Participant Information Sheet

The Barrett's oESophagus Trial 4 (BEST4) Screening Trial

We invite you to take part in a research trial

The BEST4 trial is offering people with heartburn, indigestion or acid reflux a 'Heartburn Health Check'. This could help find health problems in the oesophagus (food pipe), including pre-cancer or, in rare cases, cancer. Before you decide to take part, it is important to know why we are running this research and what it will involve. Please take time to read the following information carefully:

Why are we running this trial?

Many people experience heartburn, indigestion or acid reflux. They can usually be treated with medication or lifestyle changes. However, some people who have symptoms over a long time develop a condition called Barrett's oesophagus. This is when the cells in the food pipe change shape. About 3-6 people in every 100 with regular heartburn develop Barrett's oesophagus. The reason we are interested in Barrett's oesophagus is because people with Barrett's have a slightly higher chance of developing oesophageal cancer and we know that earlier detection improves outcomes.

Until now, endoscopy has been used to look for these health problems. An endoscopy is where a doctor looks at your oesophagus (food pipe) using a camera on a thin tube. In the last few years, a quicker and simpler test has been developed, called the capsule sponge test. This can be used to look for signs of health problems first, to see if an endoscopy is needed.

In BEST4, we are offering some people with heartburn, indigestion or acid reflux, a Heartburn Health check with the capsule sponge test. The aim of this trial is to see if Heartburn Health checks help to find these health problems early when they are easier to treat. We will then collect data held about people in the trial from NHS records for up to 12 years to see how this impacts their health. You can find more details about which health problems the capsule sponge tests for at https://best4trial.org/health-problems-1

Why have I been invited to take part?

We have invited you because:

- you joined Heartburn Health and expressed interest in having the capsule sponge test
- you are aged between 55-79 (for males) or 65-79 (for females)
- you regularly experience symptoms of heartburn, indigestion or acid reflux, or take medication for these symptoms
- you have not had an endoscopy in the last 3 years

You were then selected at random by a computer program to be invited. We plan to invite 40,000 people.

Do I have to take part?

No. It is your decision whether to take part. If you decide not to take part, your standard of care will not be affected in any

way. You can also continue in Heartburn Health.

What does taking part involve?

Taking part involves having a one-off Heartburn Health Check with the capsule sponge test at one of our Community Clinics.

You can book an appointment at a Community Clinic near you using the details in your text message invitation. Community clinics may be held in a mobile unit or at a Community Diagnostic Centre (CDC). The mobile units will be based in easy to access car parks, like the mobile units used for breast cancer screening.

You can find accessibility information for the mobile units here https:best4trial.org/faqs

As the sponge will sit briefly in your stomach, it is important that your stomach is empty. **You must not eat or drink for at least 4 hours before the test.** You can still use small sips of water to take medication. If you take blood thinning medication, you may need to skip this before the appointment. There are detailed instructions later in this information sheet. You can continue to take other daily medications.

At the appointment, a trained healthcare professional will discuss the trial and the test with you in detail. They will ask you a few questions about your health to check the trial is right for you. This will include checking whether it is appropriate for you to have the capsule sponge test. If you cannot have the capsule sponge test due to a health reason identified during the visit, you will not be invited again for a capsule sponge test as part of BEST4. However, you might be contacted about future studies related to this research, as part of Heartburn Health.

Please bring a list of your medications and your NHS number to your appointment. You may not be able to take part without this information. If you still want to take part, the trained healthcare professional will ask you to complete a consent form. If you are unable to sign forms, please read the relevant section below.

You will then have the capsule sponge test, which takes about 10 minutes. We describe the test in the next section. The whole appointment will last 30 to 45 minutes. We will let you have your results within a few weeks by text message or letter.

If the test result is abnormal, the research team will book an endoscopy for you. You may need to travel to a participating hospital other than your local hospital to have your endoscopy. The endoscopy will confirm if you have any health problems or not.

Abnormal cells may indicate cancer. The capsule sponge test is not a diagnostic tool, so if abnormal cells are found, you will need further tests. The trial team will be able to answer any questions and refer you to support if needed. Based on the results, your doctors will decide whether further tests or treatment are required.

It is important to remember that abnormal cells do not necessarily mean you have cancer.

If you have an endoscopy, we may also ask if you are willing to give a blood sample. These samples will be used for future research and will not inform your care.

If your capsule sponge test did not capture enough cells to analyse your sample properly, we may invite you to have a repeat test. If a repeat test is available, we will send this invitation by text message. As our Community Clinics may be held in different locations over time, you may have to travel further than your original appointment to have your repeat appointment. You will be able to see the available options at the time of booking your repeat appointment online. You do not need to attend the repeat appointment if you would rather not. If you have a second test and it is also inadequate, we will let

you know, but we will not ask you to do the test again.

If the capsule sponge test shows no signs of health problems, there will be nothing more you need to do for the trial.

The tests will be in addition to any care you normally receive for your symptoms. You can carry on with your heartburn medication as normal. Abnormal results may be shared with your GP or regular care team. They will not be informed of normal capsule sponge test results.

If you have any non-urgent medical problems following your capsule sponge test appointment, please contact our clinical team on 01223 761 085 The unit is open Monday – Friday 8 am to 5pm. Outside these hours please contact your GP for advice. As your GP will not have detailed information about this test, we recommend that you bring the discharge summary provided to you after your capsule sponge test appointment.

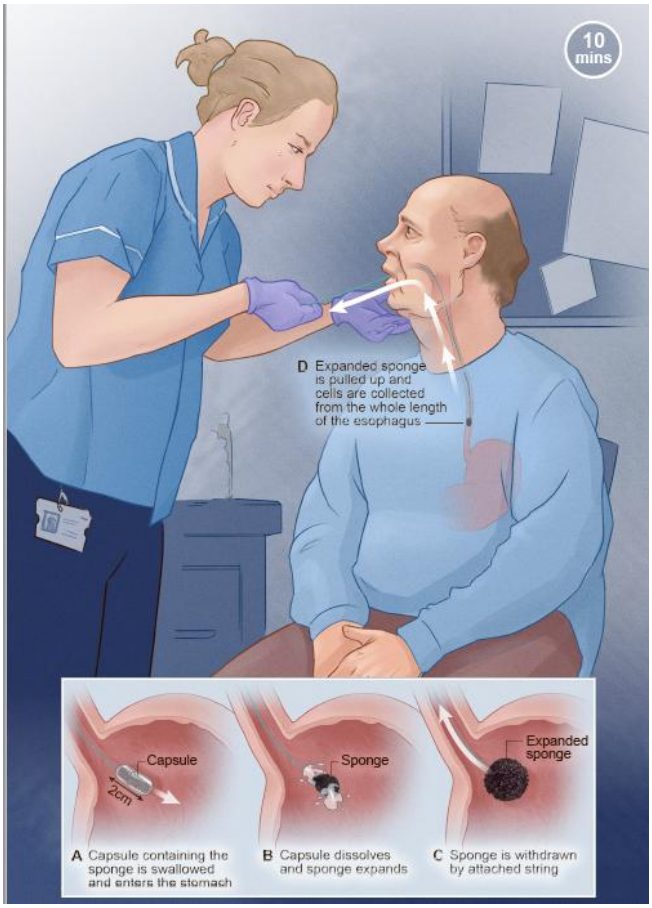
How does the capsule sponge test work?

The test is a small sponge compressed inside a capsule made of plant fibres attached to a thin thread. The capsule is similar in size to a vitamin pill.

With the help of a trained healthcare professional, you will swallow the capsule and thread with a glass of water. Once swallowed, you wait about 7 minutes while the capsule dissolves in your stomach, releasing the sponge. The trained healthcare professional will then remove the sponge by pulling the thread. As it is pulled out, the sponge collects a sample of the cells lining your oesophagus (food pipe).

The sample of cells from your test will then be sent to experts for testing.

The test has been approved by UK regulatory authorities and thousands of people have had the test. You can find more details about the test at https://best4trial.org/the-capsule-sponge



Will I need to stop my blood thinning medication?

If you take medication that thins your blood (i.e. heparin, warfarin, apixaban, rivaroxaban etc.), you may need to skip any doses you would usually take the night before and on the morning of your test. This is because there is a very small risk of bleeding when the sponge is removed.

This depends on the type of medication you take. Guidance can be found below. **Please check with your doctor before stopping your medication.**

Medication	Stopping instructions
Dabigatran	Do not take the night before or on the morning of your test.
Rivaroxaban	Do not take the night before or on the morning of your test.

Apixaban	Do not take the night before or on the morning of your test.
Edoxaban	Do not take the night before or on the morning of your test.
Warfarin	Get an INR blood test in the week before your capsule sponge test. If your INR is above 3.5, contact your doctor and do not attend your capsule sponge appointment. If your INR is below 3.5, you can attend your appointment and take your Warfarin as normal.
Aspirin	Continue to take as normal.

At your appointment the healthcare professional will tell you when you can take your next dose.

If you feel unable to stop your medication or have questions, please contact our clinical team at cuh.best4.trial@nhs.net or01223 761 085.

What are the possible benefits of taking part?

The NHS cannot offer endoscopies to everyone with heartburn, indigestion or acid reflux symptoms because of limited resources. By having the test, you will have the chance to check the health of your oesophagus (food pipe). If problems are found, your doctor will be able to offer an endoscopy or treatment if needed.

What are the possible risks of taking part?

Over 15,000 people have had the capsule sponge test with no serious side-effects. Swallowing the capsule is not painful and most people find it easy. Following the capsule sponge test, you should be able to carry on with your day as normal.

The most common complaint is a mild sore throat for 24 hours after the test. For some people, this may last a few days. Painkillers like paracetamol and throat lozenges will soothe this and it will get better naturally.

There is a very small risk (less than 1 in 2,000) that the sponge comes off the thread or the healthcare professional is unable to remove it. If this happens, we will arrange an endoscopy at a local hospital to remove the sponge within 4-6 hours. The procedure itself will take up to 30 minutes. If the sponge has to be removed in this way, you will remain in the study, and the removed sponge will be sent to the central laboratory for testing (see "What will happen to any samples I give?" below). You will not need to have a repeat capsule sponge test.

There is a very small risk of some bleeding (less than 1 in 10,000). This is likely to stop quickly on its own - the healthcare professional will check. If needed, we will arrange an endoscopy at a local hospital right away to stop the bleeding.

If you are offered an endoscopy as a result of the capsule sponge test, this will be part of standard care rather than the trial. You will be able to discuss the risks involved in having an endoscopy with the doctor at your appointment.

What will happen to any samples I give?

We will send your capsule sponge sample to a central laboratory for testing. We work with Cyted UK Ltd, a laboratory that analyses capsule sponge tests for the NHS. Your sample will carry your study ID, NHS number, initials and date of birth. Once they have been tested, your samples will be pseudonymised (coded).

If you give a blood sample, this will be stored at the University of Cambridge with a code number instead of your personal details. It will not be tested as part of this trial but will be used in future research through Heartburn Health.

In some cases, researchers may do DNA testing on your samples. They may use your capsule sponge and endoscopy biopsy

samples. This is to explore whether DNA tests could give more information about cell changes. As this is very early-stage work, we will not be able to share results with you.

More details about how your samples will be used can be found on the BEST4 website https://best4trial.org/.

What other information will you collect?

We will need to use information from you and your medical records for this trial. People will use this information to do the research or to check your records to make sure that the research is being done properly.

As part of Heartburn Health, you gave us permission to collect information from your NHS records. We will use this information as part of this trial. We will also collect information from your hospital records. If you have an endoscopy, this will include these results.

How will my personal details be handled?

We will need your personal details to run the trial. This will include your full name, NHS number, date of birth and contact details. We may use these details to contact you directly about the trial. This may include to book appointments, share trial updates, ask about your health or update your contact details.

We will handle your data in line with the UK General Data Protection Regulation (GDPR) and the Data Protection Act 2018. All third parties handling your personal details, including any organisations based outside the UK, must also meet these standards and security arrangements as set out in relevant contracts.

People who do not need to know who you are will not be able to see your name or contact details. Your research data will have a code number instead. This means no one will be able to work out who you are from the data. We will keep all information about you safe and secure.

Your data will be stored securely on a database by Queen Mary University of London (QMUL). QMUL are a Data Processor for the study on behalf of trial sponsors and will be responsible for handling your data safely.

We will use a third party called iPLATO to process your personal details, contact you about the trial and manage appointment bookings. You can find out more about how they handle your personal details here https://www.iplato.com/privacy-policy/index.html.

Your personal details will be shared with Cyted UK Ltd to process your capsule sponge test sample. Cyted UK Ltd also use third parties to process your personal details. You can find out more here, https://cyted.ai/privacy.

Your personal details may be reviewed by trial monitors, auditors, regulatory bodies and members of the research team during the trial. This is to check the quality and safety of the trial. These people will be required to keep your details secure.

For more information about how we will use your personal details, please visit https://best4trial.org/ or **www.hra.nhs.uk/patientdataandresearch**

Once we have finished the trial, we will keep some of the data so we can check the results. We will only store your personal details for up to 5 years after the study closes. We will write our reports in a way that no-one can work out that you took part in the trial.

What will happen with my research data and samples after the trial?

Once the trial has finished, all data and samples stored at Cyted UK Ltd will be returned to the University of Cambridge for

future approved research. All samples and data will be coded, this means no one will be able to work out who you are.

The clinical data and samples (without your personal details) will become part of your Heartburn Health record. This includes any blood samples given. The left-over samples will be stored at The University of Cambridge in a long term HTA (Human Tissue Authority) licenced facility.

Residual capsule samples may be used in the future by researchers for ethically approved studies and may be shared with external collaborators and organisations through Heartburn Health. These researchers may be from academic, non-profit or for-profit organisations in the UK or abroad. Future researchers may run DNA testing on the blood samples. The coded samples will not include your personal details. This testing will only take place with ethical approval and your information will be closely protected.

The University of Cambridge will be the sample custodians of any samples collected as part of the BEST4 Platform and will follow all the requirements set out by the Human Tissue Act 2004.

The coded research data will be kept as long as Heartburn Health exists and protected in accordance with the Data Protection Act 2018.

Can I stop taking part in the trial?

You can stop taking part in the trial at any time, without giving a reason. We will keep the samples and information about you that we already have, but we will collect no new information for the trial. This includes if you pass away or lose the ability to consent.
If you choose to stop taking part in the BEST4 Screening Trial, you will still be part of Heartburn Health.

https://best4trial.org/leaving-the-best4-trial

If you want to leave Heartburn Health as well, you can fill in the withdrawal form on the Heartburn Health website https://www.heartburnhealth.org/aboutthe-programme/leaving-the-programme/.
We need to manage your records in specific ways for the research to be reliable. This means that we will not be able to let you see or change the data we hold about you.

What will happen with the trial results?

As data will be collected over 12 years, results will not be available for some time. Trial updates can be found at https://best4trial.org/best4-trial-updates.

Trial results will be shared in academic journal articles and at conferences. No personal information will be used. We will write our reports in a way that no-one can work out that you took part in the trial.

If the capsule sponge test works, we hope the test can become part of usual care for people with heartburn, indigestion and acid reflux soon after the trial ends.

The research results may feed into a discovery of commercial value. You will not benefit financially from any findings. Cyted UK Ltd was founded by people from the University of Cambridge. Rebecca Fitzgerald (the lead researcher at the University of Cambridge) is a <3% shareholder and unpaid advisor for Cyted UK Ltd.

What if something goes wrong?

The risks of participants suffering harm as a result of taking part in this study are minimal, but insurance (provided by the University of Cambridge and the NHS indemnity scheme and the mobile unit provider) will provide compensation for any negligent harm caused by participation.

Cambridge University Hospitals NHS Foundation Trust and the University of

Cambridge have specific arrangements in place if you suffer any harm as the result of negligence within this trial as a result of protocol design and for non-negligent harm arising through participation in the trial.

Who can I contact if I have any questions or concerns about the trial?

If you have any questions about the BEST4 screening trial, please visit our website https://best4trial.org/ or contact us by email at cuh.best4screening@nhs.net or by telephone on 0808 281 4772.
You can contact Dr Thomas Round , who is the Principal Investigator on this trial, at thomasround@nhs.netif you wish to complain or report a problem about any aspect of the trial at any time.

Please only contact the CUH Patient Advice and Liaison Service (PALS) if you would prefer to speak to someone who is not involved in running the trial. PALS is at 01223 216756 available Monday to Friday from 9 am to 4 pm.
For any complaints or queries you may have regarding the care you receive as an NHS patient, please contact your local PALS at your local hospital who will be able to help you.

Who is organising and funding the trial?

The University of Cambridge and Cambridge University Hospitals NHS Foundation Trust are joint sponsors of this trial. This means they oversee the trial.

The Cancer Prevention Trials Unit at Queen Mary University of London is coordinating the trial. The clinical team at University of Cambridge are sharing results and making referrals.

The Principal Investigator and lead researcher responsible for the BEST4 screening trial is Dr Thomas Round.

The Chief Investigator, Professor Rebecca Fitzgerald, leads this work which is funded by Cancer Research UK (SEBSTF-2021\100036, CRUK/22/005) and the NIHR HTA programme (NIHR135565).

Who has reviewed the trial?

This trial has been reviewed and approved by the Health Research Authority (HRA) and the National Research Ethics Service (NRES) West Midland – South Birmingham Research Ethics Committee. It has also been reviewed and supported by members of the public with heartburn, acid reflux, Barrett's oesophagus and oesophageal cancer experience.

What if I am unable to sign forms?

A witness is required for participants who can understand the study and give their consent verbally but are not able to sign the consent form. For example:

- The participant cannot read or write
- The participant is visually impaired
- The participant is physically disabled

The witness must be present during the entire consent process to observe that the participant is provided with all necessary information and their decision to participate in the trial is voluntary. The witness will sign the informed consent form to confirm their presence and observation of the consent process.

The witness must be independent of the trial team (must not be involved in the conduct of the trial), such as a family member or friend.

Translation services will be available on the day of your capsule sponge test appointment for anyone who requires assistance.

Share Feedback

We welcome your thoughts or suggestions about the BEST4 Screening Trial. If you would like to share feedback, please contact us by email at cuh.best4screening@nhs.net or by telephone on 0808 281 4772.