THE UNIVERSITY OF QUEENSLAND

Participant Information and Consent Form

Title: Improving the Variability of Response to High Intensity Interval Training (Improve HIIT)

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This document has been designed to give you information to allow you to decide whether you wish to voluntarily participate in a research study investigating the association between your fitness and genes, and whether altering your gut via diet can influence your ability to improve fitness after high intensity interval training (HIIT).

This research is being done as part of the principal investigator's PhD studies.

Introduction:

Cardiorespiratory fitness (CRF) is the biggest predictor for chronic disease morbidity and mortality; however, one in five adults report little to no improvement in CRF ($\dot{V}O_{2max}$) following exercise training. Variability can be attributed to a myriad of factors, such as age, sex, gender and baseline $\dot{V}O_{2max}$. One of the biggest predictors is genetic make-up; which contributes to approximately 50% of $\dot{V}O_{2max}$ trainability. In a recently published systematic review, we identified nearly 100 genetic variants associated with $\dot{V}O_{2max}$ trainability. Individuals can be given a gene predictor score (GPS) based on how many genetic variants they have that contribute to a high or low $\dot{V}O_{2max}$ training response.

Typically, there are fewer low responders with high intensity interval training (HIIT) compared to other forms of training. Individuals with a low GPS ideally should be prescribed a HIIT intervention over other forms of training for greater adaptations. Despite this, variability will still exist.

There has been minimal, if any, research to identify the association between the gut microbiome (the bacteria that lives within our large intestines) and its effect on $\dot{V}O_{2peak}$ trainability (our improvement in cardiorespiratory fitness). More specifically, is our GPS related to the bacteria within our gut; and can this gut bacteria be positively influenced to improve our cardiorespiratory training response?

The overall objective of IMPROVE HIIT is to contribute to evidence-based personalised medicine. Understanding the factors that influence training variability that could be used to improve individualised exercise prescription, thereby contributing to health maintenance and treatment/prevention of disease.

Aims:

The aims of IMPROVE-HIIT include:

1) determining the association between our genetic make-up and the bacteria within our gut
2) investigating whether improving our gut bacteria via diet can influence our cardiorespiratory training response

Subject involvement and study procedures:

N.B. All the information collected from the procedure described here will not be stored with you name, but instead with a number. This means it cannot be linked directly to your personal details (see Confidentiality section).

Participation in this study will require:

- Attending two testing sessions before and two testing sessions after the training intervention (testing session 1 = 60-90 minutes and testing session 2= 30 minutes).
- Attending three supervised exercise training sessions per week at The University of Queensland (UQ) for 6 weeks (each session will be for ~ 60 minutes).
- Consuming prebiotic powder or a placebo daily for 8 weeks (initially once per day progressing to twice per day with either food or fluids).

Study Groups:

After initial testing, you will be randomly selected (like tossing a coin) to go into one of 2 groups:

1. High intensity interval training plus placebo (maltodextrin) (HIIT-M)
2. High intensity interval training plus prebiotic powder (HIIT-P)

The mode for exercise training will be treadmill running.

For both protocols, the high intensity interval training (HIIT) will involve a 10-minute warm up at 60-70% of maximal heart rate (HRmax). After this, you will work at 90-95% of your HRmax for 4 minutes, followed by a

3-minute active recovery (50-70% of HRmax). This will be repeated 4 times (4x4), followed by a 5-minute cool down.

If you are randomised into the placebo group, you will be asked to consume 12g of maltodextrin per day (2 x 6g/day) during the 6-week exercise intervention. During the two weeks prior to this 6-week exercise intervention, you will be asked to start at 2g/day and progressively increase the dose of the placebo so that by the end of the two weeks you are consuming the required 12g/day. You will be provided with a diary to indicate when and by how much to increase the dosage. Maltodextrin is a polysaccharide that has a tasteless to slightly sweet taste that is often used a food additive to improve texture, and as a body-building supplement. Maltodextrin can increase blood glucose levels quickly.

If you are randomised into the prebiotic fibre group, you will be asked to consume 12g (2 x 6g/day) of oligofructose enriched inulin (chicory root) each day of the 6-week exercise intervention period. During the two weeks prior to this 6-week exercise intervention, you will be asked to start at 2g/day and progressively increase the dose of the inulin so that by the end of the two weeks you are consuming the required 12g/day. You will be provided with a diary to indicate when and by how much to increase the dosage. Inulin has a slight sweet taste and may cause some bloating and gas.

Note: you will not know which group you are allocated to. You will be asked to stay on your usual diet and to avoid any drastic dietary changes.

Testing Visits:

For both groups, testing visits will occur at baseline and after 6 weeks (the intervention period).

Testing Visit 1 (60-90 minutes) will involve:

- Providing consent to participate (approximately 5 minutes to complete).
- Completing of a questionnaire assessing physical activity readiness (Australian Physical Activity Readiness Questionnaire – see appendix). This will take approximately 5 minutes to complete.
- Providing a saliva sample (DNA sample). This involves spitting into a tube (2ml required). This will take approximately 5 minutes to complete.
- Completing of a fasted blood test. A small sample of blood (two 10ml tubes, ~1 table spoon) will be collected to measure fasting glucose, triglycerides and cholesterol. This will take approximately 15 minutes to complete.
- Measuring your weight, waist and hip circumference. This will take less than 5 minutes.
- Measuring your fat mass and muscle mass via a body composition x-ray (DEXA machine). This involves laying still on a scanner for 7 minutes.
- Consuming a Sustagen popper after your body composition x-ray (to prepare you for your fitness test).
- Providing you with a stool collection kit and associated questionnaires (approximately 20 minutes to complete). You will be asked to:
    - collect a stool sample the day before your second testing visit
    - record the date and time and immediately freeze the sample in the containers provided (you will be provided with detailed instructions about collection and hygiene)
    - complete a consent form provided by the stool collection company, 'Microba'
    - complete a food frequency questionnaire
    - complete a questionnaire related to your mental health (CESD), exercise habits, medical history and what you did the day of taking your stool sample.
    - return the frozen samples at the second testing visit

- Measuring your resting blood pressure and heart rate (~ 5 minutes to complete).
- Completing a maximal exercise test (VO_{2max} test/fitness test). This test is completed on a treadmill and gradually increases in intensity (speed and incline). You will be asked to go to exhaustion (which is usually less than 16 minutes). You will also be monitored by an electrocardiogram (ECG) throughout the test.

Testing Visit 2 (30 minutes) will involve:

- Providing the researchers with your frozen stool sample (~1 minute to complete).
- Completing a 24-hour diet recall. This will take approximately 20 minutes to complete.
- Being randomly allocated to one of two intervention groups (~1 minute to complete).
- Providing you with your supplement (based on your randomisation). This will take approximately 1 minute to complete.
- Providing you with a diary to monitor supplementation compliance, and to monitor exercise attendance. This diary will also include instructions on when and how to take the supplement, and to highlight that dietary habits should not be changed during the intervention period. This will take approximately 5 minutes to explain.
- Booking in for your first supervised exercise session. The two-week supplementation adjustment period will begin two weeks before this date (~1 minute to complete).

Risks involved with the study:

- Although very unlikely (less than 1 in 100,000), a cardiac event may occur during exercise. However, the supervising Exercise Physiologists are well trained to recognise and prevent any early signs and symptoms of a cardiac event occurring. In the unlikely situation of a cardiac event, a defibrillator will be available for use. Furthermore, the Adult Pre-Exercise Screening Tool will be used to assess your risk of an adverse event during exercise; and you will be wearing an ECG during your fitness test to analyse our cardiac rhythm during exercise.
- An x-ray scan is used to determine fat mass and muscle mass and involves emission of a very small amount of radiation. However, approximate dosage received from one scan is around 0.06 mSv which equates to 9 days of natural background radiation and the corresponding risk is extremely low.
- The discomfort associated with the blood drawing procedures is minimal. There is a risk that bruising, and infection may occur and that the arm might become sore. Risk of bruising or infection from the blood draws will be minimised because all blood draws will be performed by a trained phlebotomist. The total amount of blood drawn during each testing session will be 20 ml, which is equivalent to approximately 4 teaspoons. No syringes, lancets, needles or other devices capable of transmitting infection from one person to another shall be reused. All of these items, which are disposable, will be destroyed after each use. As an additional safeguard in preventing contamination, new disposable gloves will be worn for all blood draws. All needles will be disposed of promptly in sharps containers.
- You may experience some bloating or gas when initially taking the prebiotic fibre supplement (made from chicory root, which is oligofructose enriched inulin). However, the supplementation dose will be started low and gradually increased to minimise these side-effects. For 2 weeks prior to the 6-week exercise intervention, the dose will be gradually increased (starting with 2g/day) so that by the start of week 3, 12g/day is consumed (6g twice daily).
- Maltodextrin is a tasteless to slightly sweet tasting high glycemic index (GI) food that can raise blood sugar levels quickly, but if consumed after a meal/with a meal, the peak should not be as high. The maltodextrin product may contain traces of soy, egg and milk. For 2 weeks prior to the 6-week exercise

intervention, the dose will be gradually increased (starting with 2g/day) so that by week 3, 12g/day is consumed (6g twice daily).

- If you are concerned that you have any allergies or intolerances to any food (particularly inulin, fructans, oligosaccharides, soy, milk and egg) please consult with your doctor before proceeding.
- You may be at risk of infection if adequate measures are not taken during your stool sample collection. A document will be provided to you outlining the safe collection procedures (please refer to handout).
- During the genetic analysis of your saliva, we may detect a defect in a gene that is associated with an increased risk for an untoward health condition or an inherited disease (e.g. Huntington's Disease). We ask you to please keep in mind that this study is for research purposes only and further testing will be required for clinical diagnosis. Additionally, the chance of detecting a rare heritable disease in this study is very unlikely as we are looking for common gene variants that may be associated with cardiorespiratory fitness and the gut microbiome. We will not specifically be looking in regions where known disease variants are located; therefore, the chance of identifying an inherited disease is extremely low. You can specify on the consent form if you want to be informed about such findings. If you choose to be informed, we will encourage you to see your general practitioner (GP). If warranted, your GP may refer you to a specialised genetic counsellor who will arrange for further testing. The costs associated with this additional testing will be your responsibility. We recommend that you seek clinical advice or talk to a genetic counsellor and your family members about your decision to donate your DNA sample for this study and for further research. If you become upset or distressed as a result of your participation in the research, the researchers are able to arrange for clinical advice, counselling or other appropriate support. Any counselling or support will be provided by staff who are not members of the research team. Genetic counsellors can be contacted through Australasian Society of Genetic Counsellors website https://www.hgsa.org.au/asgc. You will always have the option to suspend or end your participation in this research project if distress occurs.

Will my sample be used for future studies?

No. Your DNA samples will be destroyed once the study is complete.

Concerns, complaints or feedback related to participation in the study:

Please feel welcome to discuss participation in this study with a friend, family member or your doctor.
If you have any immediate concerns or feedback, please contact Professor Jeff Coombes on 07 3365 6767.

Alternatives to Participation:

If you choose not to participate, you can still be entitled to a copy of the overall findings. Please let the principal investigator know if wish to choose this option.

Investigator Benefits:

There are no monetary benefits allocated to investigators for their involvement in this study. Investigators are participating in this study to advance their knowledge of genes, the gut microbiome and how to affect trainability; thereby influencing health outcomes of future populations.

Termination of Study:

You will be notified by the principal investigator if the study is terminated.

What if new information arises from participating in this study?

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will only be told about this new information and the researcher will discuss whether this new information affects you, if you have given consent for us to contact you.

What is the Privacy Statement for this study?

The conduct of this research involves the collection, access, and / or use of your identified personal information. The information collected is confidential and will not be disclosed to third parties without your consent, except to meet government, legal, or other regulatory authority requirements. A re-identifiable copy of this data may be used for other research purposes; however, your anonymity will at all times be safeguarded. For further information, consult the National Health and Medical Research Council of Australia website https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/e39.pdf

Injuries related to participation in the study:

If you think you have any side effects that are related study you should immediately contact Professor Jeff Coombes, 07 3365 6767.

If you have a study-related illness, the investigator and the study staff will make sure that you receive necessary treatment.

Confidentiality:

Personal information gained from this study will be recorded but not easily identified to any one individual. Once all the measures are completed and the study outcome is verified, subject data will be de-identified and filed in a locked cabinet within the supervisor's office. To ensure longevity of the data, results will also be kept in a password locked computer with access granted only to the primary investigators. Data will be kept for a minimum of 5 years at the university before being shredded.

Access to Results:

When the study has finished you will provided with all of you results. You will also be given the opportunity to ask any questions regarding the results and anything else to do with the study in a de-briefing session.

Reimbursement:

There is no reimbursement for your involvement in this study. However, you will receive free parking, snacks after the testing, and your results to informative health tests.

Ethical considerations:

This study adheres to the Guidelines of the ethical review process of The University of Queensland and the *National Statement on Ethical Conduct in Human Research*. Whilst you are free to discuss your participation in this study with project staff (contactable on 07 3365 6767 or at camilla.willliams@uq.net.au), if you would like to speak to an officer of the University not involved in the study, you may contact the Ethics Coordinators on +617 3365 3924 / +617 3443 1656 or email humanethics@research.uq.edu.au.

PARTICIPATION IS ENTIRELY VOLOUNTARY AND SUBJECTS ARE FREE TO WITHDRAW FROM THIS STUDY AT ANY TIME WITHOUT PENALTY.

Participant Consent Form– Agreement to participate in study

Title: Improving the Variability of Response to High Intensity Interval Training (IMPROVE HIIT)

The investigators of this study conform to the principles governing the ethical conduct of research, and will protect the safety, interests and well-being of subjects at all times. This consent form and information sheet has been given to you in the interest of your own protection. They contain an outline of procedures and possible risks involved. By signing this consent form you are indicating that:

1. You are 18 years or older
2. You have read or had read to you in a language that you understand, this Participant Information Sheet and you understand the purposes, procedures and risks of this research project as described within it. You have had the opportunity to ask questions and you are satisfied with the answers you have received.
3. You are willing to provide a saliva sample for genetic analysis.
4. You are willing to provide a blood sample.
5. You are willing to complete the questionnaires.
6. You are willing to provide a faecal sample to analyse your gut health.
7. You are willing to complete the necessary fitness and biometric tests.
8. You give permission for the investigators to genetically analyse your blood and faecal sample.
9. You are aware that you can withdraw from the study at any time without prejudice or discrimination.
10. You understand that the data you provide to the researchers is confidential and can only be identified by using a master code sheet that is held by the Principal Investigator and one Co Investigator (Williams). Whilst not regular or common practice, access to your data may occur for specific purposes such as quality assurance, auditing, research and in the situation of a serious adverse event.
11. You give permission for your de-identified data published and or discussed during presentations/conferences.
12. You understand that there may be no direct clinical benefit to you because of this or future studies.
13. You understand that there is a small chance that this study could identify a genetic defect that increases your risk for an untoward health condition. If you choose to receive such information, you will be encouraged to see your general practitioner, who may refer you to a genetic counsellor.

Would you like to be informed if a risk factor for an untoward health condition or inherited disease is identified in this current study? Please tick:

- ☐ Yes
- ☐ No

Can the researchers contact you in the future if the need arises? Please tick:

- ☐ Yes, via email/phone/mail (please select)
- ☐ No

I freely agree to participate in the procedures outlined in the patient information sheet (#1) for the study: **Improving the Variability of Response to High Intensity Interval Training**

_____	_____	_____
Name of Participant	Date	Signature

Address:_____Mobile:_____Email:_____

_____	_____	_____
Witness Name	Date	Signature

Witness: I declare that I have been present when the research was explained to the above-name participant and to the best of my observation and belief was understood and the consent freely given.

_____	_____	_____
Investigator Name	Date	Signature