A blood test for dementia? A cohort study to assess the diagnostic utility of plasma neurofilament light chain protein in all-cause dementia

Participant Information Sheet/Consent form

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Participant Information Sheet/Consent Form

Non-Interventional Study - *Adult providing own consent*

Title	A blood test for dementia? A cohort study to assess the diagnostic utility of plasma neurofilament light chain protein in all-cause dementia
Project Sponsor	Eastern Health
Principal Investigator	Professor Amy Brodtmann
Locations	Any location within Eastern Health network

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project: **A blood test for dementia? A cohort study to assess the diagnostic utility of plasma neurofilament light (NfL) chain protein in all-cause dementia.**

You have been invited because you have come to Eastern Health with a cognitive complaint or potential diagnosis of dementia.

The diagnosis of a progressive brain disease is not always clear at the start. Often further testing is required 6-12 months later. This delays diagnosis, resulting in increased stress for you and your loved ones. It also means that it delays access to early therapies if they are available.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and research involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part, and be seen by the same health professional staff in the same services.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read

• Consent to take part in the research project

• Consent to the tests and research that are described

• Consent to the use of your personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The purpose of this research study is to assess the diagnostic utility of a simple blood test for all-causes of dementia.

3 What does participation in this research involve?

You have been invited to take part in the study because you are presenting with a cognitive complaint or potential diagnosis of dementia to Eastern Health.

This is a *cohort* study, which means we will follow your progress at one year. Participation involves a single blood test, speech analysis and consent to be contacted in one year. Blood will be drawn on one occasion only, and we will take contact details at that time. The blood test can be done at one of the participating institutions at Eastern Health. In some circumstances we may be able to arrange to have the blood taken from other locations such as your home. For your convenience, sometimes the blood test can be scheduled for when you arrive at clinic or are in hospital for another reason. A trained staff member will collect approximately 50ml of blood (about 2-3 tablespoons) from a vein, for storage and later analysis. Participation also involves providing speech samples to gather data on speech and language function. You will be asked to log into a web page from Redenlab and complete speech tasks that have been designed to be carried out online and to be a quick to give a quantified measure of brain health. As an example, some of these tests will assess speech timing, voice quality, sentence structure and verbal ability.

We will assign you a unique participant number (participant identification), which means you will remain anonymous in the research project. Your clinical details will be entered into a secure database using this number. Every 2 months, we will hold a meeting called a Clinical Diagnostic Consensus Meeting (CDCM), where we will discuss the blood test result, any brain imaging you have had, and your symptoms. The CDCMs will involve disclosure of your name for the purpose of your clinician identifying a diagnosis, however the storage of all data will remain de-identified using your unique participant number.

We plan to contact you at 12 months (follow-up review), either via seeing you in clinic if your treating doctor has booked this, or via a phone or video call. We will also send you some forms in the mail you for you to complete before the review. At the follow-up review, we will ask you questions about your level of function and mood, and perform some memory and thinking tasks. These questionnaires will include a routine screen of psychological distress. As your wellbeing is our priority, we will notify your nominated physician (e.g, General Practitioner, Geriatrician) if your results are clinically significant who may then decide whether this warrants follow up. We will not be discussing these results with you, and encourage you to contact your physician if these questions raise any concerns for you. This review and testing and questionnaire completion should take approximately 1 to 1.5 hours.

The details of each study visits are summarised in Table 1.

Table 1. Details of each study visit.

Visit	Study procedure
Baseline	• Consent to be obtained from participant and/or Medical Treatment Decision Maker • Participant's blood will be drawn • Participant's speech will be recorded
12-month follow-up review	• Participant to be reviewed in clinic or via a phone call (includes cognitive and wellbeing testing) • Participant's speech will be recorded

Should you wish to participate, you will be asked to sign the consent form attached. If you have problems with your memory or thinking, you will also be required to discuss your participation with a Medical Treatment Decision Maker (MTDM, Person Responsible) who has the ability to help you with making decisions about your participation. This person can be a spouse or close relative or friend. We will also ask them to sign a similar consent form on your behalf.

For the purpose of analysing the cost-benefits of this blood test, data from the Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) will be requested from services Australia. You will be asked to sign a separate consent form authorising the study to access your Commonwealth health information provided by Services Australia (see the separate Services Australia Participant Information Document and Participant Consent Form). Participation in this economic analysis is optional and will not impact your involvement in main study procedures. Services Australia is not involved in this research other than to provide the information that you have consented to the release of, should you decide to participate in this study. Services Australia has confirmed that this research and any associated documents have received approval from a Human Research Ethics Committee (HREC) that is registered with and operate within guidelines set out by the National Health and Medical Research Council (NHMRC).

If English is not your first language an interpreter can be arranged through Eastern Health as part of the study. This person will interpret the content of this form and all the information provided by the study team.

Study Procedures

There will be only one visit required for this study, which will likely be the day that you see your doctor in clinic. During this visit we will review your medical history and current medications and you will have blood drawn from a vein. The blood will be processed for storage, and then kept until all blood samples from participants have been collected. The sample will then be analysed in "batches" and results compared with each participant's clinical diagnosis. Speech will also be recorded in the clinic or via a secure weblink in your home.

There are no additional costs associated with participating in this research project, nor will you be paid to participate. All tests and medical care required as part of the research project will be provided to you free of charge.

If you have a local doctor, we strongly recommend that you inform them of your participation in this research project.

4 What do I have to do?

If you decide to take part in this study, you will have a single blood draw at the time of consent. The only test above routine clinical care will be this blood draw and speech analysis testing. If you are due to have a blood draw as part of your visit, an additional amount of blood will be taken for the purpose of this research project. If you are not scheduled to have a blood draw, then a member of our research staff will conduct a blood draw specifically for the purpose of this study.

5 Other relevant information about the research project

If you agree to take part in this research project, you will be one of about 1000 participants. This research project is open to all adult people who are presenting to Eastern Health services with a problem with thinking or memory. There are no other inclusion or exclusion criteria. This is to ensure that the findings from this research represent as many people as possible, regardless of level of education, language spoken, or identity. It ensures that they can be generalised to other national healthcare networks and can provide maximum information on the utility of using blood-biomarker estimation in real-world clinical settings.

By consenting to participate you will also be allowing your data from the study to be shared with The Markers In Neurodegenerative Disease (MiND) study. The MiND study is a 5-year study investigating the utility of plasma NfL and other markers in distinguishing neurodegenerative from non-neurodegenerative and primary psychiatric disorders in patients with cognitive, neurological and psychiatric symptoms. It is hoped that by sharing clinical and biomarker data, evidence base development will be accelerated.

As well, this study intends to contribute to international collaborations and biobanking. This means that for the first time, a truly representative sample of Australian people are being offered biobanking of plasma and DNA to advance dementia research. A biobank is a type of biorepository that stores biological samples for use in research. If you would like to participate in the DNA and plasma banking there is an additional consent option in the consent form at the end of this document.

You will complete online speech testing, which can be completed on a computer or other electronic device such as an iPad, tablet, or phone. This computer or device can belong to you, a family member, or a friend, or can be a public device such as a computer in a local library. You will need to be able to access the internet with whichever device you choose. Unfortunately, if you are not able to access the internet you will not be able to participate in this part of the study.

The Redenlab online speech tests consist of six short tasks, each taking a few seconds or a few minutes to complete. It will take approximately seven minutes to complete all the tasks. It is divided into sections so that you can complete part of it and return to it later.

6 Do I have to take part in this research project?

Participation in this research project is completely voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Eastern Health.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that the participant will receive any benefits from this research, however you will be making a valuable contribution to understanding the utility of neurofilament chain (NfL) in dementia which may help us in the future to improve diagnosis of all-cause dementia.

9 What are the possible risks and disadvantages of taking part?

A blood test is very safe but may cause some discomfort, bruising, minor infection or bleeding at the site of injection. If this happens, it can be easily treated.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

10 What will happen to my test samples?

The blood samples obtained from you will be processed, frozen and stored. This is a requirement of the study. Your blood samples will be processed at the Florey Institute, Austin campus and stored at the Alfred Centre. The stored samples and the information collected about you during the study may be used by the research partners to perform analyses during the course of the study. This blood sample will be stored with a number that can only be linked to your details via a secure database.

You will be asked to indicate at the end of this Informed Consent Form if you also agree to your samples being retained for optional future testing to help answer questions that are not part of the main study. This means that we store your samples indefinitely. You can always withdraw your

consent at any time. The samples obtained from you will then be destroyed. If your samples have already been analysed, you can tell us if you want the results to still be used.

Non-identifying testing information will be collected via Redenlab which is the third party speech testing platform. Information will be stored on their servers for the duration of the study. Data is stored in accordance with local legislation that provides data privacy and security provisions for safeguarding medical information. Redenlab may use aggregated testing information and demographic data that does not contain personal information for research purposes to augment their normative data set. The use of this data is strictly governed by a research licence agreement. No personal identifying information will be given to any third party.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your regular health care will continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

12 Can I have other treatments during this research project?

Yes. Participation in this study does not prevent you from having any treatments or being involved in any other study.

13 What if I withdraw from this research project?

Please notify a member of the research team if you decide to withdraw the participant from this research project. A member of the research team will inform you if there are any special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the investigators up to the time you withdraw will form part of the research project unless you chose to have that data removed.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include problems with the machine used to test the blood, changes to staff, or issues with funding of the project. However, this is unlikely as the research team have close to 100 years of trial experience between them, and have successfully run many cohort studies in patients.

15 What happens when the research project ends?

The findings will be submitted for presentation at conferences and publication. The publications will not include any information that allows identification of individual participants. You will always remain anonymous. You may request a copy of any publications once they are completed.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the consent form you consent to the research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project (e.g. personal identification number, gender, health data such as previous disease and study records) that can identify you will remain confidential. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about you may be obtained from your health records held at this and other health services for the purpose of this research. By signing the consent form you agree to the research team accessing health records if they are relevant to your participation in this research project.

This review may be done by the relevant authorities and authorised representatives of Eastern Health, the institution relevant to this Participant Information Sheet, Eastern Health, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant research personnel and regulatory authorities as noted above.

During the study, all the participants' records will be kept strictly confidential. This means that only the Investigator and the study staff directly involved in this study will have access to them and the records will be kept in a secure office at Eastern Health.

Information about your participation in this research project may be recorded in your health records.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the research team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project and for the future research described in Section 16 that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

The only test in addition to your routine medical treatment is the blood test and speech analysis. Although problems following a blood test are rare, you will receive any medical treatment required to treat any injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

This research has been funded by the Ian Potter Foundation Grant (Medical Research; $150,000), supported by the Eastern Health Foundation Research Grant (two grants, $150,000 and $21,600), and the Florey Institute of Neuroscience and Mental Health Dementia Research Centre ($20,000).

This research is being conducted by researchers from Eastern Health, The Florey Institute, Australian Dementia Network (ADNeT) Registry, Melbourne Health, The University of Melbourne and Mayo Clinic in the United States of America.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Eastern Health.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2018). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor or any of the following people:

Clinical contact person 1

Name	Professor Amy Brodtmann
Position	Chief Investigator
Telephone	03 9094 9540
Email	agbrod@unimelb.edu.au

Clinical contact person 2

Name	Ms Tracy Morris
Position	Study Coordinator
Telephone	03 9094 9542
Email	tracy.morris@monash.edu

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

Complaints contact person

Name	Eastern Health Human Research Ethics Committee
Position	Chairperson
Telephone	03 9895 3398
Email	ethics@easternhealth.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	Eastern Health Human Research Ethics Committee
HREC Executive Officer	Chairperson
Telephone	03 9895 3398
Email	ethics@easternhealth.org.au

Local HREC Office contact (Single Site - Research Governance Officer)

Name	Eastern Health Human Research Ethics Committee
Telephone	03 9895 3398
Email	ethics@easternhealth.org.au

Eastern Health

Consent Form - *Adult providing own consent*

Title	A blood test for dementia? A cohort study to assess the diagnostic utility of plasma neurofilament light chain protein in all-cause dementia
Project Sponsor	Eastern Health
Principal Investigator	Professor Amy Brodtmann
Locations	Any location within Eastern Health network

Consent Agreement

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

☐ I agree to participate in DNA and plasma banking as an optional part of the study.

Declaration by Participant – for participants who have read the information

Name of Participant (please print) _____

Signature _____ Date _____

Declaration - for participants unable to read the information and consent form

See Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 Section 4.8.9. A Medical Treatment Decision Maker may be a witness*.

Witness to the informed consent process

Name (please print) _____

Signature _____ Date _____

*Witness is not to be the Investigator, a member of the study team or their delegate. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.

Eastern Health

Form for Withdrawal of Participation - *Adult providing own consent*

Title	A blood test for dementia? A cohort study to assess the diagnostic utility of plasma neurofilament light chain protein in all-cause dementia
Project Sponsor	Eastern Health
Principal Investigator	Professor Amy Brodtmann
Locations	Any location within Eastern Health network

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Eastern Health.

Name of Participant (please print) _____

Signature _____ Date _____

In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.