PROJECT PROPOSAL

2025/6 Academic Entry Year – Cohort 4

Supervisory Team

Primary Supervisor

Name: Prof. David Stensel
Input (%): 50
Email: d.j.stensel@lboro.ac.uk
Centre/Institute/School/University: School of Sport, Exercise and Health Sciences, Loughborough University
Website: https://www.lboro.ac.uk/schools/sport-exercise-health-sciences/people/david-stensel/

Second Supervisor

Name: Dr Matthew Graham-Brown
Input (%): 25
Email: mgb23@le.ac.uk
Centre/Institute/School/University: Department of Cardiovascular Sciences, University of Leicester
Website: https://le.ac.uk/bhf-accelerator/people/previous-researchers/matthew-graham-brown

Third Supervisor

Name: Prof. Sally Singh
Input (%): 25
Email: ss1119@le.ac.uk
Centre/Institute/School/University: University Hospitals of Leicester NHS Trust; Department of Respiratory Sciences, University of Leicester
Website: https://le.ac.uk/people/sally-singh

Project Details

Title: Quantifying individual responsiveness to exercise to improve prescription and health outcomes in women and minority ethnic groups

Summary: Physical activity and structured exercise have profound benefits for primary, secondary and tertiary prevention of chronic disease (1). The World Health Organization recommends 150 to 300 minutes of moderate-intensity aerobic activity or 75 to 150 minutes of vigorous-intensity aerobic activity weekly for adults (2). Yet responses and adaptations to exercise vary widely between individuals for reasons that are not well understood. This limits the effectiveness of exercise prescription for health. This project will use a novel research design – the replicated crossover study – to precisely quantify variability in exercise responses within and between individuals. This information

will subsequently be used to personalize exercise prescription with the aim of optimizing the effectiveness of exercise for enhancing health outcomes. Recruitment to the studies will focus on minority ethnic groups and females due to their underrepresentation in the research literature. AI will be applied to the datasets generated to optimize exercise prescription and to explore the factors responsible for inter- and intra-individual variability in response to exercise.

Aim: To implement the replicated crossover research design to quantify individual variability in responses to acute and chronic exercise interventions in minority ethnic groups and females. The information generated will be used to improve exercise prescription for preventing and managing chronic disease.

Background: The term precision medicine is widely used but application of this concept in exercise science is limited. Waterfall plots are often used to display 'responsiveness' but these capture 'responses' to a single intervention and do not account for random variation or natural day-to-day variability. To precisely assess responsiveness to an exercise intervention, repeated bouts/doses of exercise are required, and each must be paired with a control condition to quantify the true exercise 'response'. This can only be achieved using a replicated crossover design. An example is shown in the figure displaying responses of the hunger hormone ghrelin (3). Ghrelin is suppressed by acute vigorous exercise. Panel A in the figure shows two responses. Response 1 is calculated as the change in the first exercise trial minus the change in the first control trial. Response 2 is calculated as the change in the second exercise trial minus the change in the second control trial. There is a moderate positive correlation between responses (r = 0.57, 95% CI 0.08 to 0.84, P = 0.025). Panel B displays the two individual responses for each participant and the mean response of the two (horizontal lines between each pair of circles). Ghrelin suppression is demonstrated for most individuals, but some are more responsive than others. Similar findings were observed for the hunger suppressing hormone peptide YY and for hunger perceptions assessed using visual analogue scales (3). It may be hypothesized (but remains unproven) that the 'responders' are more likely to benefit from exercise as a tool for weight management. In contrast to this finding for appetite, study of cardiovascular disease risk marker responses to acute exercise using the replicated crossover design revealed large trial-to-trial within subject variability which inhibited detection of 'responders' and 'non-responders' (4). More recently, the replicated crossover design has been implemented to demonstrate substantial heterogeneity in blood pressure responses to drug therapy for hypertension (5).

Research Plan: This project will entail three parts: 1) a systematic review to identify and assess all exercise studies with health outcomes which have employed the replicated crossover design. 2) An acute exercise study using the replicated crossover design to examine responsiveness to exercise for relevant outcomes in a patient group. This may be a group with chronic kidney disease, asthma, chronic obstructive pulmonary disease or an apparently healthy group with overweight/obesity. 3) Using the outcomes from 2 together with relevant literature, a chronic exercise intervention replicated crossover trial will be conducted. This will involve two intervention periods (each of 2 months duration) paired with two, 2-month control periods. The PhD fellow will undergo training in relevant statistical techniques and potentially qualitative research techniques also to tease out if there are social or other non-biological factors influencing inter-individual variability to exercise. AI will be used to enhance the prediction of exercise responsiveness using the datasets obtained from parts 2 and 3.

Expected outcomes and impact: At least three high quality publications together with dissemination at appropriate conferences. The findings will be used to support a major grant bid to further this work in larger samples. This work will generate valuable data in females and minority ethnic groups both of whom are underrepresented in the exercise literature.

References:

1. Stensel DJ, Hardman AE and Gill, JRM (Editors) (2022) Physical Activity and Health: The Evidence Explained. (3rd Edition) Routledge Taylor and Francis Group, London. ISBN: 978-0-415-63295-9 (Hardback) ISBN 978-0-415-63296-6 (Paperback) ISBN 978-0-203-09527-0 (E-book)
2. WHO Guidelines on physical activity and sedentary behaviour, https://www.who.int/publications/i/item/9789240015128, Date accessed 24 September 2024
3. Goltz FR, Thackray AE, King JA, Dorling JL, Atkinson G, Stensel DJ (2018) Individual responses of appetite to acute exercise: A replicated crossover study. *Medicine and Science in Sports and Exercise*. 50:758-68.
4. Shen T, Thackray AE, King JA, Alotaibi TF, Alanazi TM, Willis SA, Roberts MJ, Lolli L, Atkinson G, Stensel DJ (2024) Are there interindividual responses of cardiovascular disease risk markers to acute exercise? A replicate crossover trial. *Medicine and Science in Sports and Exercise*. 56(1):63-72. doi: 10.1249/MSS.0000000000003283.
5. Sundström J, Lind L, Nowrouzi S, Hagström E, Held C, Lytsy P, Neal B, Marttala K, Östlund O (2023) Heterogeneity in blood pressure response to 4 antihypertensive drugs. A randomized clinical trial. *Journal of the American Medical Association* 329:1160-69.