

PARTICIPANT INFORMATION SHEET

REACTIVE: A clinical Investigation to determine the accuracy of cognitive monitoring and feedback app, REACTIVE, to detect and predict cognitive decline in older adults

Chief Investigator: Professor Anne Corbett

Invitation to take part in a research study

We would like to invite you to take part in our research study, REACTIVE, which is being run at the University of Exeter. Before you decide, we would like you to understand why the research is being done and what it would involve for you.

Please take time to read the following information carefully and we recommend that you discuss it with family or friends if you wish. We recognise that there is a lot of information contained within this document. If you have any questions about this study, we encourage you to contact a member of the study team. Our contact details are on the last page of this information sheet and on the REACTIVE app and website www.reactivestudy.org.uk

You are under no obligation to take part in the study, and if you do take part you are free to withdraw at any time. If you decide to take part, we will ask you to read and sign a statement of consent on the app or website when you register.

Why are we doing the study?

Changes in brain function such as memory, attention and problem-solving can be an early sign of dementia. These changes are subtle, and doctors do not have any tools that can pick them up, meaning that people with early symptoms do not receive any support or treatment. In fact, 99% of people with early symptoms, called Mild Cognitive Impairment (MCI), do not see a GP and do not get a diagnosis. There are promising new treatments in the pipeline, and we know much more about preventing dementia than previously. It is therefore very important that we identify people with early symptoms and make sure they are in touch with their GP. This will ensure they have the best possible chance of preventing dementia, or that they get a proper diagnosis and access to treatment and support.

We know that loss of brain function and dementia is a major fear for older adults. People need a way to check their brain health and to know when to seek help from a doctor. Doctors also need a better tool for tracking people's brain health and deciding

when someone needs a full assessment. Currently they have to rely on simple tests that are not good enough to detect very early symptoms.

Computerised testing is now very good at picking up changes in people's brain function. We have developed an App (IOS and Android) called REACTIVE to help people and their GP monitor their brain health. People download the app or access the website and complete regular brain tests as well as providing information about their health and lifestyle. The app will analyse this information and send feedback to the person using the app or website and their doctor to make sure they are notified, and any changes are detected early.

Blood tests can also be used to detect changes linked to dementia risk. At-home test kits can be used to detect these changes, and this could be used alongside the REACTIVE app to give people a better idea of their brain health. It is important that we understand how these two technologies could be used together.

What is the purpose of the study?

This is a 30-month research study that will test the REACTIVE technology and see how well it performs when it is used by people at home. The trial will answer four main questions:

1. Can REACTIVE accurately detect people who are in the early stages of dementia?
2. Is the information collected on REACTIVE more accurate when it is combined with a blood and/or DNA test?
3. Will older adults use REACTIVE and find it easy to understand?
4. Do GPs find the REACTIVE information useful and easy to understand?

The study will recruit 1306 people over 65 who are experiencing concerns about their brain health. Of these, 628 participants will have MCI. They will download the app or use the REACTIVE website for 30 months, which will involve completing brain tests every six months. REACTIVE will identify people whose brain function suggests they may be developing dementia, and we will use statistical tests and clinical review to check whether REACTIVE has correctly identified the right people. Participants will also provide saliva and blood samples through the post. We will analyse these samples to look for biological indicators of dementia risk. The saliva sample will be analysed to look for genes that are known to be linked to Alzheimer's Disease and other causes of dementia. The blood sample will be analysed to look for proteins in the blood that are linked to changes in the brain. These indicators are still being confirmed by research so we cannot be certain that the information we find will affect participants' chance of developing dementia. For this reason, we will not let participants know the results of these tests as part of the REACTIVE study.

The study is being led by the University of Exeter Medical School, in partnership with the Royal Devon University Healthcare NHS Foundation Trust and a network of NHS centres.

Why have I been invited?

We are inviting adults aged 65 and over to volunteer to take part in this study. Participants will either already have Mild Cognitive Impairment (MCI) or will have concerns about their memory or brain health and are at risk of MCI or dementia.

To participate, you will need be registered with a GP practice in England and be able to use a computer, smartphone, or tablet with internet access. You will also need to either have a diagnosis of MCI or have at least two of the following risk factors for MCI or dementia:

- A first-degree family member who developed dementia when they were 75 years old or younger
- A diagnosis of one or more of these conditions: depression, diabetes, high blood pressure, cardiovascular disease, stroke
- Current smoker
- BMI of 30 or above

If you are already enrolled in a clinical trial, please contact us at reactive@exeter.ac.uk to check whether you can take part.

If you wish to ask us any questions, please use our contact details at the end of this information sheet.

Do I have to take part?

It is entirely up to you to decide whether to join the study. The purpose of this information sheet is to describe the study in detail and help you make your decision.

If you do wish to take part, you will need to read and sign a consent form on the app or website. Please note that if you do join, you will be free to withdraw at any time without giving a reason. Withdrawing will not affect the standard of care you receive through your own GP or local NHS services, or your legal rights. This study does not replace those services and if you feel less well during the time you are part of this study, it is important that you seek help from your doctor or local health professionals in the usual way.

If you do not wish to participate, this will not change your treatment or rights in any way, nor affect your participation in any research studies you are involved in. If you choose to withdraw after consenting to the study; data collected prior to your withdrawal will be retained using a participant ID. No further data will be collected from you. You will also have the option of requesting the deletion of any information that identifies you.

What will happen if I take part?

If you decide to take part, you will be asked to complete an online brain health test and some questionnaires every six months for a total of 30 months. These will take about an hour to complete each time. The REACTIVE app or website will monitor your brain health test scores and will let you know how well you are doing each time you complete

the tests. We will ask you to provide one saliva sample for genetic analysis and two small finger-prick blood samples for protein analysis using a kit that we will send to you. You will also be able to play our brain training games as often as you would like.

Specifically, the following steps will take place:

1. You will be directed to the section of the REACTIVE app or website where all instructions, assessments and study information can be found.
2. You will be asked to complete a short checklist to confirm your eligibility. .
3. You will be asked to confirm that you have read this Participant Information Sheet. A downloadable copy of this is available on the app and website www.reactivestudy.org.uk.
4. You will be asked to read a consent form and provide your consent to a series of statements on the app or website to confirm you understand what the study involves and that you are happy to participate in the study.
5. You will be asked to complete a screening questionnaire and to provide information about how you feel about your current brain health.
6. Provided you are eligible, you will be asked to register with the REACTIVE study.
7. You will be asked for some additional information including your contact details, NHS number, and GP details.
8. You will have the option of nominating a friend or family member as a study partner and provide their email address. This person will be asked to consent to participate as your study partner and complete two brief questionnaires about your brain health and behaviour.
9. You will then be asked to complete your first brain health assessment. This is a set of tests to measure brain function (called a cognitive test battery), which need to be completed in full. You will first complete a short 5-minute practice session to make sure you understand how the tests work, and then the full session. The full session lasts for up to 50 minutes. The tests are designed to test different aspects of how your brain work, such as your memory, problem-solving and concentration. They are meant to be difficult and can be tiring. We ask you to do your best and try to avoid pausing or leaving the tests, although you can take a rest during the tests if you need to. If you do, you will need to return to the tests within 50 minutes. This is to make sure we get the most accurate information about your brain health on that day.
10. We will check your test data to make sure it has arrived correctly and review your scores to see how you have done. If your tests show a lower score than expected for someone of your age, our study team will contact you to arrange a more detailed assessment with a study nurse. This process is described in detail below.
11. We will send you blood and saliva testing kits through the post. The saliva sample will just be sent at the beginning of the study and the blood sampling kit will be sent to you twice over the course of the study, once at the beginning and

once at the end. The testing kit will include full instructions for how to use them and a pre-paid envelope to return them. The test kit will contain:

- a. A saliva sample kit to collect your saliva for extracting DNA. This involves spitting saliva into a small plastic tube and is completely painless. It takes less than five minutes. The genetic information gathered from this sample will be for research purposes only and will not be made available to you. This is because the medical value of this information is not yet sufficiently understood to give people clear guidance about their current or future health. Your saliva samples will be stored anonymously at the University of Exeter in a secure research facility, and processed by our genetic analysis partner, deCODE Genetics Ltd (see below).
- b. Two finger-prick blood sample kits to collect a small sample of your blood to test for proteins that may indicate changes in your brain. This involves using a needle to prick two of your fingers and placing a drop of blood into the test kit. This can be a little painful but takes less than ten minutes. Your blood test results will not be sent to you for the same reason as the DNA results will not be sent. Your blood samples will be stored at the University of Exeter in a secure research facility and will be sent to our partner, the University of Gothenburg, for processing and analysis. The samples will be stored using a unique participant ID. No one outside of the study team will be able to identify you or your biological samples.

12. You will then be asked to complete a series of questionnaires about your health. These will take around one hour to complete and will include questionnaires that will ask about:

- a. Your existing medical conditions and current prescriptions.
- b. Your lifestyle, such as how often you exercise and whether you smoke.
- c. Your family's history of dementia.
- d. How you are managing as you go about your day-to-day activities.
- e. How you are behaving and whether you feel your behaviour has changed in recent times.
- f. Your mental health including your mood, and whether you experience anxiety and depression.
- g. Your overall health and wellbeing on the day you take the tests.
- h. Your recent use of health services such as GPs, pharmacies, and hospitals.

13. Once you have completed your questionnaires, you will then have access to the rest of the REACTIVE study. This will include:

- a. Access to a set of brain training games that help to maintain brain health. You can play these as often as you wish. The data from playing these games will be collected so we can see who is playing, and how often.
- b. A regular newsletter and updates with news and advice on how to keep your brain healthy and reduce your risk of dementia.
- c. Reminders and notifications to continue taking part in the study.

14. You will be asked to complete the same set of brain health tests and questionnaires every six months. We will send you an email and/or SMS reminder every week when your assessments are ready and if you are taking part through the App you will receive app notifications and reminders as well. If you have one, your study partner will also receive notifications and reminders to complete two questionnaires about you at each assessment point.
15. Each time you complete a brain health assessment we will give you feedback about your performance. This feedback will be available within five days of the tests being completed and will let you know what your best area of brain health is.
16. If the REACTIVE technology detects a drop in your performance, the following will happen:
 - a. Our team will first check your test results.
 - b. Our team will send an email message to let you know that we have seen a change in your scores, and you will be notified through the app / website.
 - c. We will contact you by telephone within 24 hours to arrange a further assessment with a study nurse.
 - d. We will send your GP a message to let them know that this has happened. The message will include information about your test results and will let them know that we have contacted you.
 - e. A study nurse will arrange a video call with you to complete an assessment of your brain health. You will be asked to bring a study partner with you if you have one, or to nominate a partner if you can. The assessment will involve questions and a conversation with you and your study partner to check your brain health. It will take up to one hour. Both of you will be asked questions. At the end of the assessment the study nurse will talk to you about how it went.
 - f. If this assessment suggests you may have problems with your brain health, they will talk to you about this and help you make an appointment with your GP for further assessments. This will not necessarily mean that you have dementia, but it does mean that there are some signs in your brain health that could be due to early dementia, and these should be checked fully. The nurse will also provide you with information about where to find out more and will make sure you fully understand what this result means for you. We will let your GP know that this has happened and will make sure that they are expecting your appointment. You can continue to use REACTIVE and complete your regular assessments if you wish, and you will be asked to complete a brief questionnaire about the tests or treatments that your GP has given you. We will also ask your GP to send us any medical notes about your assessments or treatments during the REACTIVE study.
 - g. If the test result shows that your brain health is normal, the nurse will discuss this with you and make sure you are happy to continue in the study. You can continue using REACTIVE. We will let your GP know that

our assessments did not indicate that you have problems with your brain health that need any further assessment.

17. In addition to the process described above, we also recommend that if you experience any ill health or have concerns about your brain health you contact your GP for advice. There will also be a section on the REACTIVE app for you to report any illness or events that you experience when using the app.
18. We will ask you to complete occasional feedback forms to provide us with suggestions and feedback on your experience with REACTIVE. These will be brief and optional.
19. We may ask you to complete a brain health assessment with the study nurse even if the system did not detect a drop in your performance. This is done to check that the system is working as expected. In this instance, you will have the option to accept or decline this assessment.
20. At the end of the study, we will contact you to let you know that REACTIVE is closing. You will have the option of registering as a participant on a similar study if you wish to continue completing the brain health tests. We will also make the findings of the research available through the study website, app, and a newsletter. These findings are not individual to you as they will be anonymised.

All the information we collect will be secure and confidential. Analysis will be completed using anonymous data. We will keep your personal data in case we need to contact you as part of the study, but this will be for no more than 10 years after the study has finished and then it will be securely destroyed.

How will we use information about you?

We will need to use information about you for this research project including:

- Name and Initials
- Date of Birth
- Contact details (email address, home address and telephone number)
- NHS number

People will use this information to do the research or check your records to make sure the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. If we need to contact your GP, we will share your name and NHS number with them.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep your data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

What is deCODE Genetics and the University of Gothenburg, and how will they handle my DNA and blood samples?

deCODE Genetics will handle your saliva sample. The University of Gothenburg will handle your blood samples. These organisations are independent of each other.

deCODE are an international genetics company. The University of Gothenburg is an education and research institution in Sweden. Both organisations work in partnership with the University of Exeter to process and analyse DNA and blood samples respectively for research under a Research Collaboration Agreement. Your samples will be sent to them as an anonymous sample for processing and analysis as part of the overall REACTIVE Study. The data will be returned to the University of Exeter for future analysis. DeCODE and the University of Gothenburg may also receive anonymised data from the study (including results from your tests and other questionnaires). However, we will never send your personal details to deCODE or the University of Gothenburg so your data will remain anonymous.

Both organisations operate under the strict international regulations for genetics and human research and are bound by the Collaboration Agreement with the University of Exeter, which protects the confidentiality and usage of any samples and data processed within the REACTIVE Study.

What are the possible benefits and risks of taking part?

This study is aiming to improve how we detect the early symptoms of dementia in people who are not yet in touch with their GP about their brain health. By taking part in this study, it could help move forward our understanding of MCI and dementia and how it should be managed and supported. You will receive feedback on your brain health and information to help you make decisions about how to reduce your risk of dementia. This could help you to improve your brain health as you age.

There is a chance that you will receive a message telling you that you may have problems with your brain health. This will happen if your test results show a drop in your performance on the tests compared to other people your age. This may be distressing and may cause anxiety for you and your loved ones. We will support you during this process to ensure you understand what this information means and what will happen next. We will also work closely with you and your GP to make sure you receive the assessment and treatment that you need during this time. We will make sure you have access to information and support beyond the scope of this study. If you have any further concerns, then you will be able to contact the study team or your GP for support.

There is a small risk with providing a finger-prick blood sample. Most people experience mild discomfort when they complete these tests. Some people experience bruising or additional bleeding. Any more serious complications are extremely rare, but we will monitor your safety during the study, and you will be able to report any safety concerns through your REACTIVE account or by contacting the study team.

This study does not replace National Health Services and if you feel less well during the time you are part of this study it is important that you seek help from your doctor or local health professionals in the usual way.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

Where can you find out more about how your information is used?

You can find out more about how we use your information

- at <https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/data-protection-and-information-governance/gdpr-guidance/templates/transparency-wording-for-all-sponsors/#GDPRtemplate>
- in our leaflet available from www.reactivestudy.org.uk
<https://www.exeter.ac.uk/about/oursite/privacy/research/#a5http://www.hra.nhs.uk/patientdataandresearch>
- by asking one of the research team
- by emailing dataprotection@exeter.ac.uk
- by sending an email to Suzy Wignall, Senior Clinical Research Governance Manager (Contact details at the end of this information sheet), or
- by ringing us on 01392 727581.

Who is organising and funding the research?

The study is funded by the National Institute for Health & Care Research and is sponsored by the University of Exeter. You will not receive payment for participating in this study.

Who has reviewed and approved this study?

The study has been reviewed by a UK Health Department's NHS Research Ethics Committee (**Yorkshire & The Humber – Leeds West Research Ethics Committee**), **the Medicines and Healthcare products Regulatory Agency** and the Health Research Authority who are the regulatory authority for research involving the NHS.

What will happen at the end of the study?

At the end of the study, you will complete your final tests for the REACTIVE study on the app or website. We will then contact you to let you know the study has ended and to thank you for your contribution. The results of the study will be published in a scientific journal. We will provide you with a lay summary of our findings in the form of a newsletter. The findings will also be available on the study website. The information

collected will be totally confidential and no individuals will be identified in any reports/publications or presentations. A description of this clinical study will be available at <https://www.isrctn.com/>.

What if there is a problem?

If you have a concern or complaint about any aspect of this study contact the research team or the Sponsor using the details below.

Additional information and Frequently Asked Questions are available on the study website and app. If this does not answer your query you can contact the research team on 01392 727581 or email us on reactive@exeter.ac.uk.

For independent advice and information, you can contact the PALS Service at the Royal Devon University Healthcare NHS Trust.

Patient Advice and Liaison Service (PALS)

Royal Devon University Healthcare NHS Trust PALS:

- Telephone: 01392 402093
- Email: rde-tr.PALS@nhs.net

University of Exeter

Sponsor Representative

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REACTIVE Study Team Contact (Study Helpline)

Email: reactive@exeter.ac.uk

Tel: 01392 727581

Further Information

Thank you for taking the time to read the information about this study. If you would like to take part, please register for the study through the app or website at www.reactivestudy.org.uk. If you would like more information about the study before you decide whether or not to take part, you can contact a member of the study team by ringing the study help and information line 01392 727581.

Please note that this helpline is for general information and support for the study. It will connect you to a member of the study team who will be able to talk about the study but will not be able to provide medical advice. Please also note that we are not able to give out information about your personal performance or progress in the study.

Thank you for your interest in taking part.