FINAL PUBLISHABLE SUMMARY REPORT

Aims & Objectives. The primary aim of this project was to characterize the effects of a novel exercise intervention, high intensity interval training (HIIT) on systemic inflammation, immune function, and health indicators in adults with either rheumatoid arthritis (RA) or diabetes and compare them to a healthy control group. The research sought to achieve this through 4 main research objectives. Participants completed a ten week structured supervised HIIT exercise training program. The program consisted of three times per week training, 30-minute sessions consisting of short intervals of high intensity exercise interspersed by similar duration intervals of low intensity exercise. Participants were assessed for inflammatory and immune responses (RO1), broader physiological and cognitive functions (RO2), intervention efficacy in clinical populations with chronic inflammatory conditions (RO3) and characterization of the response of the metabolome and determine interactions with immune and inflammation changes to assess potential mechanisms (RO4).

Summary of Work towards Achieving the Objectives.

Research objective 1 (RO1) was addressed by Task 1, consisting of three sub-tasks. Task 1 was to determine the HIIT requirements for adaptation in the elderly. The primary measure of adaptation to HIIT was assessed by changes in aerobic capacity (VO_{2peak}). Adults undertook a maximal aerobic capacity test before and after ten weeks of HIIT. Task 1A was to determine the pro- and anti-inflammatory response to HIIT. Blood samples were analyzed for pro- and anti-inflammatory cytokines before and after training by either enzyme linked immunosorbent assays or by multi-analyte fluorescence based technology. Task 1B was to assess the immune modulation in response to HIIT. Blood immune cells were isolated before and after the training and assessed for phenotype and functions, including phagocytosis, oxidative killing, and chemotactic capacity.

Research objective 2 (RO2) was addressed by Task 2, consisting of two sub-tasks investigating the broader health effects in response to HIIT. Participants completed a number of additional measures, indicative of specific tissue/organ health. Task 2A was to investigate the effects of HIIT on muscle phenotype and function. *Vastus lateralis* muscle biopsies were taken before and after the training and quantified for inflammatory profiles, gene expression and metabolism. Task 2B was to determine the broader effects of HIIT on physiology and function. Glucose tolerance and insulin sensitivity, as measures of diabetes risk, were assessed by oral glucose tolerance tests; urine samples were analyzed for renal function; cardiovascular function was assessed by a 12-lead echocardiogram, while arterial stiffness and vascular health measured by vascular tonometry; lung function was assessed by spirometry; brain health was assessed by a number of validated questionnaires, including the hospital-anxiety-depression and the health assessment questionnaire-disease index; and body composition was assessed for total fat and lean mass changes using air displacement plethysmography.

Research objective 3 (RO3) was addressed by Task 3 – to assess the impact of HIIT on patients with chronic inflammatory conditions. Older adults with either rheumatoid arthritis or were at a high risk of developing type-2 diabetes (prediabetes) completed the exercise intervention and had measures described in RO1 and RO2 completed.

Research objective 4 (RO4) was addressed by Task 4 – to assess changes in the metabolome response to HIIT in health and disease. Plasma samples from before and after the intervention were analyzed for metabolomic signatures. Ina addition to this, immune cell and muscle samples have been assessed for DNA methylation status as a measure of biological aging, which will provide greater insight into the molecular transducers of benefits. Results from these will be correlated with other outcome measures to determine relationships between the metabolome, genome and immune/inflammatory functions and organ function.

Main Results

- HIIT training is highly effective at improving physical fitness and biological functions in older adults with and without inflammatory diseases. These findings will challenge the current paradigm that exercise

mediated health benefits can only be achieved by longer duration, more time consuming exercise exposures.

- A comprehensive database of the effects of HIIT on multiple systems in health and disease has been created.
- HIIT training is not effective in reducing systemic or tissue levels of chronic inflammation.
- HIIT training was associated with improved disease indices in those with rheumatoid arthritis or prediabetes.
- Results have shown previously unknown relationships between changes in fitness, metabolism, immune function and disease activity in older adults with chronic inflammatory diseases.

Conclusions

This project has helped identify the benefits and limitations of a novel exercise intervention on older adults with and without inflammatory diseases. Furthermore, the project has helped to better understand the molecular transducers of the exercise training, and their relationships with health on older adults.

Impact of Projected Results

It is expected that the project results will have a great impact on the research community and healthcare industry. During the project, because of his work on the effects of HIIT in health, Dr. Bartlett was invited to be support staff for the US Physical Activity Guidelines working groups, tasked with assessing the literature regarding recommendations for physical activity to the US public.

The results of RO3 challenge the conceptions that for improved health benefits in those with chronic diseases, the national physical activity guidelines are the only option. The manuscript to be published has already and will further attract attention from the scientific community and healthcare industry. This could potentially help healthcare professionals develop better strategies for implementing exercise prescriptions in older adults with and without disease.

Impact of Marie Curie Fellowship on Dr. Bartlett's Career.

The Marie Curie fellowship has been very good for Dr. Bartlett's career. Dr. Bartlett has taken a faculty position at his outgoing institution in the USA where he is leading his own laboratory investigating the effects of exercise training on immune responses in cancer patients. He continues to collaborate with his university in the UK and together they will aim to educate future researchers in the area of exercise immunology, specifically in relation to older adults and those with disease.