

Participant Information Sheet

Can loss of a ‘hunger’ hormone increase heart disease in Pacific people?



Formal Study title: *(optional)* *Ghrelin and SNA in Pacific People (SNAPP)*

Sponsor (if applicable): name and address: *University of Auckland, Office of Research Strategy and Integrity*
Email: humanethics@auckland.ac.nz

Lead Researcher: *A/Prof James P Fisher*

Study Site: *University of Auckland*

Contact phone number: *+64 9 9236320*

Ethics committee ref.: *TBC*

You are invited to take part in a study examining the link between blood levels of the ‘hunger’ hormone Ghrelin and risk factors for diseases that affect the heart and blood vessels (known as cardiovascular disease). Whether or not you take part is your choice. If you don’t want to take part, you don’t have to give a reason, and it won’t affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you’d like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 10 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

In New Zealand, Pacific Island peoples are over-represented in those with diabetes and cardiovascular disease. The reasons for this remain unclear. The ‘hunger’ hormone ghrelin is known to protect against cardiovascular disease, in part, by silencing the part of the nervous system that stresses cardiovascular system (i.e., the sympathetic nerves). The purpose of our study is to test whether ghrelin is lower in Pacific Island peoples and could explain their increased cardiovascular disease risk. It is hoped that our work will pave the way for future studies targeting ghrelin to safely lower cardiovascular disease risk.

This study is funded by the Health Research Council of New Zealand. It is being conducted by Dr. Ana Luiza Carrari Sayegh (Postdoctoral Research Fellow, University of Auckland), Dr.

James P Fisher (Principal Investigator, University of Auckland), Prof. Daryl Schwenke (Chief Investigator, University of Otago), Dr Allamanda Faatoese (Research Fellow, University of Otago), Asiata Professor Satupaitea Viali (Oceanic University of Medicine, Samoa) and Professor Rinki Murphy (University of Auckland).

This study has been reviewed and approved by Health and Disability Ethics Committee. Protocol number 2024 EXP 20637.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

We are inviting Pacific Island (both biological parents of Pacific Island origin) and non-Pacific (both biological parents of NZ European origin) people to participate in this study that are either:

- People with type 2 diabetes
- People with normal blood sugar.

You have been invited to participate because you potentially fit into one of these groups of people.

For safety and scientific reasons, you are ineligible to participate in this study if you are: younger than 18 years old, are pregnant, have a percentage body fat of mass index of greater than 30% for men and greater than 42% for women (measured at the screening visit), or have another significant medical condition (e.g., heart failure, lung disease). An investigator will carefully check the inclusion/exclusion criteria with you and answer any queries.

Studies will be undertaken at the **Human Cardiorespiratory Physiology Laboratory, Clinical Research Centre Facility, Faculty of Medical and Health Sciences, University of Auckland**. Participation involves one short Screening/ familiarisation visit and one experimental visit.

Once you have read this form, an investigator will contact you to make sure that your questions have been answered and check that you understand what is involved. They will then schedule a familiarisation visit with you.

Familiarisation/screening visit

At the familiarisation visit (~45 min) an investigator will further explain the procedures, answer any remaining questions, and ask you to complete the Consent Form below. You will be asked to complete some health questionnaires. Then, providing you meet the study inclusion/exclusion criteria, you will be enrolled in the study. Body weight, height and the circumference of around your hips and waist will be measured.

Then we will measure your body composition (amount of bone, fat, lean tissue) using a scanning method. The scanning process takes about 15 minutes and is not unpleasant. We will ask you to wear gym-style clothing and to remove any metal from your person for the scan. You will need to lie quietly without moving on an open bed whilst a scanning arm passes over the top of you. As the scanning arm passes over you it emits two types of very low dose X-ray, like the radiation dose that you would be exposed to on a 1-hour flight – e.g. between Auckland and Wellington. At the end of the scan, we will print a picture of you showing an image of the bone, fat and lean tissue in your body for you to take home with you.

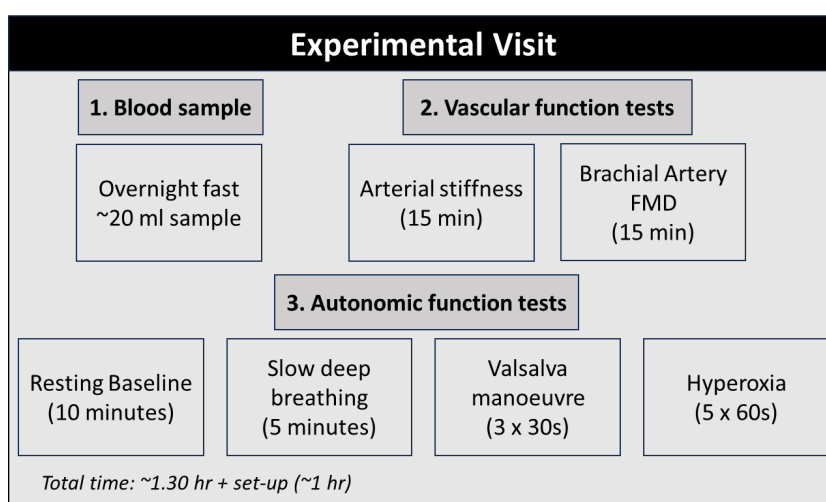
Experimental visit

A single experimental visit will last ~2-3 hours. Prior to the study visit, the following pre-study stipulations apply:

- No food intake overnight (i.e., ~8 hours prior to the study).
- No caffeine (e.g., coffee, coke, red bull) for 12 hours before the study.
- No alcohol on the day before the study and the day of the study.
- No exercise after 8:00pm the evening before the study and no exercise on the day of the study.
- No 'over the counter' (e.g., paracetamol) or prescribed medications (e.g., oral hypoglycaemics, beta-blocker, ACE inhibitor, angiotensin receptor blockers, calcium antagonists, diuretics, alpha-blockers) on the morning of the study. A study investigator will discuss this with you prior to your appointment. Please bring the medications (if you take any) to your study appointment so you can take your usual medication immediately after the research tests (by late morning).

The following procedures will be conducted:

- A **urine pregnancy** test will be taken if you are a women of childbearing age.
- A **blood sample** will be taken from an arm vein (~20 ml). We will take you over to the Clinical Research Unit at the University of Auckland for this (~200 metres from the laboratory).
- **Arterial stiffness** will be measured by the placement of a pen-shaped probe over arteries at your neck and wrist, while you lay on a bed. A cuff will be placed around your upper thigh that will inflate for a couple of minutes.
- **Flow mediated dilatation** will be used to examine the function of an artery in your upper arm. This involves the inflation (for 5 minutes) and then deflation of a standard blood pressure cuff around the upper arm (5 minutes). The amount that the artery widens will be assessed.
- **Cardiovascular tests.** Equipment will be set up for the measurement of your heart rate, blood pressure, breathing, blood flow, and sympathetic nerve activity (described below). You will then rest for 10 minutes while we collect some measurements. Then, you be asked to do some simple tests including slow deep breathing, putting your hand in cold water, doing a straining (Valsalva's) manoeuvre, and breathing 100% oxygen (hyperoxia). This will all be explained in detail.



Measurements

Arterial stiffness will be measured by the placement of pen-shaped probes over arteries at your neck, wrist, and a cuff placed at the top of your thigh. These sites correspond to your carotid, radial and femoral arteries and allow use to determine how fast the blood pressure pulse wave travels along your main arteries. During the flow mediated dilatation test, blood flow through a large artery in your arm will be measured using ultrasound. This is like the scan used with pregnant women. During the cardiovascular tests, heart rate will be measured using an electrocardiogram by placing sticky electrode patches on your chest. Your blood pressure will be monitored by a small blood pressure cuff around the finger, and another around your upper arm. A lightly placed finger clip will monitor your blood oxygen saturation. Breathing will be monitored with a lightweight nasal canula.

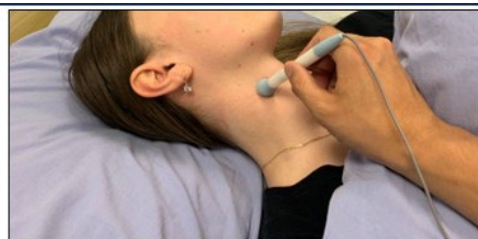
The sympathetic nervous system will be assessed using a thin wire that will be placed at the nerve just below the knee (peroneal nerve). The wires are like acupuncture needles, but the tip is very fine (it is the width of human hair). Once a good nerve recording is found, the electrodes will stay in your leg for the rest of the study. You will be asked to keep your leg as still as possible during the study. It is a well-established procedure.

All measurement equipment will be removed at the end of the session.

Pictures of the experimental setup are shown below:



Picture 2. Flow mediated dilation set up on the arm. A cuff will go around the arm and an ultrasound probe will go on the upper arm



Picture 1. Pulse wave velocity set up.



Picture 2. Microneurography setup on the leg. Two very fine electrodes wires are inserted below the knee

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

The information gathered from all the people taking part in this study will help us understand if ghrelin is a significant contributor to the unacceptably high prevalence of cardiovascular disease in NZ-based Pacific Island people and people with type 2 diabetes. In doing so, Pacific-centric treatment of the ghrelin pathway has the potential to have significant medium to long-term benefits on the quality of life, as well as alleviating the current economic burden that NZ district health boards face due to the exorbitant costs associated with ongoing clinical treatment. The results of this study will be communicated to scientific and clinical communities to raise awareness of the ethnic differences that must be considered when investigating the origin of cardiovascular disease. However, there are no individual benefits to participating in this experimental study.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS OF THIS STUDY?

The risks associated with the procedures are minimal. The research team is experienced with all the procedures employed. To further minimise the risk associated with this investigation studies will be undertaken in a clinical research laboratory. Medically trained personnel will be in close proximity, along with AED facilities, in the unlikely event that they are required. In addition, your heart rate, blood pressure, breathing, and blood oxygen levels will be very carefully monitored throughout the study. The experiment will be stopped at your request or if the investigator thinks that it is in your best interests.

Blood sample: This may cause some discomfort and local bruising. There is a very small chance of a clot forming and infection. The risk is small as the needle will remain in for a short period of time.

Sympathetic nerve recording: This procedure occasionally may result in the leg muscles feeling tired. Also, you may have a pins-and-needles feeling or a greater sensitivity to touch in the leg. However, these side effects are rare and if they occurred, would only be temporary (e.g., lasting for a day or two at the most).

100% oxygen breathing: This may cause your breathing rate to increase. There is a chance you may feel breathless or light-headed. Before the test begins, you will receive instructions to remove the mouthpiece if symptoms develop. The risk of this is low, and further minimized by being applied for a short period of time (5 minutes), but if this does occur symptoms rapidly reverse (in a few seconds) by breathing normal room air again. In addition, your heart rate, blood pressure, breathing and blood oxygen levels will be carefully monitored by an experimenter throughout the study.

Detection of Abnormalities: The measures made are for research purposes and are not a medical exam or diagnostic test. There is a small possibility that we may incidentally find an abnormality that can impact your health conditions, such as a heart rhythm abnormality. If this happens, we will write to your general practitioner to notify them. If you do not wish to know about this type of finding, please do not participate.

With-holding morning medications: Cardiovascular medicines are given to provide protection over years/decades and therefore the delay in medicines in this study (of 3-4 hours) will be extremely unlikely to cause harm over that time frame. As stated above, please bring your usual medications to your study appointment so you can take them immediately after the research tests (by late morning).

COVID-19: The study will proceed in accordance with guidance from the University of Auckland regarding practices to minimise the risk of COVID-19 transmission. This will include the researchers wearing personal protective equipment and maintaining appropriate physical

distance when able. Equipment is always sterilised between participants, and surfaces disinfected. If you feel unwell on the day of your scheduled testing, have been in close contact with a confirmed or probable case of COVID-19, or have returned from overseas in the 14 days prior to your scheduled testing, please do not come in for assessment.

WHO PAYS FOR THE STUDY?

As a participant in this study, you will not incur any costs. You will receive a \$100 voucher per experimental visit in recognition of your participation in this study. At the end of the experimental visit you will be offered refreshments.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT ARE MY RIGHTS?

Your participation in this study is entirely voluntary. You are free to decline to participate, or to withdraw from the research at any practicable time, without experiencing any disadvantage. You can withdraw by notifying an investigator verbally or by writing. You have the right to access information collected about you as part of the study and change any information that is incorrect. Please write to us if this is the case. You will be informed of any new information related to the study that becomes available during the study that may have an impact on your health. Your identity will be kept strictly confidential, and you will not be identified in the publication of the research findings.

WHAT HAPPENS AFTER THE STUDY?

During this study the research team will record information about you and your study participation. This includes the results of any study assessments (e.g., heart rate, blood pressure, breathing and blood vessel function). If needed, information from your hospital records and your GP may also be collected. You cannot take part in this study if you do not consent to the collection of this information.

Identifiable Information: Identifiable information is any data that could identify you (e.g., your name, date of birth, or address). The following groups may have access to your identifiable information:

- Research team (to complete study assessments)
- Sponsor study monitors, to make sure the study is being run properly and that the data collected is accurate.
- The sponsor and its representatives if you make a compensation claim for study-related injury. Identifiable information is required to assess your claim.

- The sponsor, ethics committees, or government agencies from New Zealand, if the study or site is audited. Audits are done to make sure that participants are protected, the study is run properly, and the data collected is correct.
- Your usual doctor, if a study test gives an unexpected result that could be important for your health. This allows appropriate follow-up to be arranged.

De-identified (Coded) Information: To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by the research team, or any study information sent to the sponsor. Instead, you will be identified by a code. The research team will keep a list linking your code with your name so that you can be identified by your coded data if needed. The following groups may have access to your coded information:

- The sponsor, for the purposes of this study.

The results of the study may be published or presented, but not in a form that would reasonably be expected to identify you.

Security and Storage of Your Information: Your identifiable information is held at University of Auckland in a locked filing cabinet in a department with security-limited access, along with all paper records (e.g., health history forms) during the study. After the study it is stored for at least ten years, then destroyed. Your coded information will be entered into electronic case report forms stored in secure and password protected University of Auckland servers. Coded study information will be kept by the sponsor in secure, cloud-based storage for 10 years. All storage will comply with local and/or international data security guidelines.

Risks: Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee that you cannot be identified. The risk of people accessing and misusing your information (e.g., making it harder for you to get or keep a job or health insurance) is currently very small, but may increase in the future as people find new ways of tracing information.

Rights to Access Your Information: You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected. Please ask if you would like to access the results of your screening and safety tests during the study. If you have any questions about the collection and use of information about you, you should ask the research team.

The full results of the studies being conducted will not be known until after the last participant has been tested and the data analysed (up to two years). The results will be reported in professional publications and meetings but will not be published in a form that identifies individual participants. If you are interested in receiving a summary of the results, please indicate as appropriate on the consent form below.

Rights to Withdraw Your Information: You may withdraw your consent for the collection and use of your information at any time, by informing the research team. If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you. If you agree, information collected up until your withdrawal from the study will continue to be used and included in the study. You may ask for it to be deleted when you withdraw unless you withdraw after the study analyses have been undertaken.

HDEC Auditing: An approved auditor appointed by New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative may review your medical records for the sole purpose of checking the accuracy of information recorded for the study, for auditing purposes.

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns, or complaints about the study at any stage, you can contact:

Name, position: Dr Ana Luiza Carrari Sayegh, Postdoctoral Research Fellow

Telephone number: 09 373 7599 | Ext 81438

Email: ana.sayegh@auckland.ac.nz

Or:

Name, position: Dr James P. Fisher, Principal Investigator

Telephone number: 09 373 7599 | Ext 86320

Email: jp.fisher@auckland.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050

Fax: 0800 2 SUPPORT (0800 2787 7678)

Email: advocacy@advocacy.org.nz

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS

Email: hdecs@moh.govt.nz

Consent Form



Please tick to indicate your consent to the following

I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.

I have been given sufficient time to consider whether or not to participate in this study.

I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.

I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.

I consent to the research staff collecting and processing my information, including information about my health.

If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.

I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.

I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.

I understand the compensation provisions in case of injury during the study.

I know who to contact if I have any questions about the study in general.

I understand my responsibilities as a study participant.

I wish to receive a summary of the results from the study.

Yes No

Declaration by participant:

I hereby consent to take part in this study.

Participant's name: _____

Signature: _____

Date: _____

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: _____

Signature: _____

Date: _____