# **The Effects of High Intensity Exercise on Cardiovascular Function in Men with Metastatic Castrate-Resistant Prostate Cancer (MCRPC): A Control Group Sub-study (NG4) Participant Information Sheet**

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

Research has shown that cardiovascular function can potentially be decreased in men with metastatic castrate-resistant prostate cancer (MCRPC). Therefore, the purpose of this sub-study is to further investigate cardiovascular function in men with MCRPC. This will be achieved by investigating various measures of cardiovascular function, as well as assessments of habitual physical activity, dietary intake, aerobic exercise capacity/fitness and body composition.

## **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.

Please note that involvement in this sub-study means you will not be randomised to an exercise intervention group. You will continue with your usual care only.

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

You will be asked to attend two testing sessions at baseline, 3 months, 6 months, 12 months and 24 months. These testing sessions will last for 90-150 minutes each and will assess measures of aerobic fitness, cardiovascular structure and function and body composition. Your dietary intake for the 24-hours prior to your first two testing sessions at baseline will be recorded. At each time point, you will also be asked to complete a health history and demographics survey, a three-day food diary and wear a physical activity monitor for 7 days after the second testing session.

Tests will be performed across two testing sessions, to be held approximately 2-5 days apart. A list of the tests to be conducted in both sessions are provided below:

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| **Testing Session 1** |
| Questionnaires *(Complete at Home)** Health History and Demographics Survey
* 24-hour Diet Recall
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| Three-day Food Diary *(Complete at Home)* |
| Body Composition* Weight and Height
* Waist and Hip circumferences
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| Aerobic Fitness* Resting Blood Pressure
* Cardiopulmonary Exercise Test (CPET) with Electrocardiogram (ECG)
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| **Testing Session 2** |
| Questionnaire* 24-hour Diet Recall
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| 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
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| Body Composition* Dual Energy X-ray Absorptiometry
* Peripheral Quantitative Computed Tomography
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| *Take home:* * ActiGraph for 7 days
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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.

**Testing Session 1**

Prior to testing session 1, you will be required to avoid consuming any stimulants or depressants (e.g. coffee, tea, alcohol) for 24 hours and not perform any vigorous exercise for 48 hours. You should take your normal daily medications. We ask that you drink an adequate quantity of water (so that you do not feel dehydrated) and consume a light meal prior to the CPET. Your consumption of food, drink, medication and water, and exercise activities, over the last 48 hours prior to the testing session will be assessed via a survey. You will also be required to complete both questionnaires and the food diary prior to attending your first testing session at each time point.

**Questionnaires**

Two questionnaires will be provided to you to complete at baseline. Completion of the questionnaires will take approximately 50 minutes.

The first survey includes questions on your health history, demographics and smoking history. After the baseline testing session, we will provide you with a shorter version of this survey at follow-up visits which will take approximately 20 minutes to complete.

The second questionnaire can be completed online or in paper form and will ask questions about your food, drink, vitamin and supplement intake over the previous 24 hours. You will be provided with a copy of this baseline recall and will be asked to replicate this dietary intake at all follow-up assessments.

**3-Day Food Diary**

*This diary will assess your habitual dietary intake.*

You will be provided with a link to an online diet database or a paper-version food diary, whichever you prefer. You will be asked to recall your food, drink, vitamin and supplement intake over three specified 24-hour periods. It is asked that you report your dietary and fluid consumption to the best of your knowledge with as much accuracy as possible. You are encouraged to maintain your normal dietary habits.

**Cardiopulmonary exercise test (CPET) with electrocardiogram (ECG)**

*This test will be performed to determine your aerobic exercise capacity.*

A CPET is performed on an exercise bike with a face mask/snorkel to measure the amount and volume of air you expire. You will breathe normal room air throughout the test. The exercise test will last approximately 10-12 minutes, commencing at a light cycling load that will progress incrementally during the test. A pedalling frequency of 70-80 RPM should be maintain during the test. This test is terminated when cycling speed falls below 50 RPM. The test is completed with 5 minutes cycling at a low load. Blood pressure and ECG will be measured at regular intervals throughout the test and during recovery. An ECG shows the electrical activity of the heart.

**Testing Session 2**

Prior to testing session 2, 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, such as green vegetables and processed meats. 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.

**24-Hour Diet Recall**

You will be asked to perform a second 24-hour diet recall for the day prior to both your testing sessions at baseline. This can be completed online or in paper form and will ask questions about your food, drink, vitamin and supplement intake over the previous 24 hours. You will be provided with a copy of this baseline recall and will be asked to replicate this dietary intake at all follow-up assessments.

**Cardiovascular Structure and Function Measures**

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 cardiovascular tests to be conducted at baseline, 3, 6, 12 and 24 months is provided below.

***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. The probe will be removed upon completion. The taking of 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 40mmHg 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 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 32 mL; a total of about 160 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 bone, muscle and fat 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 in the image to the right. Your leg will be scanned at two different points (the shin and the thigh) in this position. Scanning will last 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 the waist worn monitor for seven days immediately after testing session 2 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 minor risks associated with participating in this study.

CPET – There is a minor elevated risk of a cardiac event occurring during maximal exercise exertion. During CPETs at all time points an ECG will be recording your heart activity and blood pressures will be taken continuously throughout the test. A medical doctor will also be present at your baseline CPET to screen for any heart abnormalities. Exercise physiologists and individuals trained in cardiac investigations will be present for all CPETs at all time points to monitor the ECG trace and blood pressure responses to exercise.

Cuff Inflation (Resting Blood Pressure, 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 (CPET, Heart Rate Variability, Valsalva Manoeuvre 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 which 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**

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 future health care.

Some personal information will be required for this sub-study, for example your date of birth and diet histories. This information is needed for accurate data collection throughout the sub-study. All data will be strictly confidential and only handled by the researchers for this sub-study. All results from testing measures will be de-identified and stored under a unique identification (ID) number which will be assigned to you at commencement of the 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?**

There are numerous benefits associated with participating in this sub-study. You will be provided free-of-charge with gold-standard measures of your aerobic fitness and body composition. The body composition measures included in this sub-study (DXA and pQCT) are highly accurate and will give you a very good understanding of your bone, muscle and fat composition in your body. Furthermore, the researchers who will be assessing you during this sub-study are Accredited Exercise Physiologists, who are experts in physical activity and exercise delivery. Finally, the data obtained during this study will help to further the knowledge of 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 ten testing sessions for this sub-study, you are entitled to a total of $70.00 over the sub-study duration. Free parking will also be provided at the clinic site.

## **Access to Results**

On 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 NG4 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 $70.00 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\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_