurses and mobile units used in the trial will be provided by EMS healthcare.

For the intervention cohort, those who attend an appointment will provide informed consent before carrying out any procedures. Participants will have the opportunity to discuss the nature and objectives of the trial, and possible risks associated with their participation with a member of the Cambridge Clinical team (prior to their appointment via telephone) or EMS Unit staff (at the time of their appointment at the mobile unit). Participants will have a baseline visit and will only have a follow-up appointment in the event of an insufficient result (repeat capsule sponge test) or positive capsule sponge test (endoscopy).

Capsule sponge samples collected during the trial will be sent to a central laboratory (Cyted Ltd) to look for specific markers such as TFF3, p53 and atypia. The results of the capsule sponge test will be shared directly with the BEST4 Clinical Team via the BEST4 database. Participants with a negative result will be informed by text message. If a participant receives a negative result with other relevant clinical findings, they will be sent a letter and an email will be sent to their GP. If the participant receives a positive result, the Cambridge Clinical team will telephone the participant to discuss their result and advise an endoscopy. If the participant accepts the invitation to endoscopy, a referral will be requested at their local participating Secondary Care site. On the day of the participant's endoscopy, saliva and/or blood samples will also be taken for the Bioresource collection.

The researchers will seek permission to keep leftover capsule sponge samples (coded with personal details removed) for long-term storage at the University of Cambridge for future research. The samples may be shared in future with research from academic, non-profit and for-profit organisations in the UK and abroad.

Data usage & long-term follow up:
The researchers will seek permission from participants to collect health information from hospital records and NHS England (National Cancer Registration Service) in order to run this trial. This will include information held about appointments, test results, medications, conditions and treatment. The researchers will seek permission to collect long-term follow-up data from NCRAS; incidence of stage II+ or fatal adenocarcinoma and death from oesophageal adenocarcinoma at 4, 6, 8.5 years and 6, 7.5 and 12 years, respectively. To find this information, the researchers will use the participant's personal details (name, date of birth and NHS number).

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. Diagnosis of stage II+ oesophageal adenocarcinoma, ascertained from the baseline endoscopy (intervention arm, TFF3 positive only) and from National Cancer Registration and Analysis Service (NCRAS) data (years 1-12)
2. Deaths from oesophageal adenocarcinoma, including those arising at the gastro-oesophageal junction, obtained from National Cancer Registration and Analysis Service (NCRAS) data (years 1-12)

Secondary outcome measures
1. Deaths from oesophagogastric cancer, obtained from National Cancer Registration and Analysis Service (NCRAS) data (years 1-12)
2. Diagnosis of dysplastic BE or intramucosal OAC, ascertained from the baseline endoscopy (intervention arm, TFF3 positive only) at 6, 7.5, and 12 years
3. Booking a screening appointment, obtained from Case Report Forms (intervention arm, TFF3 positive only) at 3 years (end of active recruitment)
4. Attendance at a screening appointment, obtained from Case Report Forms (intervention arm, TFF3 positive only) at 3 years (end of active recruitment)
5. Ability to swallow the capsule sponge in those who attend a screening appointment, obtained from Case Report Forms (intervention arm, TFF3 positive only) at 3 years (end of active recruitment)
6. Attendance at endoscopy appointment in those referred for endoscopy following a positive screen, obtained from Case Report Forms at 3 years (end of active recruitment)

Overall study start date
01/10/2022

Completion date
29/06/2036

Eligibility

Key inclusion criteria
Heartburn Health Programme:
1. Have given electronic informed consent to participate
2. Males aged 55 - 79 years and Females aged 65 - 79 years (sex at birth)

3. Have a mobile phone number
4. Self-confirmed symptoms of heartburn, acid reflux and indigestion

Screening Trial:
5. Meet same criteria as Heartburn Health
6. Self-confirmed regular use (biweekly) of a prescription or over-the-counter acid-suppressant medication in the last 6 months

Participant type(s)
Patient

Age group
Adult

Lower age limit
55 Years

Upper age limit
79 Years

Sex
Both

Target number of participants
Planned Sample Size: 120,000; UK Sample Size: 120,000

Key exclusion criteria
Screening Trial:
1. Patient-reported a previous diagnosis of BO confirmed on histology
2. Patient-reported upper GI endoscopy in the last 5 years
3. Patient-reported Cytosponge/Capsule Sponge procedure in the last 5 years
4. Meet the guidelines for an urgent endoscopy referral according to NICE guidelines (dyspepsia with acute GI bleed, dyspepsia that fails to respond to PPI or H2R antagonist with negative Helicobacter Pylori test, unintentional weight loss, persistent vomiting, iron deficiency anaemia, epigastric mass, suspicious barium meal indicating risk of cancer)
5. Recorded diagnosis of an oro-pharynx, oesophageal or gastro-oesophageal tumour (T2 staging and above), or symptoms of dysphagia
6. Difficulty in swallowing due to a known cerebrovascular accident or neurological disorder
7. Recorded oesophageal varices, cirrhosis of the liver, portal hypertension
8. Received prior endoscopic (photodynamic therapy or radiofrequency ablation) or surgical intervention to the oesophagus
9. Inability to temporarily discontinue anti-thrombotic medication prior to the procedure as per clinical JAG guidelines
10. Known pregnancy
11. Lack of capacity to provide informed consent
12. Procedural: Having eaten or drank within the last 4 hours

Date of first enrolment
30/09/2024

Date of final enrolment

31/12/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
RRDN East of England
20 Rouen Road
Norwich
United Kingdom
NR1 1QQ

Study participating centre
RRDN East Midland NUH NHS Trust
F11 Curie Court
Queen’s Medical Centre Campus
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
RRDN Yorkshire and Humber
21 Queen St
Leeds
United Kingdom
LS1 2TW

Study participating centre
RRDN South East Central UHS,
Tremona Rd
Southampton
United Kingdom
SO16 6YD

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
R&D Department, Box 277
Addenbrookes Hospital
Cambridge
England
United Kingdom
CB2 0QQ
+44 (0)1223 348490
cuh.research@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.cuh.org.uk/

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal in 2037.

Intention to publish date
29/06/2037

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 4.0	30/05/2024	26/07/2024	No	Yes