



Participant Information Sheet:
Does Lifelong Exercise Preserve Capacity to Build Muscle in Master Athletes?

You are being invited to take part in a research study that forms part of a PhD project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

- Part 1 tells you the purpose of this study and what will happen to you if you take part.
- Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?

Ageing is characterized by a loss of muscle mass that is necessary for physical function and metabolic health. This has important implications for our society, because although we are living longer, we are not necessarily living healthily. Therefore, many older individuals may not be physically independent and may have a reduced quality of life. Currently, the most effective and safe means by which to maintain muscle mass in old age is exercise, which as well as being helpful in its own right, can help to restore a 'youthful' metabolism. Individuals that have undertaken lifelong exercise (termed Master athletes) maintain higher levels of physical function in old age compared with their less active counterparts. At present, the mechanisms of



how the muscles of older Master athletes are so well preserved are poorly understood. The aim of the current study is to characterise the extent to which the ability to build muscle is preserved when individuals have continued to exercise throughout their lifetime. By understanding the mechanisms through which muscles of master athletes differ from those of their less active counterparts, we want to find out whether changes in muscle that we often see in older people are actually due to age; or whether they are due to reduced physical activity.

Why have I been chosen?

You have been chosen because we are aiming to recruit 3 different sub-populations for our study including:

- Young men (18-35 years, healthy, non-obese, non-diabetic, non-smoker, no muscular dystrophy, normal activity (not partaking in structured training)).
- Older men (60-80 years, healthy, non-obese, non-diabetic, non-smoker, no muscular dystrophy, normal activity (not partaking in structured training)).
- Master athlete (aged 60 years or over, healthy, non-obese, non-diabetic, non-smoker, no muscular dystrophy, training 2 times/week or more, for 20 years or more).

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You



will still be free to withdraw at any time in the future and without giving a reason.

What will happen to me if I take part?

Enrolment - If you are interested in taking part and following explanation of the study, we would like you to answer some brief health-related questions. We will use your responses to the questionnaire to help determine whether you are eligible to take part in the study. If you are willing and eligible to participate, you will be enrolled in the study and we will ask that you sign a consent form.

Visit 1 – First, you will undergo some non-invasive assessments of height, weight and blood pressure. This will be followed by bioelectrical impedance analysis (BIA), which will determine your body composition (fat and fat-free mass). You will be asked to provide a saliva swab and a blood sample. You will undertake assessments of strength and function and be familiarised with the exercise protocol to be undertaken during Visit 3. Following this, you will be required to drink a small dose of 120-200ml (final amount dependent on the amount of lean body mass (LBM) you have) of a stable isotope tracer (called D₂O or ‘heavy water’). D₂O is naturally occurring, non-radioactive and completely safe for human consumption. You will be provided with further smaller doses to consume at set time-points during the remainder of the study (10-25 ml every day in your own home, equivalent to 1-2 tablespoons). The D₂O equilibrates in body water, and is slowly incorporated in to muscle protein. D₂O can be measured in tiny amounts of saliva/blood and muscle biopsy



samples. This will enable us to determine the rate at which you are able to 'build' skeletal muscle. Before leaving, you will be provided with a pedometer (step counter) and a wrist worn accelerometer that will help us to assess your activity levels. We will also provide you with a standardised diet (50% carbohydrate, 30% fat and 15% protein) to consume starting the morning of visit 2 and finishing the evening prior to visit 4. You will also be given additional saliva swabs to take away in order to provide further daily saliva samples in the comfort of your own home (these can be stored in your fridge and brought to us at each visit).

Visit 2 – Three days after Visit 1, you will arrive at the laboratory at approximately 0800 in an overnight fasted state having refrained from strenuous physical activity and alcohol for the previous 48 hours, and having refrained from caffeine consumption on morning of the visit. A single blood sample will be obtained from a vein in your forearm, followed by a single needle muscle biopsy sample from your quadriceps (thigh) muscle under local anaesthesia and finally a saliva sample.

Visit 3 – 48 hours following the 2nd visit you will arrive at the laboratory, again at approximately 0800 in an overnight fasted state having refrained from strenuous physical activity and alcohol for the previous 48 hours, and having refrained from caffeine consumption on morning of the visit. A resting blood sample will be obtained from the vein in your forearm. Prior to exercise, a single muscle biopsy will be obtained from your quadriceps muscle under local anaesthesia using a small biopsy needle. Following this biopsy, you will perform a session of lower-limb resistance-type exercise, followed by



consumption of a protein-based drink, 1 hour after which a second biopsy and a blood sample will be obtained to understand the metabolic processes in your muscle.

Visit 4 – 48 hours following the 3rd visit you will arrive at the laboratory at approximately 0800 in an overnight fasted state having refrained from strenuous physical activity and alcohol, and having refrained from caffeine consumption on the testing day. A single needle muscle biopsy will be obtained from the quadriceps muscle under local anaesthesia.

Visit 1 and 3 will take approximately 2-3 hours, whereas enrolment, visit 2 and 4 will be shorter in duration lasting approximately 1 hour. We will ask you to wear comfortable clothing, appropriate for exercise (e.g. shorts, t-shirt, trainers).



Time point	Enrolment	Visit 1	Visit 2	Visit 3	Visit 4
Enrolment					
Eligibility screen	X				
Informed consent	X				
General health questionnaire	X				
Assessments					
Body mass/height		X			
Blood pressure		X			
Bioelectrical impedance analysis (BIA)		X			
Leg strength (dynamometry)		X			
Exercise Familiarisation		X			
D20 Dosing		←			→
Physical activity assessment		←			→
Dietary Control			←		→
Exercise				X	
Muscle biopsy			X	XX	X
Blood sampling		X	X	XX	X
Saliva Sampling		←			→

What tests and procedures will be carried out as part of this study (along with key instruction for selected procedures)?

Blood pressure: We will measure blood pressure as a baseline measure. This will take approximately 5 minutes during visit 1.



Assessment of body composition: Body composition will be assessed using bioelectrical impedance analysis (BIA). Bioelectrical impedance analysis (BIA) is a rapid and non-invasive, method of measuring body fat and lean tissue. We will ask you to lie on your back on an examination couch and will attach the electrodes to your wrist and ankle after first cleaning the skin. This technique consists of the passage of a very low amplitude electrical current applied through cables connected to electrodes where they are in contact with the skin. The current is so low that you will not feel anything during the test, which will take only a few minutes. Height measurements will also be measured using a standard stadiometer and weight measurements will be made using a standard digital scale.

Test of muscle strength & exercise familiarisation: Your leg muscle force will be measured using specialised equipment and will involve simple pushing movements against a lever arm which you will be asked to hold for a few seconds. These tests will take about 20 minutes so you may feel a little tired afterwards but the tests should not cause any pain or discomfort. You will also be familiarised to the lower-limb exercise protocol you will perform during testing visit 3.

Food Provision: You will be provided with a standardised, weight-maintenance, diet (50% carbohydrate, 30% fat and 15% protein) to consume during your involvement in the study; you will be able to choose from a selection of pre-packaged food options. It will consist of 3 main meals (breakfast lunch and dinner), between-meal snacks and beverages. If you have any special dietary requirements (e.g., vegetarian), please inform us and



we can arrange alternative food provisions. The diet provision will begin on visit 2 and continue until study completion on visit 4.

Blood Samples: You will undergo five blood sample collections from the vein in your forearm over the duration of the study, totalling approximately 40 ml (less than 1/10th of what you would typically donate or equivalent to about eight teaspoons). These blood samples are going to be used to measure a number of inflammatory and metabolic health markers. This may be a little uncomfortable, although you should not experience any excessive pain or discomfort. Each sample provided will take about 5 minutes and will be taken by a trained individual.

Muscle Biopsy: During this procedure a tiny piece of muscle from your thigh will be sampled (~100mg or roughly the size of a pea), under local anaesthetic. You may experience some discomfort during administration of local anaesthetic. Thereafter, feelings of pressure and/or discomfort may be felt at the biopsy site, but only for a short time. This muscle sample will be used to determine the rate at which you build muscle and properties of your muscle fibres. The 4 muscle biopsies required for the study will not have any effect on any future biopsies that the participants could potentially require for medical reasons.

Administration of stable isotope tracer: So that we can measure the growth activity in your muscle during your participation in the study, we will need to provide you with a D₂O stable isotope tracer (also known as ‘heavy water’) to drink at specified times over the course of the study involvement.



D₂O is naturally occurring, non-radioactive and completely safe for human consumption. One potential side effect that you may experience is a temporary feeling of nausea and/or dizziness. These feelings are rare and generally subside within 1-2 hours after consumption. However, these side effects are usually only experienced when a large dose (>300ml) or a number of high doses are provided in quick succession; and this dosing protocol (100-200 ml + 10-25 ml daily top ups) has been chosen to reduce such risk.

Saliva Sample: You will be required to provide a saliva sample every morning upon waking. This will be collected by chewing on a swab until completely saturated (approximately 2-4 minutes). This can then be stored in a collection tube provided to you, in your fridge until you come into the lab.

What are the possible disadvantages/burdens and risks of taking part?

We have taken every precaution to minimise risk to participation in this study participants. You may find the tests of muscle function a little uncomfortable, especially if you are not accustomed to this type of activity. However, if you experience any pain or if you want to stop the procedures, you may do so immediately. Refraining from exercise, outside of our lab, during study involvement is required as this can drastically influence a number of the measurements made within the study. The blood sampling and muscle biopsy procedures may also cause slight discomfort but the procedure is quick and a member of the study team who has received appropriate training will conduct the sampling. Risks can include bruising, infection or insensitivity of the skin although these risks are very small. Aseptic conditions and the provision of detailed written instructions for aftercare of the biopsy site greatly reduce risk



associated with the procedure. To date there have been no complications with muscle biopsies in our experience (more than 700 from 2009–present in the School of Sport, Exercise and Rehabilitation Sciences).

What are the possible benefits of taking part?

You will receive £100 remuneration for taking part. Should you withdraw from the study at any point you will receive remuneration on a pro-rata basis at the discretion of the Chief Investigator. It should be noted that as a volunteer for this study remuneration for taking part will not affect any benefits/pension that you receive. Further, we can provide the results from your body composition analysis if requested. The results from the study will also help us to provide practical messages to older adults and inform policy about the benefits of lifelong exercise. It will also provide valuable information to health care professionals working with older adults. Finally, the members of staff carrying out the investigation are highly experienced in all aspects of exercise physiology, nutrition and metabolism and will be able to provide expertise and answer questions you may have about any of these matters.

What will happen to my samples?

Blood, saliva and muscle samples will be stored in a -80 degree freezer until analysis. All samples collected during the course of the research will be kept strictly confidential, with unique study identification codes, identifiable only by the research team. Samples will be stored in accordance with current University guidelines and guidance from the UK Research Councils. With your consent, samples which remain at the end of the study can be stored for use in future ethically and scientifically approved research in the UK or overseas,



including genetic studies, research which may use animals or in vitro models, and research involving private or commercial companies.

Part 2

What if relevant new information becomes available?

Though unlikely, if any clinically significant information comes to light as a consequence of taking part in this study, we will inform your GP (with your permission).

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time without having to give a reason. However, we may still choose (with your permission) to use any data obtained as a result of your participation.

What if there is a problem?

Complaints: If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (please refer to contact details on subsequent page). If you remain unhappy and wish to complain formally, you can do this by contacting Dr Sean Jennings, Research Support Group, University of Birmingham (0121 415 8011 or s.jennings@bham.ac.uk)

Harm: In the event that something does go wrong and you are harmed during the research study, the University has in force a Public Liability Policy and/or Clinical Trials policy, which provides cover for claims for "negligent harm" and the activities here are included within that coverage.



Will my taking part in this study be kept confidential?

Yes. All information, which is collected, about you during the course of the research will be kept strictly confidential in a locked cabinet, with unique study identification codes; only known to the research team. All other information which leaves the University of Birmingham, including any subsequent publications, will have your name, address and date of birth removed so that you cannot be recognised from it.

What will happen to the results of the current research study?

The results of this study will be published in medical journals, reports and textbooks. You will not be identifiable in any publication or report.

Who is organising and funding the research?

The research is being organised and sponsored by the University of Birmingham.

Who has reviewed the study?

This study has been given a favourable ethical opinion for conduct in the NHS by the East Midlands - Derby Research Ethics Committee.

Contact details

You may contact James Mckendry (the student investigator) directly by telephoning 07879332731 or email jxm965@student.bham.ac.uk for further information at any time.



You may contact Dr. Leigh Breen PhD (one of the Principal Researchers) directly by telephoning 0121 414 4109 or email l.breen@bham.ac.uk for further information at any time.

You may contact Dr. Carolyn Greig PhD (one of the Principal Researchers) directly by telephoning 0121 414 8743 or email c.a.greig@bham.ac.uk for further information at any time.

If you wish to speak with an independent individual with no direct study involvement, please contact Professor Janice Thompson PhD (Director of Research & Head of School) directly by telephoning 0121 414 4119 or email J.Thompson.1@bham.ac.uk for further information at any time.

If you wish to obtain more general information on participating in research, please contact The Health Research Authority by telephoning 020 797 22545 Or emailing HRA.Queries@nhs.net.

Many thanks for taking the time to read this information.

James Mckendry, Dr Leigh Breen PhD and Dr Carolyn Greig PhD

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The University of Birmingham