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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 27/07/2026	**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

To join Heartburn Health, visit https://www.heartburnhealth.org/

Contact information

Type(s)
Scientific

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Additional identifiers

Integrated Research Application System (IRAS)
332589

Central Portfolio Management System (CPMS)
57984

National Institute for Health and Care Research (NIHR)
135565

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

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Screening

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

Interventions
Current interventions as of 27/07/2026:
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 different Regional Research Delivery Networks (RRDNs) and Devolved Nations. 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 (or devolved nations equivalent) will employ the specified inclusion and exclusion criteria via in their search of the NHSE Patient Demographic Service (or devolved nations equivalent) 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. Self-enrolment

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 healthcare professionals 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 their GP will be informed. If the participant receives a positive result, the Cambridge Clinical team will contact the participant to inform them of 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).

Previous interventions as of 07/10/2025:

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 different Regional Research Delivery Networks (RRDNs) and Devolved Nations. 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 (or devolved nations equivalent) will employ the specified inclusion and exclusion criteria via in their search of the NHSE Patient Demographic Service (or devolved nations equivalent) 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:
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Previous 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.

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Intervention Type
Other

Primary outcome(s)
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)

Key secondary outcome(s)
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)

Completion date
29/06/2036

Eligibility

Key inclusion criteria
Current inclusion criteria as of 07/10/2025:

Heartburn Health Programme:
1. Have given electronic informed consent to participate
2. UK resident

3. Males aged 55 - 79 years and Females aged 65 - 79 years (sex at birth)
4. Have a mobile phone number
5. Patient reported symptoms and/or use medication for heartburn, acid reflux and indigestion.

Screening Trial:
1. Meet same criteria as Heartburn Health
2. Patient reported regular symptoms of heartburn, acid reflux and indigestion
in the last 6 months AND/OR
3. Confirmed regular use of a prescription or over the counter acid-suppressant medication in the last 6 months
4. Express interest in a capsule sponge test

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Previous 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)
All, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
55 Years

Upper age limit
79 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 07/10/2025:

Screening Trial:
1. Patient reported difficulty swallowing pills
2. Patient reported previous diagnosis of BO
3. Patient reported upper GI endoscopy in the last 3 years
4. Patient reported Cytosponge/capsule sponge procedure in the last 3 years
5. Patient reported diagnosis of oesophageal cancer
6. Patient reported prior surgical intervention to the oesophagus or upper stomach

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Previous 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
United Kingdom

England

Wales

Study participating centre

Heartburn Health
To join the BEST4 Screening trial, please sign up for the Heartburn Health programme at:
https://www.heartburnhealth.org/
London
England
E1 1HH

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

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

Individual participant data (IPD) sharing plan

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
Participant information sheet	version 9.0	02/04/2026	15/07/2026	No	Yes
Study website		11/11/2025	11/11/2025	No	Yes