Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Title	Optimised Transcranial Magnetic Stimulation for the Treatment of Depression (OptiTMS)
Short Title	Optimised TMS for Depression
Ethics Number	RMH HREC 2024.326
Project Sponsor	The University of Melbourne
Coordinating Principal Investigator	*Dr Robin Cash*
Participant study ID	OptiTMS – _ _ _

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project because you have been experiencing major depression and have expressed interest in the study. This research project is testing a new way of delivering Transcranial Magnetic Stimulation (TMS) for the treatment of people experiencing major depression. The new treatment method is optimised TMS.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments 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 your 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 have the tests and treatments 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?

Major Depression is a leading cause of disability worldwide and often difficult to treat. TMS is a promising non-invasive therapy (i.e. it does not involve surgery or the introduction of instruments into the body) for treatment of difficult to treat depression, but while life-changing for some individuals, others receive little benefit. Emerging research suggests that TMS clinical effects might be related to the precise part of the brain at which TMS is delivered.

This study aims to compare the clinical benefits of two different methods of TMS treatment delivery. We will compare current TMS treatment where the stimulation target is based on the size of a person's scalp to a newer approach where the stimulation target is more tailored and specific **(optimised)** and based on a person's brain Magnetic Resonance Imaging (MRI) scan image. Both treatment methods target areas in the front of the brain and use a standard 4 week course of TMS normally used in clinical care. In sum, this project aims to determine whether optimised TMS is more effective than standard TMS therapy for individuals with MDD. We are internationally recognised for our expertise in this area.

TMS is a non-invasive method of brain stimulation that involves application of brief magnetic pulses to your head. TMS is delivered through a coil that is positioned at the stimulation target site, typically at the front of the brain (on the outside of your head) as this area is known to be involved in depression. Many people describe TMS as a tapping sensation on the head. This sensation is usually mild but may be associated with some discomfort. The sensation typically becomes less uncomfortable over the first few sessions of treatment.

TMS is an established and approved therapy for treatment of difficult to treat depression under the Medicare Benefits Scheme. The TMS device used in this study has been cleared for marketing by the Therapeutic Goods Administration in Australia and the U.S. Food and Drug Administration (FDA) for the treatment of MDD, particularly in cases where patients have not responded adequately to antidepressant medications.

Furthermore, the study aims to understand the immune and metabolic health status in people with depression, and to create a way to use immune and metabolic information to help predict how well a patient will respond to TMS treatment for depression.

The study is to be conducted at three sites in Australia, and it will involve 310 participants, randomised in 1:1 ratio to the standard TMS treatment or the optimised TMS treatment group. The study was initiated by Dr Robin Cash at University of Melbourne and is funded by a National Health and Medical Research Council (NHMRC) grant.

3 What does participation in this research involve?

You will be participating in a randomised controlled research project. Sometimes we do not know which treatment is best for treating a condition. To find out we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one treatment is better. We try to make sure the groups are the same in terms of age, biological sex etc. Group allocation is 'double-blind'. This means that neither you, your trial doctor, nor the research staff know which treatment you are receiving. At the end of the trial, the results of the two groups will be compared to see if optimised TMS or scalp based TMS is more effective in treating depressive symptoms in people who have MDD.

Participation in this study will involve completion of 4 weeks of daily TMS treatment (Monday to Friday) and an MRI scan, as well as visits at which clinical interviews and questionnaires will be completed, over a 6-month period.

We will seek your written consent before any assessment, research and treatment procedures are conducted. Each treatment session will involve you being given TMS therapy in the treatment facility under appropriately approved conditions. You will be randomly allocated to receive either TMS treatment based on your scalp dimensions or on your MRI scans. For each session you will have a trained clinician who will monitor you throughout the administration of the treatment.

For the duration of your participation in the study you will be required to not make any changes to your current medication(s) schedule for depression. On the days of study treatment, it is advised that you get good sleep the night before and are well hydrated and avoid alcohol, recreational substances, and intense physical exercises 72 hours prior to the visit.

All participants will receive daily treatment sessions (Monday – Friday) for four weeks. Clinical, mood and health care assessments will be conducted at various scheduled intervals, including at 1, 3 and 6 months after TMS therapy is completed (see Table 1 for the full schedule of visits and assessments). These are conducted via phone/video, online surveys or in person.

Table 1. Visits and assessments across the duration of study

Assessment / Procedure	**Visit**								
	Pre-Screen / Screen	**Baseline**	**TMS treatments (week)**				**Follow up (month)**		
			1	**2**	**3**	**4**	**1**	**3**	**6**
Eligibility screening	x								
Consent	x								
Demographic information, including antidepressant history		x							
Brain scan (MRI)		x							
Blood collection (optional)			x			x	x		
Randomisation		x							
Daily TMS therapy (M-F)			x	x	x	x			
TMS calibration measurements		x	x	x	x	x			
Clinical and mood assessments	x	x	x	x	x	x	x	x	x
Health care cost questionnaire		x				x	x	x	x

All medication, tests and medical care required as part of the research project will be provided to you free of charge. You may be reimbursed for any reasonable travel, parking, and meals associated with the research project visit. Reimbursement arrangements (vouchers, reimbursement following receipts) will vary across sites and will be discussed locally. There are no additional costs associated with participating in this research project.

If you decide to participate in this research project, the study doctor will inform your referring and/or treating doctor, who will also be provided with a summary of the treatment outcomes at the end of your participation.

Pre-screening assessment
Potential participants will have an option to complete a pre-screening assessment prior to meeting the team. They will access this assessment by scanning the study QR code found on study advertising material and webpages. If they screen as potentially eligible, they will be notified by an email automatically generated from the study database and contacted by the staff to determine their eligibility to attend a screen visit.

Screening interview
This will be a phone or in-person screening interview We will explain the study at this point and ask you questions to determine your eligibility. We will provide you with this participant information and consent form.

Baseline visit
During your baseline visit, we will ask you to complete questionnaires to collect your demographic information (e.g. date of birth, sex), current medications and your psychiatric and medical history. You will also complete a clinical interview assessing your depressive symptoms, as well as questionnaires about depressive symptoms. These will include pen and paper tasks as well as verbal tasks. At this time or within 7 days of this visit, you will be asked to get an MRI brain scan and have initial TMS measurements taken.

Brain scan
MRI is a scan that provides a visualisation of brain structure and activity. It is used routinely in human clinical practice and research. Each MRI scan will take approximately 45-60 minutes during which you will lay at rest in the scanner. For these sessions you will be asked to change into scrubs (provided) and remove any additional metallic objects that may interfere with the equipment (e.g., glasses, jewellery, etc.). You will be asked to lie on your back on the bed of the machine. Your head will be placed inside of a helmet-like open space so that device can make accurate measurements of brain structure and activity. You will be asked to remain as still and relaxed as possible throughout the entire scan to ensure ideal data quality. During the stimulation session you will be awake, alert and aware of what is happening at all times. During this scan, we will record heart and respiratory rate using a pulse oximeter placed on your finger and an electrode placed on your chest. These measures assist us in removing artefacts that can reduce the quality of the MRI data.

TMS calibration measurements (“Single pulse TMS”)
Before we begin the treatment course, we will conduct an initial measurement to calibrate the stimulation intensity. A TMS coil will be placed on your scalp and single TMS pulses will be administered to the area of the brain involved in the movement of your hand muscles. We will use single pulse TMS as a measurement tool to determine the minimum intensity required to cause a brief finger or hand movement. The result is used to determine the intensity applied during

treatment. Single pulses are usually delivered every 4-5 seconds. This procedure will take around 15-25 minutes.

TMS therapy ("repetitive TMS")
TMS therapy will occur daily (Monday-Friday) over the course of 4 treatment weeks. Repetitive TMS is different to single pulse TMS, in that many pulses are delivered per second, in bursts of several seconds, with the goal of causing therapeutic effects. The duration of stimulation in each TMS session will be approximately 3 minutes. Set-up time may add an extra 15-20 minutes.

Clinical assessments
Clinical assessments are questionnaires designed to evaluate the severity of your depression. Some of these are in the form of self-report (where you complete the questionnaire on your own), while others are completed with a member of the research team. You will need to repeat these questionnaires several times through the course of the study, as indicated in Table 1. Some of the questionnaires will be completed daily.

Fasting blood collections
Participants will be offered the opportunity to consent to an **optional** fasting blood draw at three different trial visits; the morning of first and last TMS treatment visit, and at 1 month post last treatment visit. The results will help develop a low-cost, personalised method to assess immune and metabolic patterns in depression and predict response to TMS treatment. If a participant does not consent to having their bloods taken, this will have no impact on their eligibility to participate in the trial.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way.

4 What do I have to do?

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 project.

You will be required to attend TMS therapy daily (Monday-Friday) for 4 weeks. In addition, you will be required to partake in various scheduled study visits and follow-up assessments as detailed in Table 1. The first follow up assessment, should be conducted in person. If necessary, subsequent follow up assessments can be conducted online. The total duration of participation in the study is seven months from the date of your **initial** TMS treatment visit.

There are some limitations on making changes to your existing medication regimen. For 4 weeks prior to baseline measures, and during the study period, you will not be able to change the type or the dose of antidepressant medications, and you will need to document and report any "as needed" psychotropic medication (for example any other prescribed medications you might be taking for depression that are not a part of your regular routine) you might be taking during your participation in the study. If you or your doctor thinks that it is necessary to alter the type or dose of medications you are taking, please discuss this with the research team before making the change. This is because if changes in your depression symptom severity occur over the study period, we need to be confident that they are the result of the study treatment, and not from alterations in your antidepressant regimen.

During the course of this study, and in particular in the days preceding, during, and after your course of TMS therapy, we ask that you avoid alcohol and recreational drug intake. These may (i) interfere with the capacity of TMS to cause antidepressant effects and (ii) may compromise the safety of TMS therapy including seizure risk and (iii) may interfere with the stability and reliability of clinical assessments.

Female participants will need to agree to use medically acceptable means of contraception while on the study and not commence new pharmaceutical forms of contraception while in the study as these can interfere with mood.

Once you have been recruited to the study, you are requested to refrain from enrolling in other clinical trials. The study will NOT require any dietary restrictions and there will not be any physical or mobility restrictions.

Should you choose to consent to having your fasting blood samples taken, please ensure that you have had nothing to eat or drink (water is okay) for 8-12 hours prior to your fasting blood test. Please ensure you drink plenty of water to stay well hydrated and take any medication as normal. A trained professional will insert a cannula (thin tube) into your arm and then proceed to fill three tubes with your blood (21.5mL in total). The cannula is then removed, and pressure is applied to the insertion point to stop the bleeding with a bandage. A portion of your de-identified collected blood will be transferred to a site-affiliated facility for processing and storage. After the blood draw is completed, we will provide you with a $20 dollar voucher to purchase a breakfast before continuing with other study assessments. At the completion of the final blood collection visit you will be reimbursed $100.

One of the aims of this trial is to evaluate the cost-effectiveness of the optimised approach to TMS. As part of this evaluation, we wish to access some administrative data, held by Services Australia, collected as part of the reimbursement processes for healthcare services and prescriptions that you receive during the period that you participate in the trial. You will be invited to sign a **separate optional consent form** authorising the study to access your Services Australia information, see the separate Services Australia Participant Information Document and Participant Consent Form. 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 operates within guidelines set out by the NHMRC.

Please note, that if you do not consent for the project to gain access to this administrative data held by Services Australia or to have your bloods taken, this will have **no impact** on your eligibility to participate in the trial.

Please note that it is a condition of being in the trial that you continue to see your own regular treating doctor, psychiatrist or general practitioner (GP), as usual during the trial and that your doctor provides ongoing care after you have finished the trial. It is also essential that we inform your doctor about your participation in the trial, and if necessary, to communicate with your doctor about your progress during the trial. We do not take over your clinical care before, during or after the trial. By consenting to participate in this trial, you consent to us contacting your doctor to that end.

5 Other relevant information about the research project

Overall, we aim to recruit 310 people to this study over a four-year period. Four sites across Australia are conducting this study, and it is a collaborative project between researchers in Melbourne, Brisbane and Sydney (NHMRC Project Grant Application ID: 2032454).

This clinical trial will be registered on ClinicalTrials.gov and ANZCTR as required by the NHMRC. These websites will not contain any information that could identify you but will include a summary of the trial procedures.

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

Participation in any research project 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.

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 the institution.

Please note, there are several reasons why you may not be eligible to take part in this study:

- If you have a history of seizure or epilepsy or any other serious medical condition.
- People who have an acute brain condition, such as an acute stroke or encephalitis (inflammation of the brain).
- The presence of metal that responds to magnetic forces anywhere in the head, which may be affected by TMS's magnetic field. This includes metallic objects such as screws and clips from surgical procedures.
- Claustrophobia – this may interfere with your ability to undergo a brain scan.
- If you move excessively in MRI scanner to the extent that a TMS target cannot be computed.
- If you are currently pregnant or lactating you will not be able to be included in the trial. The effects of TMS on the unborn child and on the newborn baby are not clear. You must not participate in the research if you are pregnant or trying to become pregnant. If you do become pregnant during the course of TMS therapy, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment for your condition at the institution. Other options are available at your current clinical service, in consultation with your current treating doctor; these may include treatment with standard antidepressant or mood stabiliser medications, and psychotherapy such as cognitive behaviour therapy or acceptance and commitment therapy. You can discuss these options with your treating doctor before you

decide whether or not to take part in this research project. You can also discuss the options with your study doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any direct benefits to you from taking part in this research. However, possible benefits include a reduction in depression severity with TMS therapy. Receiving TMS therapy will not necessarily help you to reduce or cease any medication you may be taking for depression.

An indirect benefit of participation is the opportunity to help yourself and others who suffer from major depression by contributing to the development of new treatments that may be effective for this condition.

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

Medical treatments often cause side effects. You may have none, some or all of the effects listed below, and they may be mild, moderate or severe. 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.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell your study doctor immediately about any new or unusual symptoms that you get. Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

In other clinical studies/practices, the following side effects have been noted:

TMS

A very low seizure risk (standardised risk: 7/100,000 individuals). Seizures induced by TMS don't lead to the development of epilepsy or increase the probability of having subsequent unprovoked seizures. Safety standards will be adhered to, to minimise the risk of a seizure, including carefully screening participants for seizure risk by assessment of past history of seizures, any brain pathology, concomitant medications and/or substance use that are likely to increase seizure risk. A medically trained staff member will be available during TMS treatment who know how to treat a seizure should one occur.

Other adverse effects of TMS include discomfort at the scalp stimulation site, headache, fatigue or a neck ache. These are generally mild in severity and resolve quickly with paracetamol or other analgesics. Neck ache can often be avoided by ensuring that you are comfortably seated during TMS and communicating with the TMS administrator to avoid pressure being placed on the neck when the TMS coil is positioned on your head. You will be able to drive post treatment. TMS can occasionally cause transient ringing in the ears. All participants will be provided with earplugs to prevent this from occurring. There are no reports in the literature relating TMS to hearing loss.

There is also the possibility your depression will not improve with TMS. Over the course of your participation in this trial, we encourage you to continue seeing your usual clinical treatment provider. If study personnel observe a significant deterioration in your mood or your risk to yourself or others, the study personnel will inform a study doctor, your clinical treatment provider and/or local authorities, so they can discuss the most appropriate course of action with you.

MRI

We will ask you to lie on a table inside the MRI scanner. The scanner will record information about your brain. It is very important that you keep very still during the scanning. When you lie on the table, we will make sure you are in a comfortable position so that you can keep still. The MRI scanner is very noisy, and we can provide earphones to help with this. Some people may experience symptoms of claustrophobia from lying in a confined space. If you do experience discomfort at any time during the scan, you will be able to alert staff by pressing on a call button provided to you.

There are no proven long-term risks related to MRI scans as used in this research project. MRI is generally well-tolerated when conducted at a centre with established procedures. However, the magnetic attraction for some metal objects can pose a safety risk, so it is important that metal objects are not taken into the scanner room.

We will thoroughly examine you to make sure there is no reason for you not to have the scan. You must tell us if you have metal implanted in your body, such as a pacemaker or metal pins or metal piercings.

This study is for research purposes only and the MRI scan is not a clinical examination. However, a radiologist will review one of your brain scans as routine procedure. If an incidental (i.e., unexpected) finding is observed, you will be contacted and provided with advice on how to seek further medical assistance. We will also provide this information to your treating doctor. Please be aware that these findings may reflect normal differences in brain anatomy, however as the MRI scans that we are conducting are not diagnostic, we cannot make any judgement about such findings. Therefore, we will inform you of the finding and advise you about further investigation you may wish to obtain.

Psychological distress

You may feel that some of the questions in the questionnaires may be stressful or upsetting. If you do not wish to answer a question, you may skip it and go to the next question, or you may stop immediately. In the instance where you become upset with involvement in clinical research AND no longer wish to continue in the trial you can be discharged back to your referring practitioner with correspondence indicating why.

Blood draws

Risks associated with drawing blood from the arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely. You will be asked to report any side effects to the study team immediately so we can assist you. The noted side effects are readily treatable. To minimise the risk of side effects, blood will be drawn by a trained professional, using sterile techniques. You will have your blood drawn at three study visits.

There may also be other risks associated with this trial that are presently unknown or unforeseeable.

10 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 study doctor will make arrangements for your regular health care to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/ she will explain the reasons and arrange for your regular health care to continue.

11 Can I have other treatments during this research project?

You are able to continue your medication(s), including antidepressant medication(s), while participating in the trial.

As described in section 4, there are some limitations on making changes to your existing medication regimen. You should tell the study doctor about any changes to your treatment / medication regime during participation in the research project. Most importantly let the team know if starting concurrent treatment with another investigational agent or enrolment in another clinical study.

It is also important to tell the research team about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments, during the study. You should consult with the research team **prior** to making any changes to your treatment / medication regime during your participation in the study.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although your 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 sponsor (University of Melbourne) up to the time you withdraw will form part of the research project results. This is because regulatory bodies, such as the FDA, consider the removal of already collected data to undermine the scientific validity, and therefore the ethical integrity, of the research. If you do not agree with this, you should choose not to enter into the study.

13 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons and if this occurs you and your treating doctor will be notified. These may include reasons such as:

- Unacceptable side effects
- The TMS treatment being shown not to be effective

• The TMS treatment being shown to work and not need further testing
• Uncertainty around participant's capacity to provide informed consent
You will be provided with as much information as possible regarding the reason for the termination and an opportunity to address questions you may have.

The researchers may also end your participation in this research program at any time if they think it is in your best interests. This may be because of an adverse event, an injury, a medical condition which may place you at risk of further complications if you continue to participate, or if you are not available to attend the TMS treatment visits. Should this occur, your treating doctor will be consulted.

14 What happens when the research project ends?

Once the study is complete and the results are known, a written plain English summary of the results of the study will be made available to you upon request. To obtain this, please contact the study team. Additionally, summary results information will be submitted to ClinicalTrials.gov and made publicly available in the databank.

The results of this study may be submitted to the Therapeutic Goods Administration in Australia FDA if the findings suggest that it would be beneficial for the personalised targeting procedures to be approved for Medicare or health insurance reimbursement.

The study treatment will not be available after the trial administration finishes. Should you wish to continue the treatment you should discuss with your treating doctor if that would be a suitable treatment.

Part 2 How is the research project being conducted?

15 Personal and health information

By signing the consent form you consent to the research team collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential and will be securely stored. Your information will only be used for the purposes stated in this document, and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

We aim to keep all the information about you that we collect for this study strictly confidential. However, there are some exceptions to this: 1) information from the assessments may be communicated with your treating doctor/case manager/clinician to ensure that you receive the best care possible; 2) if we are concerned about risk to you or to someone else, we may need to discuss this with your treating doctor/case manager/clinician at the service where you receive treatment; 3) if we observe an incidental finding on your MRI scan, we will need to provide this information to your treating doctor/case manager/clinician.

Information about you may be obtained from your health records held at this and other health organisations for the purpose of this research. By signing the consent form, you agree to the

research team accessing health records that are relevant to your participation in this research project.

Paper based forms collected from you as part of this research study will be stored in locked filing cabinets at the trial site accessible only to the investigators involved in this research project. Electronic data will be stored on password-protected computers accessible to authorised users only.

Your information will be identified with a unique code assigned to you for the study, not your name or other identifying information. This unique code (your study identification code) will be linked to your personal details securely stored separately by the Principal Investigator at your study site. All study documentation is to be retained for a minimum of 15 years (following the publication of results from this study) including participant files and other essential documents. In addition, the Principal Investigator will notify the University of Melbourne and Royal Melbourne Hospital prior to destruction of any study documentation, regardless of the timeframe lapsed.

Your health records and any information obtained during the research project may be inspected for the purpose of verifying the procedures and the data by the relevant authorities, authorised representatives of the research team, or as required by law. This may include inspection of the study deidentified data by ethics committees or regulatory agencies, such as the FDA, in which case your permission to access these records will not be required. By signing the consent section, you authorise release of, or access to, this confidential information to the relevant study personnel and regulatory authorities as noted above.

In accordance with relevant Australian and state 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.

Consent to use of data for future research:

At the end of this form, you will have the opportunity to consent to allowing information collected about you to be used for future research, except for Medicare and Pharmaceutical benefits (MBS/PBS) information. Consenting to allow the use of your data for future research is optional. If you provide consent for your data to be used in future research, it will be held indefinitely on the password-protected databank at the University of Melbourne, and it will not include any personal details that could identify you. Future research projects may be closely related or unrelated to this research project but might for example be aimed at advancing our understanding of depression or how to further improve the effectiveness of therapies for depression. It is unlikely that these studies will have a direct benefit to you. They may benefit people in future who are in a similar position and suffer from mental health conditions. Such projects will have to be reviewed and approved by a recognised Human Research Ethics Committee. Any future research will involve members of the research team at University of Melbourne and may involve collaboration with other researchers in the mental health field.
Your Services Australia data will only be used for future studies for related (or similar) to the current research to this approved study.

16 Complaints and compensation

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 the Royal Melbourne Hospital HREC.

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

17 Who is organising and funding the research?

This research has been initiated by Dr Robin Cash at The University of Melbourne and is being funded by an NHMRC Investigator grant.

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

18 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 Royal Melbourne Hospital HREC. This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2023)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

19 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.

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

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC Name	The Royal Melbourne Hospital HREC
HREC Executive Officer	Manager HREC
Telephone	03 9342 8530
Email	research@mh.org.au

Consent Form - *Adult providing own consent*

Title	Optimised Transcranial Magnetic Stimulation for the Treatment of Depression (OptiTMS)
Short Title	Optimised TMS for Depression
Ethics Number	RMH HREC 2024.326
Project Sponsor	The University of Melbourne
Coordinating Principal Investigator	Dr Robin Cash
Participant study ID	OptiTMS – _ _ _

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

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 study without affecting my future health care.

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

I understand that, if I decide to discontinue the study treatment, I may be asked to attend follow-up visits to allow collection of information regarding my health status. Alternatively, a member of the research team may request my permission to obtain access to my medical records for collection of follow-up information for the purposes of research and analysis.

I understand that unless I complete the withdrawal form, my data will form part of research.

- ❑ I certify that I am not currently pregnant or trying to become pregnant during the course of the study. I agree to use medically acceptable means of contraception while on the study and not commence new pharmaceutical forms of contraception while in the study (female participants only).

- ❑ I consent to the use of my deidentified data for future unspecified research, except for Medicare and Pharmaceutical benefits (MBS/PBS) information.

- ❑ I consent to having a blood draw at three different study visits and to the storage and use of the de-identified blood samples for use in future research that is closely related to this research study (i.e. for future research relating to mental health).

- ❑ I would like to receive a summary of study findings via (please circle): Email or Post

Declaration by Participant

Name of Participant (please print) _____

Signature _____ Date _____

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.

Release of medical information

❑ In case of an adverse event during the study period, I consent to the study site doctor contacting my GP/clinician to obtain my information for follow up if required.

Name of GP/clinician _____

Address _____

Contact number _____

Name of Participant (please print) _____

Signature _____ Date _____

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

Title	Optimised Transcranial Magnetic Stimulation for the Treatment of Depression (OptiTMS)
Short Title	Optimised TMS for Depression
Ethics Number	RMH HREC 2024.326
Project Sponsor	The University of Melbourne
Coordinating Principal Investigator	Dr Robin Cash
Participant study ID	OptiTMS – _ _ _

Declaration by Participant of a research project

Option 1 – Intervention withdrawal

I wish to:

- ❑ Withdraw from the investigational intervention **only** (i.e. study treatment) and
- ❑ Complete post treatment follow-up visits 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 the institution.

** Please note, to confirm your withdrawal from the intervention **only**, please ensure you have checked all boxes above.*

Option 2 – Withdrawal from blood collection

I wish to:

- ❑ Withdraw my previous consent to having blood taken **only**.

** Please note, to confirm your withdrawal from having blood taken **only**, please ensure you have checked the box above.*

Option 3 – Full withdrawal

I wish to:

- ❑ Fully 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 the institution.

- ❑ I understand that, as per my previous consent, the data collected **before today's date** will form part of the research project results

** Please note, to confirm your withdrawal from the study, please ensure you have checked all boxes above.*

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.