Participant Information Sheet/Consent Form

Non-Interventional Study - *Adult providing own consent*

Royal North Shore Hospital

Title	A Multi-centre, Prospective, Observational Cohort Study of Patients Attending the National Health & Medical Research Council (NHMRC) Centre for Research Excellence for Coronary Artery Disease without Standard Modifiable Cardiovascular Risk Factors
Short Title	The SMuRFless CAD Registry
Protocol Number	2021/ETH12501
Project Sponsor	University of Sydney
Coordinating Principal Investigator	Professor Gemma A. Figtree
Principal Investigator	Professor Gemma A. Figtree
Location	Royal North Shore Hospital

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project, which is a study to learn more about coronary artery disease (CAD) in people without standard modifiable cardiovascular risk factors (SMuRFs). These standard modifiable risk factors include high blood pressure (hypertension), high cholesterol (hypercholesterolaemia), diabetes, and a history of smoking tobacco. This study is also referred to as "The SMuRFless CAD Registry." You are being invited to participate because you have been diagnosed with CAD and do not have any of the four main standard modifiable risk factors, or you are a family member of someone who has been diagnosed with CAD who has no standard modifiable risk factors.

Scan to access the SMuRFless CAD Registry eConsent

The SMuRFless CAD Registry is a research project in the National Health & Medical Research Council (NHMRC) Centre for Research Excellence for CAD clinic.

This Participant Information Sheet & Consent Form (PISCF) tells you about the research project. It explains the processes involved with taking part. 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 do not understand or would like to know more about. Before deciding whether to take part or not, you might want to talk about it with a relative, friend, or local health worker.

Participation in this research is voluntary. If you don't want to take part, you don't have to. You will receive the best possible care whether you decide take part or not.

If you decide that 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 be involved in the research described
- Consent to the use of your personal and health information as described.

You will be given a paper or electronic copy of this PISCF to keep based on your preference.

2 What is the purpose of this research?

This research aims to better understand why some people develop CAD in the absence of standard modifiable risk factors. The establishment of the SMuRFless CAD Registry will provide information on risk factors for CAD that occur less frequently, the effect of targeting these risk factors for preventing heart attacks, 1- and 5-year outcomes in people with CAD but without standard risk factors, and test how effective the NHMRC CRE for CAD specialty clinics are in treating people with CAD without standard modifiable risk factors.

Scientific and medical advancements have improved doctors' abilities to identify and target heart disease at the population level by identifying and treating standard modifiable risk factors (high blood pressure, high cholesterol, diabetes, and tobacco smoking). However, these risk factors alone do not adequately explain CAD in all individuals. The proportion of patients suffering with life-threatening events despite the absence of these risk factors has increased from 13 to 27% over ten years at one institution participating in this research study, highlighting the need for new discoveries and solutions for this previously "invisible" but critically important population at risk.

The information that will be collected through your participation in the SMuRFless CAD Registry will provide insight into new or less frequently encountered risk factors for CAD with the potential for treatment to reduce the future risk of suffering a heart attack, and inform new evidence-based pathways for the care of people with CAD. In addition, this information collected will be used to analyse the cost effectiveness of the NHMRC CRE for CAD specialty clinic.

The NHMRC CRE for CAD is an initiative funded by the Australian Government, seeking to improve the diagnosis, treatment, and quality of care of people with CAD. This research has been designed by a network of more than twenty internationally recognised experts on CAD. These experts form a part of the NHMRC CRE for CAD study team.

3 What does participation in this research involve?

If you decide to take part in our study, you will be required to sign this PISCF prior to undertaking any of the study assessments being performed.

Participation in this study involves completion of a Participant Questionnaire around the same time as your SMuRFless CAD clinic visit, which requires about 10-15 minutes of your time. This questionnaire can be completed on the same day as your clinic visit or at home before attending the clinic, depending on your preference. You can complete this questionnaire electronically—

using your own computer to access a secure study database (i.e., REDCap)—or by paper form. This questionnaire will ask questions about the following:

- Your age, sex, country of birth, education level, occupation, diet and physical activity, smoking status, any exposure to environmental pollutants
- A history of gum disease and the health of your teeth, information about snoring, quality of sleep and a history of sleep apnoea
- A health-related survey about your general quality of life

On the same day as your NHMRC CRE for CAD clinic visit, you will complete a screening questionnaire for depression, which is an important risk factor for heart disease.

Information will be recorded from your NHMRC CRE for CAD clinic visits for research purposes. For most people, this will include:

- Measurement of blood pressure, heart rate, weight, height, and waist/hip circumference
- 12-lead electrocardiogram (ECG)
- Ankle-brachial index (ABI)
- Comprehensive medical history and family history of cardiovascular disease
- Blood test or other diagnostic tests ordered by your doctor

The information included on the Participant Questionnaire will be supplemented with data from your medical record from the NHMRC CRE for CAD clinic visit.

Depending on the results of your clinic visit, your doctor may ask you to return for a follow-up visit (either in-person or via telehealth). The results from these follow-up visits will also be recorded for research purposes.

There are no costs associated with participating in this research project, nor will you be paid.

4 Other relevant information about the research project

The study is expected to enrol approximately 1,000 participants in clinics across Adelaide, Melbourne, and Sydney.

The study seeks to maximise and add to the information that has already been collected about you and your disease. By consenting to this study, you also consent to the use of your previously obtained clinical data for research purposes, including medical record information from your referring physician and the NHMRC CRE for CAD. If you have had a coronary angiogram, CT coronary angiogram (CTCA), or echocardiogram, by consenting to this study you also consent to the use of these studies for research purposes. This information is important to be able to confirm a diagnosis of CAD and to understand the location of the disease and its severity.

5 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 PISCF 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 any of the institutions participating in this research project.

6 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research. However, possible benefits may include the development of improved clinical management for you and similar types of people with CAD in the absence of traditional risk factors.

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

This study does not involve any medications. However, some of the tests that will be done as part of the study may have some risks. You may have none, some, or all of these listed below; 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.

- You may feel that some of the questions we ask are 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. If you become upset or distressed as a result of your participation in the research project, the research team 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 team. The counselling will be provided free of charge.
- This research project will record information about current and past use of recreational (or illicit) drugs such as cannabis, cocaine or amphetamines. Questions on this subject have been included as use of these substances has been associated with CAD in some previous studies. You may feel the questions are embarrassing or stressful and you may decline to answer these questions. All information collected in this study will remain confidential and will be disclosed only with your permission, except as required by law. The researchers are obligated to protect your privacy, including regarding any illegal use of recreational drugs, except where a serious threat to someone's life, health, or welfare is disclosed.

8 What if I withdraw from this research project?

If you do consent to participate, you may withdraw at any time. If you decide to withdraw from the project, please notify a member of the research team. A member of the research team will inform you if there are any special requirements linked to withdrawing. You will also be able to withdraw by completing and signing a 'Withdrawal of Consent' form provided to you by the research team.

If you decide to leave the research project, the researchers will not collect additional personal information from you, although the information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with the law. You should be aware that data collected up to the time you withdraw will form part of the research project results. If you do not want your data to be included, you must tell the researchers when you withdraw from the research project.

9 Could this research project be stopped unexpectedly?

It is not expected that this research project will need to be stopped before completion. If it does need to be stopped, we will contact you via email or phone.

10 What happens when the research project ends?

At the end of the research project, collected data will be used to learn more about people with CAD and without traditional risk factors. This information will be used to potentially inform future changes to the diagnosis and treatment of the disease, seeking to provide more personalised, evidence-based therapies and improving medical practice.

Part 2 How is the research project being conducted?

11 What will happen to information about me?

By signing the consent form, you consent to the study doctor and relevant research staff 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. All data will be labelled with a study code, rather than any information that can directly identify you. This means that this information will be 're-identifiable'. The master list that links your study code to your identity is stored on a secure networked computer database that is only accessible by senior researchers. It may be necessary at times to share identifying information between approved study sites in order to execute the study as described. 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.

All data will be stored electronically on secure, password-protected servers and internet-based database called REDCap (Research Electronic Data Capture), all hosted by the University of Sydney. All servers and the REDCap database will be managed by the study investigators, are password-protected, and only accessible to study investigators. The research data will be stored in accordance with research guidelines for 15 years after participant follow-up and data analysis is completed.

If you have an electrocardiogram (ECG) performed as part of your clinic visit, it will be securely stored for clinical use by the study site according to their standard practices. By consenting to the SMuRFless CAD Registry, you consent to the use of this ECG for research purposes. The ECG data will be labelled with a study code, rather than information that can directly identify you. The master list that links the ECG to your identity will also be accessible only by the senior study investigators on a need-to-access basis. After de-identification, the ECG data will be transferred electronically onto a password-protected research server, hosted by the University of Sydney and only accessibly by study researchers.

If you have had a CT coronary angiogram (CTCA) or invasive coronary angiogram, the results of these studies will be de-identified similar to the procedure described above. After de-identification, these images will be stored on an external research server, hosted by the University of Sydney, and accessible by study investigators only.

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 if they are relevant to your participation in this research project.

The study doctors seek your permission to store your information for future, unspecified health and medical research after approval by a Human Research Ethics Committee (HREC). In the future, other doctors and scientists at this and other medical and research centres may use your information to learn about many different diseases and conditions. Their goal is to improve health outcomes and develop new treatments. We will not use your information for a different research project without the permission of a HREC.

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.

In accordance with relevant Australian and/or NSW 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.

12 Accessing Medicare Data

One of the goals of the research project is to better understand whether there is a health benefit, and an overall cost or a savings to individual patients or the government through the use of the NHMRC CRE for CAD specialty clinics. In order to enable this, we would like to collect information about your Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) claims from Services Australia. MBS collects information on your doctor visits and the associated costs; PBS collects information on prescription medications you have filled at pharmacies. This part of the SMuRFless CAD Clinic is optional. You will be asked if you agree to the collection of the MBS and PBS information on a specific consent form from Services Australia. There is nothing further needed from you if you agree. At the end of the study, the study doctors will securely send Services Australia your Medicare number and your study ID. The information will be password-protected so only those authorised at Services Australia can access the data. Services Australia will send the study doctors your MBS and PBS information attached to your study number. None of the data will have any personally identifiable information.

13 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.

If you suffer any distress or psychological injury as a result of this research project, you should contact the research team as soon as possible. You will be assisted with arranging appropriate treatment and support.

14 Who is organising and funding the research?

The research is being conducted by Professor Gemma A. Figtree, Royal North Shore Hospital, in collaboration with Professor Stephen Nicholls, Monash Medical Centre, and Professor Alex Brown and A/Professor Peter Psaltis, Royal Adelaide Hospital. It is being funded by a NHMRC Centre for Research Excellence Grant (GNT1196629), awarded to Professor Gemma A. Figtree.

You will not benefit financially from your involvement in this research project even if, for example, knowledge acquired from your involvement proves to be of commercial value to one of the study institutions. In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to the study institution, there will be no financial benefit to you or your family from these discoveries.

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

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 approved by the HREC of Northern Sydney Local Health District (NSLHD).

The 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 problems which may be related to your involvement in the project, you can contact the coordinating principal investigator, Professor Gemma A. Figtree, at +61 (02) 9926 4915 or any of the following people:

Research contact person

Name	Professor Gemma A. Figtree
Position	Professor / Interventional Cardiologist
Telephone	+61 (02) 9926 4915
Email	gemma.figtree@sydney.edu.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 the HREC and quote HREC reference number: 2021/ETH12501:

Reviewing HREC approving this research and HREC Executive Officer details:

Reviewing HREC name	Northern Sydney Local Health District HREC
HREC Executive Officer	Research Ethics Manager
Telephone	+61 (02) 9926 4590
Email	NSLHD-research@health.nsw.gov.au

Research Governance Officer at Northern Sydney Local Health District (NSLHD) authorising the conduct of this study at Royal North Shore Hospital:

Position	Research Governance Officer
Telephone	+61 (02) 9926 4589
Email	NSLHD-Research@health.nsw.gov.au

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

Title	A Multi-centre, Prospective, Observational Cohort Study of Patients Attending the National Health & Medical Research Council (NHMRC) Centre for Research Excellence for Coronary Artery Disease without Standard Modifiable Cardiovascular Risk Factors
Short Title	The SMuRFless CAD Registry
Protocol Number	2021/ETH12501
Project Sponsor	University of Sydney
Coordinating Principal Investigator	Professor Gemma A. Figtree
Site Principal Investigator	Professor Gemma A. Figtree
Location	Royal North Shore 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 North Shore Hospital.

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.

Health
Northern Sydney
Local Health District

Consent Form – *Adult providing own consent*

Title	A Multi-centre, Prospective, Observational Cohort Study of Patients Attending the National Health & Medical Research Council (NHMRC) Centre for Research Excellence for Coronary Artery Disease without Standard Modifiable Cardiovascular Risk Factors
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Site Principal Investigator	Professor Gemma A. Figtree
Location	Royal North Shore 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 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 care.

I understand that I can withdraw my consent at any time by contacting the SMuRFless CAD Registry study team without any impact on any future treatment.

I am aware that I may not be personally informed of the general research results of studies using my samples, but these may be published, taking care not to disclose the identities of those who have contributed samples.

I permit the SMuRFless CAD Registry study to store clinical data collected from me for 15 years after the conclusion of the research and for the data to be used in an anonymous form for Human Research Ethics Committee (HREC) approved future unspecified health and medical research.

I permit the transfer and sharing of my de-identified health information to other researchers both interstate and internationally for HREC approved health, medical, healthcare, or health outcomes research.

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

Name of Participant (please print) _____

Date of Birth: _____

Signature _____ Date _____

Communication Preferences

I permit the study team to contact me for study communications and approved questionnaires through the following:

☐ **EMAIL:** _____

☐ **TELEPHONE:** _____

Notification of Study Publications

I would like to receive updates from the study team on presentations and publications arising from the research project. I understand that I will not be able to be identified in any of the publication data.

YES ☐ **NO** ☐

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.