Participant Information Sheet

For Healthy Control Participants

MASSEY UNIVERSITY
COLLEGE OF HEALTH
TE KURA HAUORA TANGATA

Te Whatu Ora
Health New Zealand

Nutritional response to chyme reinfusion in intestinal failure – a pilot study

Formal Study Title:	Investigation into the nutritional response to chyme reinfusion in patients with type 2 intestinal failure – a pilot study
Sponsor (if applicable): Name and Address:	Massey University, Albany, Auckland, New Zealand
Lead Researchers:	Professor Rozanne Kruger and Professor David Rowlands
Study Site:	Massey University Human Nutrition Research Centre
Contact Phone Number:	+64 21 88 77 30
Ethics Committee Ref.:	HDEC: Northern B: 2023 EXP 15600

Kia ora,

You are invited to take part in a study on investigating the nutritional response to chyme reinfusion in patients with type 2 intestinal failure. You are being invited as a control participant with normal gut function and metabolism.

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 or any other prejudices. 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 11 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THIS STUDY

You are under no obligation to accept this invitation. If you decide to participate, you have the right to:

- withdraw from the study at any time,
- decline to answer any specific questions,
- ask any questions about the study at any time during participation,

- provide information on the understanding that your name will not be used unless you give permission to the researcher,
- be given access to a summary of the project findings when it is concluded.

Withdrawing from the study, should you choose to do so, will not result in any disadvantage to you.

WHAT IS THE PURPOSE OF THE STUDY?

Intestinal failure (IF) happens when your gut loses the ability to absorb enough essential nutrients from food to sustain life. After major gut surgery, IF could develop and may last for several months. Main symptoms include diarrhoea or a large amount of watery gut content coming out from a stoma or fistula into an attached stoma bag. Both a stoma and fistula are an opening on the abdominal wall, connected to the gut to divert gut contents (also called chyme) out of the body when the rest of the gut cannot be used. When the output of chyme from the stoma/fistula is low, it can be discarded as a waste without changing normal body function (Figure 1). Since chyme comprises valuable nutrients and electrolytes from food eaten, when the amount of output becomes high and watery, it can lead to dehydration, weight loss and malnutrition. Nutrition through a vein, termed intravenous or parenteral nutrition (PN), is often given to treat dehydration and malnutrition, but PN is costly and has its own complications. Therefore, it is important to find ways to use the nutritious chyme within the body.

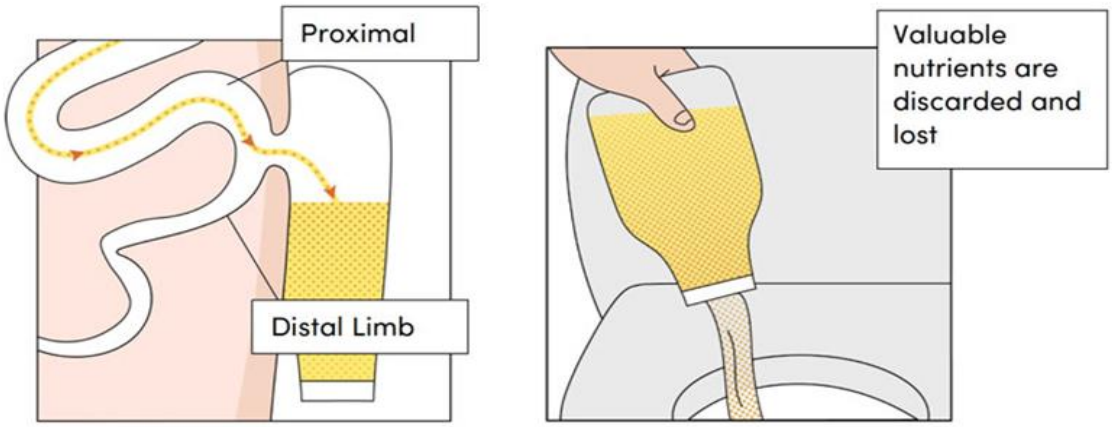

Figure 1. Chyme is collected in the Ostomy Appliance and discarded. The Distal Limb experiences atrophy (shown) from inactivity

In recent years, an automated device has been developed to reinfuse the chyme collected in the stoma bag back into the gut (Figure 2). This process is called Chyme Reinfusion Therapy (CRT). Chyme reinfusion therapy has showed to be safe and effective in reducing stoma output and achieving independence from PN.

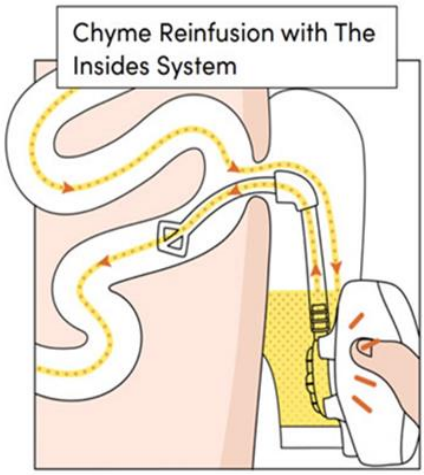

Figure 2. Chyme Reinfusion with The Insides System enables patients to recycle Chyme at both hospital and home, when needed.

Although CRT has been adopted as a usual treatment for T2IF nowadays, the effect of CRT on both the digestion and absorption of protein and the effects of soluble fibre intake on the colon's function in the unused gut, have not been studied before. Hence, in this study we plan to use stable isotope processes (explained below) to help us quantify the effect of CRT on the body's ability to digest, absorb and use the protein and soluble fibre consumed from food. We will do this by measuring the exact amounts of 'labelled' nutrients that appear in the blood stream by using stable isotopes.

Stable isotopes are variations of the same element that have a different atomic mass but are not radioactive. This means they can therefore be safely added as a label on any nutrients of interest in food such as protein in a nutritional supplement drink. Once you drink it, the movement of the 'labelled' protein can then be tracked through your stomach and gut into our body. We can therefore measure how much more protein and soluble fibre from food are digested, absorbed, and utilised by the body after the chyme has been reinfused into the lower part of the gut.

Therefore, the aim of this study is to utilise stable isotope tracer protocols to determine the nutritional response to and explore the impact of CRT on protein and fibre metabolism. This information will further guide us to develop new diets to help patients, to improve muscle mass, restore colon function and return to eating more quickly without relying on long-term PN.

As a healthy participant with normal gut function, we will make the same measurements of nutrient absorption, but without any CRT, just as you normally are.

HOW IS THE STUDY DESIGNED?

We are looking for three health adult men and women to participate in this study as a reference to participants receiving CRT.

There will be one 8-hour stable isotope investigation day taking place in the Human Nutrition Research Centre, Massey University, Albany Campus, Auckland.

WHO CAN TAKE PART IN THE STUDY?

To take part you need to:

- Be an adult younger than 70 years
- Not be pregnant or breastfeeding
- Not have intestinal failure or any gastrointestinal diseases such as inflammatory bowel disease
- Not have any diagnosed chronic diseases such as heart disease, diabetes or cancer

Apart from overnight fasting prior to the investigation day, no other lifestyle restrictions are required for the study.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

The investigation day will start in the early morning after overnight fasting for eight hours.

Investigation for protein and fibre metabolism will involve:

- having a blood sample taken via a line placed into one of your hand veins to measure natural background levels of two amino acids (phenylalanine, Phe, and tyrosine, Tyr) and three short chain fatty acids (SCFA) (acetate, propionate and butyrate) in your body.
- shortly after, we will place another line into a forearm vein and start an intravenous infusion of Phe and Tyr to assess whole body protein metabolism affected by the ingested test drink.
- at the same time, a one-off pulse of microgram amounts stable isotopically labeled SCFAs will also be given.
- then four blood samples will be taken at 4, 8, 15 and 30 minutes (to assess whole body SCFA production).

After two hours:

- you will start sipping a 200ml stable isotope tracer-enriched, spirulina flavoured oral nutritional supplement (ONS) drink every 30 minutes for the next five hours orally.
- six blood samples will be taken using the existing line in 60-minute intervals (to measure the amounts of Phe and Tyr):

Stable isotope tracer and drink ingestion protocol:

Time (min)	0	4	8	15	30	120	180	240	300	360	420
	IV primed continuous infusion: L-[ring-$^{2}H_5$]-phenylalanine & L-[$^{13}C_9$, ^{15}N]tyrosine										
Blood	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Labelled ONS drink*						✓	✓	✓	✓	✓	✓
IV pulse solution **	✓										

* ONS drink containing [^{13}C]-Phe and [^{15}N]-spirulina; ** IV pulse solution containing [1,2-^{13}C2]- acetate, [1-^{13}C]-propionate, and [1-^{13}C]-butyrate

You will be also asked to:

- have body weight and height measured using a digital scale and stadiometer to determine body mass index (BMI), body fat and lean mass and hand grip strength.

- complete validated semi-quantitative food frequency and dietary diversity questionnaires (to measure diet quality and diversity).

WHAT WILL HAPPEN TO MY BLOOD SAMPLES?

Blood samples will be collected by a certified phlebotomist (using standard operating procedures) in labelled tubes using a de-identifiable unique participant code. Blood samples will be immediately put on ice to minimize enzymatic reactions, and centrifuged to obtain plasma. All samples will be snap-frozen in separate aliquots in Eppendorf tubes and stored at -80ºC until analysis. All biohazard waste products will be disposed of in a biohazard waste container.

Samples will be stored in a secure laboratory freezer at the Human Nutrition Research Unit until completion of the study for a maximum of 10 years. Samples will be analysed by the Centre for Translational Research in Aging & Longevity, Texas A&M University, College Station, Texas, United States of America (USA). No individual will be identified during data analysis. After analysis, any additional blood will be destroyed following usual procedures. Unfortunately, for the samples that are sent to the USA, a karakia will not be available at the time of tissue destruction. However, if you prefer to have your blood samples, it can be returned to you if you request it.

You may hold beliefs about a sacred and shared value of all or any tissue samples removed. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.

WHAT ARE THE POSSIBLE RISKS OF THIS STUDY?

There are no major risks involved in taking part. Some people may fear having a blood sample taken or experience discomfort when the blood sample is taken. Occasionally, a slight bruise or an infection of the blood draw site may result. We will take every measure to ensure you are comfortable and respected. You may also be accompanied by a support person if required.

Stable isotopes (such as deuterium (^{2}Hydrogen), ^{18}Oxygen, ^{13}Carbon and ^{15}Nitrogen)) have been used as tracers in human nutritional studies for many years to assess body composition, energy expenditure, protein turnover and other metabolic studies. Nevertheless, as their name implies, none of these stable isotopes are radioactive, and no adverse biological or physiological effects have been reported at the very low levels of enrichment that are used in human studies. There are ample data to reaffirm the safety of stable isotopes at the levels used in nutritional research. In our study, only very tiny amount of stable isotopes will be ingested by and infused to the participants. Hence, our stable isotope protocols are very safe to use.

Any abnormal findings of potential clinical significance that arise during the study will be escalated by the research team to your General Practitioner (GP) if at home via a phone call and letter/email.

You will be told of any new information about adverse effects related to the study that becomes available during the study that may have an impact on your health.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

You will be contributing to a more in-depth understanding of the nutritional response to CRT in patients with T2IF.

You will also receive a brief report summarising the main findings of the project via mail or e-mail after analysis of the data has been completed. If any of your blood results are outside normal parameters you will be advised to talk to your medical practitioner or at your request, we can send your results directly to them to ensure that you receive the required treatment.

WILL ANY COSTS BE REIMBURSED?

There will be no charges made for any of the tests that you undertake. You will receive information about your body composition and dietary intake in recognition of your participation, you will receive a $100 supermarket or petrol voucher at the end of the study.

WHAT IF SOMETHING GOES WRONG?

If an unforeseen medical event occurs (e.g. a fall or cut), depending on the nature of the incident the following steps will be taken: a) when onsite at Massey University we will accompany the injured/sick participant to the health & counselling service on campus, (b) if outside of regular working hours instruct the participant to use the nearest first aider, or if needed, call 111 for an ambulance.

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 WILL HAPPEN TO MY INFORMATION?

During this study the researchers and research assistants will record information about you and your study participation. This includes the results of any study assessments. 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.

<u>Identifiable Information</u>

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 staff (to complete study assessments)
- Your GP may be notified of your participation in this study with your consent.
- 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 or overseas, 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 (your GP or specialist), if a study test gives an unexpected result that could be important for your health or well-being. This allows appropriate follow-up to be arranged.
- The Medical Officer of Health if you return a positive test for any nutrient deficiencies.
- Rarely, it may be necessary for study researchers to share your information with other people – for example, if there is a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations.

<u>De-identified (Coded) Information</u>
To make sure your personal information is kept confidential, information that identifies you will not be included in any report generated by the researchers. Instead, you will be identified by a code. The researcher will keep a list linking your code with your name, so that you can be identified by your coded data if needed. Only the researchers will have access to this identifier.

The following groups may have access to your coded information, which may be sent and stored overseas:

- The researchers, for the purposes of this study.
- People and companies working with or for the researchers, for the purposes of this study (this may include approximately 20 people and companies).

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

<u>Anonymised Information.</u>
The sponsor may remove the code from your de-identified information – this is called ‘anonymisation’. This makes it very difficult (but not impossible) to identify the information that belongs to you. The sponsor will share this anonymised information with the groups described in the De-identified information section. Anonymised data and/or tissue may also be made available to other researchers, as described below.

<u>Security and Storage of Your Information.</u>
Your identifiable information is held at Massey University during the study. After the study it is transferred to a secure archiving site and stored for at least 10 years, then destroyed. Your coded information will be entered into electronic database and retained by the researchers in secure, cloud-based storage indefinitely. All storage will comply with local and international data security guidelines.

<u>Risks.</u>
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.

Your deidentified coded information is being sent overseas. Other countries may have lower levels of data protection than New Zealand. There may be no New Zealand representation on overseas organisations which make decisions about the use of your information. There is a risk that overseas researchers may work with information in a way that is not culturally appropriate for New Zealanders.

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 researchers.

Rights to Withdraw Your Information.
You may withdraw your consent for the collection and use of your information at any time, by informing your study researchers.

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

Information collected up until your withdrawal from the study will continue to be used and included in the study. This is to protect the quality of the study.

Ownership Rights.
Information from this study may lead to discoveries and inventions or the development of a commercial product. The rights to these will belong to Massey University. You and your family will not receive any financial benefits or compensation, nor have any rights in any developments, inventions, or other discoveries that might come from this information.

Māori Data Sovereignty
Māori data sovereignty is about protecting information or knowledge that is about (or comes from) Māori people. We recognise the taonga of the data collected for this study. To help protect this taonga:

- We have consulted with Dr Bevan Erueti (Taranaki, Te Ati Haunui-ā-Papārangi, Ngāti Tūwharetoa), Associate Dean Māori, School of Health Sciences, Massey University about the collection, ownership, and use of study data.
- We allow Māori organisations to access de-identified study data, for uses that may benefit Māori.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

If you wish to withdraw during the study, you can inform the study researchers. The study team will stop collecting data from you. Information and samples collected up until your withdrawal from the study will continue to be used and included in the study. This is to protect the quality of the study. Any collected tissue will be retained for up to five years, then destroyed by incineration or returned to you on request.

CAN I FIND OUT THE RESULTS OF THE STUDY?

You will receive a brief summary of the main findings of the study via mail or e-mail after analysis of the data has been completed by the 31st of December 2025.

WHO IS FUNDING THE STUDY?

The research is funded by the Massey University Strategic Research Excellence Fund (SREF).

WHO HAS APPROVED THE STUDY?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The Northern B Committee has approved this study.

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:

Andrew Xia, Advanced Dietitian and Co-Investigator
Telephone number: +64 21 88 77 30
Email: a.xia@massey.ac.nz

Professor Rozanne Kruger, Primary Investigator
Telephone number: +64 9 213 6661
Email: r.kruger@massey.ac.nz

Professor David Rowlands, Co-Investigator
Telephone number: +64 9 213 6616
Email: D.S.Rowlands@massey.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
Website: https://www.advocacy.org.nz/

For Māori cultural support please contact:

Dr Bevan Erueti, Associate Dean Māori, School of Health Sciences
Telephone number: +64 6 951 6087
Email: b.erueti@massey.ac.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

Consent Form

Nutritional response to chyme reinfusion in intestinal failure – a pilot study

Healthy Participants

An interpreter is available on request.

Please tick to indicate you consent to the following

I have read the Participant Information Sheet, or have had it read to me in a language I understand, and I fully comprehend what it says.		
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.	Yes ☐	No ☐
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 my blood samples being sent overseas and I am aware that these samples will be disposed of using established guidelines for discarding biohazard waste.		
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 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: _____