

Evaluating Feijoa for Diabetes prevention in a multi-ethnic New zealAND cohort

the FERDINAND study

PARTICIPANT INFORMATION SHEET

You are invited to take part in the FERDINAND STUDY in the Peak Nutrition for Metabolic Health (PANaMAH) Programme, within the National Science Challenge High Value Nutrition (NSC-HVN) Programme. Whether or not you take part is your choice. If you do not want to take part, you do not have to give a reason. 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 (PIS) will help you decide if you would 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 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.

The study investigators also understand that the body is considered tapu (sacred) and therefore such sampling should be treated with special consideration and respect. While individuals have the right to choose whether to participate in this study, we encourage you to discuss this project with your whānau and friends, especially with regard to the collection of your blood, faecal and urine samples before agreeing to participate. If you have any personal or cultural requirements or questions that relate to your potential participation in this project, please ask the research team before signing this document. It is the role of the investigators to ensure that you understand all procedures and risks: please feel free to ask any questions.

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 Forms to keep.

This document is 22 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

This is a **6-month weight loss study (2 months weight loss + 4 months weight loss maintenance/prevention of weight re-gain)** which aims to investigate whether 1150 mg/d whole fruit feijoa powder, both during and following weight loss, can lower your risk of diabetes long-term, i.e., over a 6-month period.

The study will be held at the University of Auckland Human Nutrition Unit (HNU) in Mt Eden, Auckland.

Who can take part?

Any man or woman in the Auckland area, who:

- is overweight or obese (BMI \geq 26 kg/m²) and body weight \leq 150 kg
- between 18 - 70 years
- is at high risk of diabetes, based on a blood glucose test (*prediabetes* with fasting glucose between 5.6 - 6.9 mmol/L)
- is happy to join in a 2-month rapid weight loss plus 4-month dietary study

IMPORTANT: You cannot be in the study if you have ALREADY been diagnosed with diabetes

Who designed the study?

This study was designed by the research staff at the Human Nutrition Unit and Department of Medicine, University of Auckland, AgResearch Metabolomics Unit, the University of Otago, the Malaghan Institute of Medical Research Immunology Group and the Plant and Food Research Consumer Insights Group, as part of the NSC-HVN Programme, funded by the New Zealand Ministry of Business, Innovation and Enterprise (MBIE).

What is the purpose of the study?

Individuals with excess weight are at higher risk of developing type 2 diabetes (T2D). Recent studies have shown that body weight (and fat) loss, using a low energy diet (LED) and longer term weight loss maintenance (prevention of weight re-gain) can successfully improve metabolic health, including stabilising blood sugar. Identifying food and beverages that can help with short-term weight loss and long-term weight loss maintenance is important to achieve this. We also know that each individual may have a different response even when they eat the same diet. A range of lifestyle and physiological factors, including genetic factors, gut bacteria, and physical activity etc. may contribute to these differences. So additionally, the FERDINAND research team will look at these various factors, including demographic (such as your age, gender, and ethnicity), anthropometric (such as your height, weight, and waist), clinical (such as your blood sugar and lipids), as well as ‘cutting edge’ novel biomarkers (e.g., faecal microbiome, which are gut bugs) to better understand how these various factors affect an individual’s blood sugar.

How is the study designed?

The FERDINAND study comprises of 2 STUDY ARMS, with different people in each group. The study is randomised, which means that neither you nor the HNU researchers can decide which study arm you take part in – that is decided by chance during the randomisation process. You will be randomised to 1 of the 2 study arms. You and study investigators won’t know which of the intervention arms you have been receiving until the end of the study. This is done so that we do not influence the results/outcomes of the study in any way. The diets across both study arms adhere to the New Zealand dietary guidelines for improving metabolic health.

As seen from the figure below, both the diet groups consist of two phases:

Phase 1 is a low energy diet (LED)-driven weight loss phase of 2 months, where you may expect to lose between 5-10% of your body weight;

Phase 2 is weight loss maintenance phase of 4 months, where you will receive healthy diet/weight loss advice to help prevent any weight re-gain.

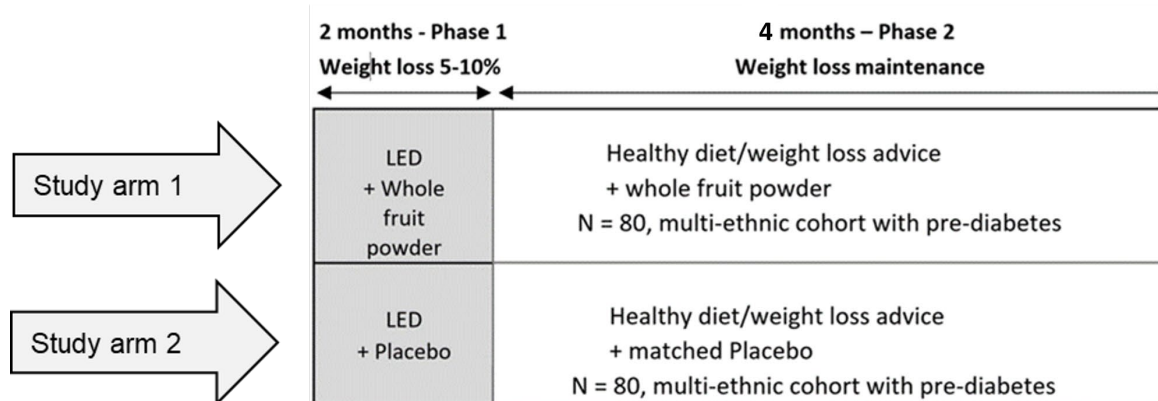


Figure 1: 2 study arms – you could be randomised (by chance) to either of these two groups

STUDY ARM 1: Healthy diet/weight loss advice + feijoa whole fruit powder

- You will receive a commercial LED meal replacement (Cambridge Weight Plan™ Ltd) which will fully replace your daily meals during Phase 1, in addition to 1150 mg feijoa whole fruit powder which will be provided as a daily sachet during both Phase 1 and Phase 2; which is to be eaten daily with breakfast

STUDY ARM 2: Healthy diet/weight loss advice + placebo control

- You will receive a commercial LED meal replacement (Cambridge Weight Plan™ Ltd) which will fully replace your daily meals during Phase 1, in addition to 1150 mg placebo (a control powder) which will be provided as a daily sachet during both Phase 1 and Phase 2; which is to be eaten daily with breakfast.

What are the aims of the study?

We aim to:

- Measure the change in your body weight and body composition** during 2 months of weight loss, using a low energy diet (LED)/meal replacement sachets, provided for free by the FERDINAND study team.
- Measure the change in your body weight and body composition** during a further 4 months of weight loss dietary advice/prevention of weight re-gain.

- iii. **Measure the change in clinical markers of diabetes** in your blood, urine and faecal samples on 4 occasions during the full 6-month dietary intervention (m0, m2, m4, m6); as well as **measure your minute-by-minute blood glucose response** over 3 days, during which we will give you a series of standardised breakfast test meals to eat at home (these are called ‘*mixed meal tests*’, or MMTs).

What happens if I decide to take part?

If you are interested in being a study participant, a member of the research team from the HNU will speak to you over the telephone or by email to ask you some questions about your age, height, body weight as well as about your family and medical history. The questionnaire is important to understand whether you might be eligible for the study.

After assessing this questionnaire and if you appear to be eligible for the study, researchers will invite you to come to the HNU in Mt Eden for a morning (before breakfast) screening visit. This will be your first clinical visit. The visit will take approximately 1 hour. You will be required to fast for 8-10 hrs prior, i.e. no food or drink to be consumed after your dinner the previous evening. However, you can still take your regular medication on the morning (e.g. blood pressure pills) of the clinic visit. During the screening visit we will talk to you, explaining the study in more detail and you will have the opportunity to ask questions. Once you are well informed about the study, we will give you enough time to decide if you want to participate or not. If you decide to take part in the study, we will ask you to sign a form stating that you do agree to be a participant in the study. This is called an ‘informed consent form’ or ICF – by signing it, you consent to take part in the study. Please note that you may always withdraw from the study at any time.

If you would like to take part, we will then carry out a clinical assessment of your health, which is very similar to a visit to your family doctor/general practitioner (GP). We will ask you again about your medical and medication history, and we will ask some other personal questions (e.g., lifestyle, exercise and diet habits). We will request you to bring any GP prescriptions you may have or any other information that is important, so that we can record your health information accurately. Were you to be unsure of these details then please do let us know, as once you have provided written consent for us to contact your GP, we can confirm this information you have provided with them. We will also do some body measurements (height, body weight, body mass index/BMI, waist and hip circumference, blood pressure). You do not have to answer all the questions and you may stop the interview and measurements at any time. You are welcome to ask us questions whenever you like.

We will also take a blood sample to check your fasting blood glucose (sugar) levels to assess how likely you are to have a high risk of diabetes. If you have had a diabetes blood test anytime in the previous 4 weeks and have been shown to be at high risk of diabetes, we will be happy to repeat this to confirm whether you can be enrolled.

What happens once I am enrolled into the study?

If you are eligible for the study, we will give you an ID number, which will be used throughout the study to keep all your personal and medical details confidential (de-identified). We will use this ID throughout the study and the samples you will provide during the study will only contain this de-identified number. When the data is collated for presentation at conferences, or publication in an international journal your data will not be able to be identified.

You will be randomised to one of the two study arms. We will then arrange with you the clinical assessment dates for your study. After you are enrolled into the study, you will have a **total of 6 clinical visits** [Figure 2: 2 visits to collect “homework” and 4 clinical investigation days (CID) where we will conduct body measurements and collect blood samples and your completed “homework”] **over the 6-month study period**. You will also attend **9 group diet advice sessions**, either in person or via online virtual mHealth platform, throughout the study to provide dietary advice and support you through the programme and help you meet your body weight goals.

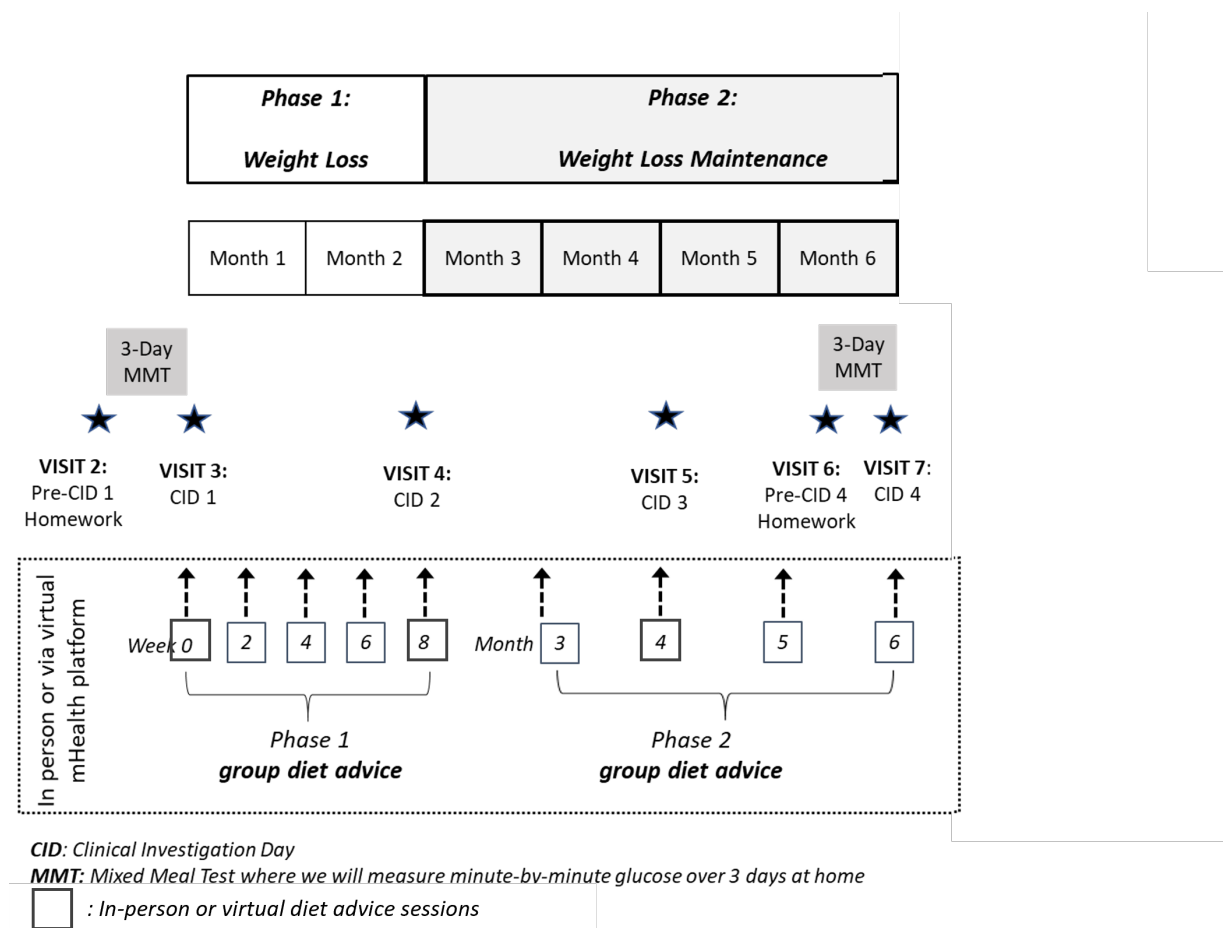


Figure 2: Study design: 2 months weight loss + 4 months prevention of weight re-gain

What happens during the clinical visits (clinical investigation days/CID)?

In addition to your screening visit, you will have the following 6 clinical visits:

1. Pre-start of study CID ‘Homework,’ VISIT 2:

Prior to the start of the study you will need to complete a series of simple assessments. We will provide you with written and verbal instructions, and also organise a video call, to help and guide you through some of these assessments.

Assessment 1: Body composition scans

We will measure your body composition (how much muscle and fat that you have) using a body scanner DeXA machine which is located at the Clinical Research Centre, Grafton Campus, University of Auckland (please see the section below for the full description of the measurement. It takes about 15 min for the scan).

We will also measure how much ‘risky’ fat you have stored in your body. Storing a lot of fat around your stomach (‘belly’ fat) or inside important organs can increase your risk of diabetes. We don’t yet understand why some people store fat in these risky sites and yet other people don’t. We will measure the fat in your abdomen (stomach area), in your liver and in your pancreas; using a Magnetic Resonance Imaging (MRI) scanner which is located at the Centre for Advanced MRI at the University of Auckland, Grafton Campus (please see the section below for the full description of the measurement. It takes about 30 - 45 min for the scan).

Assessment 2: Collect a faecal/stool sample

We will give you a home faecal sample collection kit (Omnigene·GUT) with verbal and written instructions on how to collect the sample. This small sample can be stored at room temperature, before bringing to your clinic visit or you can post it back to us in a prepaid envelope that we will provide to you. Alternatively, you may also collect your sample at the HNU, during your next study visit, and we will immediately store the container in the -20°C freezer at the HNU. You will also need to use a simple routinely used visual guide designed for self identification and classification of the type of feces passed to assess how long the feces has spent in the colon called the Bristol Stool form scale.

Assessment 3: Record all food and drink

You will need to keep a record of your diet, verbal and written instructions on how to do this will be provided. You will need to record everything that you eat and drink (all your meals and snacks) over 4 consecutive days, which must include 3 weekdays and 1 weekend. In other words, you will record your food diary either from Wednesday-to- Saturday or from Sunday-to-Wednesday. You are encouraged to weigh all the food and drinks using an electronic scale (provided by us), otherwise you will record the amount of food that you eat using common household measures, such as a teaspoon, a tablespoon, a fist, a palm, etc. You must record the food as you eat it, do not wait until later as you may forget some important details. If there are any leftovers, please do record that in the diary too. We need you to give us detailed information regarding the foods/drinks, including the brand name (e.g. Heinz, Watties, Anchor) cooking method (e.g. steamed, baked, fried), packaging (e.g. fresh, frozen, tinned), and if there is anything added to the food (e.g. type of condiment, sugar, salt).

3 days prior to starting the weight loss phase of the study the following will be done:

Assessment 4: Record your physical activity

You will need to start recording your daily step count over 3 days. We will do this by downloading a free app on your mobile phone e.g. Apple Health or Google Android fit. Over the 3 days, you will be requested to carry your smartphone with you so that data is continuously collected. Your daily step count over the 3 days will then be transferred to the HNU datahub at the end of the 3 days. If you do not access or are unable to use your smartphone we will provide you with a pedometer so that you can record your step count.

Assessment 5: continually measuring your blood glucose levels over 3 days at home

We will provide you with a continuous glucose monitor (CGM, Photo below) to measure your blood glucose levels at home over 3 days. These monitors are used very commonly by people with diabetes and are water resistant so you can shower etc. as usual; but please don't swim with it attached. They are a needle-free, single use units. The sensor filament has a short plastic probe that will be inserted a few millimetres under your skin, e.g. on the upper arm (as seen in image). We will show you what the sensor looks like during your screening visit and also give you verbal and written instruction as well as a guide on how to fit it on a video call. If you are uncomfortable doing this yourself our study nurse can do this for you.



Once the CGM is inserted you will then eat a standardised breakfast meal, which we will give you to take home, every morning for 3 consecutive days (3 breakfasts in total).

Each of the three breakfast meals will be of fixed energy and macronutrient composition (fat, carbohydrate and protein). Over the 3 days, you will consume one of these breakfast meals in the morning instead of your normal breakfast. The entire meal must be consumed in full, no other foods consumed, and you will be asked to avoid any exercise, including walking (driving the car to work, or sitting on the bus is fine) for 2 hours after finishing the meal. We call this a 'mixed meal test' (MMT). Upon completion of the two hours you may eat your regular lunch and dinner.

2. Start of the LED-weight loss, VISIT 3:

It is expected that during the 8 week weight loss phase of the study you may lose ~5-10% of your body weight (e.g., 8 kg if you weigh 100 kg = approx. 2 kg every 2 weeks).

On both study arms, *we will provide you with Cambridge Low Energy Diet (LED) meal replacements* (Cambridge Weight Plan™ Ltd) as your daily diet at no cost. The LED meal replacements come in the form of either a meal sachet or a bar. Each sachet or bar provides you with an exact serving to replace your regular meal. Therefore, when you consume the meal replacement instead of your regular meal, you consume less energy (calories) than usual, which helps you to lose weight in the longer term. Many health professionals and clinical trials recommend this Cambridge LED meal replacement as it has delivered promising weight loss to many people who have used it. If you stick to the diet for the full 8 weeks you can expect to lose

approximately 8% of your body weight. For example, if you weigh 100kg now, then after the 8 weeks diet you can expect to have lost 7-8kg.

For more information about Cambridge LED meal replacements, please visit: <https://www.cambridgeweightplan.co.nz/>.

The following assessments will be conducted at Visit 3:

Assessment 1: Collection of ‘homework’ and baseline measurements

You will attend the HNU clinic after an overnight fast of approximately 10 hrs (nothing to eat or drink, except water) following the last evening meal. We will collect all of your ‘homework’ from you, including the step count data. Your compliance to the diet and adherence to the study protocol will be monitored from the analyses of a 24-hr urine sample that we will be collecting from you. We will give you a urine sample collection kit with verbal and written instructions on how to collect the sample. You will be provided with plastic urine collection bottles, including brown paper bags to facilitate ease of transporting the bottles on the day of collection, so that you can collect all urine for a whole day and night (i.e. 24 hours). It is not essential that you store your sample in a fridge but you may keep it in a place that is cool/store in your home prior to bringing it to the HNU.

CGM will be checked and you will be asked to continue wearing it until completion of assessment 2 and 3.

We will give you a glass of water (250mL) to drink upon your arrival. Then, we will measure your body weight, height, waist-hip circumference and blood pressure. After that, a Research Nurse will collect a fasting blood sample (32.5mL).

Assessment 2: OGTT challenge

This is a test that is often carried out by your family doctor for anyone who is thought to be at risk of diabetes. The test takes 2 hours. We will collect a blood sample (approximately 7 mL; t=0) before giving you a 75g glucose drink to consume. We will collect small amounts of blood (approximately 7 ml) at 15 min (t=15), 30 min (t=30), 60 min (t=60), 90 min (t=90) and 120 min (t=120) after you have the glucose drink (our nurse will tape a butterfly needle or cannula into your vein, so only 1 needle jab). This blood test will measure what happens to your blood sugar levels when you consume a sugary drink. Up to 74.5 ml blood will be collected at each OGTT. Once the OGTT is completed we will remove the CGM monitor from your arm as well.

We will also look for new blood markers of diabetes, using a method known as ‘metabolomics’ which will be conducted in the research laboratory at AgResearch, Palmerston North. Immune and antioxidant markers will also be assessed at the Malaghan Institute in Wellington and the University of Auckland respectively. If you would like to perform a karakia (blessing) at the time of blood collection, you are encouraged to do so. Once your blood has been collected, it is sent for storage and then analysed as a group with all other participants later. If you agree, then your blood will be stored in our long-term biobank. We will ask you to sign a separate consent form for this. If you would like to request a specific tikanga (Māori custom) or other process, please feel free to talk with the research team.

Assessment 3: Measurement of metabolic rate

We will measure resting metabolic rate (BMR) using Indirect Calorimetry (IC) which will take approx. half an hour to complete. Not all participants are required to participate in this measurement. You can choose whether you would like to participate or not. BMR is also sometimes called resting metabolic rate and is the minimum amount of energy needed to keep your body functioning. For example, the energy you need to keep breathing and your heart beating. This will be conducted non-invasively using a ventilated hood/canopy system. We will ask you to sit in a comfortable chair to which a canopy is attached (as shown in the image), with fresh air coming into the canopy through the opening at the top. We will measure the amount of oxygen you consume and the amount of carbon dioxide you produce in your breath to calculate your metabolic rate. Also, measurements of blood pressure and heart rate will be recorded. This is a relatively easy process however during all of the measurements it is important that you relax and avoid large movements, but if you need to re-adjust your position or you need to itch or scratch in order to be more comfortable, of course you may do so. The same procedure will also be applied after you consume the standardised glucose (sugar) drink, described above, but as mentioned this will be a longer assessment over 2 hours. This will measure how fast you 'burn' glucose.



We will remove the canopy and carry out an OGTT, as described above. While you are relaxing in the chair during the OGTT, we will continue with the metabolic rate measurements under the canopy. Although you cannot use your phone or a laptop during this measurement (as we need you to relax and stay quite still – although don't fall asleep!) we will set up an iPad for you to watch some films or TV series, so that you are not too bored during the measurement. Your CGM will be removed at the end of the OGTT and IC measurements.

Assessment 4: Understanding your views about diet, health and how you feel

You will complete a quick short questionnaire which will ask for your views about your quality of life (QoL) e.g., your health, how you feel and how well you are able to do your usual activities.

Assessment 5: Scheduling group sessions over the 8 week weight loss period

During the 8-week weight loss phase, you will attend, either in person or via virtual mHealth platform, a total of 5 group diet advice sessions, at week 0 (baseline, before the start of intervention), 2, 4, 6, 8 (see Figure 2). At each group diet advice session, any adverse events (AE) that you may have encountered, and your current medications will all be recorded privately; and dietary and behavioural guidance will be provided. You will be given recommendations to maintain your physical activity at a low level (no increase) throughout the weight-loss phase. This is important because we want to measure the effect of the diet and not the effect of exercise.

3. End of the LED-weight loss, VISIT 4:

Once you finish the 8-week weight loss phase, you will enter the weight loss maintenance phase. The aim of this phase is to maintain your successful ~5-10% weight loss and prevent weight regain in the following 4 months, to ensure that your risk of diabetes is kept low. You will transition from the LED diet to a healthy diet (with weight loss advice) that adheres to the New Zealand Ministry of Health healthy eating guidelines.

A week prior to Visit 4, we will schedule you for your ‘end of weight loss phase’ body compositions scans, i.e. DXA and MRI (as described on Page 6).

At Visit 4, you will attend the HNU clinic after an overnight fast of approximately 10 hrs. We will collect all of your ‘homework’ from you, which includes a 4-day diet diary, the step count data and a faecal sample collected in the provided Omnigene·GUT collection kit and complete the Bristol stool form scale. Your compliance to the diet and adherence to the study protocol will be monitored from the analyses of a 24-hr urine sample. We will give you a glass of water (250mL) to drink upon your arrival. Then, we will measure your body weight, waist-hip circumference and blood pressure. A repeat OGTT and IC measurement will be conducted in a sub-group of participants, from each of the two intervention arms (see page 8).

During the 4-month weight maintenance phase, you will continue to attend group diet advice sessions, either in person or via virtual mHealth platform. There will be 4 sessions in total, scheduled at months 3, 4, 5, 6 (see Figure 2). At each group diet advice session, any adverse events (AE) and your current medications will be recorded privately; and dietary and behavioural guidance provided. You will be given recommendations to maintain your physical activity.

4. Month 4 - mid trial visit, VISIT 5

You are now half way through the study! On this day you will have a DXA body composition scan and your body weight, waist-hip circumference and blood pressure measured. We will also ask you to record your diet over a 4-day period and record your step count on your mobile device. A 24-hr urine sample will be collected to assess compliance and you will be provided the quick short questionnaire survey which will ask for your views about your health, how you feel and how well you are able to do your usual activities.

5. Pre-end of study CID ‘Homework’, VISIT 6

You have now almost completed the study! Prior to the ‘end of the study visit 7’ you will need to complete a series of simple assessments as done when you started the study. You will have all of the assessments as described for Visit 1 (Page 5 -7). You will be provided with written and verbal instructions, and also a video call, to help and guide you through some of these assessments.

6. End of study VISIT 7

We will repeat all of the assessments that were conducted at VISIT 3 to the HNU, i.e. at the start of the intervention. These include collection of your homework and a 24-hr urine sample to assess compliance to the diet, measurements of body weight, waist-hip circumference and blood pressure, body composition measurements including MRI in a sub-group of participants, and an OGTT (for additional measurement of novel blood markers) and metabolic rate only in a sub-group of participants. Your CGM will be removed. You will again be provided the quick short questionnaire survey to complete.

Additional Focus Group Interview: thoughts and insights in relation to the intervention, diet and health

Your thoughts and insights about the intervention will be collected during the study during two virtual sessions at week 6 (mid-way during LED phase) and month 4 (mid-way during weight maintenance phase). A survey, and/or an interview, will be conducted by Research Staff from Plant and Food Research, so that we may understand your thoughts about food and your health, as well as your thoughts on this clinical trial. This will help provide information regarding formulation and feasibility of diets designed for prevention of type 2 diabetes. The survey will be administered in the form of an anonymous questionnaire consisting of 6 open-ended questions. *Participation is entirely voluntary, and you may choose to take part in either the survey or the focus group interview, or both.* The virtual Focus Group will last approximately one hour and will be audio recorded by the Researcher and later transcribed. If you agree to participate in the survey and/or the Focus Group, you do not have to answer any question you are uncomfortable answering or contribute to any discussion you do not wish to. Upon completion your survey questionnaires will be kept anonymous by the Researchers. Please be assured that all names or other identifying information will be removed, and the data will be de-identified and only be used for research purposes. Your individual thoughts will not be reported, just group opinions, and only after the trial has finished. No names will be associated with anything reported.

Summary of measurements that you will have during the study

- **Height:** measured at the HNU at baseline (before the start of the study).
- **Bodyweight** measured at the HNU in the morning at Visit 3, 4, 5, 7.
- **Waist circumference** measured using a simple plastic measuring tape at Visit 3, 4, 5, 7.
- **Blood pressure and heart rate**, measured at the HNU using an automated machine, whilst you are sitting quietly in a chair at Visit 3, 4, 5, 7.
- **Blood samples** (no more than 75 ml of blood, which is 7x less than you would give if you were a blood donor) - to measure factors in your blood that are related to diabetes and heart disease, including glucose, insulin, HbA_{1c}, lipids, CRP, liver enzymes, markers of inflammation, cytokines, immune cells, peptides and also novel metabolomic markers at Visit 3, 4, 5, 7.

- **Continuous glucose monitoring** to automatically record your blood glucose every 3-5 minutes during the mixed meal tests (MMTs) at home over the Homework Visit 2, 6
- **24-hour urine collection**, collect all urine produced for 1 day + 1 night collected at Visit 3, 4, 5, 7
- **Questionnaires e.g., quick short questionnaire** collected at Visit 3, 4, 5, 7.
- **Body composition using Dual X-ray Absorptiometry (DXA)**, measured at the Grafton Campus of University of Auckland. DXA is a scanning method, to measure quantity of bone, fat and muscle in the body. The scan takes about 10 minutes. You lie quietly on an open bed and a scanning arm passes quickly over the top of you. You have to lie quietly/still without moving, but it is not an unpleasant measurement. As the scanning arm passes over you it emits 2 types of very low dose x-ray, similar to the radiation dose that you would receive if you took a short flight – perhaps between Auckland and Wellington. The DXA then measures the density of the different tissues in your body. Bone is very dense so it appears bright white on the scan. Muscle is less dense and so it is less white, and fat even less dense and so it is the least white of all. At the end of the 10 minute 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 away with you.
- **Magnetic Resonance Imaging (MRI) (sub-group)** measured at the Centre for Advanced MRI (CAMRI), Auckland Medical School, Grafton Campus. MRI is a body scanning method that has been used in hospitals worldwide for many years. It uses a magnetic field and radio frequency pulse to obtain detailed images of your organs. It does not involve radiation. It will scan your abdomen (stomach area) and identify if any fat has been stored in your liver or pancreas. You will be asked to lie down in a relaxed state, without movement if possible, within the chamber of the machine whilst it scans your abdomen and legs. The scan will take around 30 to 45 minutes. Some people may feel a little claustrophobic while having an MRI. Please let us know if this is the case for you.
- **Oral Glucose Tolerance Test (OGTT)** – 2-hour test after drinking a 75g sugary drink at Visit 3 (all participants), 4 (subgroup), 7 (subgroup).
- **30-minute basal metabolic rate and metabolic rate during the 2-h OGTT (subgroup)**, measured using Indirect Calorimetry at the HNU at Visit 3, 4, 7.
- **Microbiome, faecal sample and Bristol stool form scale** – We will ask you to collect a small faecal sample, at Homework Visit 2, 6 and Visit 4, to analyse your intestinal bacteria (gut bugs), which recent research has shown to possibly be associated with good or poor health. The test can be done on a very small sample. If you do not wish to collect your faecal sample, you can still be part of the study. You will also complete a quick and simple visual guide for self identification and classification of the type of feces passed
- **4-day food diary** we will ask you to collect this at Homework Visit 2, 6 and Visit 4, 5.
- **Physical activity** – using your smartphone or pedometer.

| Visit | Location | Time point during study | Approximate time for completion of study assessments |
|-------|---|--|---|
| 1 | HNU | Screening | 1 hour Explanation of study, written informed consent, collection of demographic information (medical and medication history, lifestyle, exercise and diet habits), body measurements, fasting blood sample. |
| 2 | CRC | Pre-Weight Loss | 1.5 hours 'Homework' collection and explanation |
| | | | 20 minutes DeXA scan |
| | CAMRI | | 45 minutes MRI/S scan (sub-group) |
| | Home | | 15 minutes Diet diary; record food and drink before/after <i>each</i> meal |
| | Home | | 15 minutes Faecal sample collection + Bristol stool form scale |
| | Home | | 2 hours MMTs (<i>each</i> of the 3 days; CGM inserted prior to start) |
| 3 | HNU | Start of Weight Loss [CID1] | 3.5 hours Collection of homework, body measurements, OGTT; questionnaires, provision of meal replacements, schedule group diet sessions |
| | | | <i>Additional 1 hour Metabolic rate (subgroup)</i> |
| 4 | CRC | End of Weight Loss/start of Weight Maintenance [CID 2] | 20 minutes DeXA scan |
| | CAMRI | | 45 minutes MRI/S scan (sub-group) |
| | HNU | | 1 hour Collection of homework, body measurements, questionnaires, schedule group diet sessions |
| | | | <i>Additional 1 hour Metabolic rate (subgroup)</i> |
| | | | <i>Additional 2.5 hours OGTT (subgroup)</i> |
| Home | 15 minutes Faecal sample collection + Bristol Stool form scale | | |
| 5 | CRC | Mid-trial [CID3] | 20 minutes DeXA scan |
| | HNU | | 1.5 hours Body measurements, questionnaires, schedule of group diet sessions |
| 6 | CRC | Pre-End of study assessments | 1.5 hours 'Homework' collection and explanation |
| | | | 20 minutes DeXA scan |
| | CAMRI | | 45 minutes MRI/S scan (sub-group) |
| | Home | | 15 minutes Diet diary; record food and drink before/after <i>each</i> meal |
| | Home | | 15 minutes Faecal sample collection + Bristol Stool form scale |
| | Home | | 2 hours MMTs (<i>each</i> of the 3 days; CGM inserted prior to start) |

| Visit | Location | Time point during study | Approximate time for completion of study assessments |
|-------|----------|-------------------------|---|
| 7 | HNU | End of Trial [CID 4] | 1 hour Collection of homework, body measurements, questionnaires |
| | | | <i>Additional 1 hour Metabolic rate (subgroup)</i> |
| | | | <i>Additional 2.5 hours OGTT (subgroup)</i> |

CRC = Clinical Research Centre at the University of Auckland Grafton Campus, 30 Park Avenue, Grafton, Auckland 1023.

CAMRI = Centre of Advanced MRI, 85 Park Road, Grafton, Auckland 1023.

How will my samples and data be stored?

Your eligibility will be assessed and you will need to provide written consent to participate. Following this, at the screen visit (and clinical days) we will always store a small sample of blood (and urine and faeces on clinical days) that has been collected from you, to be further analysed for markers of diabetes and metabolic disease. The screening blood sample will allow us to correlate markers of diabetes in the general population with bodyweight, for example, at a given time point. On the other hand, the blood, urine and faecal samples collected during the visits will allow us to see differences in the marker of diabetes following a nutritional intervention

All blood, urine and faecal samples will be stored in -20°C and -80°C freezers (urine and faecal samples will be stored separately from the blood samples) within a secure facility in the School of Biological Sciences, University of Auckland. Only the FERDINAND research team will have access to these samples. Samples to be analysed for immune function will be sent to the Malaghan Institute of Medical Research, and for metabolomics to AgResearch Mass Spectrometry facility. The biological specimens collected during this research will not be destroyed at its conclusion but will be stored long-term at the School of Biological Sciences, University of Auckland; and may be used for future analyses by the HVN researchers to address questions related to the primary and secondary outcomes of the study.

All your data will be securely stored at the HNU in Auckland and at AgResearch (metabolomics), the Malaghan Institute (immune cell profiling), and at Plant and Food Research (focus groups). Data will be both written and on computer files which can be accessed only by the study staff, using security codes. No one else at the University or outside the University will have access to your information. If you drop out of the study at any time (perhaps you become too busy), we ask that all of the data that we have collected can remain in the database in Auckland – we respect your right to withdraw from the study. All data collected from you to that point will remain in our database and be analysed as part of the study however, we will collect no further samples or data from you from that point onwards. The research team will need all data collected from study participants to report to regulatory authorities and to publish the findings from the study.

What if the researcher discovers incidental/unexpected findings?

It is possible that you may be diagnosed with abnormal blood results, such as diabetes or adverse liver enzymes, during the study. If so, we will discuss this with our clinician Dr. Rinki Murphy (Endocrinologist) who will advise us how to proceed. Were she to consider this to be a significant

abnormal result she may contact your GP directly following discussion with you. If this is not considered significant you will be informed, provided with the results, and advised to contact your GP directly. Our research staff will discuss with you the significance of any abnormal result and will suggest that you contact your GP or specialist to ensure adequate follow-up is in place, since these disorders can have significant impact on your health. If you were to request that we discuss the results with your GP, then we could do so.

MRI scans, which are for research only and not diagnostic, may also pick up incidental findings that could result in a new diagnosis or require further investigation. Again, our research staff will develop a report and discuss this with our clinician Dr Rinki Murphy. She will discuss with you the significance of the results. We will also suggest that you take the report to your GP or specialist to ensure adequate follow-up is in place. However, follow-up investigations would not be paid for by the researchers.

Will I get my test results?

You will get results of certain body measurements including weight, BMI, blood pressure, metabolic rate and DXA scan every time that you visit the research unit, if you would like them. At the end of the study, we will also give you your own information on blood tests such as blood sugar, HbA_{1c} (diabetes test), and cholesterol.

Other tests will be performed in a research laboratory and the results will not routinely be made available to you. This is to safeguard you from Insurance companies who demand to know ANYTHING you know about your health. While these tests may give research information about how you might respond to different diets, they will not provide information that is useful to your own health or wellbeing or could be used for medical treatment in any way. These measurements are for research purposes and are not diagnostic. However, you have a right to specify on your consent form if you want to receive information about findings that may indicate potential or actual risk to health. Such results will however be available only at the end of the study.

What are my rights?

You are free to decline to participate, or to withdraw from the research at any practicable time, without experiencing any disadvantage. You have the right to access information collected about you as part of the study. We will provide you with a report of all of your results, as outlined above, at the end of the study (there may be a delay between you completing the study and receiving these results, as researchers have to wait until everybody has completed the study before reporting on the outcomes). You will be told of any new information about adverse or beneficial effects related to the study that becomes available during the study that may have an impact on your health.

What are the possible benefits and risks of this study?

It can be quite hard to follow a low energy diet (LED) for weight loss. The diet contains all the nutrients (mineral and vitamins) the body needs, but with very little energy. This means you must use up or burn your own fat stores over this time, and so you lose weight. During the LED you may get some mild symptoms which might include headaches, dizziness, constipation (hard or

not much bowel motion) or stomach cramps, some tiredness and bloating particularly in the first few days. This is due to the reduced 'food' and particularly the low fibre in the LED diet. All these possible effects are normal and should disappear in a few days. You may be advised to take some fibre gel like Metamucil, which we will provide to you free of cost, and keep your water intake above 2 litres a day.

Overall, there is a low risk associated with taking part in this research study. The dose of x-rays involved in the DXA scan is similar to the radiation exposure on a 1-hour flight from Auckland to Wellington. It is important to explain to the Research Nurse if you feel any discomfort during the blood sampling. Research personnel will monitor you during the trial. The research will be stopped should any harmful effects appear or if research investigators feel that it is not in your best interest to continue.

Incidental findings might be discovered during the MRI research scans (e.g., fatty liver). In the large majority of the cases, these findings have no relevant health significance, and you can continue in the study without follow up. However, all incidental findings are reviewed by a clinician at CAMRI and if he/she suspects that there could be some relevant health issue, you will be informed of this by our clinician and you will be asked to contact your GP with these results. ***If you decline to contact your GP after being advised of an incidental finding, we must exclude you from the study for safety reasons. All incidental findings will be reported to you.***

There will be some benefits for your participation: you will be provided with the LED weight loss diet products for free and you will be provided with regular diet advice sessions. All diets meet with the healthy guideline recommendations during the intervention. We may see improvements in your blood sugar levels, cholesterol and other markers of disease, although as this is a clinical study, we cannot guarantee that this will happen. You will also be contributing to important science knowledge in the field of nutrition and health.

Will I be compensated for my participation?

You will receive a **\$10 voucher** when you come to the HNU for your screening visit /study visits to cover your travel costs (**\$70 total in vouchers**).

If you are selected in a **subgroup** that undertake the following procedures, additional compensation will be provided to you:

MRI Scan: You will receive **\$20 voucher** for each of your MRI scan at Visit 2, 4, and 6

Metabolic Rate: You will receive **\$10 voucher** for each metabolic rate measurements at Visit 3, 4, and 6)

OGTT: You will receive **\$10 voucher** for each OGTT measurement at Visit 4 and 6.

Irrespective of the study arm you are randomised to, you will also receive all weight loss meal replacement products in the LED diet free of charge, funded by the High Value Nutrition Programme.

What if something goes wrong?

The University of Auckland is sponsoring this study. 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.

Confidentiality

Study files, including conversation recordings at the Focus Group interview by Plant & Food Research scientist, and all other information that you give will be strictly confidential. Nothing that could identify you will be used in any reports on this study. On enrolling in the study, you will be given a *de-identified study number*, e.g., AB51025, and all forms and other types of data collection will use only this study number. Your name will never be linked with any data at any time either during or after the study. If an unusual blood result is found, the lab would let us know which *de-identified study number it is linked to* and then the clinical researchers would be able to access your confidential file and talk to you about the result. At the end of the study your records will be stored for 10 years in a secure place at the research units at the University of Auckland, AgResearch and Malaghan. All computer records will be password protected. Study data will be under the care of the main study investigators. All future use of the information collected will be strictly controlled in accordance with national regulations.

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.

A copy of your results will be sent to you at the end of the study if you would like to have them. Please note that there will be a delay between conducting the study, analysing the blood samples, and telling you the results. This will be done at the very end of the study when all participants have completed.

Who do I contact for more information or if I have concerns?

If you would like some more information about the study please feel free to contact the study investigators: Dr. Jia Jiet Lim, Mr. Kurt Grayson and Mr Ibrahim Mohamed at the Human Nutrition Unit, University of Auckland on telephone: (09) 630 1162/ mobile: 02109196703 / 02109195443

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent Health & Disability Advocate on:

Phone 0800 555 050

Free fax 0800 2787 7678 (0800 2 SUPPORT)

Email: advocacy@advocacy.org.nz Website: <https://www.advocacy.org.nz/>

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

Phone: 0800 4 ETHIC

Email: hdecs@health.govt.nz

This study has received Ethical Approval from the Southern Health and Disability Ethics Committee (2022 EXP 12032).

The investigators of this research are:

Principal investigators

A/P. Jennifer Miles-Chan PhD

Director, Human Nutrition Unit

School of Biological Sciences

University of Auckland

Telephone: 09 923 4322

Email: j.miles-chan@auckland.ac.nz

Dr. Ivana Sequeira PhD

Senior Research Fellow, Human Nutrition Unit

Unit School of Biological Sciences

University of Auckland

Telephone: 09 6301162

Email: ivana.sequeira@auckland.ac.nz

Associate Investigator/Research Students

Mr. William Zhu, BMed

Research Nurse

Human Nutrition Unit, University of Auckland,

Telephone: 09 6301162

Dr. Jia Jiet Lim, PhD

Post doctoral Research Fellow

Human Nutrition Unit,

Telephone: 09 6301162

Mr Kurt Grayson, BSc
Research Assistant
Human Nutrition Unit,
University of Auckland,
Telephone: 09 6301162

Mr. Saif Faraj,
PhD Candidate
School of Biological Science,
University of Auckland
Telephone: 09 6301162

Mr Ibrahim Mohamed, BMLSc, PGDipSci
PhD Candidate
Human Nutrition Unit,
University of Auckland,
Telephone: 09 6301162

Dr Ivy Gan, PhD
Scientist,
Consumer and Product Insights Group
Plant and Food Research, Auckland
Telephone: 09 925 715

Dr Shakeela Jayasinghe, PhD
Research Assistant,
Human Nutrition Unit,
University of Auckland
Telephone: 09 6301162

Please keep this information sheet for your records

Evaluating FEijoa foR Diabetes prevention in a multi-ethnic New zealAND cohort

the FERDINAND study

Consent Form

Please tick to indicate you consent to the following

I have read and I understand the Patient Information Sheet (dated _____) for volunteers taking part in FERDINAND Study

I have had the opportunity to discuss this study with the investigator. I am satisfied with the answers I have been given.

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.

I am aware that the Focus Group interview will be audio-recorded and transcribed; with information kept securely by researchers at Plant & Food Research, Auckland.

I understand that as part of the reporting process, quotes the Focus Group interview may be used but that no information that personally identifies me will be used.

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 consent to having a metabolic rate measurement, fasting blood test, OGTT, MRI/S and DXA scans, 24-hour urine collection, and faecal microbiome tests.

I also agree for my blood samples to be processed for novel risk markers, i.e., for metabolomics at AgResearch, Palmerston North and for immune profiling at the Malaghan Institute of Medical Research. I understand that no information that may identify me personally will be provided.

I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics 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 that the Researchers may use my de-identified study data for future research related to the study aims and that I may not receive a copy of these results

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>Participants to Complete (Please circle as appropriate)</i> | | |
|---|-----|----|
| I wish to receive a summary of the results from the study. | Yes | No |
| I wish to receive a copy of my results. I understand that there may be a specific delay between data collection and the availability of research results. | Yes | No |
| I consent for research staff at HNU contact me at a later date if there are future studies for which I am eligible. | 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:

*A copy of this consent form is to be given to the participant
and a copy to be kept in their research file by the Investigator at HNU.*