PARTICIPANT INFORMATION SHEET

Version 2.51. Date: 14-Aug-2024

Studying a biomarker screening platform to identify Alzheimer's Disease at point of care: PREDICTOM

What is the purpose of the study?

The study is being led by Helse Stavanger HF (Stavanger University Hospital), and aims to look at how lifestyle, genes, and changes in our body are linked with the risk for getting Alzheimer's disease (AD). We want to develop tests that people can take at home or at their General Practitioner (GP) surgery. This will provide valuable information about how to reduce the risk of developing Alzheimer's disease.

Why have I been invited?

You are invited to participate in our research study if you are aged 50 or over and do not have a prior diagnosis of dementia.

We know some of the factors linked with an increased risk of developing AD, we are particularly interested in individuals experiencing mild memory problems, sleep problems, and mild mental health symptoms (low in mood), obesity, hearing loss, diabetes, high cholesterol, hypertension, or those with a first-degree relative who has Alzheimer's Disease or dementia. In addition, if your lifestyle includes risk factors such as smoking, poor diet, and limited social and physical activity, you may be eligible to participate.

To be eligible for this study, you should not have any life-threatening physical diseases, or any other conditions that would make participation impossible. You should be able to communicate in your native language, have access to a computer or touchscreen device with an internet connection, and be willing and able to provide informed consent for your participation in the study.

Your involvement can greatly help our understanding of these conditions and their potential risk factors. Thank you for considering participating in our research.

Do I have to take part?

No. It is up to you whether or not to join the study. The purpose of this information sheet is to describe the study in detail to help you make your decision. If you agree to take part, you will then need to read and sign a consent form on the PREDICTOM pages of the PROTECT study website. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive through your own General Practitioner or local health services. 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.

Why are we doing the study?

Alzheimer's disease and other diseases affecting the brain cause memory decline and other changes leading to dementia. The number of people with dementia is already high and is expected to increase markedly during the next decades. We know that lifestyle changes can reduce the risk of dementia, particularly in people with increased risk. Also, there are some new medicines that can slow down memory loss. It is important to diagnose Alzheimer's and other conditions that cause dementia as soon as we can. This way, people can make changes to lower their risk. Today, the only way to reliably diagnose Alzheimer's disease is to have an expensive and generally not available imaging scan of your brain, or by testing the fluid around your brain after a procedure called a lumbar puncture. There is a need to find simpler tests for people to access easily. In this project, we will explore a number of relevant tests that can be performed in people's homes to help us diagnose Alzheimer's disease. To help our ability to prevent and treat AD, it is important to gain a deeper understanding of the key factors that influence it. This study will address these important issues by measuring key risk markers (e.g., memory function, genes, gut microbiome (bacteria living in the gut), blood, and brain activity) over 4 years in 4000 adults over the age of 50, through an online or in-clinic study. You will do some tests, and we will see how well you do compared to your genes and other things that might affect your brain as you get older. We will look at things like your lifestyle and health too. By putting all this together, we will learn more about how memory changes as people age.

What will happen if I take part?

If you want to participate in this study you will to need to register and provide informed voluntary consent. To do so:

- Complete the registration online. During registration you will be asked to provide some basic personal details including your name, address, email address, NHS number (UK) and doctor/general practitioner details. These details will allow us to contact you for subsequent research purposes and to send you important information about the ongoing study.
- Study Consent form: You will be asked to sign the informed consent form for this study on the website. Once you have registered and signed the consent form you will be asked to provide some basic demographic information including age, gender (including an expanded question for inclusivity), marital status, ethnicity, employment, and education.

What would my participation involve?

- Once you have registered and provided consent, you will then be asked to complete the following tests and provide various samples. All the assessments, tests and the samples will be done at home on your own.
- Please see below a list of the assessments, tests and samples that you will be asked to complete or provide Memory Assessments

1. Online Memory Assessments

   You will take memory tests on the PREDICTOM website by logging in with your study details. Once logged in, you will see simple on-screen directions to start the memory tests. These tests relating to memory and hearing abilities should be conducted in a quiet, focused environment for optimal results. Some online assessments require you to have certain computing equipment. Don't worry if you don't have the equipment needed for all the tests as we may be able to lend you an iPad, or you can opt out.

   The online tests related to your memory and cognitive abilities will include:

   i. FLAME Memory Assessment

   - This tests memory, reasoning, and attention. Some of these tests have certain similarities and are designed to challenge you.

- There are some similarities in some of these tests, which allow us to detect subtle changes in performance.
- These will take around 30 minutes to complete in total using a tablet or a laptop.

ii. BrainCheck

- The BrainCheck test looks at memory, focus, and other thinking skills by giving you different tasks and memory exercises online.
- Overall, this test will take 5 minutes to complete, using a tablet or a laptop / desktop computer.

iii. Cognitive Battery: Altoida

- The Altoida app has games that check how good you are at moving around and finding things using "augmented reality," which mixes real and virtual items (like fruits) on your phone screen.
- You will play games where you have to hide and find objects in this mixed reality world.
- It should take about 10 to 15 minutes to finish the test on your iPhone or an iPad.

iv. Banking app

- Changes in everyday activities can be early indicators of cognitive impairment. The Banking app is a virtual or 'fake' ATM. You will be asked to enter a PIN, withdraw money, and confirm choices on your tablet or computer. This is a fake ATM, and it is not linked to any real credit card or bank.
- The 'Banking App' will help us see how well somebody is able to handle daily tasks, like managing money, which is a key part of daily living. The test should only take around 5 minutes to complete using a tablet or computer.

v. Eye tracking app

- The eye-tracking test monitors your gaze as you follow the movement of on-screen images. It measures tiny eye movements that are associated with cognitive health.
- The test consists of three blocks and will take 15 minutes to complete. You will be asked to calibrate your gaze by looking at 5 points on the screen. Once this is done, you will be able to control the test in the first block directly with your eyes; the remaining two blocks are controlled with your mouse.
- To complete this test, you will need a Windows 10 computer with a web camera and a mouse with 1GB of free space on your hard drive to install an app. We will give you instructions to do install the app as well as how to uninstall the app when you are finished. You can opt out of this activity if you do not have the necessary equipment or are unable to install the app.

2. Online Hearing Screening

- This assessment aims to explore if hearing problems are linked to thinking and memory issues.
- You will answer questions about your hearing concerns, like pain or ringing in the ears, and where you struggle to hear.
- You will be guided on how to perform the test, and we recommend you use headphones.
- The test will check hearing in each ear separately at different pitches.
- If you use hearing aids, you should take them out for the test.
- The whole test takes about 5 minutes.

3. Online Questionnaires

These include information about your:

- Medical history, diagnoses and prescribed medication.
- Use of health services (time spent in recent appointments)
- Functional abilities (doing daily chores) and mental health, including low moods, depression, anxiety.
- Other lifestyle factors including alcohol use.

The online questionnaires will take 50 to 70 minutes to complete.

4. Samples that can be taken at home (Finger prick saliva and stool sample)

To complete these assessments, you will receive a kit by post. The kit will include instructions about how to use the kit and a pre-addressed and stamped envelope for you to post your samples back to us.

i. Finger Prick Blood Test

- This involves pricking the tip of your finger with a lancet to obtain a small blood sample, allowing a drop to be absorbed into the test strip for the finger prick test.
- This will allow us to possibly analyse the level of proteins, related to Alzheimer's disease.
- The procedure is safe and minimally invasive. There may be minor discomfort or pain during the prick; there may be a small bruise or bleeding at the site of the prick.

ii. Saliva Sample

- This involves spitting into a tube. It is a simple, quick and painless procedure.
- The activity of relevant genes for healthy or unhealthy ageing can be switched on and off by means of external factors including dietary factors, in a process called epigenetics, which includes methylation and other specific reactions. We will collect saliva to check the pattern of DNA methylation. This can tell us about how the body is ageing. Muhdo Health will analyse your genetic and epigenetic information.

iii. Microbiome Stool Test

There is recent evidence suggesting a link between the bacteria in the gut ('microbiome') and brain health, this test will allow us to study how microbial factors that could influence the development or progression of Alzheimer's disease.

Participants will receive their Microbiome stool test kit with detailed instructions to follow. A small sample of your stool will be collected. This is a safe and straightforward procedure. It includes:

- Providing you with a sterile collection kit, including a container and instructions.
- Collecting a small stool sample in the provided container.

Properly seal the container and return it to the study team as instructed. Participating in the stool microbiome analysis is generally low risk. People may feel mild discomfort or inconvenience associated with collecting the stool sample and there may be risk of having some mess during the collection process.

5. Feasibility questionnaire

   We will ask you about your experience of completing the PREDICTOM study using a brief online questionnaire after you have completed all the study assessments.

6. Consent for Contact for Future Research

   Based on research scores from the current study, a subgroup, approximately 15%, of the participants from the current study will be asked to take part in a follow-up study. By signing this part of the consent form you are only agreeing to receive information about this next study, and you are under no obligation to take part. None of your personal details will be passed on to any other researcher, institution, or company without your specific consent. Participants enrolling in the follow-up study will receive a separate information sheet along with a consent form. This documentation will outline detailed and study-specific information regarding the assessments involved in the follow-up study.

   There is a small chance that by taking part in this study we may identify findings indicating high risk for a specific serious disease. In that situation, we will contact you by email to let you know our concerns and give you the opportunity to discuss them with one of our study doctors. We will also write to your doctor/general physician to recommend they arrange an appointment with you to carry out further tests. Your involvement in the study would not be affected by this process and it is your decision as to whether you wish to continue to take part.

How will we use and keep information about you and your data safe and secure?

1. Initial storage of information

   The Helse Stavanger HF (Stavanger University Hospital) is the sponsor for this study based in Norway. We will be using information from you in order to undertake this study and will act as data controller for this study. This means that we are responsible for looking after your information and using it properly.

   All the information you provide will be kept strictly confidential and stored either on a protected electronic database or a password protected computer and will only be accessed by the PREDICTOM research team. The information we collect will be kept anonymous and confidential.

   - Information about personal details such as your name and contact details will be held at the University of Exeter (as part of your PROTECT study records) and on site in a secure separate database. It will be available to some members of the PREDICTOM study team to support you should you contact the PREDICTOM team to communicate study information, or for sending and receiving study sample kits. People will use this information to do the research or to check your records to make sure that the research is being done properly.
   - Research data, such as answers to the questionnaires, blood tests and hearing tests will be collected in a study database. The study database will not include your name, just a study number (code). People who do not need to know who you are will not be able to see your name or contact details.

The anonymised research information collected via the study website is transferred in encrypted form to two separate databases that are configured behind a firewall. The databases are stored on Microsoft Azure Cloud servers at data centres located in the UK (UK West Region) and Norway (Norway West Region). The databases are managed by developers on the University of Exeter PROTECT research team. The storage system is structured so that it separates identifiable and non-identifiable information. University of Exeter has developed an online database to collect and process the information you provide, only approved database developers at University of Exeter will have access to personally identifiable data through the master electronic database. Other members of the research team have limited access to your personal information through an administrative area of the website. All research data about you will be de-identified, meaning that your name will be replaced by a study code that will be linked to the data.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in such a way that no-one will be able to work out that you took part in the study. The Helse Stavanger HF will keep identifiable information about you for ten years after the study has finished.

2. Information that might be shared with other researchers securely

Some of your de-identified information will be shared with researchers involved in PREDICTOM in the UK, Norway, Spain, Germany, Belgium, France, Switzerland, Sweden and the USA. They must follow our rules about keeping your information safe.

By participating in the project, you also consent to de-identified information being stored, analysed, and processed by our partners, also abroad, as part of research collaboration and publication. We will at all times use the partners who are most appropriate based on the purpose of the project. Currently collaborating research partners are University of Exeter (UK), King's College London (UK), University of Geneva (Switzerland), LMU Munich (Germany), University of Gothenburg (Sweden), Qairnel (France), Vrije Universiteit Brussel (Belgium), La Fe University/Fundacion Para La Investigacion (Spain) and other organizations such as Mudho Health Ltd , Siemens HealthCare Gmbh/Diagnostics, GE Healthcare, CERTH, Pharmacoidea, Novo Nordisk, Alzpath, Lygature, Icometrix, GN brainworks, Braincheck and Altoida. When cooperating with countries with weaker privacy legislation than United Kingdom, we will set the same strict requirements for the protection of the information, and Chief Investigator Prof. Dag Aarsland will ensure that your information is safeguarded in a safe manner. An updated list of partners can be obtained by contacting PREDICTOM support (contact information at the bottom of the page).

We will never pass your personal information on to any third party without your written consent. All study data will be stored securely according to Data Protection Laws* and the security procedures in place at the University of Exeter, Helse Stavanger HF (Stavanger University Hospital in Norway) and King's College London.

Data may be used by other researchers in the future; however, they will be completely de-identified before they are shared with other researchers outside PREDICTOM, and it will not be possible to identify you.

3. Storage and analysis of the samples (saliva, blood and stool)

The saliva, blood and faeces samples will be stored in a general research biobank for research into age-related brain diseases (SESAM biobank) 2014/328. This is located at Stavanger University Hospital in Norway. The biobank ceases at the end of the project.

The samples taken from you will be forwarded for analysis to the following partner:

- The saliva sample will be sent to our partner Muhdo Health Ltd. in the UK for analysis.
- Finger prick blood sample will be sent to our partner University of Gothenburg, Sweden.

- The stool sample will be analysed locally at Helse Stavanger in collaboration with the University of Stavanger.

The laboratories that analyse the samples will not know your identity. The connection key that can identify you will be stored at SESAM. Chief Investigator Professor Dag Aarsland is responsible for the research biobank. All future research projects that use the material from you must be approved in advance by a research ethics committee for medical and healthcare research ethics.

About our privacy policy and how you can contact us about it

For further information on how your personal information will be processed please visit our privacy policy on the study website. In 2018 regulatory changes in the way that data is processed came into force, with the EU General Data Protection Regulation 2018 (GDPR) and the Data Protection Act 2018 (DPA 2018). Since the UK left the EU, the key principles of EU GDPR have been adopted in the UK GDPR (a 'UK-only' version) and the DPA 2018 still applies. If you have any queries about the University's processing of your personal data that cannot be resolved by the research team, further information can be obtained from the Data Protection Officer, Helse Stavanger HF, via the web-link; https://www.helse-stavanger.no/en. If you have any concerns about how your data is controlled and managed for this study, then please contact the Sponsor Representative (Contact details at the end of the information sheet). Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate.

What happens if I no longer want to be part of the study?

You can withdraw from the study at any time without giving a reason. You can do this through the study website or by contacting us on the PREDICTOM research team (predictom@kcl.ac.uk or 02078480297). If you withdraw from the study, we will ask to keep the information about you that we have already obtained. You can tell us whether you want us to retain any personal information that could be used to identify you (email address, home address and full postcode) or whether you would like us to destroy that information.

Please note we will retain the full name, partial postcode, and participant ID of any withdrawn participants to ensure we have a record of your consent when you registered. We will retain all de-identified data that we have collected up to the time you withdraw. This includes all anonymised data from assessments and questionnaires, de-identified blood sample data, genetic data and extracted DNA, which is also entirely de-identified. On the event of your death, your account would then be closed, and we would retain all anonymised information you have provided up until that date and will retain your personal information unless you have indicated otherwise. If you decide to withdraw from the study, we will keep the de-identified study data about you that we have already obtained. However, to safeguard your rights, we will use the minimum personally identifiable information possible.

Unless you opt to destroy it, any personally identifiable information you submit as part of this study (for example, your name and email address) will be held for a period of 10 years after the study has ended. We will then destroy it. De-identified information, such as your assessment data, may be kept indefinitely and up until the study objectives have been achieved. If you agree to be contacted regarding participation in future studies, you will also be given the opportunity to take part in important future research about the brain and how we can prevent conditions such as dementia.

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

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to predictom@kcl.ac.uk, or
- by ringing us on 020 3228 6000.

What are the possible benefits and risks of taking part?

This is an 'observational' study, meaning we only wish to observe your situation.

There is a small risk that some people may find certain questions difficult to answer or distressing. For example, some of the memory tests are designed to be very challenging, which may cause increased stress. In addition, some of the questionnaires include questions about mental health, which may be distressing for some participants. Please contact your general practitioner (GP) or if you are worried about your mental health, please contact Samaritans at www.samaritans.org . You can also call the Samaritans day or night if you need someone to talk to without judgement on 116 123. Mind's website at www.mind.org.uk has useful resources to help you cope if you are feeling anxious, worried or isolated.

The main advantage of this research is that participants will be taking part in an important research study that could provide valuable new knowledge about new ways to detect people at increased risk for AD.

Does this study have approval from an ethics committee and insurance coverage?

The Wales REC 4 Ethics Committee has approved this research (Ref: 24/WA/0069) and the research will be covered by normal insurance policies at the local site. Compensation for any injury caused by taking part in this study will be covered by SYB24941553A01. Insurance Scheme will be applied for negligent harm. Non negligent harm was not covered by the scheme

Will my taking part in this study be kept confidential?

In this research study we will use information from you. We will only use information that we need for the research study. Everyone involved in this study will keep your data safe and secure. We will also follow all privacy rules. At the end of the study, we will save some of the data in case we need to check it for future research. We will make sure no-one can work out who you are from the reports we write. Participants who lose capacity during the study would be withdrawn and their GP would be contacted.

What happens to samples taken by you?

If you agree, you will be sent a sampling kit for the collection of a saliva sample and blood sample (by finger prick) to your address. The trial kit you will receive contains instructions on how to use these. It is a simple, quick, and painless procedure. A pre-addressed envelope will be enclosed so that you can easily send the samples back to us.

The samples that are taken and sent to us will be stored in a general research biobank for research into age-related brain diseases (SESAM biobank) 2014/328. This is located at Stavanger University Hospital. The biobank ceases at the end of the project.

The samples taken from you will be forwarded for analysis to the following partner:

- The saliva sample is sent to our partner Muhdo Health Ltd. in the UK for analysis.
- Finger prick blood sample is sent to our partner University of Gothenburg, Sweden.
- The stool sample will be analysed locally at Helse Stavanger in collaboration with the University of Stavanger.

The laboratories that analyse the samples will not know your identity. The connection key that can identify you will be stored at SESAM. Chief Investigator Professor Dag Aarsland is responsible for the research biobank. All future research projects that use the material from you must be approved in advance by a research ethics committee for medical and healthcare research ethics.

What will happen at the end of the study?

At the end of the study period, you will complete your final assessments, we will 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 if you so wish. The findings will also be available on the study website. The information collected is totally confidential and no individuals will be identified in any reports/publications or presentations.

What if there is a problem?

If you have a concern about any aspect of this study, please contact the research team on 02078480297 or email us on predictom@kcl.ac.uk.

For independent advice and information, you can contact the South London and Maudsley Trust Patient Advice and Liaison Service (PALS):
Tel: 020 3228 6000
Webpage: https://www.helse-stavanger.no/en
Study Chief Investigator (CI) details can be found below:
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Further Information

Thank you for taking the time to read the information about this study. If you would like more information before you decide whether or not to take part, you can contact a member of the study team by calling the study helpline on 02078480297 or emailing your query to predictom@kcl.ac.uk. Please note that this helpdesk is for general information and support for the study. It will connect you to the study team who will be able to tell you about the study but will not be able to provide medical advice.

Consent to Take Part

- I am aged over 50 or older, live in the UK and have access to a computer or touchscreen device with internet access.
- I confirm that I have read and understand the Information Sheet for Participants dated 14 August 2024, V2.51 for the above study. I have had the opportunity to consider the information, seek clarification and understand my involvement in the study.
- I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.
- I understand that relevant data collected during the study may be looked at by individuals from the research team at the Helse Stavanger, PREDICTOM researchers at PREDICTOM consortium member organisations listed at www.predictom.eu, and regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.
- If I choose to withdraw, I understand that all anonymised data will be retained in the study, and that I will have the choice to destroy all identifying data about me that is held in the study with the exception of my name, partial postcode and consent form.
- I understand that the data will be stored in a way complying with the provisions of the General Data Protection Regulation (2018) and other Data Protection Laws.
- I understand that anonymous data from this study may be used by other researchers in the future.
- I understand that the storage of my biomarker samples (finger prick blood test, stool and saliva) will be pseudonymous (labelled with an ID number instead of personally identifying information) and outcomes of the analysis are unlikely to have any implications for me personally.
- I agree to provide samples (finger prick blood test, stool and saliva) for biomarker analysis as part of the PREDICTOM study.
- I agree to provide data through questionnaires and online tests (memory, hearing and eye tracking) as part of the PREDICTOM study.
- I give permission for members of the research team to contact my General Practitioner (GP) regarding any significant incidental findings.
- I give permission for my anonymised study data to be analysed by the research team and study collaborators to check my suitability for future studies involving specialised assessments such as imaging scans, lumbar puncture and face to face memory tests.
- I agree to take part in the PREDICTOM study.