**Information Letter**

The effect of exercise timing on glycemic control in individuals with Type 2 diabetes mellitus

We understand that exercise plays an important role in keeping your blood glucose levels in a healthy range. This project seeks to determine whether the time at which exercise is performed, is important. Therefore, we invite you to participate in this research study, which aims to determine whether there is a better time of day (night or morning) to exercise, when it comes to managing your blood glucose levels. This study is part of my PhD in Exercise Science at Murdoch University and is being supervised by Dr. Timothy Fairchild (Murdoch University), Dr Kym Guelfi (The University of Western Australia) and Prof Jill Kanaley (Missouri University).

**Nature and Purpose of the Study**

The primary aim of this study will be to determine whether the performance of exercise training (12 weeks) either in the morning or at night-time is better for longer-term control of your blood glucose. We are interested to see whether blood glucose response may be affected by changing the timing of exercise. This is important, since 54.2% of the Western Australian population complete their exercise in the morning before work, while 29.5% and 26.3% of the population complete their exercise in the afternoon after work or later in the evening, respectively. Currently, we do not know whether this timing of exercise can alter the blood glucose concentration.

If you consent to take part in this research study, it is important that you understand the purpose of the study and the procedures you will be asked to undertake. Please make sure you ask any questions you may have, and that all your questions have been answered to your satisfaction before you agree to participate.

**What the Study will involve**

Since this project involves exercise training and measurement of blood glucose, we are looking for a specific population group to participate in this study, namely those:

1. Non-smoking, sedentary (defined as the accrual of <150 min of exercise per week) male and females participants between the ages of 20 and 60 years
2. Overweight (body mass index ≥ 27 kg/m2)
3. Who have an existing diagnosis of T2DM

You may be ineligible if you:

1. Are currently on insulin
2. Have had surgery for weight loss
3. Have prior history of heart, lung, kidney, endocrine or liver disease
4. Have experienced recent weight loss ≥4kg in previous month
5. Are screened as ineligible from the Exercise and Sports Science screening tool.
6. You are currently pregnant or you perceive that there is a possibility that you are pregnant.
7. You have an allergy/food aversion to any foods being used in the study.

If you consent to participate in this study, you will be asked to attend the Murdoch University Exercise Physiology laboratory on forty-one separate occasions (Thirty six occasions being the training sessions).

The first visit will involve preliminary measurements and a familiarisation to the procedures and exercise intervention; whilst the second visit will be the performance of the no-exercise control (CON) condition which will consists of blood sampling. The preliminary measurements will include measurement of your height and weight, your aerobic fitness (walking on a treadmill whilst breathing into a mask and tube to assess your maximum endurance capacity) and some pen and paper questions (using an Exercise questionnaires). We will then ask that you keep a 3-day food diary, and we will monitor your physical activity and skin temperature over a 14-day period. Additionally, you will be instructed about the use and fitting of a Continuous Glucose Monitoring System (CGMS) that will be on you for a duration of approximately one week to allow for continuous tracking of your glucose concentration. Finally, we will then measure your body composition using a DEXA scan (described below) either during this session or at a later date.

On your second visit, you will be performing your CON condition. We will ask that you arrive at the laboratory at 0700h and a venous catheter will be placed into a forearm vein. A baseline blood sample will be taken at 0730h. During this session you will be instructed to remain sedentary. You will be allowed to read or bring some work-related material with you (such as a computer). We will then provide your first meal (information on meal item will be provided) between 0730h and 0800h. Blood samples will then be sampled at 0800h, 0815h, 0830h, 0845h, 0900h, 0930h and at 1000h respectively. Thereafter, we will provide a second meal at 1030h and bloods will then be sampled at 1100h, 1115h, 1130h, 1145h, 1200h and 1230h. Participants will then be free to leave the laboratory and continue with their diet. To help make this clearer for you, we can provide the experiment in a flow diagram.

Upon completion of your baseline assessments as well as the CON condition, you will then be invited to begin the 12-week exercise training intervention. You will be required to attend three supervised exercise-training sessions per week for a total of twelve weeks. The exercise training protocol that you will be completing during the 12-weeks training intervention will be a “combined exercise training” protocol of both aerobic and resistance exercises. The exercise session will consist of a walking protocol at moderate intensity (somewhat hard, but still able to maintain a conversation; 60% of VO2peak) for 30mins followed by 5 types of resistance-training exercises (e.g. Push Ups, Squats). The duration of each exercise session will be approximately 1 hour, which will begin and end with a 10min warm-up and 10min cool-down, respectively. The intensity of both aerobic and resistance training is prescribed according to the American Heart Association scientific statement. A mid-intervention assessment will occur during Week 6 (Blood sample and fitness test only). After the 12-weeks of exercise training, we will repeat the CON condition along with the baseline measurements (height, weight, body composition, physical activity levels, skin temperature) that is identical to the pre-intervention testing sessions.

The expected overall time commitment for the study is 14 weeks, which includes all the training sessions, mid-intervention and post-intervention testing sessions.

**Further information of procedures**

Aerobic Fitness: VO2 peak test/Graded treadmill test:

This test is used to measure fitness assessment to determine the maximum amount of oxygen the body can consume and this is typically measured during a bout of exercise. This test will consist of walking on a treadmill at progressively difficult workloads while breathing through a mouthpiece connected to a metabolic cart. This test continues until volitional exhaustion. The highest oxygen uptake measured will then be deemed as VO2 peak. Heart rate will be continuously monitored throughout the test, and rating of perceived exertion (RPE; Borg scale) recorded every minute.

Anthropometric measurements:

Height and weight will be measured using a stadiometer and weighing scale, respectively, and the Body Mass Index (BMI) calculated. Waist circumference will also be measured.

Body composition analysis:

A Dual Energy X-ray Absorptiometry (DEXA) scan will be completed to determine body composition. DEXA is a form of ionising radiation and is considered the gold standard in body composition assessment. While ionising radiation presents with risks, the amount of ionising radiation will be low (0.15 microsievert) compared to other forms such as chest X-ray (microsievert)(Albabese et al., 2003).

Blood collection:

A total of 15 blood samples (Approximately 45 ml; baseline sample [6ml] and 14 additional blood samples [3ml]) will be collected during each condition from the antecubital vein (region of the arm in front of the elbow). In total, we will be collecting approximately 250 ml over the 18 weeks of phase one and two. To minimize the discomfort of these interventions, we will be using a catheter to minimize the pain associated with the needle insertion.

Continuous Glucose Monitoring System (CGMS)

The CGMS allows the monitoring of glucose concentration over a maximum period of 6 days. It is a common tool used in a clinical population and in research in order to track the changes of glucose concentration over a period of time. You will be instructed to complete a finger prick test at least twice daily to calibrate the device throughout the day. Additionally, you will be asked to complete one test each night.

**Voluntary Participation and Withdrawal from the Study**

Your participation in this study is entirely voluntary. You may withdraw at any time without discrimination or prejudice. All information is treated as confidential and no names or other details that might identify you will be used in any publication arising from the research. If you withdraw prior to completion of data collection, all information you have provided will be destroyed.

**Benefits of the Study**

Benefits of participation include a free fitness test (the gold-standard VO2max test) and body composition analysis by DEXA (gold-standard body composition analysis). Additionally, you will be able to master new exercise techniques that will be beneficial for you when it comes to

treatment/lifestyle management of T2DM. Furthermore, you will be provided with 36 free exercise training sessions!

**Possible Risks**

It is possible that you may experience some discomfort during the session as a result of some of the tasks such as the exercise or the blood sampling. You will be monitored closely during the study and you are free to withdraw at anytime during the study.

There are only minor risks associated with the exercise protocol and blood sampling, although there will be some level of discomfort during the study. Some individuals may suffer light-headedness or fainting during the blood collection process, please inform the investigators if you have experienced this previously. You may experience muscle soreness either immediately or a few days after due to the performance of unaccustomed exercises. However, this soreness would typically disappear within a few days. Additionally, you will be constantly monitored during all exercise sessions but please inform the researchers if you experience any feeling of great discomfort during the exercise conditions. It is important for you to understand that you can ask the investigator to stop the experiment at any stage without having to provide an explanation. With regards to the possible risks involved with the DEXA scan, the radiation (DEXA: 0.37 microsievert) that you will be exposed to will be well within NHMRC Recommendations for limiting exposure to ionizing radiation guidelines, which states that the accumulated effective dose to any individual in any year shall not exceed 5 millisievert [5000 microsievert) All researchers in this study are trained (and current) in Senior First Aid. If you have any questions about this project please feel free to contact myself Mr Shaun Teo (0423 716 780; or shaun.t12@hotmail.com) or Dr Fairchild (9360 2959; or T.Fairchild@murdoch.edu.au). We will be happy to discuss with you any concerns you may have about this study.

Once we have analysed the information from this study we will publish the results of the study on the Murdoch University School of Psychology and Exercise Science website:

http://www.murdoch.edu.au/School-of-Psychology-and-Exercise-Science/Research/Exercise-Science-Research/Research-findings/. You can expect to receive this feedback within 12 months.

If you are willing to consent to participation in this study, please complete the Consent Form. Thank you for your assistance with this research project.

Sincerely,

Mr Shaun Teo

This study has been approved by the Murdoch University Human Research Ethics Committee (Approval 2015/170). If you have any reservation or complaint about the ethical conduct of this research, and wish to talk with an independent person, you may contact Murdoch University’s Research Ethics Office (Tel. 08 9360 6677 (for overseas studies, +61 8 9360 6677) or e-mail ethics@murdoch.edu.au). Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.