MD FluNCS: Managing delirium with Fluvoxamine treatment for non-cardiac surgery

PARTICIPANT INFORMATION SHEET

Title	***Managing delirium with Fluvoxamine treatment for Non-Cardiac Surgery***
Short Title	*MD FluNCS*
Protocol Number	*X00-0000*
Coordinating Principal Investigator/ Principal Investigator	*Professor Robert Sanders*
Location	*Royal Prince Alfred Hospital*

1. Introduction

You are invited to take part in a research study looking into the prevention of delirium post-surgery. The aim of the study is to see whether a drug called fluvoxamine (selective serotonin reuptake inhibitor) will reduce delirium symptom severity. This pilot study will focus on determining the feasibility of this research project on a bigger level and assist us to modify the study activities based on the feedback we receive from this research project.

The study is being conducted by Professor Robert Sanders (Academic Head of the Anaesthetic Department) and is supported by the department, Royal Prince Alfred Hospital and Sydney Local Health District.

This Participant Information Sheet (PIS) will tell you what is involved in the study and help you decide whether or not you wish to take part. Please read this information carefully. If there is anything you do not understand or if you feel you need more information about anything, please ask. Before you make a decision, please feel free to talk things over with a relative, a friend or your doctor.

2. Study Procedures

If you agree to participate in this study, you will be asked to sign the Participant Consent Form at the end of this document. You will then be asked to undergo the following study activities:

- Brief physical examination as part of the normal pre-admission visit – this is not outside of normal care. Pre-admission clinic activities will be communicated to you by your treating team prior to your surgery. During this visit you will see an anaesthetic doctor who will assess you and ask about your current medical status, medication and medical history. In addition to this you will be asked to do a baseline cognitive assessment and delirium assessments. These assessments may be done face to face or over the phone and will take approximately 20-30 minutes.

- As a participant you will be randomly allocated to one of two study groups (like a flip of a coin). Both groups will receive oral tablets to take prior to surgery, on the day of surgery and on post-operative day one. One group of patients will be given the active drug and the other group will receive a placebo. If allocated to the active drug group, you will receive: 100mg of Fluvoxamine on the night before surgery, 100mg Fluvoxamine in the morning and evening on the day of surgery and 100mg fluvoxamine in the morning and evening on post-operative day one.

- Prior to the procedure you will have an intravenous cannula placed in order to receive standard anaesthetic drugs. Your blood samples will be collected during insertion of the cannula. This is often standard procedure for surgeries and will not involve additional invasive procedures. A small amount of blood (10ml) will be collected for this research project. Bloods collected at this time will be processed and stored securely at Royal Prince Alfred Hospital. All blood samples will be safely destroyed and disposed of in hospital provided clinical waste once it has been analysed and data collected for this project.

- On the day of surgery a member of the research staff will visit you in the evening to preform a brief delirium assessment which will take less than 10 minutes.

- On post-operative days one through four you will be followed up in the ward or ICU by research staff who will perform a brief adverse event assessment, delirium assessments and routine

bloods will be collected. Bloods will be collected when possible from an existing access device in order to minimise invasive procedures.

- On post-operative day one a member of the research staff or anaesthetic doctor will also preform a brief physical examination and EEG (electroencephalogram) which is a test that measures the electrical activity of your brain. This is a non-invasive procedure that involves wearing a cap with electrodes and will take around 30 minutes.

- On post-operative day 7 if you are still in hospital research staff will perform a cognitive assessment. If you are no longer an inpatient you will be contacted on the telephone. This will take around 15 minutes in total.

The treatment being investigated in this study differs from the standard treatment offered at Royal Prince Alfred Hospital because of its use of the drug fluvoxamine, a commonly used anti-depressant (selective serotonin reuptake inhibitors (SSRIs)). This drug works by increasing the amount of serotonin, a natural substance in the brain that helps maintain mental balance, and by reducing inflammation. This study will look at the effects this drug has on post-operative delirium.

Medications, drugs and devices have to be approved for use by the Australian Federal Government. Currently Fluvoxamine is approved for use in Australia for the indication of depression/OCD. This study will be conducted under the Therapeutic Goods Administration (TGA) Clinical Trials Notification (CTN) Scheme. This allows the Investigators to use this product for medical research purposes once the research has been assessed and approved by an authorised Human Research Ethics Committee (HREC).

If you agree to participate in this study, you will be asked to sign the Participant Consent Form prior to participating, in addition, the researchers would like to have access to your medical record – namely medical history, medications and current medical status -to obtain information relevant to this study.

If the study data will be used for future research purposes and / or shared with national and international collaborators, Ethics Approval will be required to be sought prior to the access of any de-identified data.

3. Risks

All medical procedures - whether for diagnosis or treatment, routine or experimental – involve some risk of injury. All risks associated with your planned procedure and general anesthetic will be discussed prior to admission with your treating team/anesthetic doctor in the pre-admission clinic.

In addition, there may be risks associated specifically with this study that are presently unknown and unforeseeable. In spite of all precautions, you might develop medical complications from participating in this study.

During the procedure a blood sample will be collected following the insertion of a cannula (standard practice prior to anaesthesia). Please be aware that you will need a cannula inserted for your procedure regardless if you participate in this research project. There are no additional invasive procedures required for this research project. The EEG monitoring is non-invasive and involves the placement of a cap on your head which can be slightly uncomfortable but poses no risk to health/wellbeing.

The additional risks of participating in this study are:
Potential side effects from the interventional drug- fluvoxamine. Please note the side effects noted below are related to ongoing use of these medications and are very rare in single doses.

Fluvoxamine

Possible Risk/Side Effect	How often this may occur?
Loss of appetite, nausea, diarrhoea, gas, sore throat, dizziness, drowsiness, anxiety	Rare
Serotonin Syndrome (if administered with other serotonergic medications eg. SSRIs, MAOIs, TCAs, tramadol, triptans)	Rare- will assess medication list pre-operatively
Pharmacokinetic Interactions (CYP1A2 eg. Warfarin, phenytoin, carbamazepine, clopidogrel)	Rare- will assess medication list pre-operatively
Hyponatraemia (low sodium)	Very Rare (patients will have sodium levels checked post-operatively)

4. Benefits

While we intend that this research study furthers medical knowledge and may improve treatment of post-operative delirium severity but it may not be of direct benefit to *you.*

5. Funding and Costs

This study is funded internally by the Department of Anaesthetics at Royal Prince Alfred Hospital and is sponsored by the Sydney Local Health District.

Participation in this study will not cost you anything, nor will you be paid.

6. Voluntary Participation

Participation in this study is entirely voluntary. You do not have to take part in it. If you do take part, you can withdraw at any time without having to give a reason by contacting a member of the research staff (contact details listed below). Whatever your decision, please be assured that it will not affect your medical treatment or your relationship with the staff who are caring for you.

Sometimes during the course of a study, new information becomes available about the treatment that is being studied. While you are participating in this study, you will be kept informed of any significant new findings which may affect your willingness to continue in the study.

If you decide to withdraw from the study, we will not collect any more study-related information from you. If you want to withdraw please let us know and tell us what you would like us to do with the information we have collected from you up till then. If you wish, your information will be removed from our study records. It will not be included in the study results, unless we have analysed and published the results.

7. Confidentiality

All the information collected from you for the study will be treated confidentially and will be stored on a research database within the Department of Anaesthetics Royal Prince Alfred Hospital. Only the authorised research staff will have access to this data.

Any identifiable hardcopy data will be stored on either a secure, password protected shared drive (supported by the hospital Information Technology Department) or in a locked cabinet in a locked office within the Department of Anaesthetics at RPAH.

The data will be analysed by the researchers at the Royal Prince Alfred Hospital. All data for use in journal publications and presentations will be de-identified. The files will be retained for 15 years from the day the study is completed. Once the retention expires the files will be disposed of in a secure manner.

Blood samples will be stored securely Royal Prince Alfred Hospital and analysed by lab staff. Any data collected from this analysis will be de-identified* and stored in the secure online server.

*de-identified data means that you/your information will not be identifiable

8. Storage of Data

The SLHD software licence for REDCap (Research Electronic Data Capture) will be used for to manage the collection and storage of research data. REDCap is a secure, web-based, non-commercial, data management tool designed for research purposes. Data collected by REDCap is stored on servers in the SLHD data centre. Data is secured, and back-up, privacy and confidentiality.

9. Future use of Data

The data collected in this project may also be used in future research studies. The results of this study and de-identified data may be shared in the future with national and international collaborators, any stored samples/data that is used for related or future research, will first be reviewed and approved and approved by an appropriately constituted Ethics Committee. You can indicate your agreement to this on the Participant Consent Form.

10. Complaints and Compensation

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. In the event that you are physically injured as a result of participating in this research, emergency care will be available. Please contact the investigator, Professor Robert Sanders (contact details below).

11. Ethics Approval and Complaints

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 Prince Alfred Hospital.

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 02 9515 8564 or contact any of the following people.

Clinical contact person

Name	Prof Robert Sanders
Position	Principal Investigator
Telephone	02 9515 8564
Email	Robert.sanders@sydney.edu.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

If you have any complaints about any aspect of the project, the way it is being conducted or any

This study has been approved by the Ethics Review Committee (RPAH Zone) of the Sydney Local Health District. Any person with concerns or complaints about the conduct of this study should contact the Executive Officer on 02 9515 6766 and quote protocol number XXX-XXXX.

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	Sydney Local Health District (RPAH Zone)
HREC Executive Officer	Merela Ghazal
Telephone	02 95115 6766
Email	SLHD-RPAEthics@health.nsw.gov.au

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

Name	Maree Larkin
Position	**Research Governance Officer**
Telephone	02 9515 7899
Email	SLHD-RPAEthics@health.nsw.gov.au

Consent Form - *Adult providing own consent*

Title	***Managing delirium with Fluvoxamine treatment for non-cardiac surgery***
Short Title	MD FluNCS
Consent Version	V.1, 10.5.2022
Coordinating Principal Principal Investigator	Professor Robert Sanders MBBS Ph FRCA
Location	Royal Prince Alfred Hospital

Declaration by Participant

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 Royal Prince Alfred Hospital concerning my health purposes of this project. I understand that such information will remain confidential.

I understand that my participation in this study will allow the researchers and others, as described in the Information for Participants, to have access to my medical record, and I agree to this.

I understand that the SLHD software license for REDCap (Research Electronic Data Capture) will be used to manage the collection and storage of my research data.

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 acknowledge that my de-identified data may be shared with other local or international collaborators and used for future research purposes, and I agree to this: □Yes □No

Name of Participant (please print) _____

Signature _____ Date _____

Name of Witness* to Participant's
Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. 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.

_____

I consent to the storage and use of blood and tissue samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for:

- This specific research project
- Other research that is closely related to this research project
- Any future research.

By signing this consent section, I agree to the use of my blood samples for this research project.

Name of Participant (please print)_____
Signature_____ Date _____

Name of Witness* to
Participant's Name (please print)_____
Signature_____Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent p

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

Signature_____ Date _____

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

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

Title	*Managing Delirium with Fluvoxamine for non-cardiac surgery*
Short Title	MD FluNCS
Consent Version	V.1 dated 10.5.2022
Coordinating Principal Investigator/ Principal Investigator	Professor Robert Sanders MBBS Ph FRCA
Location	Royal Prince Alfred Hospital

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 Royal Prince Alfred Hospital.

Name of Participant (please print) _____

Signature _____ Date _____

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