THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Information Statement for the Research Project:

Enhancing Exercise Prescription and Adherence for Type 2 Diabetes Management for Adults with Long-COVID: A Randomised Pilot Trial

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You are invited to participate in a research project from a team of researchers from the University of Newcastle, Hunter Medical Research Institute, John Hunter Hospital, and The University of Queensland. This project is funded by a Diabetes Australia Research Program grant. This document provides information about the project. It explains the tests and research involved. Knowing what is involved will help you decide if you want to take part in the research. You will be given a copy of this information statement to keep.

What is the aim of this research?

Our project aims to improve the prescription and delivery of exercise to people with type 2 diabetes and long-COVID symptoms (e.g., shortness of breath, fatigue) to allow a return to, or uptake of, regular exercise. This project will mirror the structure of the current Medicare-subsidised type 2 diabetes group exercise scheme. We will compare the effects of a long-COVID symptom-guided eight-week exercise program with usual care.

Why is this research being done?

The time it takes to recover from COVID-19 is different for everyone. For most people, a mild or moderate COVID-19 infection will cause them to feel unwell for a short time and then get better within a few weeks. Others may experience ongoing health problems for several weeks or months after their initial infection, even though they no longer test positive for the virus. Long-COVID refers to those who experience ongoing symptoms more than 12-weeks after first testing positive to COVID-19. These symptoms can affect all parts of the body and may be physical, mental, or emotional, mild or severe, and can change day-to-day. Common symptoms in those with long-COVID are shortness of breath and fatigue.

People with type 2 diabetes are more likely to develop a severe COVID-19 illness than the general population, and are therefore at a greater risk of developing Long-COVID. The continued impact of Long-COVID can aggravate diabetes management and make it difficult to control. Symptoms such as shortness of breath and fatigue impact the ability to function, and have a negative impact on daily life by reducing the capacity to be physically active. This is a problem as exercise is a key component for the management of type 2 diabetes, providing benefits for blood sugar control, heart health, body composition, and reducing the risk of diabetes-related complications.

What are the benefits of participating?

While exercise interventions often provide health benefits, we cannot guarantee or promise that you will receive any benefits from this research. However, you may find improvements in your blood sugar, blood pressure, strength, fitness, and/or sense of wellbeing; you will receive a copy of your results at the conclusion of the program. Overall, it is hoped this research will contribute to the currently limited evidence base for utilising exercise in people with type 2 diabetes and long-COVID so that it may be recommended as part of routine clinical care.

In addition to the 8week, individualised supervised exercise program, you will be compensated $20 for completing the two baseline assessment visits and $30 for completing the two final assessment visits, in the form of a gift card. That is, if you complete the study, you will be receive a $50 gift card at the end of the study to compensate you for your time. If you start the study and then are unable to continue and withdraw, you will be compensated $20 for completing the two baseline assessment visits.

Another benefit is that the assessments conducted as part of this research are expensive to be completed outside of research and/or may not be available to you. Once you have completed these assessments as part of the research, we will provide you with a copy of these.

Who is conducting the research?
This project is being conducted by Dr Emily Cox, Dr Hayley Lewthwaite, Professor Ronald Plotnikoff, Dr Myles Young, and Professor Peter Gibson from the University of Newcastle and Hunter Medical Research Institute, in collaboration with Dr Shelley Keating from The University of Queensland and Associate Professor Shamasunder Acharya from the John Hunter Hospital.

Who can participate in the research?
You will be eligible for this research if you:

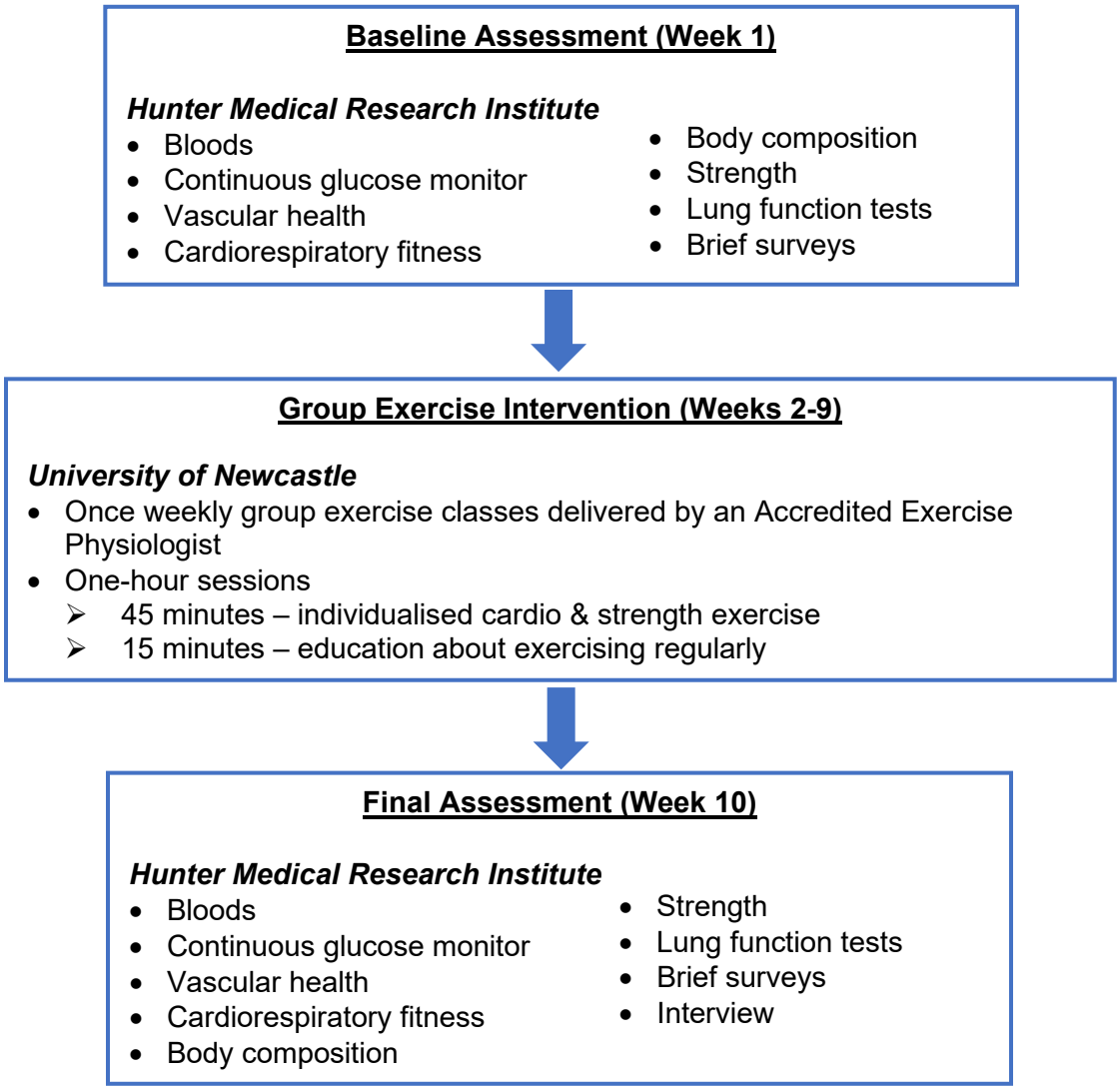
- Have been diagnosed with type 2 diabetes (including a HbA_{1c} of ≥7.0%)
- Are experiencing long-COVID symptoms.
- Are over 18 years of age

You will not be eligible to participate if you:

- Have type 1 diabetes
- Are not able to do the daily activities (e.g., housework, occupation) you would have been able to complete pre-COVID infection
- Have uncontrolled or severe heart, lung or kidney disease
- Are currently undertaking 150 minutes or more of moderate intensity/75 minutes or more of vigorous intensity exercise per week
- Have had changes to medication or weight (+/- 5kg) in the last three months
- Have any planned medical operations during the research period
- Have a physical condition whereby exercise training would be inappropriate
- Are pregnant or expecting to be pregnant during the study period
- Are non-English speaking
- Have cognitive deficits such as Dementia

What would you be asked to do? How much time will it take?

Before commencing in the project, you will be screened for eligibility, and you will sign the consent form prior to any study assessments being performed. The research project will be conducted in the Exercise and Sports Science Laboratories at the University of Newcastle Callaghan Campus and Hunter Medical Research Institute. The total duration of the study will be 10 weeks – this includes one baseline assessment visits in week 1, eight weeks of supervised exercise in weeks 2-9, and one final assessment visits in week 10. The visits are outlined in the figure:



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At the beginning of the study, you will be required to attend the Hunter Medical Research Institute for a baseline assessment (180 minutes). This will be scheduled at a time that is suitable for you, and you will be given free parking. The assessments will include:

- **Bloods**: You will be asked to provide a small blood sample of 30mL. This will be collected under sterile conditions by a trained phlebotomist. This blood test will be collected to measure your HbA1c, blood glucose, blood insulin and cholesterol profile. After your sample is analysed, it will be destroyed.
- **Continuous glucose monitor:** You will be asked to wear a continuous glucose monitor for two weeks to measure fluctuations in your blood sugar levels. This is a small device the size of a 50cent coin; the monitor is inserted through a small needle (5mm) into the back of your upper arm and is secured with an adhesive patch. The monitor measures your blood sugar every 15 minutes; you will not need to interact with the monitor in any way. You will be asked to record the timing of your meals and medications during this time. You should continue with your normal daily activities during this time (this includes showering). After two weeks of wear, you will return the monitor to us via post.
- **Lung function tests:** You will be asked to perform a simple lung function test to evaluate the health of your lungs and airways. You will be asked to breathe through a rubber mouthpiece with your nose gently clipped. You will be asked to breathe all the way in through a mouthpiece before blowing out as hard and as fast as you can for as long as you can (spirometry). In another test, you will gently “pant” through a mouthpiece while sitting inside a closed chamber; the air during panting will at first move through the mouthpiece, which will then be blocked for a few seconds while you make small efforts to pant with no movement of air (lung volumes). In a final test, you will breathe all the way in until your lungs are full, hold your breath for ~8 seconds, and then breathe out again at a comfortable pace (diffusing capacity).
- **Vascular health:** You will be asked to lie down for 10 minutes. Following this, you will have your blood pressure taken three times. Then, the stiffness of your blood vessels will be measured with an automated blood pressure cuff around your thigh which will be inflated to a low pressure, while simultaneously putting a small pen like device (probe) on your neck.
- **Cardiorespiratory fitness:** You will complete a graded cardiopulmonary exercise test using a ramp exercise protocol with simultaneous electrocardiogram analysis (12 lead ECG) and regular measures of blood pressure and ratings of perceived exertion. This test will be conducted on a treadmill or bike.
- **Body composition**: You will undertake a whole-body dual-energy X-ray absorptiometry (DXA) scan to measure lean and fat mass, as well as height, weight, and waist and hip circumference.
- **Strength:** You will undertake an assessment of your grip strength, as well as your lower body strength (30 second sit-to-stand test) and upper body strength (30 second bicep curl test)
- **Physical activity:** You will be asked to wear a physical activity monitor on your wrist for two weeks, for all waking hours, except when sleeping or if the monitor could get wet, at the beginning and the end of the program.
- **Brief surveys/interview**: You will complete surveys assessing your ongoing symptoms related to COVID-19, physical activity enjoyment, shortness of breath levels, physical activity levels, diabetes-related quality of life, and dietary intake at all time points. Each questionnaire will take between 5-20 minutes to complete, and will either be self-administered or researcher-guided. You will also complete a short (~10mins) interview to

assess your experiences in the program (final assessment only). Your responses will be audio recorded and transcribed.

Following your baseline assessment, you will participate in once weekly group exercise sessions, under the supervision of an Accredited Exercise Physiologist (a university qualified health professional), for eight weeks. You will also be asked to exercise at other times throughout the week, in your own time. Your group will include up to four other like-minded people with type 2 diabetes (up to five participants total). Each session will be one hour – 45 minutes will be dedicated to exercise, and 15 minutes dedicated to education. The exercise program will include both cardio and strength-based exercise and will be tailored to your individual needs and preferences; for example, you may be given a different way to complete an exercise compared with another member of your group (e.g., to make it easier or harder). The education component of these sessions will cover such topics as guidelines for exercising with type 2 diabetes, goal setting, and behaviour change. These sessions will be scheduled based on your availability (e.g., around work, health appointments, carer duties, social activities).

At the end of the training period, you will attend the Hunter Medical Research Institute for your final assessments (180 minutes), which will involve the same assessments as the baseline assessment. You will also be asked to complete a short interview to rate your experiences in the program.

What choice do you have?
Participation in this research is entirely your choice. Participants have the right to consent, or not to consent to participate in the research. Whether or not you decide to participate in this study, your relationship with the course staff and the University of Newcastle will not be affected in any way. In addition, if you decide to participate in the study, you have the right to withdraw your consent and discontinue participation in the study at any time, and your relationship with the University of Newcastle will not be affected. If you do decide to withdraw from the research project for any reason, any data that may have already been collected may still be utilized towards the final analysis.

***What are the risks of participating*?**
The current study carries a small risk of discomfort to participants. All assessments will be performed in a controlled environment. All staff involved in this study are trained and procedures are put in place to minimize the risks to you. In the unlikely event that a serious event occurs, medical advice will be sought.

A qualified person will take a blood sample from a vein in your forearm; the total amount of blood drawn during each testing session will be approximately 30mL, which is equivalent to approximately 1.5 tablespoons. This is a very common procedure and causes little discomfort or risk other than minor pain from the needle. Rarely, blood may leak from a vein, but this is easily stopped by applying pressure over the vein. However, a bruise may still appear at the site. The risks and discomfort will be minimised, as this procedure will be performed under sterile conditions by highly experienced and qualified personnel. No syringes, lancets, needles, or other devices capable of transmitting infection from one person to another will be reused. All these items will be appropriately disposed of after each use.

While wearing the continuous glucose monitor, there is a small risk of irritation or discomfort at the sensor site and/or around the clear adhesive dressing that is placed over the sensor. To minimise this risk, you will be screened for allergy to adhesives prior to application of the monitor. If you notice skin irritation around or under the sensor or adhesive dressing, you will be asked to remove the sensor immediately.

There is a small risk of discomfort when performing lung function testing, including mild light-headedness, shortness of breath or cough. However, this is uncommon and these discomforts go away as soon as the test is stopped. Major discomfort is uncommon during lung function tests.

During the assessment of your arterial stiffness and central blood pressure, there is minimal risk of mild discomfort that normally occurs when having your blood pressure taken (e.g., limb numbness, pins-and-needles, and possibly pain). This feeling is temporary and subsides immediately when the blood pressure cuff is deflated.

This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 to 3 millisieverts (mSv) each year. The effective dose from this study is about 0.02 mSv. At this dose level, no harmful effects of radiation have been demonstrated and the risk is believed to be negligible.

There is some risk of adverse events with exercise testing and training. These include risks of a cardiac event or stroke in addition to musculoskeletal injuries. The risk of heart rate abnormalities (including heart attack) during supervised exercise are reported to be rare (less than 0.1%) and no different than if such exercise were performed at home or in a local gymnasium. To help reduce these risks, a pre-exercise health screening (Adult Pre-Exercise Screening Tool), standard procedures for risk assessment, and monitoring of exercise responses (e.g., heart rate, blood pressure) will be employed. The supervising Accredited Exercise Physiologists are well trained to recognise and prevent any early signs and symptoms of a cardiac event occurring. Short-term muscle soreness may be experienced if you are unaccustomed to exercise, however this typically resolves within a few days following exercise. You will be given the opportunity to warm-up prior to exercise to reduce the risk of musculoskeletal injuries. Whilst exercising you may feel fatigued or tired and this may make you feel uncomfortable.

If you are experiencing ongoing fatigue following your COVID-19 infection, it may be increased in the days following exercise. However, the supervising Accredited Exercise Physiologists are trained to prescribe and adjust your exercise program to avoid this happening. You will be asked to keep a symptom diary throughout the study so your fatigue may be monitored, and exacerbations can be avoided.

During the assessments, and at regular intervals throughout the program, we will ask you to inform us of any side effects that you may experience. It is important that you contact the study staff immediately if there are any unusual feelings, injury, or bad effects. This notification should take place whether you believe that the problem is related to the program or from some other cause.

In the case of any abnormal findings, we will refer you back to your general practitioner and/or an appropriate medical specialist with copies of your results.

How will your privacy be protected?

Data will be retained securely for a minimum period of 15 years from completion of the research and managed/stored in accordance with the University's Research Data and Materials Management Guideline (see https://policies.newcastle.edu.au/document/view-current.php?id=72) or any successor Guideline, and applicable University of Newcastle policy provisions (as amended from time to time).

Access to any identifiable data will be restricted to members of the research team, unless:

- you have consented otherwise; or
- disclosure is required by law in order for us to comply with our regulatory obligations.

All information related to your assessments will be labelled with a numerical identity code and will therefore be anonymous. Any identifiable information will not be associated with this identity code.

All surveys will be administered using REDCap, a secure web application for building and managing online surveys. The 24-hour dietary recalls will be administered and managed using the web-based Automated Self-Administered 24-Hour Dietary Assessment Tool (ASA24). Your responses will be encrypted and only associated with your study identify code (not your name). Both REDCap and ASA24 use the same Secure Sockets Layer (SSL) protocol as online retailers and banking organisations. SSL creates a secure connection between the user and the server to encrypt the information being transmitted through the web page. Only members of the research team will have access to the data. For more information about privacy and data security with REDCap, please visit the following link: https://redcap.hmri.org.au/surveys/?s=XXJYFKJYFKHD3PR8. For more information about privacy and data security with ASA24, please visit the following link: https://epi.grants.cancer.gov/asa24/respondent/confidentiality.html.

How will the information collected be used?

The results of the study may be reported in peer-reviewed journals, and conference presentations, posters, and proceedings. Only general results will be published. Individual participants will not be identified in any reports arising from the project. All participants will receive information of the findings relating to this study, via email or mail; you will be asked to indicate your preference on the consent form.

If you provide consent for us to use your deidentified data in future research, these also may be reported in peer-reviewed journals, and conference presentations, posters, and proceedings. Again, only general results will be published. Individual participants will not be identified.

***What do you need to do to participate*?**

Please read this Information Statement and be sure you understand its contents before you consent to participate. If there is anything you do not understand, or you have questions, please contact a member of the research team.

If you would like to participate in this research study, please contact a member of the research team. You will be asked to sign the consent form in-person, on your first visit to the Hunter Medical Research Institute, before initiation of the first assessment session.

Further information
If you would like further information, please contact Dr Emily Cox (Phone: 02 4985 4515, Email: emily.cox10@newcastle.edu.au).

Thank you for considering this invitation.

Kind Regards,

Dr Emily Cox
PhD, BExSS (Clinical Exercise Physiology)
School of Biomedical Sciences and Pharmacy
University of Newcastle
AUSTRALIA

On behalf of the research team

Dr Hayley Lewthwaite
School of Nursing and Midwifery
University of Newcastle
hayley.lewthwaite@newcastle.edu.au

Dr Myles Young
School of Psychological Sciences
University of Newcastle
myles.young@newcastle.edu.au

Professor Ronald Plotnikoff
School of Education
University of Newcastle
r.plotnikoff@newcastle.edu.au

Professor Peter Gibson
School of Medicine and Public Health
University of Newcastle
peter.gibson@newcastle.edu.au

Dr Shelley Keating
School of Human Movement & Nutrition Sciences
The University of Queensland
s.keating@uq.edu.au

Associate Professor Shamsunder Acharya
John Hunter Hospital
Shamasunder.Acharya@health.nsw.gov.au

Complaints about this research
This project has been approved by the University's Human Research Ethics Committee, Approval No. H-2023-0038. Should you have concerns about your rights as a participant in this research, or you have a complaint about the manner in which the research is conducted, it may be given to the researcher, or, if an independent person is preferred, to the Human Research Ethics Officer, Research & Innovation Services, The University of Newcastle, University Drive, Callaghan NSW 2308, Australia, telephone (02) 4921 6333, email Human-Ethics@newcastle.edu.au.