Participant Information Sheet/Consent Form
Optional Components for Participants
Melbourne Health

Title	Markers in Neuropsychiatric Disorders: investigating biomarkers and clinical markers in neuropsychiatric, neurological and neurodegenerative disorders
Short Title	MiND
Protocol Number	2020.142
Project Sponsor	The Royal Melbourne Hospital
Principal Investigators	Professor Dennis Velakoulis, Dr Dhamidhu Eratne and the Melbourne Health MiND Study Group
Location	The Royal Melbourne Hospital

Part 1: What does my participation involve?

1. Introduction

You are invited to take part in opt-in, optional components of the research study that you are already participating in, Markers in Neuropsychiatric Disorders (MiND). These sometimes occur in people's standard clinical care. However, if you are not having them as part of your standard clinical care, we would like to offer these to you. These additional components provide very useful data for the study, which will mean we can interpret all of the other data from your participation in this study, even better.

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.

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 brain and nervous system are extremely complicated. We still have a long way to go to improving our understanding of illnesses of the brain and nervous system. Even after seeing

many doctors and having lots of tests, many people still struggle with uncertainty, wrong diagnosis, and wrong treatments, sometimes over many years.

Research we and others have done, has started to show that measuring levels of proteins or "biomarkers", such as one called 'neurofilament light', can significantly improve our understanding of these illnesses, for example improving our ability to diagnose early, quickly and accurately.

This research study aims to study how well the biomarker neurofilament light can improve early, accurate diagnosis, to fill in many gaps in our understanding, and improve clinical care and outcomes for patients and their families.

By collecting and storing blood to measure neurofilament light biomarker levels now, and using the remaining sample for the future when new biomarkers are discovered, and linking these levels with clinical information, we will be able to significantly improve our understanding of these diseases and how neurofilament light and other biomarkers can help to better diagnose and potentially prevent and treat them.

Our research study could lead to important outcomes for patients and their families. For example, our study could lead to a simple blood test that even a general practitioner can do, right at the beginning, to diagnose and guide further tests (or not), that would be a significant improvement on how we do things currently, with positive impacts for patients and their families.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions

3. What does participation in this research involve?

Your participation is completely voluntary, and will only start after you have been given information on the study, have been able to ask all the questions you want, and after understanding the study and wish to continue, you sign the consent form to document this. You will be given the opportunity to discuss any questions with the research coordinator or one of the investigators. Your medical care will happen as normal. It will not be affected by participation in this study and there will be no consequences or negative impact on your normal course of treatment and care if you participate, or if you decide to withdraw from the study at any time for any reason.

If you agree to participate in the optional components part of this study, the study doctor will offer the following to you:

1. **Signing the consent form for the optional components**
2. Some, or all, of the following, depending on what you are having in your standard clinical care, in order to provide more comprehensive and gold-standard data to compare to and complement the other data you are providing for this study:
    a. **A neuropsychology cognitive assessment**
        - A trained professional will conduct an in-depth and comprehensive assessment of different parts of your brain functioning such as thinking, memory, language, reasoning
        - This assessment typically takes 2-3 hours

    and/or

    b. **A brain scan (magnetic resonance imaging scan, or MRI scan),** to look at the size and shape of your brain
        - This will be done by trained professionals in a radiology department
        - The MRI scan itself will take only about 30 minutes, although there might be some waiting and preparation time before and after. The whole process should only take at most a few hours

    and/or

c. **A lumbar puncture** to collect cerebrospinal fluid (CSF) and store for research testing of biomarker levels to better understand brain illnesses
    - CSF is still the gold standard for researching biomarkers of brain and nervous system functioning. This will allow analysis of biomarkers in CSF, and to compare to and understand biomarker levels in blood.
    - Preparation for the procedure can take 5-10 minutes. The lumbar puncture itself is usually fairly brief, taking about 5-10 minutes. You will be asked to lie down and observed for a little while afterwards. The whole process should take less than an hour
    - You may also require a blood test close to the time you have a lumbar puncture

There are no costs associated with participating in this research project, nor will you be paid. You may be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visit, up to a maximum of AUD$100

It is desirable that your local doctor be advised of your decision to participate in this research project. If you have a local doctor, we strongly recommend that you inform them of your participation in this research study.

4. Do I have to do anything differently? Can I have other treatments during this research project?

Participation in this study does *not* change anything else in your healthcare and standard clinical treatment. There are no lifestyle or dietary restrictions, or other changes you need to make just because you are participating in this study. You should follow your usual clinical treatment with and advice from your treating doctors and other healthcare professionals, and continue to take your usual, regular medications. You can have other treatments and participate in other research projects.

5. Other relevant information about the research project

- This research study has the potential to recruit at least 150 participants per year
- In order for a study like this to be successful, many collaborations with medical researchers from a number of organisations with expertise and equipment and technology is required

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

Participation in any research study is 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.

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 the Royal Melbourne Hospital.

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.

7. What are the possible benefits of taking part?

It is unlikely that you will directly benefit by taking part in this study, because the most important health benefits will be realised years from now. However, your participation will contribute and

benefit the advancement of scientific knowledge, our understanding of diseases, and help future generations.

8. What are the possible risks and discomforts of taking part?

This research study does not involve any interventional treatment. You may have none, some or all of the effects listed below. If you have any of these side effects, or are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

- **Blood collection**:
    - The blood test you will have in this study will follow the same procedure as a blood test you would have in your standard clinical care. The blood test will be performed by a highly trained and experienced staff member
    - The risks with standard blood tests are minimal when done by a qualified person with appropriate technique. There is a small risk of discomfort, bruising, and infection (extremely rare) at the site of the needle puncture. Some people can feel dizzy or faint after they give blood. All of these can be easily treated.
- **MRI brain scan**
    - This is another common, low-risk procedure routinely performed in standard clinical care
    - During this time you need to keep very still and we will make sure you are in a comfortable position. Some people may become anxious during the scans, especially due to the confined space (claustrophobia). The scanner is quite noisy and so you can have earphones to reduce this noise. You will be able to communicate directly with the radiology and study staff at all times during the scan and ask that the scan be stopped if you feel too anxious or want to stop for any reason
    - There are no long-term risks related to MRI scans, however a strong magnet is used so it is important that no metal objects are taken into the scanner room. You will go through rigorous standard safety screenings and checklists with radiology staff prior to the MRI scan
- **Lumbar puncture**
    - This is a low-risk procedure that is commonly performed in clinical care and part of routine care for many patients with neuropsychiatric, neurocognitive and neurological symptoms, that will be conducted by experienced clinicians skilled in the procedure
    - You must not be taking any regular blood thinning medication (for example, warfarin). After discussing the procedure again in detail with you and after confirming that informed consent has been provided for this optional, opt-in procedure, a small amount of local anaesthetic will be injected into your lower back, around the spine, in order to provide some numbing. Approximately 15mL of cerebrospinal fluid (CSF) will be collected. Routine clinical analysis is required to interpret the validity of the sample and interpret biomarkers, and the remaining CSF will be processed and stored for research analysis of biomarkers
    - Most people who have a lumbar puncture experience no side effects or mild side effects such as mild transient pain and mild transient headache. Following a lumbar puncture, you may experience minor backache or discomfort (5-17%); minor bruising or swelling at the puncture site. Typical headache or dizziness (9%) may occur due to removal of CSF. If a headache does occur, it is usually mild, easily treated, and goes away within 2 days. Occasionally, a more severe headache can develop after a lumbar puncture (uncommon, less than 5% of the time). These severe headaches can be treated. Other very rare (less than 1%), side effects are infection, damage to the spinal nerves (exceedingly uncommon) and bleeding into the spinal fluid space. You will be encouraged to see their GP or present to the emergency department, urgently, in the unlikely event that you have a severe headache or any other symptoms of concern, for assessment and treatment

- **Neuropsychological assessment**
    - This is a common clinical assessment that will be conducted by staff with training, expertise and experience in the formal neuropsychological assessment of patients with neuropsychiatric or neurological symptoms, which includes training on identifying and managing any distress or discomfort during the assessment. You may choose not to answer specific questions or do any test at any time, and end the assessment at any time. If you have any distress and discomfort, this will be addressed as described below
- **Unplanned or 'incidental findings':**
    - During research, it is possible that information is discovered that has serious and significant health implications for you. It may also reveal something about you that is unrelated to your original disease. This information is known as 'incidental findings'
    - As this study is focused on research tests (not clinical tests), it is very unlikely that there will be any of these incidental findings. However, in the unlikely event that something potentially clinically relevant is identified, this will be urgently reviewed by the senior study doctors. Only findings that meet the following criteria will be fed back urgently to your treating doctor, to then discuss and return the findings to you:
        - significant (such as one that indicates a life-threatening condition) and/or
        - clinically actionable (for which there are specific established treatments) and
        - confirmed (that has been checked by senior study doctors, and confirmed as accurate and/or valid, as far as reasonably possible in a research context)
- **Distress or discomfort:**
    - Any interaction that involves discussion or assessment of medical symptoms, particularly neurological, neurocognitive and neuropsychiatric, can potentially cause discomfort or distress. This also applies to neuropsychological examination and any incidental findings. All study staff that interact with you have training and expertise with people with neurological or neuropsychiatric symptoms. Distress or discomfort with any part of the research study will be promptly and sensitively responded to by study staff. 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

- In the event that you suffer an injury as a result of participating in this study, hospital care and treatment will be provided by the public health service at no extra cost to you

9. <u>What if I change my mind and don't want to participate?</u>

Even after your samples and health information have been collected, you are free to withdraw your consent at any time without having to give a reason. Withdrawing your consent to participate will not affect your medical treatment in any way. Your decision whether to take part or not, or to take part and then withdraw, will not affect your relationship with the researchers or your doctor, or Royal Melbourne Hospital. If you choose to withdraw, please contact the study staff (contact details below).

You may choose to withdraw from future sample and data collection while giving the study permission to keep the samples and information about you that have already been collected. You may also give the study permission to collect relevant follow-up information from your medical records for use in research and analysis. However, you will not be personally contacted by the study from then on. Should you choose to fully withdraw your consent, the study will discard your stored samples and associated personal and clinical information. However, if some

or all of your samples have already been used or provided to a research project, it will not be possible to retrieve these samples.

Also, research that has been published cannot be deleted or discarded, but you will not be able to be identified in any way. All information used in research publications will be a collation of results of all study participants and/or will be in a coded format where individual names, addresses or other identifiers are not disclosed.

10. Could this research project be stopped unexpectedly?

This research study is an ongoing study, and we do not anticipate any scenario in which this research would be stopped unexpectedly. However, in the unlikely event that it is stopped unexpectedly, you will be notified immediately and made aware of how your data will be stored and/or destroyed as required by the research and ethics departments.

11. What happens when the research project ends?

This research study aims to provide significant research findings on an ongoing basis. We want to be able to share summaries of these findings and the successes of the study, and your participation, with you. However, research of our kind can take a long time, sometimes even years, to collect, analyse, finalise and publish. Findings will be published in scientific journals, on the study and Royal Melbourne Hospital websites, and shared with community organisations.

Part 2: How is the research project being conducted?

12. What will happen to information about me?

As you are already participating in this study, all information will be stored in the same secure, password protected database specifically designed for research, and housed at Melbourne Health/Royal Melbourne Hospital, and only accessible by study researchers. Any information recorded in paper form for this research will be kept in a locked filing cabinet in the senior study doctor's office at Neuropsychiatry, Royal Melbourne Hospital, that only researchers have access to.

The results of this study will be published and/or presented in a variety of forums, such as in scientific journals and at scientific meetings. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the research team. You also have the right to request that any information with which you disagree be corrected. Please contact the study 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 future research 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.

13. What will happen to my test samples?

The samples collected from you will be labelled with a unique study code, and will be stored in freezers at a biobank such as the Florey Institute for Neuroscience, Parkville, Victoria.

Samples will be analysed for neurofilament light. In order to facilitate research on biomarkers that haven't even been discovered yet and maximise the benefits of this ongoing research study, your remaining samples will be stored indefinitely and used for any future unknown, unspecified medical research.

Your samples may be shared with study researchers in Australia and overseas in order to achieve the aims of this research study. If your samples are shared with study researchers outside of Melbourne Health, your samples will be sent in a coded manner. Any identifiable, personal information (such as name, contact details, etc.) will **not** be disclosed to them. Your samples will only be used for research purposes. No research will take place using your samples and information unless that research is first reviewed and approved by a properly constituted Human Research Ethics Committee, which will determine whether the benefits of the research outweigh the cost to you and your privacy.

Your samples will be re-identifiable, so that data from samples (such as biomarker levels) can be linked with your clinical information, which is crucial to properly understanding the biomarker levels, and the success of this study. Also, in the unlikely event of an incidental finding, study staff can de-code your sample (i.e. re-identify you) if necessary. Your privacy is paramount; only study staff will have access to the re-identifable information, which is kept in a secure, password protected, research database.

It is possible that our research might result in medications or tests that are produced and marketed by private organisations. This study may or may not benefit from any of the revenue that such research may produce. If the research does lead to discoveries that are of commercial value to the researchers and their institutions, there will be no financial benefit to you or your family. If this study were to benefit from any discoveries, any funds so derived would be used for future research.

14. Who is organising and funding the research?

This research project is being conducted by Dr Dhamidhu Eratne and Professor Dennis Velakoulis. It is funded by the Australian National Health and Medical Research Council (NHMRC) and Medical Research Future Fund (MRFF).

15. 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 reviewed and approved by the HREC of Melbourne Health.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

16. 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 on 03 9342 8750 or any of the following people:

Clinical contact person

Name	Professor Dennis Velakoulis or Dr Dhamidhu Eratne

Position	Consultant Neuropsychiatrist
Telephone	03 9342 8750
Email	Dennis.velakoulis@mh.org.au or Dhamidhu.eratne@mh.org.au

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	Director Research Governance and Ethics
Position	Complaints manager
Telephone	9342 8530
Email	research@mh.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

Name	Melbourne Health HREC
HREC Executive Officer	Manager HREC
Telephone	03 9342 8530
Email	research@mh.org.au

Consent Form – Optional Components for Participants

Title	Markers in Neuropsychiatric Disorders: investigating biomarkers and clinical markers in neuropsychiatric, neurological and neurodegenerative disorders
Short Title	MiND
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Project Sponsor	The Royal Melbourne Hospital
Principal Investigators	Professor Dennis Velakoulis, Dr Dhamidhu Eratne and the Melbourne Health MiND Study Group
Location	Melbourne Health

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 give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Melbourne Health concerning my condition and treatment for the purposes of this project. I understand that such information will remain confidential.

Optional components of the research project (please initial under your preferred response)	**Yes**	**No**	**Not Offered**
I have been offered a neuropsychology examination, and agree to it			
I have been offered a brain MRI scan, and agree to it			
I have been offered a lumbar puncture, and agree to it			

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
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/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/ Researcher (please print) _____

Signature _____ Date _____

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

Form for Withdrawal of Participation – *Optional Components for Participants*

Title	Markers in Neuropsychiatric Disorders: investigating biomarkers and clinical markers in neuropsychiatric, neurological and neurodegenerative disorders
Short Title	MiND
Protocol Number	
Project Sponsor	The Royal Melbourne Hospital
Principal Investigators	Professor Dennis Velakoulis, Dr Dhamidhu Eratne and the Melbourne Health MiND Study Group
Location	Melbourne Health

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 Melbourne Health.

Options for withdrawing (please initial under your preferred response)	**Yes**	**No**
1) I wish to withdraw but give researchers the permission to keep my samples and my personal and health information that has already been collected and to use them for future ethically approved research		
2) I wish to withdraw but give researchers the permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.		
3) I wish to withdraw fully, and for my samples and associated personal and clinical information collected to be destroyed and deleted		

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/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/ Researcher (please print) _____

Signature _____ Date _____

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