# **The Effects of High Intensity Exercise on Cardiovascular Function in Men with Metastatic Castrate-Resistant Prostate Cancer (MCRPC): A Sub-study Participant Information Sheet**

## **Introduction and Purpose of this Sub-study**

Research has shown that cardiovascular function can be decreased in men with metastatic castrate-resistant prostate cancer (MCRPC). High intensity exercise has shown to be effective in improving cardiovascular function in other clinical populations, however its effectiveness has not yet been investigated in men with MCRPC.

This sub-study will be completed within the GAP4-QLD (INTERVAL – MCRPC) study.

The purpose of this sub-study is to investigate the effects of high intensity exercise on cardiovascular function in men with MCRPC.

## **Participation and Withdrawal**

You have been provided with this information sheet as it has been determined though the GAP4-QLD (INTERVAL – MCRPC) that you are eligible for this sub-study. Participation in this sub-study is entirely voluntary. You are free to withdraw from the sub-study at any time. Withdrawal from the sub-study will not affect your involvement in the GAP4-QLD (INTERVAL – MCRPC) study or your future health care.

## **What does Participation in this Sub-study involve?**

You will be required to attend one additional testing session at baseline, 3 months, 6 months, 12 months and 24 months of the GAP4-QLD (INTERVAL – MCRPC) study. These five testing sessions are separate to and in addition to the GAP4-QLD (INTERVAL – MCRPC) testing and exercise sessions during the same period. The additional testing session will require approximately 150 minutes of your time and will assess measures of cardiovascular structure and function, and body composition. The additional tests within this session are non-invasive, and require you to lie comfortably on a bed for the majority of the time. You will also be provided with a physical activity monitor to be worn for 7 days after the testing session at each time point. The tests taken during these additional sessions include assessments of:

**Cardiovascular Structure and Function**

* Flow-mediated Dilation
* Carotid Intima-media Thickness
* Heart Rate Variability
* Pulse Wave Analysis
* Pulse Wave Velocity
* Valsalva Manoeuvre
* Deep Breathing
* Blood Draw

**Body Composition**

* Dual Energy X-ray Absorptiometry
* Peripheral Quantitative Computed Tomography

**Habitual Physical Activity *(Take home)***

* ActiGraph

These testing sessions will take place at the School of Human Movement and Nutrition Sciences, University of Queensland, St Lucia, QLD, 4072. Blood draws may also be conducted at QML Pathology, Gordon Greenwood Building, University of Queensland, St Lucia, QLD, 4072. Parking is available and can be organised for you on your behalf. Public transport options are also available.

Prior to these testing sessions, you will be required to complete a 12 hour overnight fast. For 48 hours prior to testing, you will be asked to not consume any high-nitrate containing foods. You will be provided with a list of these foods one week prior to testing to assist with abstinence. For 24 hours prior to the testing sessions you will be asked not to consume any stimulants or depressants (e.g. coffee, tea, alcohol) or perform any vigorous exercise. You should take your normal daily medications. We ask that you drink an adequate quantity of water (so that you do not feel dehydrated) prior to your blood draw, and that you bring a snack of your choice with you to eat after the blood draw. We will have snacks on hand in case you forget to bring your own. Your consumption of food, drink, medication and water, and exercise activities, over the last 48 hours prior to testing will be assessed via a survey. You will be required to complete and sign this survey, which will then be witnessed by the clinician at the testing sessions. If blood draws are conducted at the QML Pathology University of Queensland site, then you will also be required to read and sign an additional consent form prior to each blood draw.

You will then be asked to relax while laying on a (massage) bed in a dimly-lit, temperature controlled room for 20 minutes prior to testing. Further explanation of the tests to be conducted during the additional testing session at baseline, 3 months, 6 months, 12 months and 24 months of the GAP4-QLD (INTERVAL – MCRPC) study is provided below.

**Cardiovascular Function**

***Flow-mediated Dilation***

*During this test, we will be assessing the change in the width of the brachial artery in your right arm.*

You will be asked to lay on a bed with your right arm placed straight out at your side, with your shoulder at 90 degrees. Your arm will be supported by 2 pieces of foam. A small pressure cuff will then be secured around your arm just below your elbow and a probe will be placed on your skin just above the elbow. During the test, the probe will remain on the skin and the cuff will remain inflated for 5 minutes. The test will last approximately 15-25 minutes.

***Carotid Intima-media Thickness***

*This test will assess the structure of the carotid artery in your neck.*

You will be asked to remain on the bed in a relaxed state. Towels and/or pillows will be placed comfortably to support your head during the test. The probe will then be placed just above your collar bone on your neck and images of your carotid artery will be taken in 3 planes. Taking images in each of the three planes should take approximately 60 seconds each.

***Heart Rate Variability***

*During this test, we will be assessing your resting heart rate variability.*

You will be asked to remain on the bed in a relaxed state. If necessary, a razor will be used to shave any excess chest hair just above and below your sternum (breast bone) and on the left side of your ribs. An alcohol wipe will be used to wipe the skin in these spots. Three small stickers (electrodes) will then be placed on your skin: (1) above the sternum, (2) below the sternum and (3) on a rib on your left side. Leads will then be attached to each of the three electrodes. You will then be asked to lay still for 5 minutes while the computer assesses your resting heart rate variability.

***Pulse Wave Analysis***

*This test will assess the function of your blood vessels.*

You will be asked to remain on the bed in a relaxed state. A blood pressure cuff will be attached to your right arm. During the test, the cuff will inflate and deflate. Each trial will last approximately 30 seconds and three trials will be performed.

***Pulse Wave Velocity***

*This test will assess the stiffness of your blood vessels.*

You will be asked to remain on the bed in a relaxed state. A blood pressure cuff will be attached to your thigh. The clinician will then identify the location of the pulse in your neck and place a small mark (with a soft pen marker). The test will then begin when the thigh cuff inflates and the clinician will place a small blunt pen-like device on your neck. This pen will be held on your neck for the duration of the test and removed upon completion. Each trial will last approximately 30-60 seconds and three trials will be performed.

***Valsalva Manoeuvre***

*This test will assess the response of your heart and blood pressure to a Valsalva manoeuvre.*

You will be asked to remain on the bed in a relaxed state. If necessary, a razor will be used to shave any excess hair just above your wrists on your left and right arms and just above the ankle on your left leg. An alcohol wipe will be used to wipe the skin in these spots. Three small stickers (electrodes) will then be placed on your skin: (1) just above the right wrist, (2) just above the left wrist and (3) just above your left ankle. Leads will then be attached to each of the three electrodes. A small cuff will also be attached to your left index finger to measure blood pressure throughout the test. You will then be asked to remain in a lying position and blow into a mouthpiece while looking at a pressure dial. You will be required to maintain a pressure of 40 mmHg for 15 seconds, this counts as one trial. You be required to perform 3 trials in total, with rest allowed between each trial.

***Deep Breathing***

*This test will assess the response of your heart and blood pressure to deep breathing.*

You will be asked to remain on the bed in a relaxed state. Your heart rate and blood pressure will continue to be monitored in the same way as in the above Valsalva test. You will be asked to breath in for 5 seconds and then breath out for 5 seconds. This will be repeated six times in a row, leading to 6 breaths per minute. You be required to perform 3 trials in total, with rest allowed between each trial.

***Blood Draw***

This blood test will assess for pre- and post-exercise levels of oxidative stress, metabolic, inflammatory, hormonal and prostate cancer cell growth changes. Oxidative stress and inflammation causes damage to cells within the body.

While you are seated comfortably, blood will be drawn by inserting a needle into a vein in your arm. At each visit, each sample will be approximately 24 mL; a total of about 120 mL will be drawn for the whole study. Your blood sample will be labelled with your unique identification (ID) number and stored securely in a locked laboratory.

**Body Composition**

There is no pain or discomfort associated with the below measures of body composition.

***Dual Energy X-ray Absorptiometry (DXA)***

*This test will assess your whole-body composition.*

This is a routine technique for the measurement of body composition.  You will lie on a specially designed table for approximately 7 minutes and a scanning arm will move above the table.

***Peripheral Quantitative Computed Tomography (pQCT)***

*This test will assess your lower limb muscle and bone composition.*

You will be positioned in a specially-designed chair with your leg resting in a support, as shown below. Your leg will be scanned at two different points (the shin and the thigh) in this position. Scanning will take approximately 10 minutes.



**Take Home: Habitual Physical Activity - ActiGraph**

Your habitual physical activity will be assessed using the Actigraph GT3X+ accelerometer. You will be asked to wear this waist worn monitor for seven days immediately after your testing session at baseline, 3, 6, 12 and 24 months to determine time spent per week in light, moderate and vigorous physical activity. You will also be provided with a diary to record when the monitor is worn and any physical activity you perform while wearing the monitor.

## **Risks of Participating in this Sub-study**

There are minimal risks associated with participating in this study.

Cuff Inflation (Flow-mediated Dilation, Pulse Wave Analysis and Pulse Wave Velocity) – Mild discomfort (e.g. pins and needles) may arise during the inflation of blood pressure cuffs on the arms and right leg during testing measures. The longest period of cuff inflation will be five minutes. Cuffs will not be inflated to such an extent or duration that will cause permanent damage to your arms and leg.

Shaving (Heart Rate Variability, Valsalva Menoeuvre and Deep Breathing) – There is a minor risk associated with dry shaving (e.g. skin irritation, skin abrasion or incision) prior to electrode placement. However, this practice is considered to be of minimal risk. A new, clean, disposable razor will be used. An alcohol wipe will be used immediately to disinfect the shaved areas to minimise the risk of infection caused by any skin irritation and/or abrasion. All razors will be destroyed after use.

Blood Collection - There are minor risks associated with a blood draw (i.e., bruising, infection, discomfort, light-headedness). However, this procedure is considered to be of minimal risk and will be performed by a trained phlebotomist. No syringes, lancets, needles or other devices capable of transmitting infection from one person to another shall be reused. All of these items will be destroyed after each use.

Radiation (DXA and pQCT) – There is a negligible risk associated with both of these body composition measures that utilise radiation scanning. Radiation dose for the DXA equals <10 microsieverts, which is similar to normal day-to-day background radiation (5-8 microsieverts). Radiation dose for the pQCT is much lower, equating to <1 microsieverts per scan. The total radiation dose from both machines for the total number of scans to be completed over the 24-month study period is deemed to be low risk.

## **Illness or Injury**

If you become ill or injured as a result of participating in this study, please contact the sub-study’s Principal Investigator (Natalie Vear – Personal PH: 0434 904 208) and your general practitioner (GP). All appropriate measures will be taken to ensure an appropriate course of treatment.

## **Participant Confidentiality and Data Management**

The only personal information that will be required for this sub-study is your date of birth. This information is needed for the computer software which will be used to conduct the testing measures during the testing sessions.

All results from testing measures will be de-identified and stored under a unique identification (ID) number which will have been assigned to you from the GAP4-QLD (INTERVAL – MCRPC) study. All data will be stored in accordance with The University of Queensland’s relevant policies and procedures.

## **What are the benefits of taking part in this Sub-study?**

Data obtained during this study will help to develop foundational world-first knowledge on the effects of high intensity exercise on cardiovascular function in men with metastatic castrate-resistant prostate cancer (MCRPC).

## **Reimbursement**

You will be entitled to a $7.00 monetary travel expenses reimbursement per testing session. If you attend all five testing sessions for this sub-study, you are entitled to a total of $35.00 over the sub-study duration. Free parking will also be provided at the clinic site.

## **Access to Results**

At the completion of the sub-study, you will be provided with your individual results. You will be provided with published data for the sub-study once available.

## **Who can I contact?**

If you have any questions or concerns regarding this project, please contact Natalie Vear (Personal PH: 0434 904 208 - Email: n.vear@uq.edu.au).

**Sub-study Investigators:**

**Natalie Vear (Principal Investigator)**

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## **Ethical Clearance**

All research in Australia involving humans is reviewed by an independent group of people, called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been reviewed by the HRECs at all participating sites in Queensland. This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

Human Ethics Coordinator contact number: 07 336 53924

# **The Effects of High Intensity Exercise on Cardiovascular Function in Men with Metastatic Castrate-Resistant Prostate Cancer (MCRPC): A Sub-study Participant Consent Form**

## **Research Study Title:**

The effects of high intensity exercise on cardiovascular function in men with metastatic castrate-resistant prostate cancer (MCRPC).

## **Sub-study Principal Investigator:**

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| **Natalie Vear**BExSS(CEP)(Hons)PhD Candidate The University of Queensland |

## **Co-Investigators:**

|  |  |
| --- | --- |
| **Professor Jeff Coombes**PhD, MEd, BEd(Hons), BAppSc.Professor – Exercise ScienceThe University of Queensland | **Dr Tina Skinner**PhD, GCHigherEd, BAppSci(HMS – Ex Sci)(Hons)Senior Lecturer – Clinical Exercise PhysiologyThe University of Queensland |
| **Dr Tom Bailey**PhD, MSc, BSc (Hons)UQ Research FellowThe University of Queensland  |  |

## **Consent to Participate in GAP4-QLD Sub-study**

**Declaration by Participant**

1. I have read and understood the participant information sheet for this sub-study and understand the procedures and risks involved.
2. If required, someone has read the participant information sheet to me in language I can understand.
3. I understand that I am able to withdraw from the sub-study at any time without prejudice from The University of Queensland.
4. I understand that I will only be eligible to receive a maximum of $35.00 for reimbursement of travel expenses when participating in this sub-study.
5. I am aware that all appropriate measures will be taken by the investigators to maintain participant confidentiality throughout this sub-study.
6. I have been given the opportunity to discuss the sub-study contents with one of the investigators and any questions I may have had were answered satisfactorily.
7. I understand that I will be given a signed copy of this document to keep.

Name of Participant (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Declaration by Investigator**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Investigator (please print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_