

Modulating $\dot{V}O_2\text{max}$: Effects of Training Frequency, Sprint Volume, and Myokines

by

Matthew Hutchinson

A thesis submitted to the University of Stirling in partial fulfilment for the degree of
Doctor of Philosophy

Centre for Research and Innovation in Sport

Faculty of Health Sciences and Sport

University of Stirling

December 2025

I dedicate this thesis to my wife, Jodie, my late best friend, Liam, and to all those who have helped me along my journey

Declaration

I declare that this thesis was composed by myself and that all the data were collected and analysed by myself, under the supervision of Dr. Niels BJ Vollaard and Dr. Richard Metcalfe, with the following exception(s):

1. The original R Studio script and statistical advice used for the meta-analysis in **Chapter 2** was first written and provided by Dr Robert Paval, a recent doctoral graduate of the University of Stirling. The original script was continuously edited and adapted by myself for the final analysis.

Neither the thesis, nor the original work contained therein have been submitted to this or any other institution for a higher degree. This thesis does not infringe upon anyone's copyright, and any materials from the work of others included in this thesis are fully acknowledged in accordance with common reference practices.

Signed:



Matthew Hutchinson

Date: 12/12/2025

The copyright of this thesis belongs to the author, under the terms of the United Kingdom Copyright Act, as qualified by the University of Stirling regulations. Due acknowledgement must always be made to the author when using any materials contained in, or derived from, this thesis.

Abstract

Physical inactivity is a global issue; over a third of people don't exercise regularly enough to meet the recommended physical activity guidelines. This increases the risk of mortality and developing numerous chronic diseases. Regular exercise improves $\dot{V}O_{2\max}$, which is the best predictor of overall health and disease risk. The reasons for low adherence to regular physical activity are multifactorial, with lack of time among the most common reasons reported. Exercise interventions, such as HIIT and SIT, have been well researched as time-efficient alternatives to MICT. Research has demonstrated the effectiveness of HIIT and SIT at improving $\dot{V}O_{2\max}$. However, they are not without their limitations, which cast doubt on their real-world relevance and whether they would improve regular physical activity levels. REHIT has been shown to be a promising alternative, effective at improving $\dot{V}O_{2\max}$ to levels similar to MICT, HIIT, and SIT, but with a substantial reduction in total exercise volume. The minimal effective dose for improving $\dot{V}O_{2\max}$ with REHIT remains to be determined, and modifications to key parameters remain underexplored. Furthermore, the mechanisms underpinning the comparable $\dot{V}O_{2\max}$ improvements observed with REHIT despite its substantially lower exercise volume remain unclear.

Chapter 1 provides an overview of the literature surrounding the thesis topics. **Chapter 2** meta-analyses the literature and combines with previous work on the topic to provide an updated meta-analysis and systematic review of the effect of the number of sprint repetitions in a SIT session on the changes in $\dot{V}O_{2\max}$. **Chapter 3** presents an experimental trial investigating the effects of reducing the training frequency of a REHIT exercise intervention on the changes in $\dot{V}O_{2\max}$. **Chapter 4** attempts to elucidate mechanisms that affect variability in the response to exercise by examining whether there are differences in the training-induced myokine response between high- and low-responders to exercise.

Ethical Approval

All experimental research involving human participants presented in this thesis was conducted following approval from the relevant University of Stirling research ethics committee. The research was conducted in accordance with the ethical principles applicable to research involving human participants.

AI Declaration

AI was used solely to assist in the creation of Figure 3 in Chapter 1 of this thesis. The figure was generated using Microsoft CoPilot within PowerPoint, based on a text prompt provided by myself underneath the figure. The resulting illustration was subsequently annotated by me to depict central and peripheral physiological adaptations to exercise training. All scientific content, interpretations, and accompanying descriptions remain my own work.

Plagiarism Detection Consent

I consent to the University of Stirling using plagiarism detection software to assess the originality of this thesis in accordance with the University's academic integrity policies and procedures.

Acknowledgements

I would like to express my sincere gratitude to everyone who has supported me throughout my PhD journey. Completing this thesis has been an incredibly challenging yet rewarding experience, and I am fortunate to have had some wonderful people alongside me throughout.

First and foremost, I would like to thank my supervisor, Dr Niels Vollaard, for his unwavering support, guidance, and mentorship throughout my PhD. Your expertise, encouragement, and patience have been invaluable, and I am extremely grateful for the opportunities you have provided me and the confidence you have shown in my abilities. I could not have asked for a better supervisor and mentor, and I will always appreciate everything you have done to help me develop as a researcher.

A special thank you goes to Daniel Kinghorn, who has been an absolute rock and a great friend throughout this entire journey. From the challenges and frustrations to the successes and celebrations, having someone to share the experience with has made all the difference. Your friendship, encouragement, and willingness to help whenever needed have meant more than you know, and I am incredibly grateful to have had you alongside me.

Finally, I would like to thank my family and friends for their continued love, support, and understanding throughout the years. In particular, to my wife, Jodie, thank you for your patience, encouragement, and unwavering belief in me, especially during the more demanding periods of this journey. Your support has meant everything, and I genuinely could not have done this without you. Completing this PhD represents the culmination of years of hard work, perseverance, and personal growth. While this thesis bears my name, it would not have been possible without the support of those mentioned above. To everyone who has played a part in helping me reach this point, thank you.

Table of Contents

Chapter 1 – General Introduction	14
Physical Inactivity	14
Factors influencing physical inactivity	16
$\dot{V}O_2\text{max}$	18
$\dot{V}O_2\text{max}$ measurement	18
Moderators of $\dot{V}O_2\text{max}$ – Biological	20
Limiting factors of $\dot{V}O_2\text{max}$	23
Alternative exercise protocols	27
HIIT & SIT	27
REHIT	36
REHIT – Sprint Volume	37
REHIT – Additional training parameters.....	39
Interindividual Variability	42
Individual variability in responsiveness to exercise.....	42
Myokine discovery & the ‘myokinome’	46
Myokine response to exercise	47
Gaps in the literature	48
Aims and Objectives.....	49
Chapter 2 - Updated systematic review and meta-analysis of the effect of the number of sprint repetitions in a SIT session on changes in $\dot{V}O_2\text{max}$ with training.....	50
INTRODUCTION	50
METHODS.....	51
Literature search and screening process.....	51
Data Extraction.....	52
Statistical Analysis	53
Effect Size Calculation.....	53
Bayesian Model.....	53
Risk of Bias	54
Sensitivity Analyses.....	54
RESULTS.....	55
DISCUSSION.....	65
SUPPLEMENTARY DATA	68

Chapter 3 - The effect of training frequency on changes in aerobic power following reduced-exertion high-intensity interval training (REHIT)	77
INTRODUCTION	77
METHODS	78
Participants	78
Experimental Procedure	79
Statistical Analysis	80
RESULTS	80
DISCUSSION	81
Chapter 4 - Improvements in aerobic fitness with exercise training: the role of myokines	86
INTRODUCTION	86
METHODS	88
Participants	88
Experimental Procedure	88
Statistical Analysis	91
RESULTS	92
DISCUSSION	96
SUPPLEMENTARY DATA	100
Chapter 5 – General Discussion	101
Time-efficient exercise and the “minimal dose”	101
Mechanistic considerations and inter-individual variability	103
Implications for public health and exercise prescription	105
Future directions	106
Overall conclusions	108
References	109

List of Figures

FIGURE 1.1. - VALIDATES THAT THE RAMP $\dot{V}O_2$ WAS INDEED $\dot{V}O_{2\text{MAX}}$ AS EVIDENCED BY THE PRESENCE OF THE PLATEAU REGARDLESS OF AN INCREASE IN WORK RATE (POOLE AND JONES, 2017).	19
FIGURE 1.2 - LONGITUDINAL CHANGES IN $\dot{V}O_{2\text{PEAK}}$ PER DECADE FROM 20 TO 80 YEARS OF AGE PREDICTED FROM A MIXED-EFFECTS LINEAR REGRESSION MODEL (FLEG ET AL., 2005)	22
FIGURE 1.3 - CENTRAL AND PERIPHERAL ADAPTATIONS TO AEROBIC EXERCISE TRAINING THAT SUPPORT OXYGEN DELIVERY AND UTILISATION. CENTRAL ADAPTATIONS INCLUDE INCREASED STROKE VOLUME AND BLOOD VOLUME, ENHANCING OXYGEN DELIVERY TO WORKING MUSCLES. PERIPHERAL ADAPTATIONS INCLUDE INCREASED SKELETAL MUSCLE CAPILLARISATION AND MITOCHONDRIAL CONTENT, SUPPORTING OXYGEN EXTRACTION AND AEROBIC ATP PRODUCTION. PHYSIOLOGICAL ADAPTATIONS LABELLED ABOVE OCCUR THROUGH MICT, HIIT, SIT / REHIT AND ARE NOT EXCLUSIVE TO ONE EXERCISE MODE. ADAPTATIONS CONTAINED IN THE LABELS ARE TAKEN FROM MULTIPLE STUDIES LISTED IN TABLE 2	26
FIGURE 1.4 - META-ANALYSIS OF THE DECREASE IN AFFECTIVE VALENCE DURING SIT USING DIFFERENT SPRINT DURATIONS. THE SOLID LINE REPRESENTS THE POINT ESTIMATE, WHILST THE SHADED AREA REPRESENTS THE BONFERRONI-CORRECTED 95% CONFIDENCE LIMITS. THE PURPLE LINE AND SHADING ARE FOR 5–6 S SPRINTS, THE RED LINE AND SHADING ARE FOR 15–20 S SPRINTS, AND THE GREEN LINE AND SHADING ARE FOR 30 S SPRINTS (METCALFE ET AL., 2022).	38
FIGURE 2.1 - PRISMA FLOW DIAGRAM OF THE STUDY SELECTION PROCESS.	51
FIGURE 2.2 - EFFECT OF SIT ON $\dot{V}O_{2\text{MAX}}$. LETTERS A, B AND C USED IN STUDY LABELS DENOTE DIFFERENT DATASETS FROM WITHIN THE SAME STUDY.	60
FIGURE 2.3 - FUNNEL PLOT OF 93 STUDY EFFECT SIZES (BLACK CIRCLES). THE VERTICAL BLUE LINE REPRESENTS THE ESTIMATED POOLED EFFECT SIZE, AND THE DASHED BLACK LINES REPRESENT 95% CREDIBLE INTERVALS.	61
FIGURE 2.4 - RELATIONSHIP BETWEEN THE NUMBER OF SPRINT REPETITIONS PER TRAINING SESSION AND THE EFFECT SIZE FOR THE CHANGE IN $\dot{V}O_{2\text{MAX}}$ WITH TRAINING, EITHER WITH (A; N=93) OR WITHOUT (B; N=89) STUDIES IMPLEMENTING >10 SPRINTS PER SESSION.	62
FIGURE 2.5 - MODIFYING EFFECTS OF INTERVENTION DURATION (A), AGE (B), SPRINT DURATION (C), BMI (D), WORK:REST RATIO (E), AND TOTAL WEEKLY SPRINT TIME (F) ON THE EFFECT OF SIT ON $\dot{V}O_{2\text{MAX}}$. BMI DATA ARE N=73 TRIALS DUE TO MISSING DATA. EACH ADDITIONAL WEEK OF SIT (FIGURE 2.5A) WAS ASSOCIATED WITH A SMALL, POSITIVE EFFECT ON THE CHANGE IN $\dot{V}O_{2\text{MAX}}$ FOLLOWING SIT (ES = 0.05, 95% CI = 0.01 TO 0.09). CONVERSELY, EACH ADDITIONAL YEAR OF AGE (FIGURE 2.5B) WAS ASSOCIATED WITH A SMALL, NEGATIVE EFFECT ON THE CHANGE IN $\dot{V}O_{2\text{MAX}}$ (ES = -0.02, 95% CI = -0.03 TO -0.003). THERE WAS NO EFFECT OF SPRINT DURATION (ES = 0.02; 95% CI = -0.002 TO 0.03; FIGURE 2.5c), BMI (ES = 0.03; 95% CI = -0.03 TO 0.08; FIGURE 2.5d), WORK:REST RATIO (ES = 0.01; 95% CI = -1.33 TO 1.32; FIGURE 2.5e), OR TOTAL WEEKLY SPRINT TIME ON THE CHANGE IN $\dot{V}O_{2\text{MAX}}$ (ES = 0.0005; 95% CI = -0.0001 TO 0.0010; FIGURE 2.5f).	63
FIGURE 3.1 - GROUP MEAN AND INDIVIDUAL DATA WITH DIRECTIONAL CHANGES IN W_{MAX} IN RESPONSE TO 6 WEEKS OF REHIT PERFORMED AT A TRAINING FREQUENCY OF EITHER ONCE- (REHIT1) OR TWICE (REHIT2) WEEKLY. * P < 0.01 FOR THE MAIN EFFECT OF TIME.	80
FIGURE 4.1 - PERCENTAGE CHANGE IN BLOOD MYOKINES ACROSS HIGH, MEDIUM AND LOW $\dot{V}O_{2\text{MAX}}$ RESPONDER GROUPS. EACH SHAPE REPRESENTS THE GROUP DISTRIBUTION, AND EACH BOX DISPLAYS THE MEDIAN AND INTERQUARTILE RANGE. LAMA4 HIGH: N=8; LAMA4 MEDIUM: N=3. THBS4 HIGH: N=8. CCL21 HIGH: N=8. COLIVA HIGH: N=8.	94

List of Tables

TABLE 1.1 - COMPARISON OF THE TYPICAL CHARACTERISTICS OF MICT, HIIT, SIT, AND REHIT.	27
TABLE 1.2 – SELECTED STUDIES COMPARING THE EFFECTS OF MICT, HIIT, SIT AND REHIT ON AEROBIC FITNESS AND OTHER PHYSIOLOGICAL OUTCOMES. STUDY POPULATIONS, INTERVENTION CHARACTERISTICS AND REPORTED CHANGES ARE SUMMARISED.....	29
TABLE 2.1 - STUDY TRAINING INTERVENTION PROTOCOL PARAMETERS, PARTICIPANT CHARACTERISTICS, AND TRAINING EFFECTS.	55
TABLE 2.2 - BAYESIAN MODEL ESTIMATES FOR THE EFFECTS OF PARTICIPANT CHARACTERISTIC AND EXERCISE PROTOCOL VARIABLE PREDICTORS ON CHANGES IN $\dot{V}O_{2\text{MAX}}$	61
TABLE 3.1 – PARTICIPANT CHARACTERISTICS	80
TABLE 4.1 - PARTICIPANT CHARACTERISTICS (N=20)	92
TABLE 4.2 - PRE-TO POST-INTERVENTION CHANGES IN $\dot{V}O_{2\text{MAX}}$ AND PLASMA MYOKINE CONCENTRATIONS.....	92
TABLE 4.3 - PEAK POWER RELATIVE TO BODY MASS AND MAXIMUM CADENCE DURING THE FIRST AND FINAL REHIT SESSIONS.	93

List of Publications / Conference activity

Zhang J, Blaschek JLM, Hutchinson M, Kinghorn DJ, Metcalfe RS, Hall ECR, Bartie KL, Vollaard NBJ (2025). The increase in plasma IL-6 following sprint interval training does not depend on total sprint volume. *Journal of Applied Sports Sciences*, 9: 12-23.

July 2024 (10 min oral presentation): European College of Sport Science in Glasgow, Scotland.

Title: Updated systematic review and meta-analysis of the effect of the number of sprint repetitions in a SIT session on changes in $\dot{V}O_{2\max}$ with training.

List of abbreviations

ADP – Adenosine diphosphate

AMP – Adenosine monophosphate

AMPK – Adenosine monophosphate-activated protein kinase

ATP – Adenosine triphosphate

a-vO₂diff – Arteriovenous oxygen difference

BDNF – Brain-derived neurotrophic factor

BMI – Body mass index

CaO₂ – Arterial oxygen content

CCL21 – Chemokine (C-C motif) Ligand 21

CI – Credible intervals

COL4a1 – Collagen type IV alpha-1 chain

COL4a2 – Collagen type IV alpha-2 chain

COLIVa – Collagen type IV alpha

CRF – Cardiorespiratory fitness

CTHRC1 – Collagen triple helix repeat containing 1

CV – Coefficient of variation

CVD – Cardiovascular disease

FGF21 – Fibroblast growth factor-21

HIIT – High-intensity interval training

HR – Heart rate

HRmax – Heart rate max

IL-6 – Interleukin-6

IL-10 – Interleukin-10

IL-13 – Interleukin-13

IL-15 – Interleukin-15

IL-18 – Interleukin-18

IPAQ – International Physical Activity Questionnaire

LAMa4 – Laminin, alpha 4

MET – Metabolic equivalent

MHCC – Major histocompatibility complex class

MICT – Moderate-intensity continuous training

mRNA – Messenger ribonucleic acid

PA – Physical activity

PAR-Q – Physical activity readiness questionnaire

PCr – Phosphocreatine

PGC-1 α - Peroxisome proliferator-activated receptor gamma coactivator 1-alpha

PPC – Posterior predictive check

PPO – Peak power output

Q_{max} – Maximal cardiac output

RER – Respiratory exchange ratio

RPE – Rating of perceived exertion

SD – Standard deviation

SEE – Standard error of estimate

SEM – Standard error of the mean

SIT – Sprint interval training

SNP – Single-nucleotide polymorphism

SPARC – Secreted protein acidic and rich in cysteine

TE – Technical error

THBS4 – Thrombospondin 4

VEGF-C – Vascular Endothelial Growth Factor C

VEGFR2 -Vascular Endothelial Growth Receptor 2

$\dot{V}O_2$ – Volume of oxygen

$\dot{V}O_{2max}$ – (Maximal) Volume of oxygen

$\dot{V}O_{2peak}$ – (Peak) Volume of oxygen

WHO – World Health Organisation

W_{max} – Maximal Power Output

Chapter 1 – General Introduction

Physical Inactivity

Physical inactivity describes people who do not achieve enough physical activity (PA) to meet current guidelines. These guidelines recommend 150-300 minutes of moderate-intensity aerobic activity, or 75-150 minutes of vigorous-intensity activity, per week (World Health, 2020). In addition, adults are advised to perform muscle-strengthening activities involving all major muscle groups on at least 2 days per week at moderate intensity or above (World Health, 2020).

There is strong evidence that physical inactivity increases the risk of a wide range of adverse health outcomes, including major non-communicable diseases such as type 2 diabetes and coronary heart disease (Lee et al., 2012b). Conversely, regular PA can improve $\dot{V}O_2\text{max}$, which is associated with substantial health benefits. For every 1-metabolic equivalent (MET) increase in aerobic capacity, equivalent to $\sim 3.5 \text{ mL} \cdot \text{kg} \cdot \text{min}^{-1}$, the risk of mortality and cardiovascular disease (CVD) decreases by approximately 10-25% in healthy men and women (Myers et al., 2015).

The protective effects of cardiorespiratory fitness (CRF) are evident even when other risk factors are present. These include age (Lee et al., 2014, Lee et al., 2010), race (Kokkinos et al., 2008), adiposity ((Barry et al., 2014, Lee et al., 2012a), BMI (Lee et al., 2011, Fogelholm, 2010) and co-morbidities such as diabetes (Broekhuizen et al., 2011, Kokkinos et al., 2009, Church et al., 2004) and hypertension (Kokkinos et al., 2014).

Despite this evidence, the burden of physical inactivity in the UK has worsened over the last half-century. A recent report commissioned by Public Health England (gov.uk, 2022) states that the population is now 20% less active than in the 1960s, with approximately 34% of men and 42% of women failing to meet the current PA guidelines (World Health, 2020). The same report suggests that physical inactivity in the UK is associated with one in six deaths and carries an estimated annual cost of £7.4 billion.

According to Guthold et al. (2018), the prevalence of physical inactivity is particularly high and continues to rise in high-income Western countries such as the United Kingdom. Globally, it is estimated that one in four adults and three in four adolescents (11-17 years) do not meet current PA guidelines (Amini et al., 2021). Katzmarzyk et al. (2022) further report that physical inactivity is responsible for more than 7% of all-cause and CVD deaths and up to 8% of non-communicable diseases.

Importantly, these figures are likely to underestimate the true scale of the problem. Individuals often overestimate their PA levels in self-report questionnaires, as shown in several studies (Hagstromer et al., 2010, Gauthier et al., 2009, Wanner et al., 2016). For example, Wanner et al. (2016) found that total PA was self-reported as 4.2 times higher on the IPAQ than when measured using accelerometer data.

Self-report questionnaires have been, and remain, the main method of data collection for these estimates. This is largely because they are time- and cost-efficient. However, their widespread use may obscure the full scale and complexity of physical inactivity.

The most severe categorisation of physical inactivity is sedentary behaviour. This is defined as waking behaviour with an energy expenditure ≤ 1.5 METs while sitting, reclining, or lying (Tremblay et al., 2017).

Factors influencing physical inactivity

A variety of factors influence an adult's level of participation in PA. These include biological, demographic, intrapersonal, sociocultural, socioeconomic, psychological, social, and environmental factors (Allender et al., 2006).

Physical inactivity is not caused by a single factor. Rather, it arises from the complex interplay of multiple factors. For example, physical inactivity in females is shaped by a variety of factors mentioned above, with key barriers including chronic health conditions, caregiving responsibilities, low self-confidence, and cost. Together, these factors intersect and contribute to the challenges women face in engaging in PA (Ominyi et al., 2025).

Age is negatively associated with PA participation (Bauman et al., 2016, Aleksovska et al., 2019). However, lower PA levels among older adults are influenced by a range of related determinants. A large-scale review identified walkability of the environment, social support for PA, and loneliness as significant factors associated with PA in this population (D'Amore et al., 2023).

One of the most frequently self-reported reasons for physical inactivity is a perceived lack of time (Trost et al., 2002, Reichert et al., 2007, Bauman et al., 2012). This perception is partly attributable to time spent at work and exacerbated by declining levels of physical activity during the modern workday. Thivel et al. (2018) argue that the typical working day has evolved over time.

Workplaces have become increasingly sedentary, with many employees spending most of their working hours seated at a desk. This is supported by data from the United States, which suggests that many occupations have shifted away from requiring moderate-intensity PA as a necessity to complete the work required. Instead, they are now largely characterised by sitting and other sedentary behaviour (Church et al., 2011). The authors estimated that occupational energy expenditure has declined by more than 100 calories per day in both men and women.

Concerns about the reduced workplace activity are further compounded by UK transport data. The most recent survey of work-related travel found that 68% of people *always* use a car to travel to and from work (Transport, 2023). This is concerning because greater time spent using a car has been associated with obesity (McCormack and Virk, 2014, Sugiyama et al., 2020), largely due to the sedentary nature of car travel.

Furthermore, this issue appears to have been exacerbated by the recent pandemic. During this period, working from home became the norm, and has been associated with higher levels of sedentary time (Fukushima et al., 2021). For some individuals, this shift in the workplace environment may also have removed routine opportunities for habitual daily PA, particularly through active commuting (Petersen et al., 2021).

Taken together, this information highlights the need for a time-efficient exercise intervention. Such an intervention may help address the perceived barrier of limited time and increase regular PA to levels sufficient to meet current guidelines (World Health, 2020). This is important for reducing the

physiological and economic burden of physical inactivity, which remains one of the leading risk factors for non-communicable diseases and mortality (World Health, 2024).

$\dot{V}O_2\text{max}$

$\dot{V}O_2\text{max}$ measurement

CRF reflects the integrated ability of the pulmonary, cardiovascular, and muscular systems to take up, transport, and utilise oxygen in the mitochondria of working skeletal muscle to meet metabolic demand (Poole and Jones, 2017). CRF is often expressed as maximal oxygen consumption ($\dot{V}O_2\text{max}$) (Bishop et al., 2025). For the purposes of this thesis, CRF will hereafter be referred to as $\dot{V}O_2\text{max}$.

The foundational premise of $\dot{V}O_2\text{max}$ is that $\dot{V}O_2$ eventually reaches a plateau or ceiling, such that further increases in speed or workload no longer elicit further increases in $\dot{V}O_2$. This concept was first articulated by Hill and Lupton in 1923 (Hill and Lupton, 1923, Poole and Jones, 2017).

Methods for measuring $\dot{V}O_2\text{max}$ has evolved considerably since these early investigations. Initial protocols used discontinuous bouts at different constant power outputs (Hill and Lupton, 1923, Chidnok et al., 2013). Whereas now, the contemporary gold standard for measuring $\dot{V}O_2\text{max}$ is typically a maximal incremental (Davis et al., 1982) or ramp test (Whipp et al., 1981) performed to exhaustion. These tests are combined with breath-by-breath measures of ventilation and gas exchange, while speed or work rate is progressively increased until exhaustion.

Despite its widespread acceptance as an important index of aerobic and functional capacity, the conceptual and methodological basis of $\dot{V}O_2\text{max}$ remains debated. In particular, discussion has focused on its distinction from $\dot{V}O_{2\text{peak}}$ and on the criteria used to confirm whether a ‘true’ maximal value has been attained (Chidnok et al., 2013). One common method used to verify attainment of $\dot{V}O_2\text{max}$ is the ‘verification phase’. In this approach, the participant cycles for as long as possible at a power output higher than the peak power output (PPO) achieved during the incremental test, following a 5–15-minute recovery period (Thoden et al., 1991, Rossiter et al., 2006, Midgley et al., 2007). If the value obtained during the verification phase falls within the tolerance of measurement error, ~2% (Midgley et al., 2006) of the maximal value recorded at the end of the incremental phase, it is considered highly likely that a true $\dot{V}O_2\text{max}$ has been achieved (Midgley et al., 2007). **Figure 1.1** illustrates this principle.

When a clear $\dot{V}O_2$ plateau is not observed, secondary criteria are commonly used to support the attainment of $\dot{V}O_2\text{max}$ (Poole and Jones, 2017). The most frequently applied criteria include one or more of the following: heart rate (HR) within 10 bpm or within 5% of the age-predicted maximum ($220 - \text{age}$); a blood lactate concentration of ≥ 8 mmol/L; or a respiratory exchange ratio (RER) > 1.15 (Poole and Jones, 2017).

However, reliance on these criteria has been criticised because maximal values for these variables vary substantially across different populations. For example, HR_{max} derived from $220 - \text{age}$ has a standard error of estimate (SEE) of $\sim 7 - 12$ bpm (Robergs and Landwehr, 2002). Similarly, maximal blood lactate concentration shows considerable inter-individual variation, as evidenced by

Peserico et al. (2018), who reported that only 45.5% of participants reached the threshold across age groups ranging from ≤ 25 to >45 years.

This issue is even more evident in older adults. Edvardsen et al. (2014) found that the blood lactate criterion excluded 63% of participants in a cohort of 400 individuals aged 50–85-year-old, within a total sample of 861 individuals. By contrast, younger participants would likely satisfy this criterion at submaximal intensities, suggesting that a blood lactate concentration ≥ 8 mmol/L is strongly age-dependent (Edvardsen et al., 2014). The RER criterion is also problematic. RER responses can vary substantially between individuals and are influenced by both exercise modality and training status (Bentley and McNaughton, 2003, Pierce et al., 1999). This heterogeneity challenges the use of fixed verification criteria when a $\dot{V}O_2$ plateau is absent. Consequently, Midgley et al. (2007) argue that a new set of standardised criteria for $\dot{V}O_2$ max determination should be considered.

Reducing measurement noise is therefore important for strengthening research conclusions. This is particularly relevant in studies examining the effects of exercise interventions on $\dot{V}O_2$ max, where even ‘true’ $\dot{V}O_2$ max values may still be influenced by a range of methodological sources of variability.

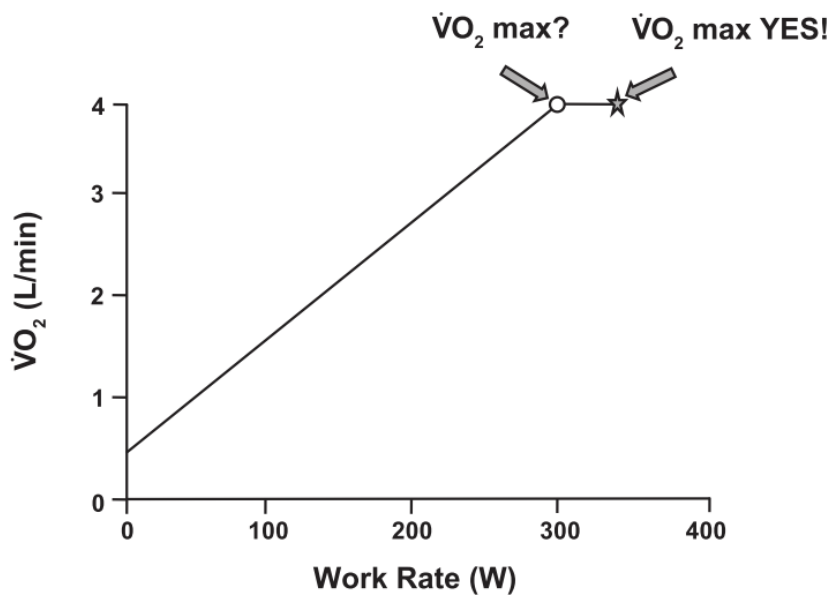


Figure 1.1. - Validates that the ramp $\dot{V}O_2$ was indeed $\dot{V}O_2$ max as evidenced by the presence of the plateau regardless of an increase in work rate (Poole and Jones, 2017).

Moderators of $\dot{V}O_2\text{max}$ – Biological

Given the importance of $\dot{V}O_2\text{max}$ for disease prevention and overall health, it is essential to understand the biological factors that underlie inter-individual variability in $\dot{V}O_2\text{max}$ within the general population (Zeiger et al., 2019). Early studies showed that a substantial proportion of variation in both $\dot{V}O_2\text{max}$ and its response to standardised aerobic exercise is genetically determined (Klissouras et al., 1973, Lortie et al., 1984).

Further evidence was provided by the multi-centre ‘HERITAGE Family Study’ (Bouchard et al., 1999). This study examined individual responses to 20 weeks of aerobic exercise, comprising 60 training sessions, in sedentary two-generation families. The change in $\dot{V}O_2\text{max}$ ranged from 0 to 1000 mL O_2 across individuals. The authors estimated that genetic factors accounted for approximately 47% of the heterogeneity in $\dot{V}O_2\text{max}$ trainability. They also reported greater between-family variation than within-family variation, further supporting a genetic contribution to both baseline $\dot{V}O_2\text{max}$ and $\dot{V}O_2\text{max}$ trainability (Schutte et al., 2016). However, an important limitation of this work was the absence of a control group (Williams et al., 2017).

Support for these early observations is provided by a meta-analysis conducted by Schutte et al. (2016). This analysis combined data from the largest twin study on directly measured $\dot{V}O_2\text{max}$ of their own with seven additional twin studies of varying sample sizes, involving monozygotic and dizygotic twins (Klissouras, 1971, Klissouras et al., 1973, Bouchard et al., 1986, Fagard et al., 1991, Sundet et al., 1994, Maes et al., 1996, Mustelin et al., 2011). The authors estimated that approximately 59% of the total variance in measured $\dot{V}O_2\text{max}$ (mL·min⁻¹) was attributable to heritable factors.

However, the precise contribution of the two components of $\dot{V}O_2\text{max}$ heritability remains unclear. These components are the genetic determinants that influence baseline levels of $\dot{V}O_2\text{max}$ and those that influence $\dot{V}O_2\text{max}$ trainability. This distinction could not be resolved in the meta-analysis by Schutte et al. (2016), because the included studies involved both sedentary participants and moderate-to-vigorous exercisers. The HERITAGE findings (Bouchard et al., 1999) are also broadly consistent with a later meta-analysis, which reported heritability estimates of 44% to 68% for endurance-related phenotypes (Miyamoto-Mikami et al., 2018). The wide range of estimates likely reflects substantial heterogeneity across the included studies. This heterogeneity arose from differences in study design, including the inclusion of both twin and family studies, the use of different exercise modes such as cycling and running, variation in participant sex, and the use of both direct maximal and indirect submaximal methods to assess $\dot{V}O_2\text{max}$.

Aerobic capacity is also well known to decline with age (Tanaka and Seals, 2008, Fleg et al., 2005, Pimentel et al., 2003) (**Figure 1.2**). In healthy sedentary individuals, $\dot{V}O_2\text{max}$ declines by approximately 10% per decade of life after the age of 25-30 years (Burtcher et al., 2022) This

decline accelerates to approximately 23% during the seventh decade of life and beyond (Fleg et al., 2005).

Although endurance-trained individuals maintain a higher $\dot{V}O_{2\max}$ than sedentary individuals across the lifespan, some studies suggest that habitual PA does not alter the rate of age-related decline in $\dot{V}O_{2\max}$ (Wilson and Tanaka, 2000, Fitzgerald et al., 1997, Fleg et al., 2005). In contrast, other longitudinal studies have shown that continued exercise can attenuate reductions in $\dot{V}O_{2\max}$ (Pollock et al., 1997, Katzel et al., 2001, Trappe et al., 1996). Importantly, the rate of age-related decline in $\dot{V}O_{2\max}$ appears to depend on both total PA volume and exercise intensity (Burtcher et al., 2022). In this context, $\dot{V}O_{2\text{peak}}$ has been shown to correlate most strongly with time spent performing high-intensity PA (Talbot et al., 2000).

The age-related decline in $\dot{V}O_{2\max}$ is thought to be driven primarily by reductions in maximal cardiac output ($Q_{\max}$). This appears to be largely mediated by reductions in maximal stroke volume, which are linked to increased left ventricle stiffness (Zile et al., 2004), and by decreases in maximal heart rate ($HR_{\max}$) (Pandey et al., 2020). A reduction in peak exercise arteriovenous oxygen difference ($a\text{-}\dot{V}O_{2\text{diff}}$) is also thought to contribute to the age-related decline in $\dot{V}O_{2\max}$ (Kitzman et al., 1988, Carrick-Ranson et al., 2012, Fuller et al., 2021). This may reflect age-related changes in skeletal muscle mass and quality, skeletal muscle blood flow, capillary density, and mitochondrial function (Subramanian et al., 2025). However, skeletal muscle adaptations that improve oxygen extraction may play a particularly important role in increasing $\dot{V}O_{2\max}$ in older adults. For example, $\dot{V}O_{2\text{peak}}$ increased by ~18% following three months of aerobic exercise in older sedentary adults, despite no change in $Q_{\max}$ (Beere et al., 1999, Subramanian et al., 2025). This suggests that peripheral adaptations may make a greater contribution to training-induced improvements in $\dot{V}O_{2\max}$ in older populations.

There is also clear evidence of sex-related differences in $\dot{V}O_{2\max}$. Women generally exhibit values that are 20-30% lower than those of men (Hakola, 2015, Zeiher et al., 2019, Loe et al., 2013). These differences are primarily attributed to lower $Q_{\max}$ and stroke volume in women (Ogawa et al., 1992). In turn, these differences are generally explained by smaller average body and organ size, as well as a higher proportion of body fat in women (Proctor and Joyner, 1997, Hakola, 2015). Notably, the magnitude of the sex difference depends on how $\dot{V}O_{2\max}$ is expressed. Fleg et al. (2005) showed that when $\dot{V}O_{2\max}$ is expressed relative to muscle mass ($\text{mL}\cdot\text{kg}\cdot\text{muscle mass}\cdot\text{min}^{-1}$) rather than in absolute terms ($\text{mL}\cdot\text{min}^{-1}$) or relative to body mass ($\text{mL}\cdot\text{kg}\cdot\text{min}^{-1}$), the difference between men and women is often eliminated (Zeiher et al., 2019).

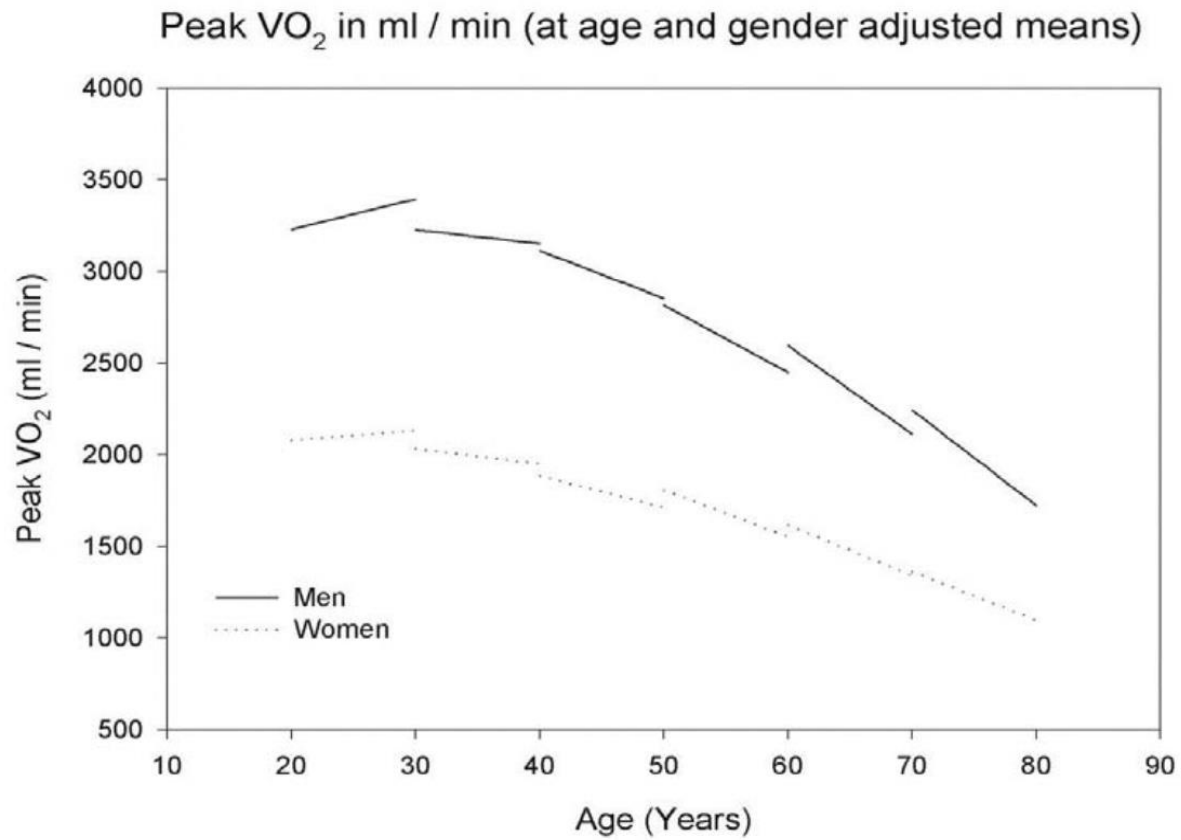


Figure 1.2 - Longitudinal changes in $\dot{V}\text{O}_{2\text{peak}}$ per decade from 20 to 80 years of age predicted from a mixed-effects linear regression model (Fleg et al., 2005)

Limiting factors of $\dot{V}O_{2\max}$

It has long been recognised that the only established method for improving $\dot{V}O_{2\max}$ is regular exercise. The specific physiological adaptations that occur depend on the type, intensity, and duration of the prescribed training (Midgley et al., 2007). However, despite the substantial body of research examining the effects of different exercise modalities on $\dot{V}O_{2\max}$, the precise physiological factors that limit $\dot{V}O_{2\max}$, and their relative contributions to training-induced improvements, remain debated.

The trainable determinants of $\dot{V}O_{2\max}$ can be divided into central and peripheral components. Central components relate to the transport of oxygen to the working muscles, whereas peripheral components relate to oxygen extraction and utilisation within the muscles themselves (Joyner and Lundby, 2018). Central mechanisms include factors such as blood oxygen-carrying capacity, pulmonary diffusing capacity, blood volume expansion, and stroke volume, all of which contribute to a greater $Q_{\max}$ (Bassett and Howley, 2000, Lundby et al., 2017). In contrast, peripheral mechanisms include factors such as capillary density and mitochondrial content, which influence the muscle's capacity to extract and utilise oxygen (Rosenblat et al., 2022).

Current evidence suggests that the primary limitation to $\dot{V}O_{2\max}$ lies in the cardiovascular system's capacity to deliver oxygen to the working muscles (Montero and Lundby, 2017). Experimental evidence supports this central limitation theory. For example, unilateral leg studies conducted under hyperoxic conditions have demonstrated higher leg $\dot{V}O_{2\max}$ values than under normoxic conditions (Knight et al., 1993, Richardson et al., 1999). In these studies, $\dot{V}O_{2\max}$ increased alongside enhanced O_2 delivery resulting from saturating the blood with higher oxygen content. If O_2 extraction were the principal limiting factor, increasing arterial oxygen content (CaO_2) would be expected to have little effect, as the rate of O_2 extraction during maximal exercise would already be at its upper limit.

Training-induced improvements in $\dot{V}O_{2\max}$ are also widely considered to be driven primarily by central adaptations. These include increases in blood volume, which contribute to a greater $Q_{\max}$ (Krip et al., 1997, Sawka et al., 2000, Lundby et al., 2017). Support for this view comes from Bonne et al. (2014), who showed that improvements in $\dot{V}O_{2\max}$ after 6 weeks of moderate-intensity continuous training (MICT) returned to pre-training levels when the training-induced expansion in blood volume was removed via phlebotomy. However, blood volume expansion is unlikely to be the sole mechanism responsible for improved $\dot{V}O_{2\max}$. Skattebo et al. (2020) reported that training-induced improvements in $\dot{V}O_{2\max}$ were maintained even after the removal of the expanded blood volume. This finding suggests that additional adaptation contributed to the observed response.

The discrepancy between these findings may reflect differences in training protocol. In Skattebo et al. (2020), participants completed a 10-week intervention consisting of one MICT session and two high-intensity interval training (HIIT) sessions per week. In contrast, Bonne et al. (2014) used a 6-week MICT-based intervention. The longer duration and higher intensity used by Skattebo et al.

(2020) may have promoted further central adaptations. Indeed, that study reported an increase in left ventricular mass, a change not observed by Bonne et al. (2014).

Such cardiac remodelling may have helped preserve improvements in $\dot{V}O_{2\max}$ through an elevated stroke volume. Skattebo et al. (2020) suggested that this effect may have been mediated by improved contractility, enhanced compliance, or faster ventricular relaxation. Importantly, the authors concluded that central adaptations remained the predominant driver of improved $\dot{V}O_{2\max}$ following endurance training, with increased $Q_{\max}$ accounting for approximately 70% of the observed $\dot{V}O_{2\max}$ improvements (Skattebo et al., 2020). Nevertheless, they also reported an increase in a- $vO_{2\text{diff}}$ of 5 ± 12 ml/l, suggesting that peripheral adaptations contributed around 30% of the increase in $\dot{V}O_{2\max}$ (Skattebo et al., 2020). Many studies also report increases in $Q_{\max}$ following HIIT or sprint interval training (SIT). These changes are generally mediated by increases in stroke volume (Warburton et al., 2004, Daussin et al., 2007, Trilk et al., 2011, Ben Abderrahman et al., 2013, Matsuo et al., 2014, Mandic et al., 2022, Astorino et al., 2017) and are associated with significant improvements in $\dot{V}O_{2\max}$. However, not all studies show this pattern. Some have reported significant improvements in $\dot{V}O_{2\max}$ despite no measurable change in $Q_{\max}$, alongside increases in a- $vO_{2\text{diff}}$ reported (Jacobs et al., 2013, Macpherson et al., 2011, Raleigh et al., 2018). These findings have led some authors to propose that peripheral adaptations may play a greater role during the early stages of HIIT or SIT interventions. Such adaptations may include enhanced skeletal muscle mitochondrial function (Vincent et al., 2015), increased mitochondrial protein content (Gibala et al., 2006, Ma et al., 2013, Granata et al., 2016), and increased capillary density (Cocks et al., 2016, Scribbans et al., 2014). Variation in the adaptations reported across studies may be explained by differences in training duration, intensity, modality and measurement techniques. Overall, the balance of evidence indicates that central adaptations are the primary drivers of improved $\dot{V}O_{2\max}$ following HIIT and SIT, although peripheral adaptations also make a meaningful contribution. This interpretation is supported by Mandic et al. (2022) and by a recent meta-analysis conducted by Astorino et al. (2022). The meta-analysis concluded that central adaptations, particularly those affecting stroke volume and therefore $Q_{\max}$, are the principal contributors to improvements in $\dot{V}O_{2\max}$ following HIIT/SIT interventions, with a greater effect size in unhealthy populations than in healthy individuals (Astorino et al., 2022).

Using data from 14 studies ($n=199$), Astorino et al. (2022) also noted that increases in a- $vO_{2\text{diff}}$ contributed to the observed improvements in $\dot{V}O_{2\max}$, indicating a role for peripheral adaptations. However, the authors cautioned against using these data to quantify the relative contributions of central and peripheral mechanisms too precisely. All included studies estimated a- $vO_{2\text{diff}}$ using the Fick equation. This approach is associated with inherent error because it depends on estimates of both VO_2 and CO , each of which contains measurement error, which in turn can amplify the inaccuracy of the derived a- $vO_{2\text{diff}}$ value (Astorino et al., 2022, Mahutte and Jaffe, 1995). Astorino et al. (2022) therefore recommend that future studies use direct measurements to clarify the relative

contribution of peripheral adaptations. However, the invasive nature of such methods may limit their practical application.

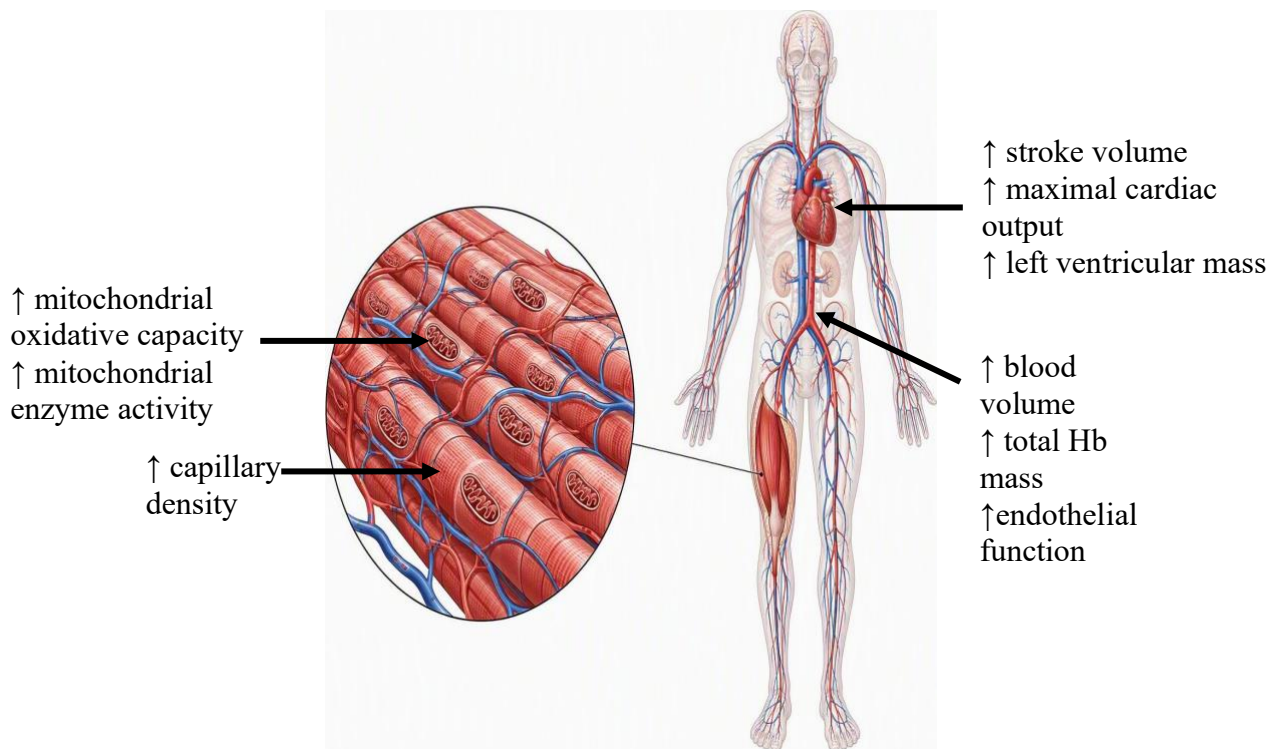


*Figure 1.3 - Central and peripheral adaptations to aerobic exercise training that support oxygen delivery and utilisation. Central adaptations include increased stroke volume and blood volume, enhancing oxygen delivery to working muscles. Peripheral adaptations include increased skeletal muscle capillarisation and mitochondrial content, supporting oxygen extraction and aerobic ATP production. Physiological adaptations labelled above occur through MICT, HIIT, SIT / REHIT and are not exclusive to one exercise mode. Adaptations contained in the labels are taken from multiple studies listed in **Table 1.2**.*

Note: For transparency, the image was created in PowerPoint using CoPilot and typing this prompt “I want to create a figure of a human being, I need a thigh muscle to be present in one leg, the heart, some blood inside the body that I’m going to annotate, then I need a zoomed in section of the muscle to the left of the body which I’ll label with capillaries and mitochondria”.

Table 1.1 - Comparison of the typical characteristics of MICT, HIIT, SIT, and REHIT.

Characteristic	MICT	HIIT	SIT	REHIT
Typical intensity	46-65% $\dot{V}O_{2\max}$ 64-76% $HR_{\max}$	64-100% $\dot{V}O_{2\max}$ 77-95% $HR_{\max}$	$\geq 91\%$ $\dot{V}O_{2\max}$ $\geq 95\%$ $\dot{V}O_{2\max}$ “All-out” / Supramaximal	“All-out” / Supramaximal
Typical session duration	30-60 min	20-40 min	20-30 min	10-20 min
Typical sprint/work bouts	Continuous	30-240 s	4-6 x 30 s	2-3 x 20 s
Recovery	None	30-240 s	3-4 min	3-4 min
Weekly exercise time	~150 min	~90-120 min	~90 min	~30 min

Adapted from Coates et al. (2023), American College of Sports Medicine (2021), and Ito (2019).

Alternative exercise protocols

HIIT & SIT

Moderate-intensity continuous training (MICT) is typically defined as PA performed at $<80\%$ of $HR_{\max}$ / $\dot{V}O_{2\max}$ in a single continuous bout, usually lasting at least 30 minutes (Steele et al., 2021). MICT has been shown to significantly improve $\dot{V}O_{2\max}$ (Milanovic et al., 2015, Su et al., 2019, Lawler et al., 2011). However, many individuals report barriers to participation. These include a perceived lack of time and the view that MICT is monotonous and therefore potentially less enjoyable (Batrakoulis and Fatouros, 2022). This has highlighted the need for alternative training modalities that may be more time-efficient and engaging.

HIIT encompasses a broad range of intermittent exercise protocols. Among the most widely studied are the 4×4 min and 10×1 min protocols (Ito, 2019). Despite the large volume of research, there is still no universally accepted definition of HIIT (Coates et al., 2023). Coates et al. (2023) describe HIIT as intermittent bouts of exercise performed at or above moderate intensity for health-related purposes, and at or above heavy intensity for performance-related purposes.

There is strong evidence indicating that HIIT is just as effective as MICT for improving $\dot{V}O_{2\max}$. This conclusion has been supported by meta-analyses across several populations, including healthy adult populations (Milanovic et al., 2015, Wen et al., 2019), overweight/obese populations (Turk et al., 2017, Su et al., 2019, van Baak et al., 2021), older adults (Poon et al., 2021) and clinical populations (Weston et al., 2014). However, the mechanisms underlying the apparently greater effect of HIIT on $\dot{V}O_{2\max}$ remain unclear (Ito, 2019). Some evidence suggests that HIIT may

enhance pathways linked to peripheral adaptations, such as mitochondrial biogenesis (MacInnis and Gibala, 2017). Other studies have reported significantly greater increases in $\dot{V}O_{2\max}$ following HIIT compared with MICT (Daussin et al., 2007). Differences between studies may partly reflect variation in the intensity prescribed in the MICT protocols (Daussin et al., 2007).

Despite its physiological effectiveness, questions remain about the suitability of HIIT as a population-level strategy to improve PA and improve long-term health in physically inactive or sedentary individuals. Reljic et al. (2019) challenge the commonly cited claim that HIIT is highly time efficient. They argue that, when warm-up, recovery intervals, and cool-down are totalled, most HIIT protocols save little time compared with MICT. Weston et al. (2014), for example, reported a median HIIT session duration of 38 minutes, equating to ~114 minutes per week. This is only slightly lower than a typical MICT prescription (~135 minutes per week).

Another key limitation of HIIT concerns the affective responses often associated with high-intensity exercise. Affective valence, defined as the experience of pleasure-displeasure during exercise (Williams et al., 2008), is an important determinant of adherence (Haines et al., 2021). Research has shown a negative relationship between exercise intensity and affective responses in inactive and overweight adults (Jung et al., 2014). Frazao et al. (2016) found that, in physically inactive individuals, affect became progressively more negative as the number of high-intensity work bouts increased. Although affect remained positive during the first few work bouts, it declined with each additional bout (Frazao et al., 2016). Reljic et al. (2019) also reported that longer session duration, greater weekly time-effort, and higher overall time-effort per intervention were associated with higher dropout rates, reinforcing the importance of both time-efficiency and minimising time spent exercising at intensities perceived as unpleasant.

These issues raise doubts about the extent to which HIIT can influence public health at the population level. As Foster et al. (2015) contend that even highly effective interventions are unlikely to produce meaningful public health benefits if participants do not find them enjoyable. SIT represents another form of HIIT and is characterised by repeated, brief, intermittent bursts of ‘all-out’ exercise, interspersed with periods of active or passive recovery (Hardcastle et al., 2014). The ‘classic’ SIT protocol commonly used in the literature typically consists of 4-6 × 30-second ‘all-out’ sprints interspersed with 4-minute rest intervals, performed 3 times per week (Weston et al., 2014). SIT has also been shown to be more effective than MICT for improving $\dot{V}O_{2\max}$, with no significant difference between SIT and HIIT (Poon et al., 2021). In addition, SIT has demonstrated benefits for other important health markers, including blood pressure, blood lipids, and insulin sensitivity (Song and Lan, 2024, Adamson et al., 2019, Richards et al., 2010). **Table 1.2** summarises the training protocols and associated changes in $\dot{V}O_{2\max}$ and other physiological outcomes reported in studies of MICT, HIIT, SIT and REHIT.

Table 1.2 – Selected studies comparing the effects of MICT, HIIT, SIT and REHIT on aerobic fitness and other physiological outcomes. Study populations, intervention characteristics and reported changes are summarised.

Reference	Duration	Population	Protocol	Outcome variables	Change in $\dot{V}O_{2\max}$	Other changes
MICT						
(Dunston and Taylor, 2023)	6 weeks, 3 sessions/week	Inactive, young adults (n = 10)	Cycling, 40 min at 40% PPO	$\dot{V}O_{2\text{peak}}$, PPO	+9.7% $\dot{V}O_{2\max}$	+10.8% PPO
(Daussin et al., 2008)	8 weeks, 3 sessions/week	Sedentary adults; (n = 11) crossover design	Cycling, approx. 61% Pmax; duration 20-35 mins	$\dot{V}O_{2\max}$; Qmax; SV; muscle oxidative capacity; capillary density	+9% $\dot{V}O_{2\max}$	Muscle capillary density +40%; NSC in Qmax, SV and mitochondrial oxidative capacity
(Gillen et al., 2016)	12 weeks, 3 sessions/week	Sedentary men; (n = 10)	Cycling, 45 min @ 70% HRmax; 50 min including warm-up/cool-down	$\dot{V}O_{2\text{peak}}$; insulin sensitivity; muscle mitochondrial markers	+19% $\dot{V}O_{2\text{peak}}$	Citrate synthase activity +27%; insulin sensitivity index +34%
(Cocks et al., 2013)	6 weeks, 5 sessions/week	Sedentary men; (n = 8)	Cycling, 40-60 min @ 65% $\dot{V}O_{2\text{peak}}$	$\dot{V}O_{2\text{peak}}$; insulin sensitivity; capillary density	+15% $\dot{V}O_{2\text{peak}}$	Insulin sensitivity index + 31%; capillary density +32%
(Trapp et al., 2008)	15 weeks, 3 sessions/week	Inactive, otherwise healthy women (n = 8)	Cycling, 40 min @ 60% $\dot{V}O_{2\max}$	$\dot{V}O_{2\max}$, total body mass, fat mass, insulin level	+19.4% $\dot{V}O_{2\max}$	-9% fasting insulin
(Burgomaster et al., 2008)	6 weeks, 5 sessions/week	Healthy young adults (n = 10)	Cycling, 40-60 min @ 65% $\dot{V}O_{2\max}$	$\dot{V}O_{2\max}$; mitochondrial markers for skeletal	+9.8% $\dot{V}O_{2\max}$	↑ in mitochondrial markers for skeletal muscle and lipid

				muscle and lipid oxidation; body fat		oxidation; NSC in percentage body fat
(Dunham and Harms, 2012)	4 weeks, 3 sessions/week	Physically active, but untrained, healthy adults (n = 7)	Cycling, 45 min @ 60-70% $\dot{V}O_{2max}$	$\dot{V}O_{2max}$; maximum inspiratory pressure; time trial performance	+5.5% $\dot{V}O_{2max}$	↑ time trial performance
(Shepherd et al., 2013)	6 weeks, 5 sessions/week	Sedentary men (n = 8)	Cycling, 40-60 min @ 65% $\dot{V}O_{2max}$	$\dot{V}O_{2max}$; fat-free mass; relative fat mass	+15.6% $\dot{V}O_{2max}$	↑ fat-free mass; NSC in relative fat mass
(Warburton et al., 2004)	12 weeks, 3 sessions/week	Untrained men (n = 6)	Cycling, 30-48 min @ ~65% $\dot{V}O_{2max}$	$\dot{V}O_{2max}$; peak stroke volume; blood volume	+23% $\dot{V}O_{2max}$	↑ peak stroke volume and blood volume
(Matsuo et al., 2014)	8 weeks, 5 sessions/week	Sedentary men (n = 14)	Cycling, 40 min @ 60-65% $\dot{V}O_{2max}$	$\dot{V}O_{2max}$; left ventricular mass; stroke volume; resting HR	+10% $\dot{V}O_{2max}$	NSC in left ventricular mass; stroke volume; resting HR
HIIT						
(Dunston and Taylor, 2023)	6 weeks	Inactive, young adults (n = 10)	10 x 1 min at 80% PPO, recovery at 20% PPO	VO_{2peak} , PPO	+5.9% $\dot{V}O_{2max}$	+8.6% PPO
(Daussin et al., 2008)	8 weeks, 3 sessions/week	Sedentary adults; (n = 11) crossover design	Repeated cycles of 4 min @ VT1 followed by 1 min	$\dot{V}O_{2max}$; Q_{max} ; SV; muscle oxidative capacity; capillary density	+15% $\dot{V}O_{2max}$	Q_{max} +11%; mitochondrial oxidative capacity

			@ 90% Pmax; 4-7 cycles			+40%; capillary density +21%
(Trapp et al., 2008)	15 weeks, 3 sessions/week	Inactive, otherwise healthy women (n = 11)	Cycling, 60 reps of 8 s sprints @ 95-100% HRmax	$\dot{V}O_{2\max}$; total body mass; fat mass; insulin level	+26.4% $\dot{V}O_{2\max}$	↓ total body mass, fat mass and insulin level
(Dunham and Harms, 2012)	4 weeks, 3 sessions/week	Physically active, but untrained, healthy adults (n = 8)	Cycling, 5 x 1 min work intervals @ 90% $\dot{V}O_{2\max}$; 3 min active rest intervals	$\dot{V}O_{2\max}$; maximum inspiratory pressure; time trial performance	+9.6% $\dot{V}O_{2\max}$	↑ time trial performance and maximum inspiratory pressure
(Warburton et al., 2004)	12 weeks, 3 sessions/week	Untrained men (n = 6)	Cycling, 8-12 reps; 2 min work intervals @ 90% $\dot{V}O_{2\max}$; 2 min active rest intervals @ 40% $\dot{V}O_{2\max}$	$\dot{V}O_{2\max}$; peak stroke volume; blood volume	+22.2% $\dot{V}O_{2\max}$	↑ peak stroke volume and blood volume
(Matsuo et al., 2014)	8 weeks, 5 sessions/week	Sedentary men (n = 14)	Cycling, 3 work intervals @ 80-90% $\dot{V}O_{2\max}$; 2 min rest intervals @ 50% $\dot{V}O_{2\max}$	$\dot{V}O_{2\max}$; left ventricular mass; stroke volume; resting HR	+15.7% $\dot{V}O_{2\max}$	↑ left ventricular mass and stroke volume
SIT						
(Cocks et al., 2013)	6 weeks, 3 sessions/week	Sedentary men; (n = 8)	Cycling, 4-6 30 s Wingate sprints	$VO_{2\text{peak}}$; insulin sensitivity; capillary density	+8% $VO_{2\text{peak}}$	Insulin sensitivity index +27%; capillary density +27%

(Burgomaster et al., 2008)	6 weeks, 3 sessions/week	Healthy young adults (n = 10)	Cycling, 4-6 30 s all-out Wingate sprints	$\dot{V}O_{2\max}$; mitochondrial markers for skeletal muscle and lipid oxidation; body fat	+7.3% $\dot{V}O_{2\max}$	↑ in mitochondrial markers for skeletal muscle and lipid oxidation; NSC in percentage body fat
(Shepherd et al., 2013)	6 weeks, 3 sessions/week	Sedentary men (n = 8)	Cycling, 4-6 30 s Wingate sprints	$\dot{V}O_{2\max}$; fat-free mass; relative fat mass	+7.6% $\dot{V}O_{2\max}$	↑ in fat-free mass; NSC in relative fat mass
(Hazell et al., 2010)	2 weeks, 3 sessions/week	Healthy, young adults (n = 12)	Cycling, 4-6 30 s Wingate sprints; 4 min rest-intervals	$\dot{V}O_{2\max}$; 5 km time trial performance; peak power; average power; lean and fat mass	+9.3% $\dot{V}O_{2\max}$	+5.2% time-trial performance; +12.1% average PO; NSC in any body composition values
(Astorino et al., 2011)	3 weeks, 2 sessions/week	Recreationally active adults (n = 20)	Cycling, 4-6 30 s Wingate sprints; 4 min active recovery intervals	$\dot{V}O_{2\max}$; Wingate power and fatigue index; submaximal RER; body fat; waist-to-hop ratio	+6.3% $\dot{V}O_{2\max}$	+10.5% mean power; NSC in other outcomes
REHIT / LOW-VOLUME SIT						
(Gillen et al., 2016)	12 weeks, 3 sessions/week	Sedentary men; (n = 9)	Cycling, 3 x 20 s all-out sprints, separated by 2 min cycling @ 50 W; 10 min/session	$VO_{2\text{peak}}$; insulin sensitivity; muscle mitochondrial markers	+19% $VO_{2\text{peak}}$	Citrate synthase activity +48%; insulin sensitivity index +53%

(Leahy et al., 2022)	8 weeks, 2-4 sessions/week	Physically inactive (n = 12)	Cycling, 2 x 20 s all-out sprints; 3 min recovery intervals	$\dot{V}O_{2max}$; FFI; waist circumference; waist-to-height ratio	+12.3% $\dot{V}O_{2max}$	+13.3% FFI; NSC for other outcomes
(Nalcakan et al., 2018)	6 weeks, 3 sessions/week	Healthy, sedentary / recreationally active adults (n = 17)	Cycling, 2 x 20 s all-out sprints; 3 min active recovery intervals	$\dot{V}O_{2max}$; body mass; RPE; affect and mood; intervention acceptability	+10% $\dot{V}O_{2max}$	+1.3% Body mass
(Bostad et al., 2023)	12 weeks, 3 sessions/week	Untrained adults (n = 20)	Cycling, 3 x 20 s all-out sprints; 2 min active recovery intervals	VO_{2peak} ; Q_{max} ; estimated peak a- vO_{2diff} ; peak aerobic power; blood pressure; vascular function	+9.3% VO_{2peak}	+9.1% estimated peak a- vO_{2diff} ; +8.4% peak aerobic power; -3.5% systolic BP; NSC in other outcomes
(Aslankeser and Balci, 2017)	2 weeks, 5 sessions/week	Recreationally active young women; (n = 8)	Cycling, 2 x 20 s all-out sprints; 4 min active recovery intervals	$\dot{V}O_{2max}$; Wingate peak and mean power; substrate oxidation; maximal fat oxidation; body mass	+9.1% $\dot{V}O_{2max}$	+25.4% Wingate peak power; +7.5% mean power; +12.4% CHO oxidation; NSC in other outcomes

Percentage changes refer to changes from pre-to post-intervention. ↑, increase; ↓, decrease; NSC, no significant change; $\dot{V}O_{2max}$, maximal oxygen uptake; VO_{2peak} , peak oxygen uptake; HRmax, maximal heart rate; PPO, peak power output; PO, power output; Pmax, maximal power output; Q_{max} , maximal cardiac output; SV, stroke volume; VT1, first ventilatory threshold; n, sample size. Changes within a group do not necessarily indicate a significant difference between training groups.

However, despite often being described as time-efficient, the classic SIT protocol is not especially economical in practice. When warm-up and recovery intervals are included, the weekly time commitment is approximately 90 minutes (Vollaard and Metcalfe, 2017). Since both time-efficiency and exercise intensity influence affective responses and participation, this remains a significant limitation. As Ekkekakis et al. (2011) note, an exercise prescription may be physiologically effective, but its public health relevance is questionable if very few want to follow it. Importantly, Vollaard and Metcalfe (2017) observed that none of the studies using the classic SIT protocol provide a specific justification for their chosen exercise intervention parameters. This suggests a need to investigate shorter and less demanding SIT protocols. Such work may be achieved by modifying key variables, including sprint duration, intensity, number of sprint repetitions, and training frequency. Collectively, these findings indicate that although HIIT and SIT can produce meaningful physiological benefits, important questions remain regarding their practicality, tolerability, and public health relevance, particularly in insufficiently active populations.

REHIT

HIIT and SIT have well-established health benefits. However, their use as exercise interventions for physically inactive individuals outside laboratory setting has been met with scepticism. This concern largely reflects the protocol-specific drawbacks discussed above (Metcalf and Vollaard, 2024). In response, researchers began to explore modified approaches that might retain efficacy while improving feasibility. One such approach was introduced by Metcalfe et al. (2012), who reduced the sprint volume of the ‘classic’ SIT protocol and developed the low-volume all-out sprint interval protocol, Reduced Exertion High Intensity Interval Training (REHIT). Each session involved 10 minutes of unloaded cycling, interspersed with 2×20 -sec all-out sprints against a resistance equivalent to 7.5% of body weight. Despite the low exercise volume, the intervention increased $\dot{V}O_{2\max}$ by 15% in men and 12% in women after six weeks (Metcalf et al., 2012).

Since then, numerous studies have investigated the beneficial effects of REHIT on other health parameters and found significant positive effects on blood pressure (Cuddy et al., 2019, Ruffino et al., 2017, Bostad et al., 2023) and insulin sensitivity (Gillen et al., 2014, Gillen et al., 2016, Metcalfe et al., 2012, Ruffino et al., 2017), although there is considerable variability in response (Metcalf et al., 2016). The most striking point here is that REHIT interventions elicit these reported health benefits with around 80% less time commitment than MICT (Ruffino et al., 2017).

The mechanisms responsible for providing sufficient stimulus to mediate the training adaptations that lead to increases in $\dot{V}O_{2\max}$ after only ~40 s of supramaximal sprint volume per session are still relatively unknown. Training adaptations have been reported to result from disturbances in physiological homeostasis (Egan and Zierath, 2013). Metcalfe and Vollaard (2024) describe multiple ways in which supramaximal exercise induces rapid and pronounced metabolic, cardiovascular, and respiratory disruption. For example, a single 30-second all-out sprint can reduce intramuscular ATP by ~50%, with corresponding significant increases in intramuscular ADP, AMP, lactate, and glycolytic intermediates (Esbjörnsson-Liljedahl et al., 2002, Esbjörnsson-Liljedahl et al., 1999, Gibala, 2009, Metcalfe et al., 2015, Parolin et al., 1999). The rapid utilisation of phosphocreatine and glycogen during the initial seconds of supramaximal exercise creates a substantial oxygen deficit, driving $\dot{V}O_2$ towards maximal values during repeated sprint exercise and the subsequent recovery periods, this results in a markedly greater excess post-exercise oxygen consumption than that observed following 30 minutes of MICT (Metcalf and Vollaard, 2024, Metcalfe et al., 2015).

Furthermore, blood flow to the active musculature can increase by up to ~100-fold (Hawley et al., 2014). During supramaximal exercise, near-infrared spectroscopy studies demonstrate substantial reductions in muscle oxygenation, reflecting a dynamic mismatch between oxygen delivery and mitochondrial oxygen utilisation as metabolic demand rapidly increases (Bhambhani, 2004, Bhambhani et al., 2001, Metcalfe and Vollaard, 2024). The accompanying rise in heart rate, cardiac output, and peripheral hyperaemia elevates mean arterial pressure and endothelial stress (Hawley et al., 2014). The recovery following a sprint is characterised by a pronounced reduction in plasma volume, far greater than that observed after MICT, driven by osmotic fluid shifts into muscle

following the accumulation of glycolytic intermediates (Esbjörnsson et al., 2012, Mandić et al., 2021, Metcalfe et al., 2015, Metcalfe and Vollaard, 2021).

Collectively, the severity of these acute disturbances associated with SIT activates various signalling kinases, which subsequently activate transcriptional co-activators, leading to increased gene expression and protein synthesis (Egan and Sharples, 2023, Egan and Zierath, 2013, Metcalfe and Vollaard, 2024, Perry et al., 2010). The repeated accumulation of these molecular responses is thought to underpin mitochondrial, muscular, and cardiovascular adaptations driving improvements in $\dot{V}O_2\text{max}$ (Metcalfe and Vollaard, 2024). Although the exact mechanisms by which REHIT improves $\dot{V}O_2\text{max}$ are unknown, recent research has provided evidence that increased blood volume plays a major role (Mandic et al., 2023, Mandic et al., 2022, Metcalfe and Vollaard, 2024). At the same time, mitochondrial genesis may also contribute as a peripheral factor, since a 15-fold increase in skeletal muscle PGC-1 α gene expression has been observed following a single REHIT session (Metcalfe et al., 2015), which is responsible for stimulating mitochondrial biogenesis (Burgomaster et al., 2008, Koulmann and Bigard, 2006).

REHIT – Sprint Volume

Over the past decade, increased research has provided further support for shorter, simpler SIT protocols through modifications of one or more key training parameters. Logically, the number of sprint repetitions is the most important parameter, as it greatly influences session duration (Metcalfe and Vollaard, 2024). For example, reducing the number of sprint repetitions directly reduces the volume of supramaximal exercise performed and may also substantially shorten overall session duration, depending on the recovery period prescribed between sprints (typically 4 minutes). Additionally, sprint repetitions have been shown to be a primary factor influencing affective change during SIT, with affect decreasing proportionally with each additional sprint (Metcalfe et al., 2022). **Figure 4** shows that longer sprints cause a steeper decline in affective valence with each extra sprint, whereas shorter sprints result in a more gradual decline, further highlighting the interaction between sprint repetitions and duration.

Furthermore, Vollaard and Metcalfe (2017) note that none of the studies employing the traditional SIT protocol explain why they use 4-6 $\times$ 30-s all-out sprints, which served as the basis for their meta-analysis examining how the number of sprint repetitions influences changes in $\dot{V}O_2\text{max}$ (Vollaard et al., 2017). Their review, analysing 34 SIT studies (n=418), concluded that improvements in $\dot{V}O_2\text{max}$ are not diminished when training sessions involve fewer sprint repetitions than those in the classic 4-6 $\times$ 30-s protocol, and there appears to be no dose-response relationship with increasing sprint repetitions. However, relatively few studies used fewer than six sprints per session; for example, only 2 used 2 sprints. Since then, the number of studies with fewer sprints has increased significantly, with research reporting clinically meaningful improvements in $\dot{V}O_2\text{max}$ using 2 $\times$ 20-s all-out sprints (Cuddy et al., 2019, Haines et al., 2021, Leahy et al., 2022, Metcalfe et al., 2020, Nalcakan et al., 2018, Thomas et al., 2020), 3 $\times$ 20-s all-out sprints (Bostad et al., 2021, Bostad et al., 2023, Little et al., 2019, Opazo-Diaz et al., 2023), or 3 $\times$ 30-s all-out sprints

(Bostad et al., 2023, Mandic et al., 2023, Mandic et al., 2022, O'Driscoll et al., 2018), which adds further support for the use of fewer sprint repetitions in training interventions involving physically inactive populations.

Sprint duration is another important parameter that has been reduced as part of the REHIT protocol to address the hypothesised negative affective valence linked with SIT (Biddle and Batterham, 2015, Hardcastle et al., 2014). There are discrepancies about how much the volume can be reduced while still maintaining sufficient work to trigger physiological adaptations that contribute to clinically meaningful health improvements. For instance, some studies have demonstrated that reducing sprint duration to 10 seconds is sufficient to elicit clinically meaningful improvements in $\dot{V}O_2\text{max}$ (+8.5-14.7%) (Allen et al., 2017, Camacho-Cardenosa et al., 2017, Hazell et al., 2010, Olek et al., 2018). However, this finding has not been replicated consistently, with several studies reporting little to no improvement (- 1.7% to +3.9%) following 10-second sprint SIT protocols (Hellsten-Westing et al., 1993, Nalcakan et al., 2018, Skleryk et al., 2013).

The reasons for these discrepant findings remain uncertain. Skleryk et al. (2013) reported a 1.7% decrease in $\dot{V}O_2\text{max}$ using a similar protocol but with a greater number of sprint repetitions (8-12); however, this study used a sprint resistance of 0.05 kg per kg of body mass, which is half of that used by Hazell et al. (2010). The authors suggest that the lack of meaningful changes in key health markers may be due to lower power output during each sprint, the brief sprint duration (10 seconds), and the short intervention period (2 weeks). Isolating the independent effect of any specific parameter of interest on $\dot{V}O_2\text{max}$ adaptations is challenging due to variations in other aspects of the protocols -such as sprint duration, repetitions, intervention length, training frequency, sprint resistance, and participant characteristics.

Nalcakan et al. (2018) exemplifies how slight differences in training volume can have a significant influence on $\dot{V}O_2\text{max}$ improvements. They demonstrated that 18 sessions over 6 weeks involving 2×20 -second sprints improved $\dot{V}O_2\text{max}$ by 9.7% in sedentary/recreationally active individuals, consistent with similar REHIT research using the same format (Cuddy et al., 2019, Haines et al., 2021, Metcalfe et al., 2012, Metcalfe et al., 2016, Thomas et al., 2020). Conversely, the further reduced-volume condition involving 2×10 -second sprints produced significantly attenuated improvements of 3.5%. Collectively, these findings suggest that reducing sprint volume beyond a certain threshold may compromise adaptation. This notion is further supported by two studies (Songsorn et al., 2016, Songsorn et al., 2017) which found that a single 20-second sprint was insufficient to meaningfully increase $\dot{V}O_2\text{max}$, suggesting that a threshold in sprint duration and/or number is needed to achieve clinically relevant improvements. Although the reasons why certain combinations (1×20 seconds vs. 2×10 seconds vs. 4×10 -sec) have led to varying levels of efficacy remain unclear (Nalcakan et al., 2018, Vollaard and Metcalfe, 2017). Overall, the available evidence suggests that substantial reductions in sprint volume do not necessarily attenuate improvements in $\dot{V}O_2\text{max}$. However, the minimum effective sprint volume remains uncertain, with

evidence indicating that reducing the stimulus below a threshold (e.g., 1×20 s sprint or 2×10 s sprints) may compromise adaptation.

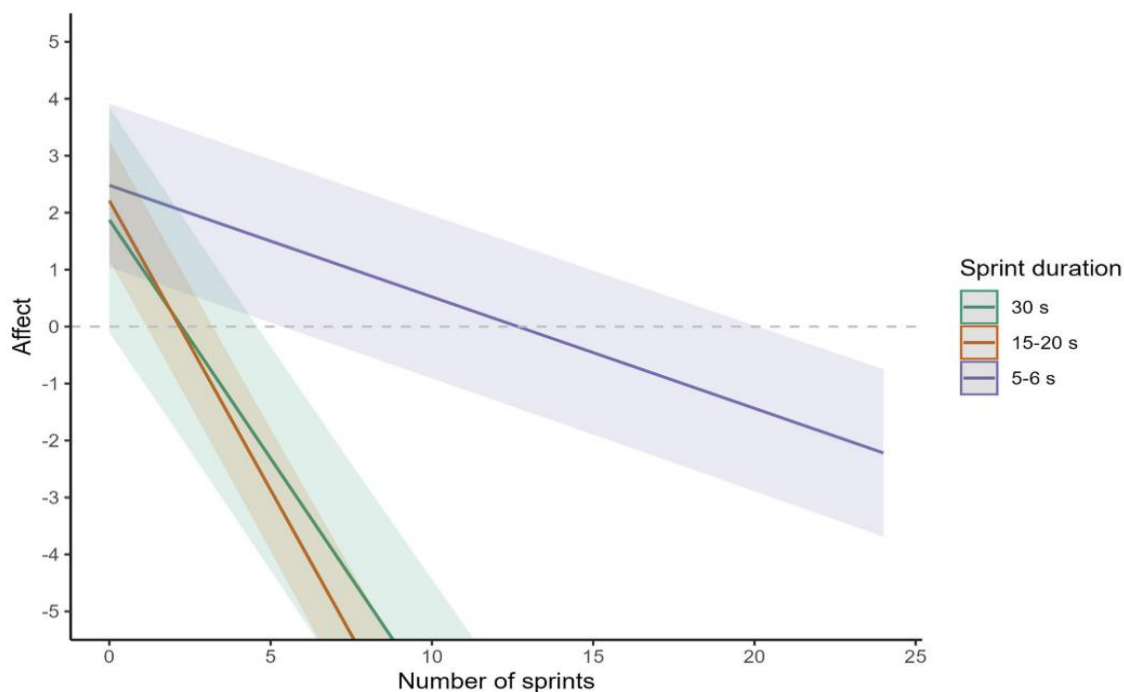


Figure 1.4 - Meta-analysis of the decrease in affective valence during SIT using different sprint durations. The solid line represents the point estimate, whilst the shaded area represents the Bonferroni-corrected 95% confidence limits. The purple line and shading are for 5–6 s sprints, the red line and shading are for 15–20 s sprints, and the green line and shading are for 30 s sprints (Metcalf et al., 2022).

REHIT – Additional training parameters

While a substantial proportion of REHIT and broader SIT research has focused on modifying sprint volume within a session, the influence of other training parameters, including recovery duration, training frequency and intervention duration, has received comparatively little attention. Yet these variables are likely to play a meaningful role in the magnitude of response and future adherence. Research investigating how training frequency influences improvements in $\dot{V}O_{2\max}$ in response to REHIT/SIT is limited (Dalleck et al., 2010, Lenk et al., 2025, Thomas et al., 2020). Typically, three sessions per week is the training frequency most commonly selected in SIT/REHIT studies, despite little justification for its use (Vollaard and Metcalfe, 2017). Thomas et al. (2020) noted the absence of a rationale to support this frequency as the standard and therefore compared the effects of performing 2, 3, or 4 REHIT sessions per week (2×20 -s sprints) over six weeks. The finding that two sessions per week elicited the largest improvement in $\dot{V}O_{2\max}$ (+10.2%) and that increasing the weekly training frequency to three (+8.1%) or four sessions (+7.3%) did not provide additional benefits was unexpected and has important implications for reducing the total weekly time commitment from 30 minutes to just 20 minutes per week without sacrificing the health benefits. Most studies examining reduced training frequency use a work-matched design (Manthou et al.,

2015, Meyer et al., 2006, Tripp et al., 2025). In these designs, the low-frequency group completes more work per session, so their total weekly volume matches that of the high-frequency group. However, this approach does not address the question relevant to this thesis, for example, finding the minimal training dose, highlighting an area for future research.

Another underexplored parameter is intervention duration. The studies that have implemented the longest intervention duration (12 weeks) using low-volume SIT (3×20 -s) have reported the greatest mean increases in $\dot{V}O_2\text{max}$ (Bostad et al., 2021, Bostad et al., 2023, Gillen et al., 2016). However, some studies have reported clinically meaningful improvements in $\dot{V}O_2\text{max}$ after just 2 weeks (Aslankeser and Balci, 2017, de Sousa et al., 2018, Hazell et al., 2010). A possible explanation for this is that the mechanisms governing inter-individual variability in responsiveness to training – primarily genetics (Bouchard et al., 1999) – may require longer periods to manifest in some individuals. Evidence from Bonafiglia et al. (2016) suggests that the physiological pathways that drive differences between high- and low-responders remain unknown and may vary substantially between individuals.

Recovery duration represents another potentially important training parameter that is independent of sprint volume. The recovery interval between sprints may influence both the ability to reproduce maximal power output and the relative contribution of aerobic and anaerobic metabolism during subsequent sprints. For sprints lasting 20-30 s, recovery periods commonly range from approximately 200-240 s, corresponding to work-to-recovery ratios of approximately 1:8 to 1:12. Lloyd Jones et al. (2019) proposed that shorter recovery periods may impose greater stress on the aerobic energy system and therefore potentially enhance $\dot{V}O_2\text{max}$ adaptation. However, the available evidence is inconsistent. In their study, participants performing 6×10 s sprints separated by 2 min of recovery demonstrated a non-significant increase in $\dot{V}O_2\text{max}$ (+3.8%), whereas groups completing either 6 x 30 s sprints or 6×10 s sprints with 4 min recovery improved $\dot{V}O_2\text{max}$ by 9.3% and 9.2%, respectively. The attenuated response with shorter recovery may reflect incomplete ATP-PCr resynthesis, reducing the power that can be generated during subsequent sprints (Lloyd Jones et al., 2019, Mendez-Villanueva et al., 2012). Consequently, the reduced work performed during subsequent sprints may diminish the metabolic stress proposed to underpin peripheral adaptations (Burgomaster et al., 2005). Conversely, A similar pattern was observed by Hazell et al. (2010), who reported that reducing recovery from 4 to 2 min during repeated 10 s sprints attenuated improvements in $\dot{V}O_2\text{max}$ from 8.5% to 3.9%.

In contrast, Olek et al. (2018) reported a 14.7% increase in $\dot{V}O_2\text{max}$ despite employing an even shorter 60 s recovery interval within an otherwise similar 10 s sprint protocol. However, this apparent discrepancy should be interpreted cautiously, as the studies differed in other important training parameters. Participants in Olek et al. (2018) cycled against a resistance equivalent to 7.5% of body mass, compared with 10% in Hazell et al. (2010), which may have enabled a higher average power output to be maintained across repeated sprints. Furthermore, participants in Olek et al. (2018) had a substantially lower baseline $\dot{V}O_2\text{max}$ (36.4 ± 1.4 vs. 47.0 ± 6.7 mL·kg⁻¹·min⁻¹),

potentially providing greater scope for improvement. Collectively, these findings suggest that recovery duration may influence training adaptation, but its independent effect remains difficult to isolate because alterations in recovery are frequently accompanied by differences in participant characteristics and other aspects of the training prescription.

Interindividual Variability

Individual variability in responsiveness to exercise

Despite the well-established efficacy of exercise to improve $\dot{V}O_{2\max}$ at the group level, considerable interindividual variability exists in the magnitude of adaptation following a standardised training intervention. Rather than representing distinct groups of ‘responders’ and ‘non-responders’, current evidence suggests that individuals exhibit a continuum of responsiveness to a given exercise stimulus, ranging from large improvements to little or no measurable change (Metcalf and Vollaard, 2021, Williams et al., 2019, Ross et al., 2019). This issue has attracted research attention since early studies recognised high variability between individuals in response to standardised aerobic exercise (Bouchard, 1983, Bouchard et al., 1999, Lortie et al., 1984).

Historically, individuals who failed to exceed a predefined threshold of improvement have frequently been classified as “non-responders”. However, understanding the true incidence and mechanisms underlying interindividual variability in responsiveness has been hindered by inconsistencies in how studies define and classify individuals as “non-responders”. As Ross et al. (2019) note, many different definitions are used to classify individuals as exhibiting little or no measurable responsiveness in the literature, ranging from no absolute improvement ‘ ≤ 0 L/min’ (Sisson et al., 2009), to relative change cut-offs ‘ $< 5\% \Delta$ ’ (Pandey et al., 2015), to statistical criteria such as ‘ $< \text{within-subject coefficient of variation (CV)} < 5.6\%$ ’ (Scharhag-Rosenberger et al., 2012), ‘ < 1 or < 2 technical errors (TE)’ (Gurd et al., 2016, Ross et al., 2015), or changes failing to exceed a minimal clinically significant difference ‘ $< \text{minimal clinically important difference (3.5 mL/kg/min)} \text{ minus } 1 \times \text{TE}$ ’ (Williams et al., 2019).

The lack of a standardised definition makes cross-study comparisons difficult and increases the likelihood that individuals with small but genuine physiological adaptations are misclassified as “non-responders”. Importantly, classifying individuals as “non-responders” based on overly conservative thresholds may be misleading, particularly given normal biological variability and measurement error. Furthermore, such terminology may discourage future exercise participation, despite evidence that modifying exercise dose, modality or intervention duration can often elicit meaningful physiological adaptation (Ross et al., 2019, Metcalf and Vollaard, 2021).

Advances in molecular technologies have started to uncover the basis for this variability. The first genome-wide association study (Sarzynski et al., 2017) identified 21 single-nucleotide polymorphisms (SNPs) that explained 49% of the variance in $\dot{V}O_{2\max}$ trainability. The authors showed that individuals with more favourable alleles at each SNP experienced a greater increase in O_2 uptake; for example, those with ≥ 19 favourable alleles gained an average of $383 \text{ mL } O_2 \text{ min}^{-1}$ more than those with ≤ 9 favourable alleles (Sarzynski et al., 2017).

However, exhibiting little or no measurable improvement following a specific MICT exercise protocol, such as the one used in the HERITAGE project (30-50 min/day, 3 x weekly, 55-75% HRmax, 20 weeks), does not necessarily indicate that an individual lacks the capacity to improve

$\dot{V}O_{2\max}$ in response to exercise. Rather, responsiveness may depend on the specific exercise stimulus prescribed. Considering this, researchers have questioned whether individuals initially classified as “non-responders” simply received an insufficient exercise stimulus rather than lacking the capacity to adapt (Montero and Lundby, 2017). For example, in a study of 78 healthy adults, Montero and Lundby (2017) demonstrated that progressively increasing weekly endurance-training volume reduced the proportion of participants classified as “non-responders” (60 min, 81%; 120 min, 47%; 180 min, 50%; 240 min, 18%; 300 min, 0%), whereby those that failed to respond after the first 6-week training period were ‘rescued’ following an extra 6 weeks of endurance training with two additional sessions per week (Montero and Lundby, 2017). These findings are supported by larger exercise intervention studies, including Ross et al. (2015) ($n = 121$) and Sisson et al. (2009) ($n = 310$), both of which reported fewer participants being classified as “non-responders” with greater exercise volumes. Although these findings are broadly consistent, direct comparisons remain difficult because studies differ substantially in exercise prescription and in the criteria used to classify individuals as “non-responders” (Metcalf and Vollaard, 2021).

Nevertheless, a particularly concerning statistic is that 40-50% of participants across the aforementioned endurance-training studies (Montero and Lundby, 2017, Ross et al., 2015, Sisson et al., 2009) were classified as non-responders despite completing 150-200 min of weekly MICT which would suggest that current guidelines (World Health, 2020) may be insufficient for providing meaningful $\dot{V}O_{2\max}$ improvements in a large proportion of the population.

Although HIIT and SIT exercise protocols have demonstrated greater overall improvements in $\dot{V}O_{2\max}$ than MICT (Poon et al., 2021), it could be hypothesised that increasing exercise intensity would eliminate the occurrence of individuals demonstrating little or no measurable improvement in $\dot{V}O_{2\max}$. Evidence does support a reduction in the proportion of individuals classified as “non-responders” with increasing exercise intensity (Ross et al., 2015, Weatherwax et al., 2019), including the largest pooled analysis to date by Williams et al. (2019) (HIT/SIT pooled $n = 677$). However, there is also evidence, albeit from several smaller intervention studies, that demonstrate considerable heterogeneity in responsiveness following exercise performed within the HIIT and SIT intensity domains (Astorino et al., 2017, Astorino and Schubert, 2014, Bonafiglia et al., 2016, Bonet et al., 2020, Gurd et al., 2016), and more recently in response to REHIT (Metcalf and Vollaard, 2021) indicating that increasing exercise intensity alone is insufficient to eliminate interindividual variability in responsiveness.

Utilising the same $<1.8 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ threshold applied in the most extensive pooled HIIT/SIT analysis (Williams et al., 2019), Metcalf and Vollaard (2021) observed that the incidence of participants classified as “non-responders” following REHIT (38%; $n=117$) was similar to that reported for HIIT (35%; $n=299$) and lower than SIT (52%; $n=116$). However, it is essential to note that none of the studies categorised as SIT in these analyses used true all-out, supramaximal sprint intensities, meaning this SIT estimate may not accurately represent non-response in classical SIT protocols discussed in this review of the literature.

Crucially, 76% (228/299) of participants in the HIIT category of the Williams *et al.* (2019) analysis completed interventions lasting ≥ 12 weeks, with 77 individuals training for ≥ 1 year. In contrast, all REHIT interventions included in Metcalfe and Vollaard (2021) analysis lasted only 6 weeks and required just ~ 10 minutes per session. Despite requiring only ~ 10 minutes per session over six weeks, REHIT resulted in a proportion of participants classified as “non-responders” comparable to that observed following HIIT. This finding underscores the potential of REHIT as a highly time-efficient alternative and suggests that low responsiveness cannot be explained solely by an insufficient exercise dose.

Longer REHIT interventions appear capable of eliciting substantially larger improvements in $\dot{V}O_2\text{max}$. The greatest mean increases reported using low-volume SIT protocol (3×20 s sprints) have been observed in 12-week interventions, including +17.3% (Gillen *et al.*, 2016) and +20.9% (Bostad *et al.*, 2021). By contrast, Little *et al.* (2019), reported a smaller improvement (6.2%) using an otherwise comparable protocol over six weeks. These findings raise the possibility that the mechanisms governing inter-individual variability in response to REHIT and, potentially, high-intensity modalities require more prolonged stimulus exposure to be fully activated. However, intervention duration alone cannot explain the variability in training response. Despite employing identical exercise prescriptions (3×20 -s ‘all-out’ sprints; 7.5% of body weight; 2-min active recovery at 50 W; 3 sessions/week; 12 weeks), Bostad *et al.* (2023) and Bostad *et al.* (2021) reported markedly different improvements in $\dot{V}O_2\text{max}$ (20.9% versus 10%). Furthermore, while Bostad *et al.* (2021) observed significant increases in Q_{max} , the later study found no change despite significant improvements in aerobic fitness. The authors therefore suggest that increased skeletal muscle oxygen extraction and/or diffusing capacity are important contributors to SIT-induced increases in $\dot{V}O_2\text{peak}$ (Bostad *et al.*, 2023). However, the reason for the discrepant results between studies is unclear, as participant characteristics were also similar. Still, it may relate to interindividual differences in training responsiveness that are not explicitly linked to biological sex, as no significant sex-related differences were found (Bostad *et al.*, 2023).

This aligns with the suggestion that variability in gene expression patterns within the signalling pathways that drive central and peripheral adaptations may mediate responsiveness to specific training stimuli (Timmons *et al.*, 2010). Although associations between genetic markers and training response have been reported (Bouchard *et al.*, 2011, Timmons *et al.*, 2010), their utility in prescribing personalised exercise interventions remains unknown (Bonafiglia *et al.*, 2016).

Consequently, longer-duration REHIT interventions may help determine whether individuals demonstrating little or no measurable improvement following short interventions simply require a greater training stimulus or longer exposure to express meaningful physiological adaptation. Moreover, manipulating exercise dose within a given modality does not universally eliminate interindividual variability in responsiveness. For example, as discussed earlier, Vollaard *et al.* (2017) provided evidence showing that reducing the number of sprint repetitions in SIT does not attenuate improvements in $\dot{V}O_2\text{max}$, and that performing additional sprints does not, on average,

elicit additional gains. This supports the point that increasing the dose of exercise, through sprint repetitions in this example, does not lead to an additional increase in $\dot{V}O_2\text{max}$ response. The persistence of substantial interindividual variability in responsiveness across modalities - MICT, HIIT, SIT, and REHIT - and across varying exercise doses highlights the complexity of the underlying biological mechanisms. Although it remains possible that genuine biological non-responsiveness may exist in a small proportion of individuals, current evidence increasingly supports the concept of a continuum of responsiveness rather than discrete responder and non-responder phenotypes. This emphasises the need for a deeper mechanistic understanding of the pathways that mediate exercise-induced adaptations and how different training stimuli interact with these pathways (MacInnis and Gibala, 2017).

Myokine discovery & the ‘myokinome’

Researchers have spent decades elucidating the mechanisms by which the energy-demanding work of skeletal muscle can affect the entire human body, leading to meaningful health benefits (Hoffmann and Weigert, 2017). The earliest work to uncover the secretory function of skeletal muscle was by Goldstein (1961), who suggested that exercise stimulates the production of humoral substances capable of enhancing glucose utilisation in dogs at rest following electrically induced muscle contractions. Later, researchers identified what was then known as a cytokine: interleukin-6 (IL-6), produced and released by contracting muscles, which appeared to have metabolic effects (Ostrowski et al., 1998). This was considered a breakthrough, as it shed light on skeletal muscle being a cytokine-producing organ in response to exercise (Pedersen, 2011). Steensberg et al. (2000) then confirmed that skeletal muscle also acts as an endocrine organ, as they discovered that circulating IL-6 was significantly increased during prolonged single-limb exercise, potentially influencing metabolism in tissues and organs elsewhere (Pedersen, 2011).

However, the extent to which the endocrine actions of muscle-derived factors contribute to the health benefits of exercise in humans remains unclear (Hoffmann and Weigert, 2017). In many cases, it remains unclear whether increases in myokine mRNA and protein expression in skeletal muscle translate into elevated circulating concentrations (Geiger et al., 2013).

Following their discovery, Pedersen and Febbraio (2008) suggested that, as the field advances, cytokines and other peptides produced, expressed, and released by muscle fibres that exert autocrine, paracrine, or endocrine effects should be classified and referred to as ‘myokines’ (Pedersen, 2011). So far, myokines have been shown to facilitate communication between muscles and various organs, such as the brain (Hutton et al., 2015, Nakajima et al., 2010), adipose tissue (Tanimura et al., 2022), bones (Shahabi et al., 2021), liver (Chan et al., 2024), heart (Ho et al., 2018) and pancreas (Kostka et al., 2024, Pedersen and Hojman, 2012). Additionally, muscle-to-muscle myokine ‘crosstalk’ was demonstrated by Catoire et al. (2012), who showed that one-legged endurance exercise induced changes in gene expression not only in the active leg but also in the inactive leg.

The discovery of endogenous factors released from skeletal muscle as hormone-like mediators of the preventive and therapeutic effects of exercise has led to proteomic and transcriptomic profiling approaches to characterise the skeletal muscle secretome and identify novel myokines (Hoffmann and Weigert, 2017). Efforts have been made to identify all myokines that are secreted from skeletal muscle, along with details of their specific functions (Catoire et al., 2014, Hartwig et al., 2014, Norheim et al., 2011, Pourteymour et al., 2017, Raschke et al., 2013), giving the term “myokinome”, which now contains information on over 650 myokines (Khan and Ghafoor, 2019, Pang et al., 2021). However, much work remains to determine each myokine’s specific function(s), as only parts have been well-characterised so far (Florin et al., 2020). The benefits of mapping and understanding the myokinome in full may help reveal which myokines are dysregulated in disease states, for example there are people with diabetes that are ‘exercise resistant’ referring to the fact

that they don't benefit from the metabolic improvements associated with aerobic exercise (Garneau et al., 2024) which could then lead to targeted treatments (Di Raimondo et al., 2017, Stephens et al., 2015) Moreover, it could uncover mechanisms relating to the response variability to exercise and potentially lead to the development of tailored exercise interventions for the improvement of $\dot{V}O_2\text{max}$ in low- or non-responders to exercise and, therefore, improve overall health (Noone et al., 2024).

Myokine response to exercise

Of the myokines that are better understood, many show consistent regulation at both transcriptional and protein levels in response to acute and chronic exercise, and these changes have been associated with improvements in skeletal muscle insulin sensitivity and mitochondrial function (Garneau et al., 2024). For example, exercise-induced myokines such as IL-6, IL-10, IL-13, IL-15, IL-18, brain-derived neurotrophic factor (BDNF), fibroblast growth factor-21 (FGF21), and secreted protein acidic and rich in cysteine (SPARC) exert essential autocrine and paracrine actions within skeletal muscle, where they are known to contribute to enhancing mitochondrial biogenesis, glucose uptake, and insulin sensitivity, (Almendro et al., 2006, Busquets et al., 2006, Camporez et al., 2013, Carey et al., 2006, Darkhal et al., 2015, Garneau et al., 2024, Jiang et al., 2013, Petersen et al., 2005, Song et al., 2010, Yamanaka et al., 2007) and a large portion of these effects are mediated through activation of the AMPK pathway, a central metabolic sensor upregulated by muscle contraction (Mounier et al., 2015).

Plasma concentration of IL-6 has been shown to increase exponentially with the intensity and duration of exercise (Ostrowski et al., 2001, Pedersen and Febbraio, 2008). However, there is substantial heterogeneity in the responses of other myokines to exercise; research suggests they don't all exhibit a uniform dose-response pattern. For example, Little et al. (2018) state that myokine release is highly dependent on exercise modality and intensity, based on their work in rats, which shows a greater overlap in myokine profiles between a single bout of endurance exercise and chronic wheel running than between an exhaustive sprint bout and either condition. Furthermore, BDNF has been shown to be significantly elevated in blood plasma following high-intensity exercise (Dinoff et al., 2017, Szuhany et al., 2015) but not after endurance exercise (Catoire et al., 2014). Contrastingly, plasma SPARC concentration has been shown to be significantly increased following acute endurance exercise (50-70% $\dot{V}O_2\text{max}$) (Bettariga et al., 2024), but not after acute SIT exercise (Songsorn et al., 2017).

There is also evidence of variability in myokine response with intervention duration: Catoire et al. (2014) found 86 myokines upregulated in skeletal muscle in response to acute endurance exercise and 69 in response to chronic endurance exercise. Interestingly, only a very minor overlap was observed in the secretome analyses of acute and exercise training (Catoire et al., 2014).

Gaps in the literature

Chapter 1 has highlighted that REHIT is a genuinely time-efficient exercise protocol that has been shown to elicit health benefits similar to those of MICT, HIIT, and the classic SIT protocol. Over the last decade, researchers have sought to establish an optimal REHIT dose that maximises efficiency without sacrificing the protocol's positive health benefits. For example, 2×20 s sprints are effective at improving $\dot{V}O_2\text{max}$ (Metcalf et al., 2012), but 1 x 20 s sprint (Songsorn et al., 2016, Songsorn et al., 2017) and 2×10 s have been shown to attenuate improvements in $\dot{V}O_2\text{max}$ (Nalcakan et al., 2018). Thomas et al. (2020) found no differences in $\dot{V}O_2\text{max}$ improvements between performing REHIT two, three, or four times per week (2×20 s all-out sprints), suggesting that training frequency could potentially be reduced even further without diminishing positive outcomes. However, no study has directly compared reducing REHIT training frequency to a single weekly session, which forms the basis of **Chapter 3** in the current thesis.

Similarly, Vollaard et al. (2017) highlighted that the number of sprint repetitions in SIT protocols may not be warranted, as they may be higher than what is required to elicit meaningful health improvements in physically inactive populations. Their meta-analysis suggests that reducing the number of sprint repetitions does not attenuate the training-induced changes in $\dot{V}O_2\text{max}$, and that performing more sprints does not provide additional benefits to these changes (Vollaard et al., 2017). However, the authors noted limitations related to the small number of studies that used <4 sprints for analysis; for example, only two studies included two sprints. Furthermore, the use of magnitude-based inference has been criticised by statisticians for a lack of sound mathematical foundation, high type I error rates, and incorrect interpretation of frequentist statistics (Sainani et al., 2019), which means the reported results may not truly reflect the effects. Since its publication, research on low-volume SIT has increased substantially, thereby expanding the pool of studies eligible for analysis and providing the rationale for **Chapter 2** in the current thesis.

Despite extensive knowledge of the training adaptations that underpin improvements in $\dot{V}O_2\text{max}$ following standardised exercise interventions, the specific mechanisms that drive these adaptations remain poorly understood. Emerging evidence suggests a potential role for myokines in mediating changes in $\dot{V}O_2\text{max}$, as they are involved in ‘crosstalk’ between muscles and other organs (Severinsen and Pedersen, 2020). Previous work on the topic found that 13 genes were expressed significantly higher in the training-response transcriptome mapped by Keller et al. (2011) and that these overlapped with 13 myokines that were highly regulated in a separate training group (Catoire et al., 2014). It is plausible that the repeated release of exercise-induced myokines and their downstream signalling cumulatively contribute to training adaptations (Leuchtmann et al., 2021). Furthermore, baseline circulating levels of these specific myokines, which are thought to be linked to $\dot{V}O_2\text{max}$ -enhancing mechanisms, may differ between high- and low-responders to exercise, potentially explaining some of the variability in training-induced improvements in $\dot{V}O_2\text{max}$. This gap in the literature warrants further investigation and provides the rationale for **Chapter 4** in the current thesis.

Aims and Objectives

The aims and objectives of the current thesis are to contribute to the evidence base for identifying the minimal dose of exercise in the context of low-volume SIT targeting the physically inactive population.

The present thesis aims to address the gaps in the literature by completing the following:

1. Update the existing evidence by meta-analysing studies published from May 2016 onward and integrating these with the data of the previous meta-analysis, using a Bayesian approach to reassess whether reducing sprint repetitions in a SIT session influences changes in $\dot{V}O_{2\max}$.
2. Investigate whether reducing the training frequency of REHIT sessions from two weekly sessions to one weekly session attenuates the changes in $\dot{V}O_{2\max}$.
3. Elucidate whether the changes in $\dot{V}O_{2\max}$ with training are mediated by the release of specific myokines from exercising skeletal muscle.
4. Investigate differences in myokine responses between high- and low-responders to REHIT and whether these differences determine differences in $\dot{V}O_{2\max}$ response.

Chapter 2 - Updated systematic review and meta-analysis of the effect of the number of sprint repetitions in a SIT session on changes in $\dot{V}O_2\text{max}$ with training

INTRODUCTION

As outlined in Chapter 1, SIT is an effective strategy for improving $\dot{V}O_2\text{max}$ and other important cardiometabolic health outcomes such as blood pressure, blood lipids, and insulin sensitivity (Gist et al., 2014, Krusnauskas et al., 2020, Mattioni Maturana et al., 2021, Milanovic et al., 2015, Sloth et al., 2013, Weston et al., 2014) comparable to those achieved performing MICT. Despite this, the “real-world” relevance of both HIIT and SIT has been widely disputed, with SIT being the most heavily criticised (Biddle and Batterham, 2015, Hardcastle et al., 2014). Much of the scepticism regarding the real-world value of SIT is based on the “classic” SIT protocol involving 4-6×30-s all-out sprints (Burgomaster et al., 2005).

Recent evidence suggests that reducing the number and/or duration of sprints attenuates the negative affective responses associated with SIT while preserving improvements in $\dot{V}O_2\text{max}$ (Metcalf et al., 2022, Metcalfe and Vollaard, 2024). Moreover, there is some evidence that the volume of supramaximal exercise during SIT sessions can be substantially reduced while retaining the key health benefits (Metcalf and Vollaard, 2024). For example, we and others have shown that the REHIT protocols involving 2×20-s all-out sprints (Metcalf et al., 2020, Metcalfe et al., 2012, Metcalfe et al., 2016, Cuddy et al., 2019, Thomas et al., 2020, Nalcakan et al., 2018, Haines et al., 2021, Leahy et al., 2022) or 3×20-s all-out sprints (Gillen et al., 2016, Gillen et al., 2014, Opazo-Diaz et al., 2023, Bostad et al., 2021, Bostad et al., 2023, Little et al., 2019) within a 10-min low-intensity cycling session are associated with clinically meaningful improvements in $\dot{V}O_2\text{max}$.

To date, no studies investigating the effects of the classic SIT protocol have provided a specific justification for the use of 4-6×30-s all-out sprints. As time efficiency and affective responses appear to be key determinants of exercise participation, we previously advocated a shift in focus towards investigating shorter, more manageable, and tolerable SIT protocols (Vollaard and Metcalfe, 2017). Concomitantly, we conducted a meta-analysis of 34 SIT studies involving 418 participants and concluded that improvements in $\dot{V}O_2\text{max}$ were not attenuated when training sessions involved fewer sprint repetitions than those used in the classic protocol (Vollaard et al., 2017). This finding is important because reducing the number of sprint repetitions significantly reduces total training time commitment, making the exercise more time-efficient (Metcalf and Vollaard, 2024). Reducing the number of sprints also substantially attenuates the reduction in affective valence during exercise, making the exercise less unpleasant and more acceptable (Metcalf et al., 2022).

However, a limitation of the meta-analysis was the use of magnitude-based inference as the primary statistical analysis approach. Magnitude-based inference has recently been criticised by statisticians,

citing a lack of sound mathematical foundation, high Type I error rates, and incorrect interpretations of frequentist statistics (Sainani et al., 2019). A further limitation was the relatively low number of studies available that used fewer than six sprint repetitions per session; for example, only two studies used two sprint repetitions as part of the SIT protocol. However, since the publication of the original meta-analysis (Vollaard et al., 2017), research in this area has continued to grow, providing a marked increase in the number of eligible studies for analysis. Therefore, the present updated meta-analysis aimed to examine the modifying effect of the number of sprint repetitions in SIT exercise protocols on the increase in $\dot{V}O_{2\max}$ in untrained individuals, using an appropriate statistical analysis approach.

METHODS

Literature search and screening process

This study was registered on the PROSPERO database (registration number CRD42022349104) and was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). Online databases Web of Science and PubMed were searched for relevant journal articles published between 01/05/2016 and 01/09/2024. Articles from before 01/05/2016 were taken from the previous meta-analysis (Vollaard et al., 2017). The search strategy combined independent variable terms such as “Wingate”, “all-out”, “sprint” and “interval training” with dependent variable terms including “fitness”, “aerobic capacity”, “aerobic power”, “ $\dot{V}O_{2\max}$ ”, “ $\dot{V}O_{2\text{peak}}$ ”, “oxygen uptake” and “oxygen consumption”. These were combined using Boolean logic (“AND”, “OR”), giving a total of 28 possible combinations. The search strategy aimed to identify studies that used an exercise intervention in which human participants performed repeated all-out Wingate-type sprints, with a minimum intervention duration of 2 weeks, and in which $\dot{V}O_{2\max}$ was measured pre- and post-training. Studies were excluded if: 1) exercise was not all-out, sprints were <10 s, or intervention duration was <2 weeks, 2) participants involved clinical populations or athletes, 3) mean participant age was <18 years or mean baseline $\dot{V}O_{2\max}$ was >55 mL·kg⁻¹·min⁻¹, 4) the exercise intervention involved any exercise other than cycling or used SIT in conjunction with another intervention, 5) publication type was a review, letter, or commentary, or 6) the manuscript was not written in English.

After the removal of 6,599 duplicates, the titles and abstracts of 11,459 journal articles were independently screened for eligibility using systematic review software Rayyan (Ouzzani et al., 2016) by two authors (MH, NBJV) who were blinded during this part of the screening process. Full-text versions of the 337 remaining potentially eligible articles were reviewed for inclusion into the meta-analysis (**Figure 2.1**). The authors were then unblinded, and any discrepancies during the screening process were resolved through discussion. If the dispute(s) could not be resolved, a third reviewer (RM) was used to determine the final decision. The final data set of 44 studies selected for inclusion from the literature search in this study was combined with the studies compiled from a previous meta-analysis on the same topic (Vollaard et al., 2017). The previous meta-analysis

contained 34 studies from all years up to May 1, 2016, using an identical search strategy. This resulted in a combined data set of 78 studies for the updated systematic review and meta-analysis.

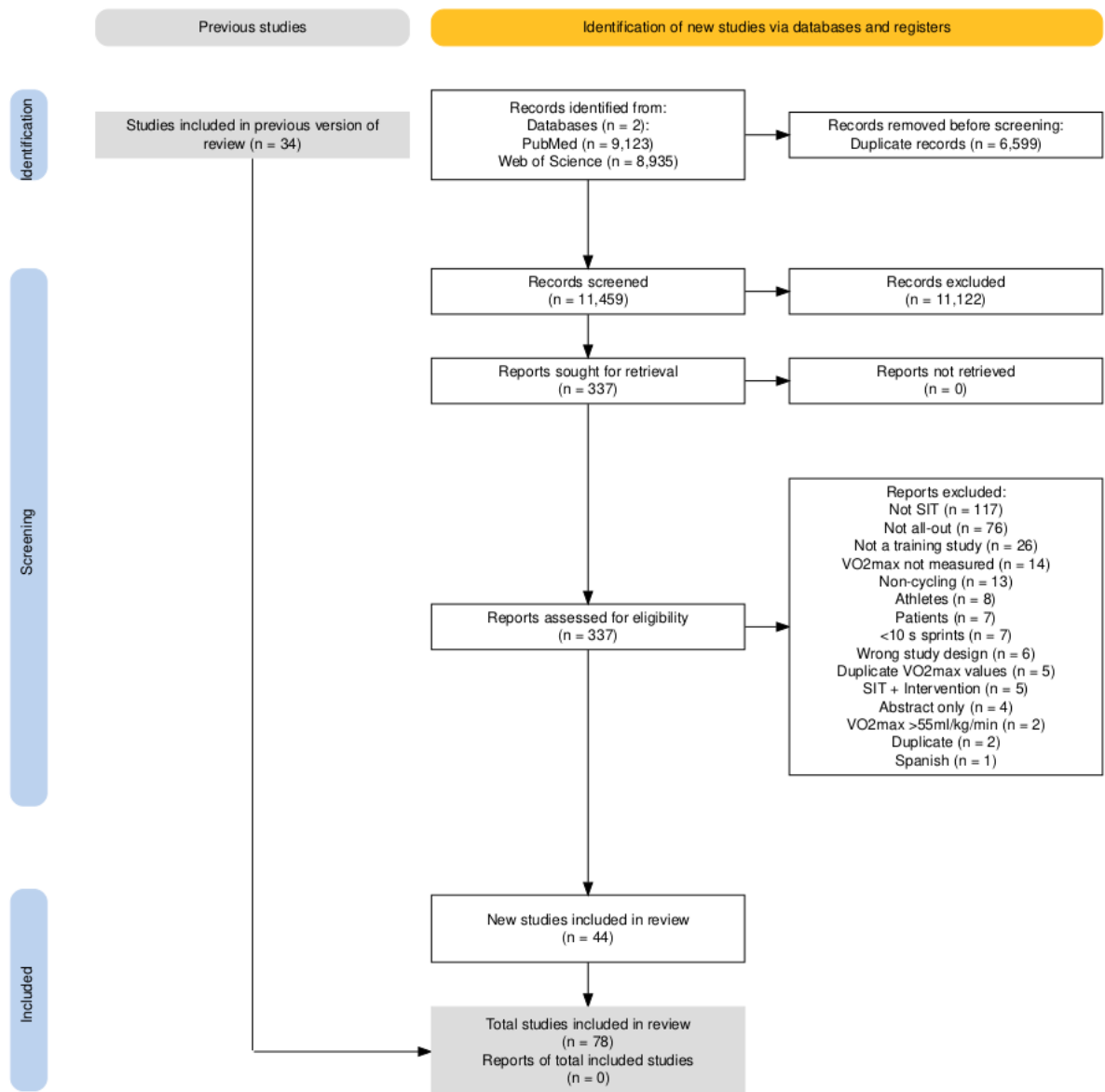


Figure 2.1 - PRISMA flow diagram of the study selection process.

Data Extraction

As the present study was an updated version of a previous meta-analysis on this topic (Vollaard et al., 2017), the methods for data extraction were similar to compile data from both studies for reliable analysis. All included articles were assessed for mean absolute pre- and post-training $\dot{V}O_{2\max}$ ($L \cdot \min^{-1}$) as opposed to relative $\dot{V}O_{2\max}$ ($mL \cdot kg^{-1} \cdot \min^{-1}$). Absolute $\dot{V}O_{2\max}$ values provide an estimate of the true change in the body's ability to take up and utilise oxygen, regardless of any accompanying fluctuations in body mass (Vollaard et al., 2017).

As 24 of the 44 newly included studies were missing mean absolute $\dot{V}O_{2\max}$ data, the authors were contacted to request this data. Nine of the 24 authors contacted were able to provide the requested missing data (Allen et al., 2017, Colpitts et al., 2021, Cuddy et al., 2019, Little et al., 2019, Muggeridge et al., 2017, Olek et al., 2018, Richardson et al., 2016, Thomas et al., 2020, Wyckelsma et al., 2020). Relative $\dot{V}O_{2\max}$ was used for 13 studies where absolute $\dot{V}O_{2\max}$ could not be obtained (Camacho-Cardenosa et al., 2017, De Smet et al., 2016, de Sousa et al., 2018, Digby et al., 2023, Haines et al., 2021, Inglis et al., 2024, Jurimae et al., 2023, Juskeviciute et al., 2024, Kavaliauskas et al., 2018, Kavaliauskas et al., 2017, Leahy et al., 2022, Naves et al., 2018, Oliveira et al., 2022). Plot digitizer software (PlotDigitizer; Version 3.1.6) was used to obtain relative $\dot{V}O_{2\max}$ (Krusnauskas et al., 2020) and absolute $\dot{V}O_{2\max}$ (Bostad et al., 2023) from the two remaining published journal articles where the relevant values were not stated and could not be obtained.

Participant characteristics (sex, age, BMI, and baseline $\dot{V}O_{2\max}$), exercise intervention variables (minimum and maximum number of sprint repetitions per exercise session, sprint duration, sprint resistance, sprint/recovery ratio, intervention duration, training frequency per week, and total number of sessions), and study design (controlled, uncontrolled) were extracted from each study as potential moderators. For effect size calculations, if the spread of the data was reported as the standard error of the mean (SEM), it was converted to the standard deviation (SD) by multiplying the SEM by the square root of the sample size (Higgins et al., 2024).

Statistical Analysis

Effect Size Calculation

Standardised mean differences were calculated to quantify effect size for each study, allowing inclusion of studies reporting different units for the outcome measure $\dot{V}O_{2\max}$ ($L \cdot \min^{-1}$ vs. $mL \cdot kg \cdot \min^{-1}$). This was calculated by dividing the mean change in $\dot{V}O_{2\max}$ by the SDchange, which was calculated using the formula below (Higgins et al., 2024).

$$SD_{change} = \sqrt{SD_{pre}^2 + SD_{post}^2 - 2 \times r \times SD_{pre} \times SD_{post}}$$

Most studies did not report either the SDchange or the pre- to post-intervention correlation coefficients (r). Based on pre-post correlation scores we routinely see in our laboratory from similar intervention studies, a correlation coefficient of $r = 0.90$ was imputed for the analysis. A sensitivity analysis using alternative correlation coefficients ($r = 0.85$ and $r = 0.95$) was conducted to assess whether the overall results were robust to the use of imputed correlation coefficients (Higgins et al., 2024).

Bayesian Model

The Bayesian analysis reporting guidelines (Kruschke, 2021) were followed to provide transparency and reproducibility of the steps carried out throughout the present study. The overall effect of sprint interval training on changes in $\dot{V}O_{2\max}$ was assessed using a Bayesian hierarchical model, which

was fit using the brms (v2.22.0) (Burkner, 2017) package within the statistical computing software R (v.4.3.2) (R Core Team, 2023). Weakly informative priors were used as recommended by the developers of the Stan probabilistic language, upon which brms is based (Stan Development Team, 2025), and model diagnostics confirmed appropriate convergence and fit. Full details of model structure, model priors, and sensitivity analyses are reported in **Supplementary File S1**. All R scripts and data required to reproduce the analysis are available at:

https://github.com/matthutch95/SIT_VO2max_Reproducibility.git

Study parameters and participant characteristics were added as moderators to the model to assess their influence on the overall pooled effect size. The following moderators were included: number of sprint repetitions, sprint duration (s), intervention duration (weeks), work:rest ratio, baseline relative $\dot{V}O_2\text{max}$ ($\text{mL}\cdot\text{kg}\cdot\text{min}^{-1}$), age (y), and BMI ($\text{kg}\cdot\text{m}^{-2}$). Total weekly sprint time was calculated as sprint repetitions $\times$ sprint duration $\times$ weekly session frequency, which was estimated in a separate model to avoid issues with multicollinearity. All reported model estimates are posterior means (Bayesian effect sizes) and 95% credible intervals (CIs) where the true effect is estimated to lie with 95% probability (Hespanhol et al., 2019). Bubble plots were used to visualise the relationships between effect size and the moderators.

Risk of Bias

A funnel plot was created to assess the risk of publication bias visually. Egger's test was conducted to determine the asymmetry observed in the funnel plot. Within-study risk of bias was evaluated using the Cochrane Risk of Bias V.2.0 tool (Sterne et al., 2019). To reduce subjective bias and improve process accuracy, two reviewers (MH, NBJV) independently evaluated the studies, with discrepancies discussed post-assessment. If the discrepancies could not be resolved through discussion, a third reviewer (RM) provided a final judgment on the rating. Risk of Bias was evaluated across five domains: the randomisation process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The RoB V.2.0 for crossover trials tool (Higgins et al., 2021) was used for any studies that implemented a crossover study design. This tool contains one additional domain: risk of bias arising from period and carryover effects. The Risk of Bias in Non-randomised studies of Interventions, Version 2 (ROBINS-I V2, 2024; 7 domains) (Sterne and Higgins, 2024) was used for studies in which participants were not randomised to their intervention.

Sensitivity Analyses

A prior sensitivity analysis was performed to assess the robustness of the model's results (Kallioinen et al., 2023, van de Schoot et al., 2018) (**Supplementary File S1**). A sensitivity analysis was conducted by removing 4 outlier datasets that contained >10 sprint repetitions, as all of these datasets involved short (10-15 s) sprints.

RESULTS

Data for the 78 included studies, with a total of 93 separate trials, are shown in **Table 2.1**. On average, SIT had a strong positive effect on $\dot{V}O_{2\max}$ with a mean effect size for training-induced improvements of 0.87 (95% CIs = -0.10 to 1.85; **Figure 2.2**). Visual inspection of the funnel plot (**Figure 2.3**) suggests asymmetry, which may indicate publication bias, whereby smaller studies with non-significant changes in $\dot{V}O_{2\max}$ may remain unpublished. The significant result from Egger's test supports the presence of funnel plot asymmetry ($p=0.010$). **Table 2.2** displays the results of the Bayesian model. **Supplementary File S1** contains tables and figures from model diagnostic checks and sensitivity analyses.

The risk of bias analysis indicated a moderate overall risk of bias. This result was largely determined by “some concerns” in three of the seven domains (Selection of the reported result, Measurement of the outcome, and Randomisation process; **Supplementary File S1; Figures 4a - c**) assessed across the three risk-of-bias tools. The issues within the three domains were due to a lack of study preregistration, non-blinding of the outcome assessors, and the absence of randomisation in some studies. Individual study results from the three risk-of-bias analysis tools are shown in **Supplementary File S1, Figures 4d–e**.

Table 2.1 - Study training intervention protocol parameters, participant characteristics, and training effects.

Reference	Study Design	N (% men)	Baseline $\dot{V}O_2\text{max}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)	Age (yr)	BMI ($\text{kg}\cdot\text{m}^{-2}$)	Training duration (wk)	Total training sessions	Sprint duration (s)	Recovery duration (s)	Resistance (% of BM)	Min sprint reps	Max sprint reps	Change in $\dot{V}O_2\text{max}$ (%)	Effect Size
<i>Metcalfe et al. (2012)</i>	C	11(45%)	34.2 ± 5.2	25.0 ± 3.0	23.5 ± 4.0	6	18	20	200	7.5	1	2	12.7	1.1
<i>Nalcakan et al. (2018)</i>	NC	18(80%)	34.0 ± 9.0	22.0 ± 4.0	25.3 ± 5.9	6	18	10	220	7.5	2	2	3.5	0.0
<i>Aslankeser and Balci (2017)</i>	C	8(0%)	34.3 ± 0.7	20.4 ± 0.6	-	2	10	30	240	7.5	2	2	9.7	2.4
<i>Thomas et al. (2020)</i>	NC	14(57%)	35.7 ± 4.8	26.0 ± 5.0	24.3 ± 4.2	6	18	20	280	7.5	2	2	7.9	0.7
<i>Thomas et al. (2020)</i>	NC	12(75%)	36.2 ± 4.8	24.0 ± 4.0	26.9 ± 2.4	6	24	20	280	7.5	2	2	7.2	0.5
<i>Haines et al. (2021)</i>	NC	12(100%)	44.7 ± 6.8	21.4 ± 2.4	25.4 ± 1.7	5	15	20	200	7.5	1	2	9.0	1.2
<i>Nalcakan et al. (2018)</i>	NC	18(61%)	39.0 ± 7.0	22.0 ± 2.0	23.8 ± 24.1	6	18	20	200	7.5	2	2	9.8	0.8
<i>Metcalfe et al. (2020)</i>	C	13(46%)	28.0 ± 7.0	46.0 ± 9.0	27.2 ± 4.5	6	18	20	180	5.0	2	2	7.6	0.5
<i>Thomas et al. (2020)</i>	NC	16(75%)	34.4 ± 6.1	26.0 ± 6.0	27.1 ± 4.6	6	12	20	280	7.5	2	2	10.1	0.8
<i>Leahy et al. (2022)</i>	NC	12(42%)	25.3 ± 2.9	40.8 ± 10.8	-	8	26	20	180	CAROL	2	2	12.3	2.3
<i>Metcalfe et al. (2016)</i>	NC	34(50%)	35.0 ± 7.4	34.1 ± 9.2	24.6 ± 2.9	6	18	20	200	5	1	2	9.6	0.8
<i>Cuddy et al. (2019)</i>	NC	12(-)	25.3 ± 2.9	40.8 ± 10.8	-	8	26	20	180	-	2	2	13.5	1.4
<i>Mandic et al. (2023)</i>	NC	9(44%)	34.8 ± 6.1	27.0 ± 5.0	-	6	18	30	120	7.5	3	3	12.1	0.7
<i>Opazo-Diaz et al. (2023)</i>	NC	9(-)	33.7 ± 5.8	21.1 ± 1.7	23.0 ± 1.5	4	12	20	120	-	3	3	9.5	0.7
<i>Bostad et al. (2023)</i>	NC	10(0%)	33.2 ± 7.2	21.0 ± 4.0	-	12	36	20	120	CAROL	3	3	9.1	0.8
<i>Bostad et al. (2021)</i>	NC	15(40%)	37.1 ± 6.9	21.0 ± 2.0	-	12	36	20	120	7.5	3	3	20.9	1.1

<i>Little et al. (2019)</i>	NC	16(56%)	34.3 ± 7.6	21.0 ± 4.0	24.1 ± 4.9	6	18	20	180	-	3	3	6.6	0.4
<i>Gillen et al. (2016)</i>	C	9(100%)	32.0 ± 7.0	27.0 ± 8.0	27.0 ± 5.0	12	36	20	120	5	3	3	17.3	1.3
<i>Mandic et al. (2022)</i>	NC	29(55%)	41.0 ± 7.8	27.0 ± 5.0	23.5 ± 2.5	6	18	30	120	7.5	3	3	10.0	0.8
<i>Ijichi et al. (2015)</i>	C	10(100%)	47.7 ± 4.8	20.4 ± 0.8	21.0 ± 2.9	4	20	30	600	5	3	3	13.9	1.8
<i>O'Driscoll et al. (2018)</i>	CC	40(100%)	42.5 ± 5.2	21.0 ± 1.7	-	2	6	30	120	7.5	3	3	5.7	0.8
<i>Gillen et al. (2014)</i>	NC	14(50%)	29.5 ± 4.0	30.0 ± 9.0	-	6	18	20	120	5	3	3	11.6	1.0
<i>Allemeier et al. (1994)</i>	C	11(100%)	48.7 ± 6.7	22.7 ± 5.0	-	6	15	30	1200	7.5	3	3	13.5	2.2
<i>Bostad et al. (2023)</i>	NC	10(100%)	41.1 ± 7.3	21.0 ± 3.0	-	12	36	20	120	CAROL	3	3	8.3	0.8
<i>Tan et al. (2021)</i>	NC	15(40%)	38.0 ± 9.3	39.0 ± 13.0	23.3 ± 3.8	6	18	30	120	-	2	4	4.5	0.3
<i>de Sousa et al. (2018)</i>	C	26(46%)	42.9 ± 8.6	23.5 ± 5.1	24.5 ± 3.4	2	6	30	180	7.5	3	4	12.5	1.2
<i>de Sousa et al. (2018)</i>	C	46(54%)	43.4 ± 9.1	23.5 ± 5.1	25.0 ± 4.4	2	6	30	180	7.5	3	4	12.4	1.1
<i>Oliveira et al. (2022)</i>	NC	21(0%)	32.0 ± 7.7	28.8 ± 6.0	25.0 ± 3.2	8	24	30	240	-	4	4	14.1	1.3
<i>Colpitts et al. (2021)</i>	NC	18(50%)	36.4 ± 8.6	41.7 ± 13.3	22.9 ± 1.6	4	12	30	240	7.5	2	4	7.4	0.5
<i>Colpitts et al. (2021)</i>	NC	16(38%)	25.8 ± 5.4	39.3 ± 11.8	34.1 ± 3.8	4	12	30	240	7.5	2	4	2.2	0.2
<i>Kavaliauskas et al. (2018)</i>	C	6 (100%)	41.5 ± 7.0	32.0 ± 7.0	23.0 ± 2.0	2	6	30	240	7.5	4	4	0.0	0.0
<i>Naves et al. (2018)</i>	NC	24(0%)	32.0 ± 7.2	29.8 ± 6.4	25.2 ± 3.2	8	24	30	240	-	4	4	14.1	1.4
<i>Kavaliauskas et al. (2017)</i>	CC	8(0%)	31.7 ± 3.0	21.0 ± 1.0	23.0 ± 4.5	4	8	30	240	7.0	4	4	-2.5	-0.4
<i>Harris et al. (2014)</i>	C	6(0%)	35.0 ± 3.0	22.0 ± 2.0	23.6 ± 1.8	4	12	30	270	7.5	4	4	9.0	1.3
<i>Bayati et al. (2011)</i>	C	8(100%)	44.6 ± 4.3	25.0 ± 0.8	-	4	12	30	240	7.5	3	5	9.6	2.3
<i>Schubert et al. (2017)</i>	C	12(42%)	32.3 ± 7.1	28.8 ± 7.6	28.4 ± 4.7	4	12	20	120	5.0	3	5	10.9	1.1

<i>Thompson et al. (2018)</i>	NC	10(60%)	43.8 ± 6.3	22.0 ± 3.0	-	4	14	30	240	7.5	4	5	5.6	0.6
<i>Kiviniemi et al. (2015)</i>	C	13(100%)	34.7 ± 3.9	48.0 ± 5.0	25.6 ± 2.7	2	6	30	240	7.5	4	6	4.7	0.8
<i>Hazell et al. (2010)</i>	C	13(81%)	47.0 ± 6.7	24.0 ± 3.2	24.7 ± -	2	6	30	240	10.0	4	6	8.3	0.6
<i>Ijichi et al. (2015)</i>	C	10(100%)	46.8 ± 6.3	21.3 ± 1.6	22.2 ± 1.8	4	10	30	600	5.0	6	6	8.4	1.5
<i>Larsen et al. (2013)</i>	NC	8(100%)	25.8 ± 4.0	27.0 ± 3.4	-	2	6	30	240	7.5	4	6	9.8	1.8
<i>Yamagishi and Babraj (2019)</i>	NC	7(57%)	43.9 ± 6.0	23.0 ± 3.0	-	2	6	30	240	7.5	4	6	1.9	0.1
<i>Yamagishi and Babraj (2019)</i>	NC	7(71%)	47.6 ± 7.2	25.0 ± 4.0	-	2	6	30	240	7.5	4	6	-0.4	0.0
<i>Shepherd et al. (2013)</i>	C	8(100%)	41.9 ± 1.8	22.0 ± 1.0	24.8 ± 0.8	6	18	30	270	7.5	4	6	7.6	1.1
<i>Olek et al. (2018)</i>	NC	7(100%)	36.4 ± 1.4	20.1 ± 0.3	23.5 ± 0.5	2	6	10	60	7.5	4	6	14.7	1.7
<i>Olek et al. (2018)</i>	NC	7(100%)	34.8 ± 1.5	20.7 ± 0.2	24.3 ± 0.5	2	6	10	240	7.5	4	6	10.9	1.8
<i>Denham et al. (2020)</i>	NC	11(100%)	43.6 ± 5.9	33.0 ± 9.6	26.8 ± 3.3	6	18	30	240	-	4	6	9.4	1.2
<i>Broatch et al. (2017)</i>	NC	8(100%)	31.5 ± 7.6	26.0 ± 7.0	25.1 ± 3.7	6	18	30	240	7.5	4	6	9.8	1.6
<i>McGarr et al. (2014)</i>	C	8(75%)	47.2 ± 11.8	25.0 ± 7.0	-	2	8	30	240	7.5	4	6	14.2	1.3
<i>Jurimae et al. (2023)</i>	NC	11(100%)	36.0 ± 7.1	63.0 ± 8.0	26.1 ± 2.1	3	9	30	240	7.0	6	6	5.0	0.6
<i>De Smet et al. (2016)</i>	NC	10(100%)	53.5 ± 2.6	23.0 ± 3.0	-	5	15	30	270	-	4	6	16.5	1.8
<i>Astorino et al. (2011)</i>	C	20(55%)	43.6 ± -	25.0 ± -	-	2	6	30	300	7.5	4	6	6.3	0.6
<i>Muggeridge et al. (2017)</i>	C	10(100%)	40.6 ± 6.6	26.0 ± 4.0	-	3	9	15	240	7.0	4	6	0.9	0.1
<i>Wyckelsma et al. (2020)</i>	NC	8(100%)	34.5 ± 6.9	64.3 ± 6.0	26.0 ± 2.4	3	9	30	240	-	4	6	-0.7	-0.1
<i>Whyte et al. (2010)</i>	NC	10(100%)	32.8 ± 1.4	32.1 ± 8.7	30.3 ± 3.7	2	6	30	270	6.5	4	6	8.4	1.2
<i>Hazell et al. (2010)</i>	C	13(81%)	47.0 ± 6.7	24.0 ± 3.2	24.7 ± -	2	6	10	240	10.0	4	6	8.5	0.9

<i>Burgomaster et al. (2008)</i>	C	10(50%)	41.0 ± 2.0	23.6 ± 3.2	-	6	18	30	270	7.5	4	6	6.3	0.6
<i>Denham et al. (2018)</i>	NC	10(100%)	42.8 ± 6.2	33.3 ± 10.9	26.8 ± 3.5	6	18	30	240	-	4	6	9.4	1.1
<i>Nalcakan (2014)</i>	C	8(100%)	40.2 ± 4.3	21.7 ± 2.2	25.5 ± 2.3	7	21	30	270	7.5	4	6	7.0	1.5
<i>Barnett et al. (2004)</i>	C	8(100%)	47.6 ± -	20.4 ± 1.2	-	8	24	30	180	-	3	6	8.2	2.1
<i>Araujo Bonetti et al. (2024)</i>	C	14(100%)	35.5 ± 4.1	30.0 ± 5.0	-	5	15	30	240	7.0	3	6	6.3	1.1
<i>Inglis et al. (2024)</i>	C	14(50%)	40.9 ± 6.6	28.0 ± 6.0	-	6	18	30	270	7.0	3	6	11.5	1.5
<i>Yamagishi and Babraj (2017)</i>	C	9(78%)	42.2 ± 5.4	27.0 ± 2.7	-	9	18	15	180	7.5	4	6	11.1	1.0
<i>Yamagishi and Babraj (2017)</i>	C	8(63%)	40.6 ± 9.6	27.5 ± 4.5	-	9	18	30	240	7.5	4	6	10.6	0.8
<i>Juskeviciute et al. (2024)</i>	NC	10(100%)	40.8 ± 6.7	21.6 ± 1.4	24.2 ± 3.1	3	9	30	240	-	4	6	5.4	0.7
<i>Digby et al. (2023)</i>	NC	9(67%)	43.8 ± 6.6	22.0 ± 3.0	25.6 ± 4.9	3	9	30	240	7.5	4	6	5.3	0.8
<i>Hazell et al. (2010)</i>	C	13(81%)	47.0 ± 6.7	24.0 ± 3.2	24.7 ± -	2	6	10	120	10.0	4	6	3.9	0.4
<i>Cochran et al. (2014)</i>	C	12(100%)	50.6 ± 6.0	22.0 ± 2.0	-	6	18	30	240	7.5	4	6	10.3	1.6
<i>Zelt et al. (2014)</i>	C	12(100%)	43.9 ± -	22.0 ± 2.0	26.0 ± 3.0	4	12	15	285	7.5	4	6	7.4	0.8
<i>Zelt et al. (2014)</i>	C	11(100%)	48.6 ± -	23.0 ± 5.0	25.0 ± 3.0	4	12	30	270	7.5	4	6	5.3	1.2
<i>Krusnauskas et al. (2020)</i>	NC	17(100%)	47.0 ± 7.0	25.9 ± 6.4	23.5 ± 2.4	3	9	30	240	7.5	4	6	4.3	0.6
<i>Krusnauskas et al. (2020)</i>	NC	9(100%)	43.9 ± 8.2	25.3 ± 5.4	24.7 ± 3.2	3	9	30	240	7.5	4	6	12.8	1.5
<i>Burgomaster et al. (2006)</i>	C	8(100%)	48.9 ± 2.1	21.0 ± 1.0	-	2	6	30	240	7.5	4	7	5.6	1.0
<i>Bailey et al. (2009)</i>	C	8(63%)	42.0 ± 6.0	21.0 ± 5.0	-	2	6	30	240	7.5	3	7	7.4	0.8
<i>Richardson and Gibson (2015)</i>	C	9(56%)	40.0 ± -	21.0 ± 1.0	-	2	6	30	240	7.5	4	7	11.2	0.9
<i>Higgins et al. (2016)</i>	NC	23(0%)	29.1 ± 4.8	20.4 ± 1.5	30.3 ± 4.5	6	18	30	240	-	5	7	17.4	2.2

<i>Richardson et al. (2016)</i>	C	14(64%)	42.2 ± 8.6	20.0 ± 1.0	-	2	6	30	240	7.5	4	7	10.7	0.9
<i>Burgomaster et al. (2005)</i>	C	8(75%)	44.6 ± 3.2	22.0 ± 1.0	-	2	6	30	240	7.5	4	7	1.4	0.2
<i>Trilk et al. (2011)</i>	C	14(0%)	21.6 ± 1.1	30.1 ± 6.3	35.7 ± 6.3	4	12	30	240	5.0	4	7	11.7	1.6
<i>Katz et al. (1984)</i>	NC	8(100%)	51.8 ± -	24.2 ± 4.3	-	8	32	30	240	-	8	8	7.0	1.3
<i>Scalzo et al. (2014)</i>	NC	21(52%)	41.5 ± 5.7	22.5 ± 1.0	22.4 ± 0.9	3	9	30	240	7.5	4	8	3.7	0.4
<i>Allen et al. (2017)</i>	C	20(35%)	41.0 ± 4.3	49.2 ± 6.1	27.3 ± 4.0	9	27	30	240	6.5	4	8	14.3	0.9
<i>MacDougall et al. (1998)</i>	NC	12(100%)	50.8 ± 1.8	22.7 ± 2.0	-	7	21	30	180	7.5	4	10	7.5	1.2
<i>McKenna et al. (1997)</i>	NC	8(100%)	47.1 ± 2.6	20.9 ± 0.6	-	7	21	30	180	7.5	4	10	13.7	2.1
<i>Stathis et al. (1994)</i>	NC	8(75%)	49.6 ± 3.6	22.1 ± 1.0	-	7	21	30	180	-	3	10	4.2	0.3
<i>Harmer et al. (2006)</i>	C	7(71%)	43.7 ± 6.2	24.0 ± 5.0	23.8 ± 5.0	7	21	30	180	7.5	4	10	8.2	0.6
<i>Harmer et al. (2000)</i>	NC	7(100%)	49.8 ± 5.9	22.0 ± 3.0	-	7	21	30	180	7.5	4	10	6.9	1.4
<i>Camacho-Cardenosa et al. (2017)</i>	C	8(-)	33.1 ± 6.7	24.4 ± 3.5	23.1 ± 2.7	4	8	10	20	-	10	10	10.2	1.7
<i>Hebisz et al. (2024)</i>	NC	10(70%)	47.7 ± 9.2	22.8 ± 2.8	-	5	15	30	90	7.0	6	10	5.8	0.8
<i>Skłeryk et al. (2013)</i>	C	8(100%)	29.7 ± 1.3	40.2 ± 2.3	32.2 ± 2.1	2	6	10	80	5.0	8	12	-1.7	-0.2
<i>Lloria-Varela et al. (2024)</i>	NC	13(38%)	37.4 ± 5.6	23.0 ± 5.0	-	6	15	15	120	7.0	8	14	8.6	0.6
<i>Hellsten-Westing et al. (1993)</i>	NC	11(100%)	53.0 ± -	23.6 ± 5.9	-	6	18	10	50	7.0	15	15	2.4	2.2
<i>Allen et al. (2017)</i>	C	21(43%)	40.5 ± 4.0	49.2 ± 6.1	27.8 ± 4.5	9	27	10	180	6.5	10	24	13.4	1.0

BM: body mass, BMI: body mass index, C: controlled, CC: crossover controlled, NC: not controlled.

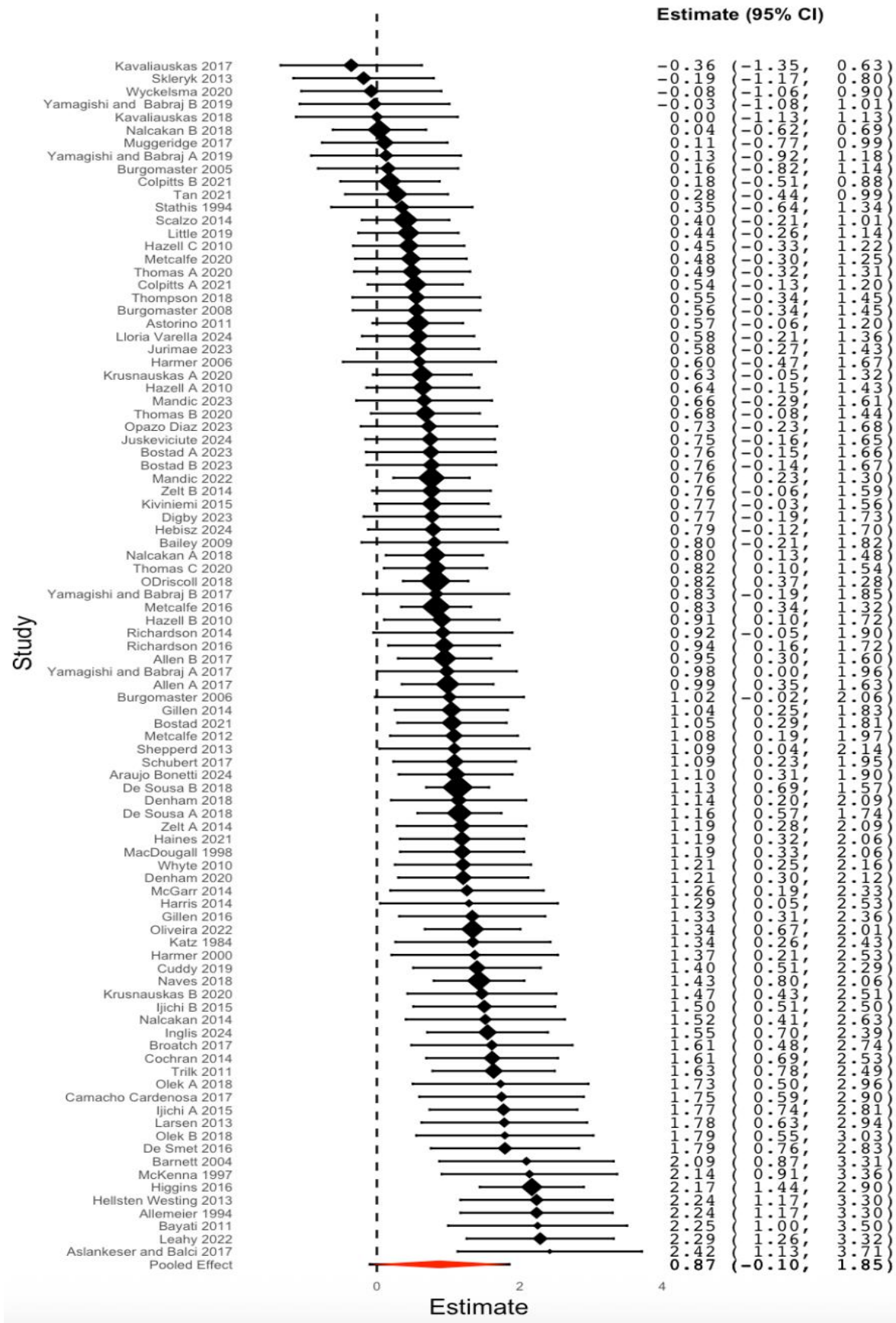


Figure 2.2 - Effect of SIT on $\dot{V}O_{2\max}$. Letters A, B and C used in study labels denote different datasets from within the same study.

Table 2.2 - Bayesian model estimates for the effects of participant characteristic and exercise protocol variable predictors on changes in $\dot{V}O_{2\max}$.

Parameter	Estimate	Est. Error	l-95% CI	u-95% CI	Rhat	Bulk ESS	Tail ESS
Intercept	0.866	0.500	-0.087	1.852	1.0003	20,133	14,284
Sprint Repetitions	0.024	0.017	-0.010	0.058	1.0001	19,746	14,178
Work:rest Ratio	0.011	0.674	-1.327	1.324	1.0003	28,315	14,354
Age (y)	-0.017	0.007	-0.030	-0.003	1.0001	20,320	14,678
Intervention Duration (wks)	0.052	0.021	0.010	0.094	1.0001	23,206	14,199
Baseline $\dot{V}O_{2\max}$ (mL·kg ⁻¹ ·min ⁻¹)	-0.007	0.010	-0.026	0.012	0.9999	18,431	14,791
Sprint Duration (s)	0.015	0.009	-0.002	0.032	1.0000	23,633	14,719

l-95% CI: lower-95% credible interval, u-95%: upper-95% credible interval, work:rest ratio: sprint duration (s) divided by recovery duration (s). Estimates are displayed as posterior standardised effect sizes.

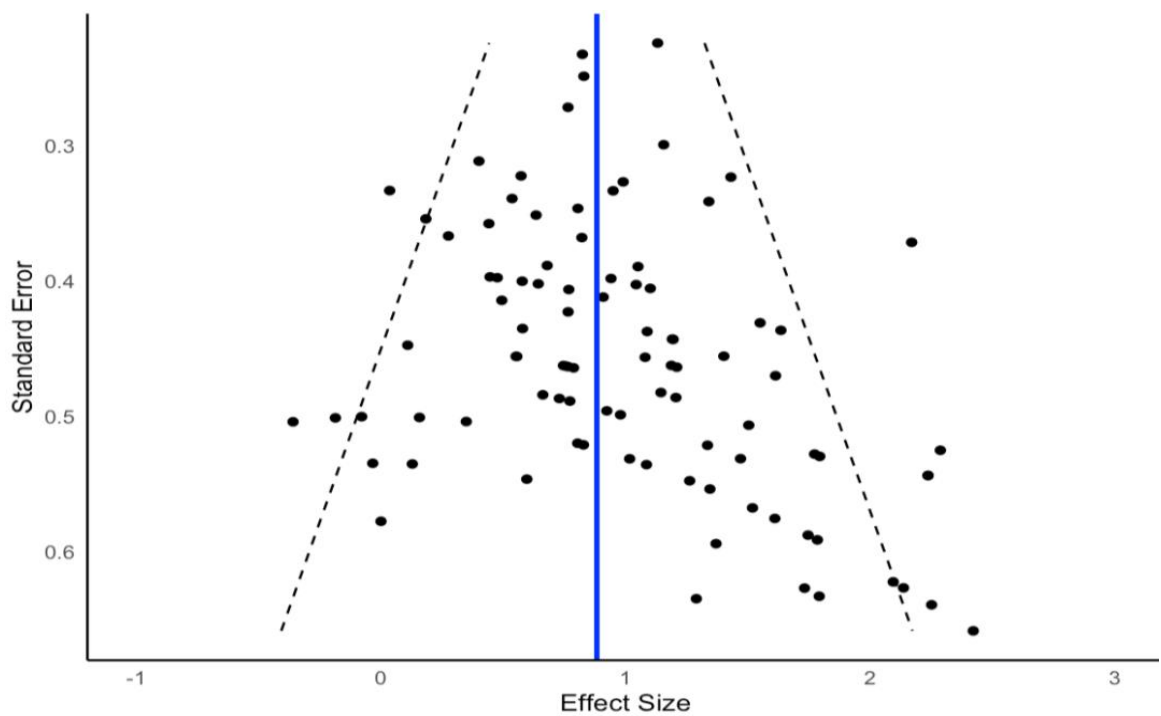


Figure 2.3 - Funnel plot of 93 study effect sizes (black circles). The vertical blue line represents the estimated pooled effect size, and the dashed black lines represent 95% credible intervals.

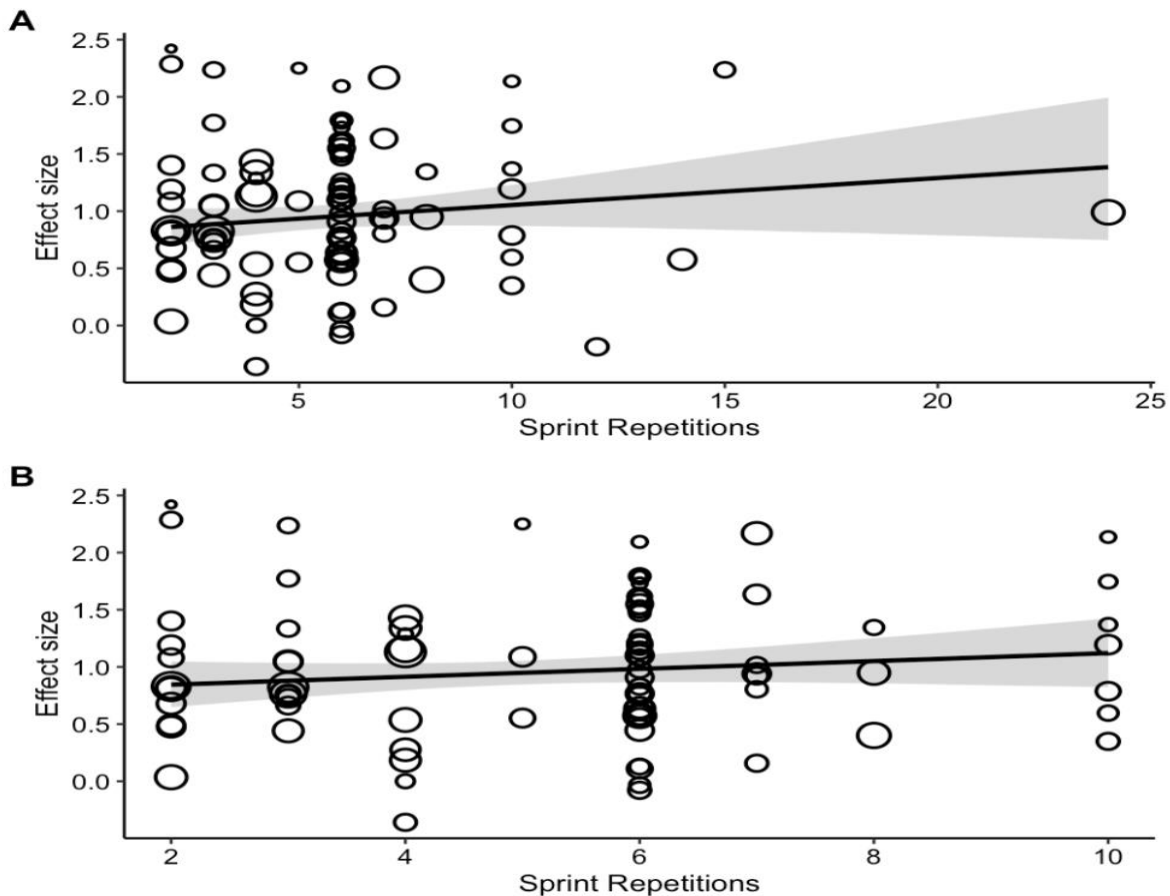


Figure 2.4 - Relationship between the number of sprint repetitions per training session and the effect size for the change in $\dot{V}O_{2\max}$ with training, either with (A; $n=93$) or without (B; $n=89$) studies implementing >10 sprints per session.

Figure 2.4A illustrates the non-significant effect of increasing the number of sprint repetitions on the magnitude of the change in $\dot{V}O_{2\max}$, with a numerical increase in effect size of 0.02 for each additional sprint, i.e., an increase of 4 sprints would equate to an increase in effect size of 0.08, and this would be considered trivial. **Figure 2.4B** displays the results of a sensitivity analysis in which atypical SIT protocols incorporating >10 sprints per session were excluded ($n=4$). Removing the studies increased the pooled effect from 0.87, (95% CI = -0.09 to 1.85) to 1.17, (95% CI = 0.18 to 2.17; **Supplementary Table 2**) and strengthened the association between sprint repetitions and $\dot{V}O_{2\max}$ improvements from ES = 0.02, 95% CI = -0.01 to 0.06 (**Table 2.2**), to ES = 0.03, 95% CIs = -0.02 to 0.09 (**Supplementary Table 2**). However, the relationship remained non-significant, and the overall interpretation did not change.

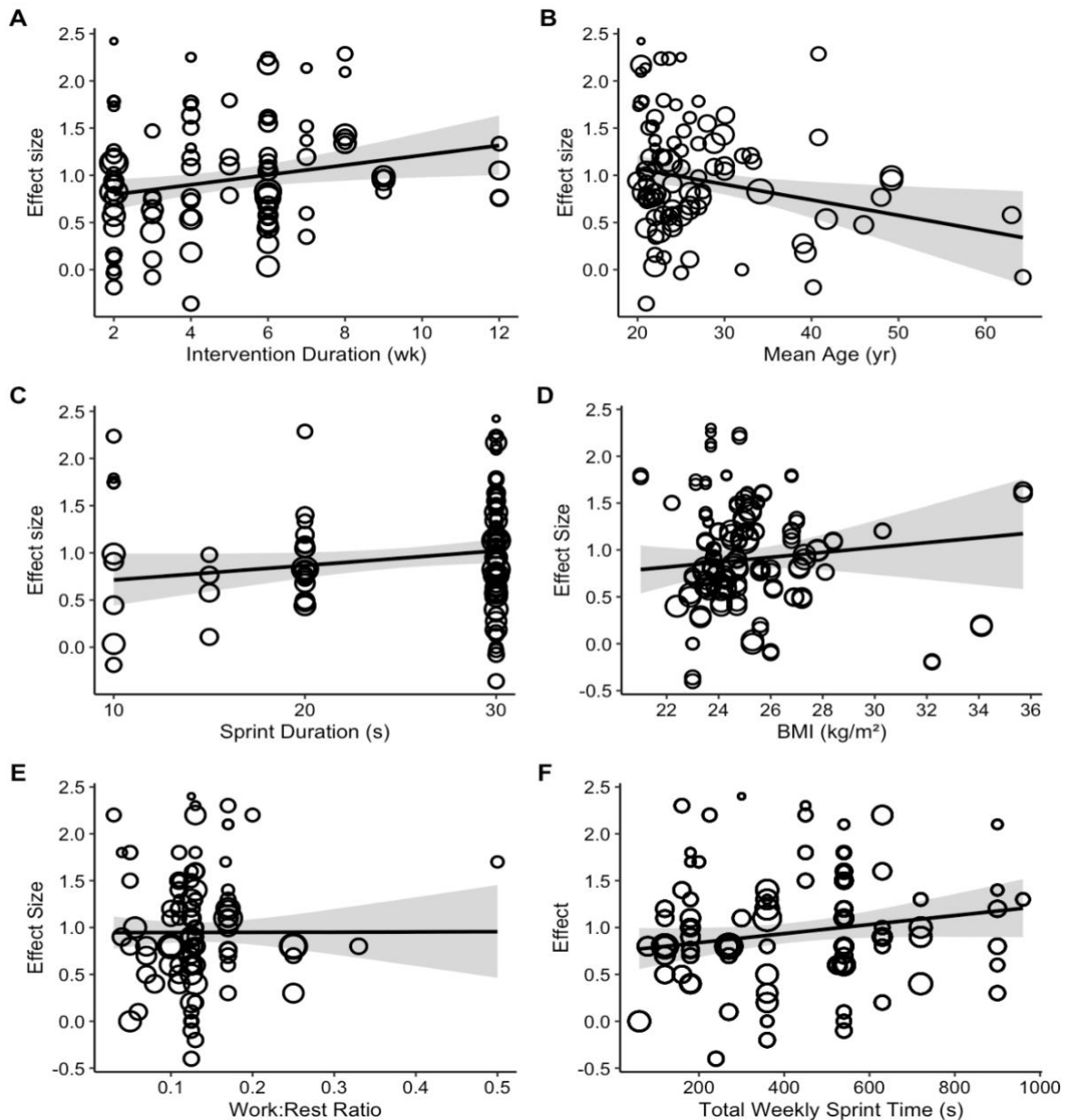


Figure 2.5 - Modifying effects of intervention duration (A), age (B), sprint duration (C), BMI (D), work:rest ratio (E), and total weekly sprint time (F) on the effect of SIT on $\dot{V}O_{2\max}$. BMI data are $n=73$ trials due to missing data. Each additional week of SIT (**Figure 2.5A**) was associated with a small, positive effect on the change in $\dot{V}O_{2\max}$ following SIT ($ES = 0.05$, $95\% \text{ CI} = 0.01$ to 0.09). Conversely, each additional year of age (**Figure 2.5B**) was associated with a small, negative effect on the change in $\dot{V}O_{2\max}$ ($ES = -0.02$, $95\% \text{ CI} = -0.03$ to -0.003). There was no effect of sprint duration ($ES = 0.02$; $95\% \text{ CI} = -0.002$ to 0.03 ; **Figure 2.5C**), BMI ($ES = 0.03$; $95\% \text{ CI} = -0.03$ to 0.08 ; **Figure 2.5D**), work:rest ratio ($ES = 0.01$; $95\% \text{ CI} = -1.33$ to 1.32 ; **Figure 2.5E**), or total weekly sprint time on the change in $\dot{V}O_{2\max}$ ($ES = 0.0005$; $95\% \text{ CI} = -0.0001$ to 0.0010 ; **Figure 2.5F**).

DISCUSSION

The main aim of the present study was to provide a robust estimate for the modifying effect of the number of sprint repetitions per training session in SIT protocols on the training-induced increase in $\dot{V}O_{2\max}$ in untrained individuals. We addressed two key limitations of a previous meta-analysis (Vollaard et al., 2017) by 1): employing a Bayesian statistical approach rather than relying on the criticised statistical method of Magnitude-Based Inference (Lohse et al., 2020, Sainani, 2018, Sainani et al., 2019), and 2): improving statistical power by more than doubling the number of trials included. Using data from 78 studies with 93 trials, involving a total of $n=1188$ participants, we confirm the previous finding (Vollaard et al., 2017) that increasing the number of sprint repetitions in a SIT protocol does not meaningfully augment improvements in $\dot{V}O_{2\max}$.

This finding is clinically important, given the overwhelming evidence that $\dot{V}O_{2\max}$ is among the most powerful independent predictors of all-cause and cardiovascular mortality (Ross and Myers, 2023). Ross et al. (2016) emphasise that the greatest health benefits occur at the low end of the cardiorespiratory fitness continuum – the population of focus in the current study – where relatively modest improvements in $\dot{V}O_{2\max}$ can lead to substantial reductions in mortality risk. The results show that these $\dot{V}O_{2\max}$ improvements are not attenuated when the number of sprints in a SIT session is reduced.

The practical implication of our finding is that reducing the number of sprint repetitions while maintaining worthwhile improvements in $\dot{V}O_{2\max}$ helps address the two common concerns that SIT is not as time efficient as proposed and that it will be experienced as unpleasant and unenjoyable (Ekkekakis et al., 2004, Ekkekakis et al., 2011, Hardcastle et al., 2014, Lind et al., 2005). For example, whereas the classic SIT protocol involving 4-6×30-s sprints take ~30 min to complete (Burgomaster et al., 2006, Burgomaster et al., 2008, Burgomaster et al., 2005, Gibala et al., 2006), a REHIT session involving 2×20-s sprint repetitions takes just 10 min (Metcalf et al., 2012, Metcalf et al., 2016). Additionally, performing fewer sprint repetitions diminishes the drop in affective valence during exercise (Metcalf et al., 2022). It has also been demonstrated that exercise enjoyment and the drop in affective valence with REHIT are not significantly different from MICT (Songsorn et al., 2019). Since $\dot{V}O_{2\max}$ can only be improved through regular exercise, developing alternative interventions that promote greater adoption of regular exercise is an important public health objective. The present findings support the use of SIT protocols with a reduced number of sprint repetitions as a viable strategy for improving $\dot{V}O_{2\max}$ in untrained individuals.

The mechanisms that mediate the training adaptations that occur following SIT are not fully understood. The evidence from the current study suggests that there may be a hypothetical threshold that is sufficiently triggered by two sprints and is not further stimulated by completing additional sprint repetitions. Vollaard and Metcalf (2017) have suggested that rapid glycogen depletion during supramaximal sprints results in a severe disturbance of circulatory homeostasis, which may provide the stimulus for the body to increase blood volume, a central adaptation to exercise proposed to be a

primary driver for improvements in $\dot{V}O_{2\max}$ following SIT (Mandic et al., 2022). It was also suggested that release and activation of glycogen-bound 5'-AMPK associated with glycogenolysis could trigger signalling pathways leading to aerobic adaptations (Vollaard and Metcalfe, 2017). The rationale for the idea that two sprints satisfy the hypothetical threshold for training adaptations stems from research showing that glycogenolysis is almost completely attenuated after two supramaximal sprints, with glycogenolytic rates depressed throughout the entirety of a third sprint (Parolin et al., 1999). Thus, performing more than two sprint repetitions may not further activate key signalling processes required for training adaptations, but will make the training session longer, more tiring, and more unpleasant.

The results of our analysis suggest that to increase the magnitude of improvements in $\dot{V}O_{2\max}$ following SIT, the most influential exercise protocol parameter is intervention duration. For example, the results show that each 1-week increase in intervention duration is positively associated with $\dot{V}O_{2\max}$ (ES = 0.052). Therefore, increasing the intervention duration from 2 to 12 weeks would have a moderate effect (ES = 0.52) on the change in $\dot{V}O_{2\max}$.

However, it should be noted that this model assumes a linear relationship, whereas a plateau in adaptation is likely to occur. Although most studies measure $\dot{V}O_{2\max}$ pre- and post-intervention, several studies have assessed the time course of changes in $\dot{V}O_{2\max}$. Some of these have observed progressive increases in $\dot{V}O_{2\max}$ over time (Bostad et al., 2021, Gillen et al., 2016, Nalcakan, 2014), but others (Burgomaster et al., 2008, Lloria-Varela et al., 2024, Yamagishi and Babraj, 2017) support comments by Sloth et al. (2013) in their previous meta-analysis, that some of the adaptations to SIT occur in the early stages of training and that the magnitude of improvements tapers off.

The reasons for the contrasting results are unclear. Conceptually, over short training periods, there must be an effect of intervention duration while $\dot{V}O_{2\max}$ improves from baseline. However, over time, the rate of improvement will slow, and a 'plateau' may be reached, with no further increases in $\dot{V}O_{2\max}$ (Bassett and Howley, 2000), thus eliminating the ongoing positive effect of intervention duration. To date, it is unknown if and when such a plateau will occur with different SIT protocols. As the longest intervention duration we identified in the current study is 12 weeks (Bostad et al., 2021, Bostad et al., 2023, Gillen et al., 2016), further research exploring longer duration SIT interventions may help to determine the, presumably curvilinear, association between intervention duration and the magnitude of $\dot{V}O_{2\max}$ response.

Another finding from the current study is that a higher mean age is associated with reduced improvements in $\dot{V}O_{2\max}$ following SIT. This is interesting because studies comparing the effects of different endurance exercise training protocols (Makrides et al., 1990, Murias et al., 2010) and HIIT protocols (Storen et al., 2017) on young and older healthy adults (≥ 60 yr) have found that older participants tend to experience $\dot{V}O_{2\max}$ improvements either similar to or greater than younger adults. To our knowledge, no studies have compared the effects of supramaximal SIT between young and older populations matched for baseline $\dot{V}O_{2\max}$. The data in our meta-analysis suggest that 40-

50-year-olds can expect moderate to large effect sizes for improvements in $\dot{V}O_2\text{max}$ with an average SIT protocol (4-6×30-s all-out sprints, three sessions/week). Although lower than that achieved by younger adults, the reductions in all-cause mortality and cardiovascular disease risk in this population are still clinically meaningful. There appears to be insufficient data on populations older than 50, which needs to be addressed in future studies.

One limitation of the present study's findings is the risk of publication bias. While a visual inspection of the funnel plot and the results of the Egger's test suggest a potential risk of publication bias, specifically an underrepresentation of studies with non-significant results, these do not necessarily confirm the presence of publication bias. Sterne et al. (2000) suggest the use of the term "small-study effects" as an alternative way of describing the observed trend, as there are a range of influences that may contribute to these small-study effects, such as outcome reporting bias, heterogeneity between studies, or other sources beyond publication bias alone (Schwarzer et al., 2015).

Additionally, the inclusion of non-controlled studies may have contributed to greater heterogeneity and potentially produced wider posterior distributions than a meta-analysis limited to randomised-controlled trials, thus increasing the uncertainty of the model's effect estimates. Furthermore, the present study focused solely on $\dot{V}O_2\text{max}$ as an outcome measure. Therefore, the finding that increasing sprint repetitions does not significantly influence improvements in $\dot{V}O_2\text{max}$ cannot be generalised to other important health markers, such as blood pressure, body composition, blood lipid profiles, or insulin sensitivity.

There is a need for studies involving larger sample sizes; still, we restate our previous recommendation (Vollaard and Metcalfe, 2017) to focus on SIT protocols involving fewer / shorter sprints in these studies. Even if publication bias / small-study effects may have masked a small but significant positive effect of the number of sprint repetitions on improvements on $\dot{V}O_2\text{max}$, the combination of effectiveness at improving key health markers (Cuddy et al., 2019, Gillen et al., 2016, Gillen et al., 2014, Metcalfe et al., 2012, Ruffino et al., 2017) and measures of acceptability (Metcalfe et al., 2020, Metcalfe et al., 2022, Songsorn et al., 2019) makes low-volume SIT protocols like REHIT better candidates for real-world implementation compared to classic SIT protocols.

In conclusion, using a more robust statistical approach and a larger dataset, we confirm previous findings that the number of sprint repetitions in a SIT session does not impact improvements in $\dot{V}O_2\text{max}$ with training. Considering the overarching aim of SIT protocols to offer a time-efficient method to improve key health markers, and the increasingly negative affective responses associated with SIT protocols involving more sprint repetitions, the implication of this finding is that low-volume SIT protocols should be the focus of research examining real-world implementation as interventions for improving general health in sedentary populations.

SUPPLEMENTARY DATA

Bayesian Model Specifications

Harrer et al. (2021) describe the model's assumptions. Weakly informative priors were used, as recommended by the developers of the Stan probabilistic language, on which brms is based (Stan Development Team, 2025). A normally distributed prior (0,1) was used for the overall pooled effect size, with the expectation that the true pooled effect size lies within ± 2 SDs with 95% probability. A normal prior (0,1) was also applied for the moderators in the model. For the between-study heterogeneity (τ), a half-normal prior (0,1) was used, assuming heterogeneity is likely small to moderate but allowing for larger values. Hamiltonian Markov Chain Monte Carlo (MCMC) methods (Carpenter et al., 2017) within the statistical package brms (Burkner, 2017) were used to estimate the posterior distribution of the overall effect and for each parameter. Four chains, each with 5,000 iterations, were run for the sampling; 500 iterations were designated as warm-up iterations, allowing the chains to stabilise before sampling (Rindskopf, 2020), resulting in a total of 18,000 posterior samples across all chains.

Study parameters and participant characteristics were added as moderators to the model to assess their influence on the overall pooled effect size. The following moderators were included: number of sprint repetitions, sprint duration (s), intervention duration (weeks), work:rest ratio, baseline relative $\dot{V}O_2\text{max}$ ($\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), age (y), and BMI ($\text{kg}\cdot\text{m}^{-2}$). All reported model estimates are posterior means (Bayesian effect sizes) and 95% credible intervals (CIs) where the true effect is estimated to lie with 95% probability (Hespanhol et al., 2019). Bubble plots were used to visualise the relationships between effect size and the moderators.

Model Checks

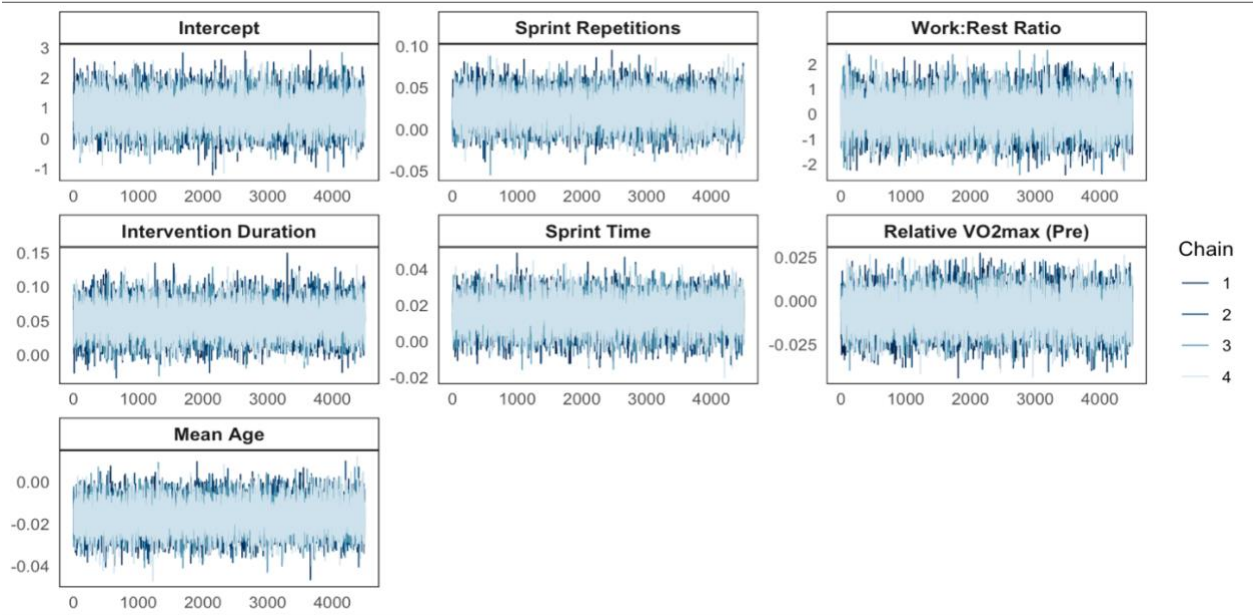
A posterior predictive check (PPC) was conducted to assess the fit of the model; a PPC plot was created to visualise whether the simulated data run by the model closely resembles the observed data (Gabry et al., 2019, Kruschke, 2013). Between-study heterogeneity (τ) was assessed within the model and summarised using a posterior density plot with 95% CIs. Convergence was assessed by visually assessing trace plots (**Supplementary Figure 1**) and confirming that 'rhat' (Gelman and Rubin, 1992) values were all close to 1 (Vehtari et al., 2019).

Sensitivity Analyses

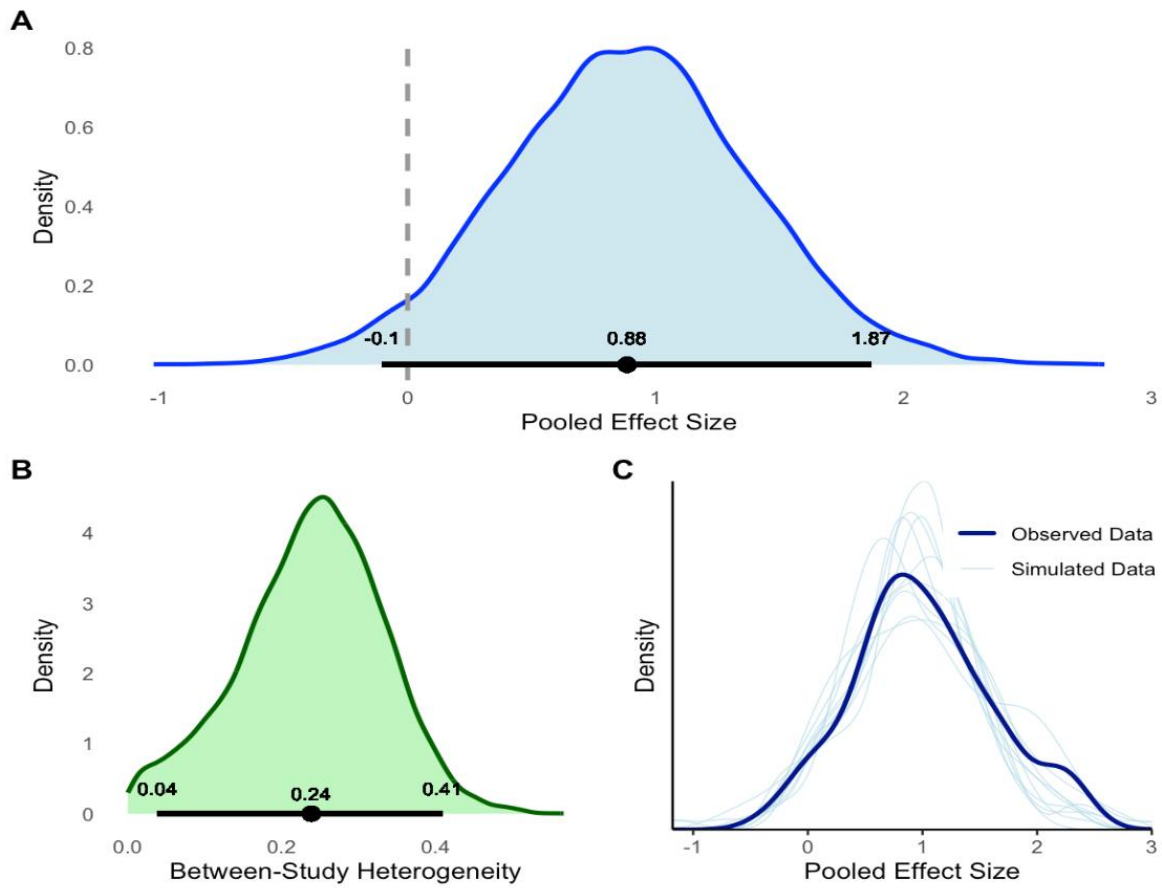
A prior sensitivity analysis was performed to assess the robustness of the model's results (Kallioinen et al., 2023, van de Schoot et al., 2018). A more diffuse prior was chosen (normal (0,5); normal (0,3); Cauchy (0,2)) based on general guidelines provided that suggest if diffuse priors were used in the original analysis, then different forms of diffuse priors would be recommended for the sensitivity analysis (Depaoli et al., 2020). A sensitivity analysis was conducted by removing four outlier datasets that contained >10 sprint repetitions, since all of these datasets involved short (10-15 s) sprints.

Supplementary Results

Supplementary Figure 2a illustrates the posterior probability distribution of the pooled effect size. There was a moderate amount of heterogeneity between studies ($\tau_{\text{between}} = 0.24$; 95% CI = 0.04 - 0.41; **Supplementary Figure 2b**). **Supplementary Figure 2c** demonstrates that the model is a good fit for the given data, as there is good alignment between observed and simulated data. The results of the prior sensitivity analysis model were similar to those of the original model; they are displayed in **Supplementary Table 1**. **Supplementary Figure 3** illustrates the similarities between the original model and the prior sensitivity analysis model for both the posterior distribution of pooled effect size (**Supplementary Figure 3a**) and between-study heterogeneity (**Supplementary Figure 3b**), implying that the posterior estimate is robust to different prior distributions and is being driven by the data rather than the choice of prior (Depaoli et al., 2020). This is expected when a large number of studies are included (Lambert et al., 2005). The moderator effect estimates (**Supplementary Table 1**) show negligible changes, further demonstrating the robustness of the original model's results.



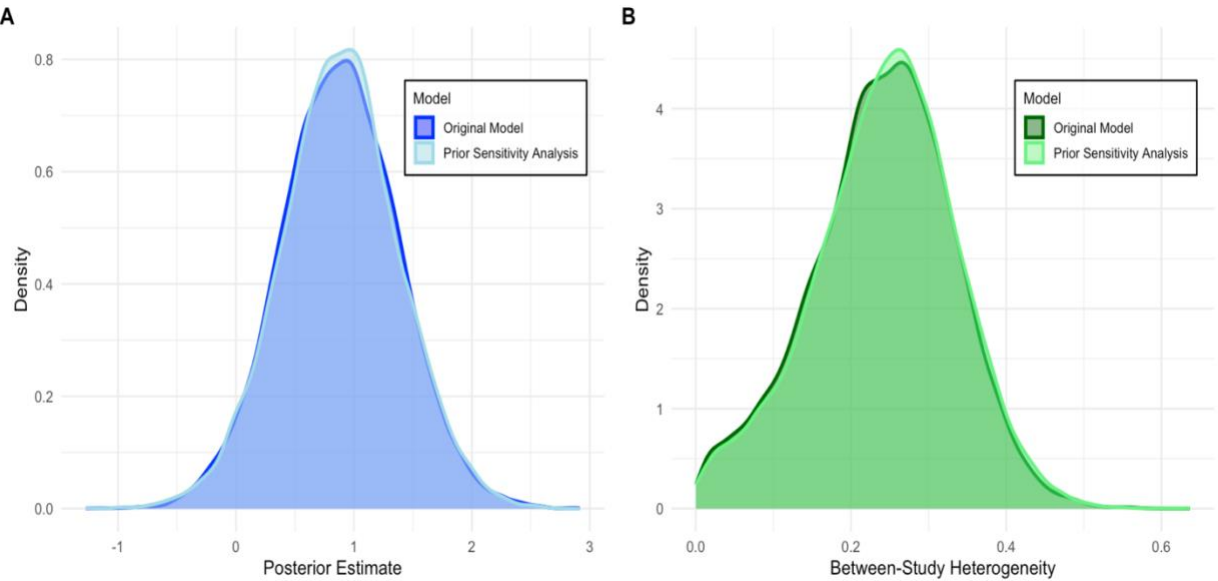
Supplementary Figure 1 - Trace plots for the original model assessing the convergence of the model. Each panel represents a different regression coefficient sampled in the model.



Supplementary Figure 2 - (A) Posterior distribution of the pooled effect size. The black circle indicates the posterior mean, while the black solid lines represent the 95% CIs. (B) Posterior distribution of between-study heterogeneity. The black circle indicates the posterior mean, while the solid black lines represent the 95% CIs. (C) Posterior Predictive Check plot.

Supplementary Table 1 – *Prior sensitivity analysis model results.*

Prior Sensitivity Analysis Results							
(No smooth terms)							
Param	Estimate	Est.Error	l-95% CI	u-95% CI	Rhat	Bulk_ESS	Tail_ESS
Intercept	0.8845	0.4991	-0.0953	1.8740	1.0002	18,575.0950	14,352.6212
Sprint Repetitions	0.0235	0.0173	-0.0102	0.0578	1.0002	16,841.6352	13,593.8021
Work:rest ratio	0.0182	0.8712	-1.7048	1.7294	1.0004	17,863.9135	13,706.0848
Age (y)	-0.0166	0.0068	-0.0300	-0.0031	1.0000	17,346.1557	15,057.6537
Intervention Duration (weeks)	0.0520	0.0211	0.0105	0.0929	1.0001	20,044.5571	13,891.5519
Baseline VO2max (mL/kg/min)	-0.0067	0.0096	-0.0255	0.0125	1.0000	16,802.7164	14,559.9802
Sprint Duration	0.0152	0.0085	-0.0018	0.0319	1.0001	17,871.4999	14,208.8210



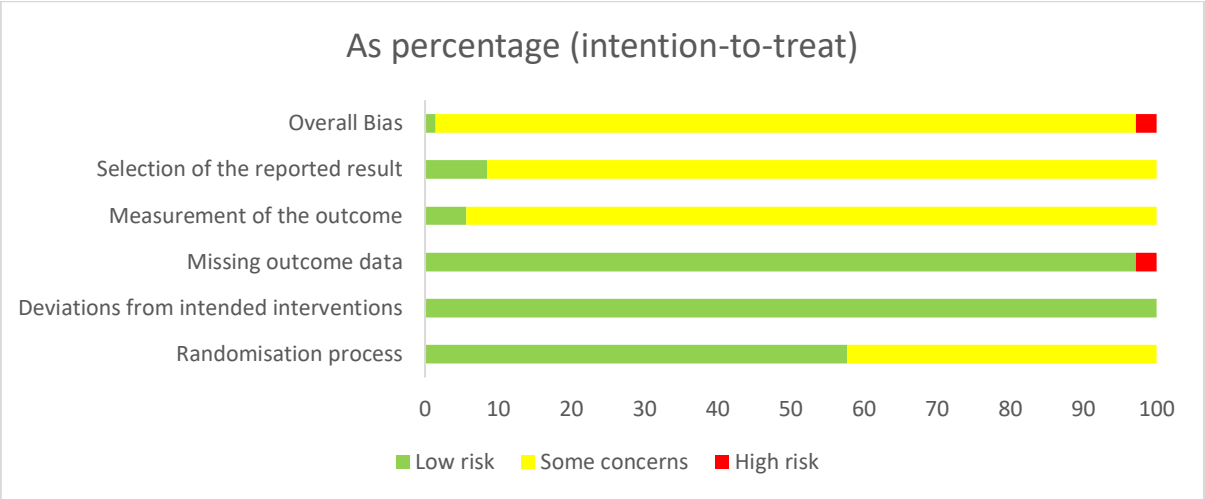
Supplementary Figure 5 - (A) *Posterior density plot for original and alternative prior models.* (B) *Posterior distribution of between-study heterogeneity for original and alternative prior models.*

Supplementary Table 2 – *Sensitivity analysis model results excluding four outlier SIT studies.*

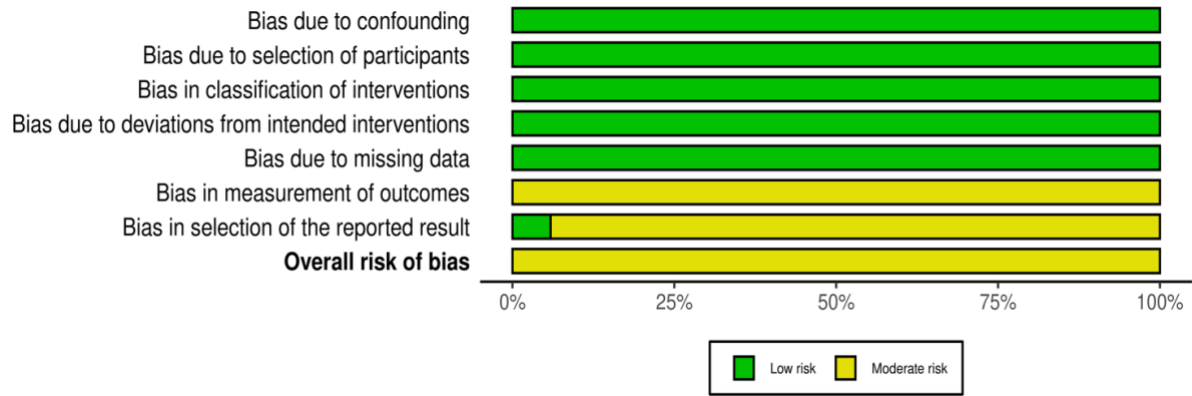
≤10 sprints sensitivity analysis							
Param	Estimate	Est.Error	l-95% CI	u-95% CI	Rhat	Bulk_ESS	Tail_ESS
Intercept	1.1701	0.5019	0.1816	2.1731	1.0001	19,140.3640	14,993.5119
Sprint Repetitions	0.0343	0.0289	-0.0224	0.0926	1.0001	15,727.1787	13,727.2170
Work:rest ratio	0.0466	0.0216	0.0045	0.0889	1.0000	18,953.7941	14,066.5494
Age (y)	-0.1476	0.6734	-1.4716	1.1685	1.0001	22,832.2302	14,146.6321
Intervention Duration (weeks)	-0.0172	0.0068	-0.0304	-0.0041	1.0002	18,971.2687	14,855.6803
Baseline VO2max (mL/kg/min)	-0.0138	0.0098	-0.0331	0.0055	1.0001	17,914.8503	13,805.0776
Sprint Duration	0.0154	0.0095	-0.0032	0.0338	1.0000	21,927.4406	14,435.1768

Supplementary Table 3 – Bayesian model results with total weekly sprint time.

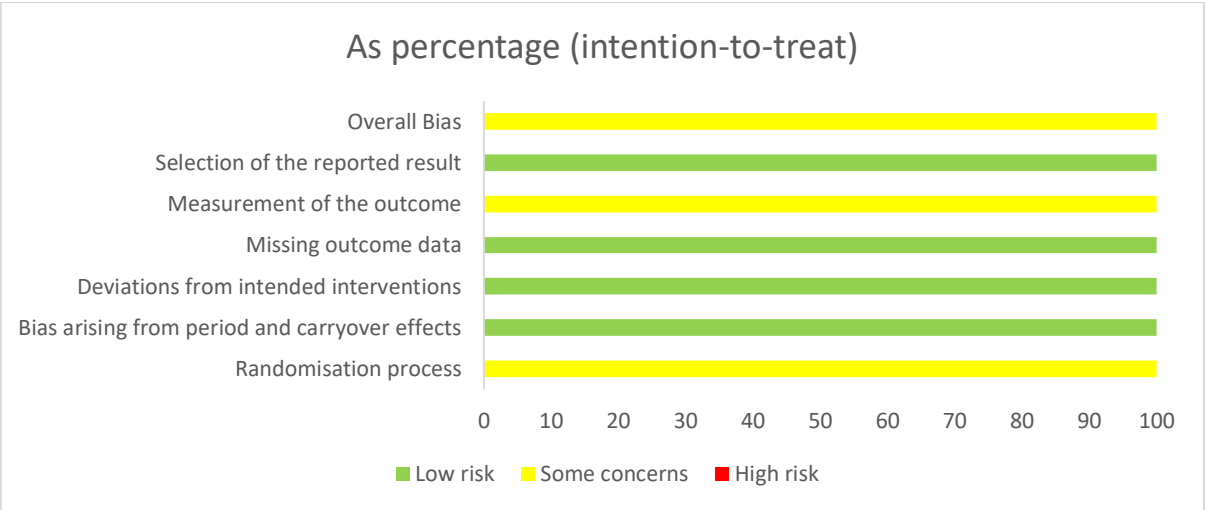
Total Weekly Sprint Time							
Param	Estimate	Est.Error	l-95% CI	u-95% CI	Rhat	Bulk_ESS	Tail_ESS
Intercept	1.1585	0.4791	0.2263	2.1131	1.0007	18,670.0527	14,611.2917
Total weekly sprint time	0.0005	0.0003	-0.0001	0.0010	1.0000	18,557.4337	14,617.6132
Work-rest ratio	0.1523	0.6638	-1.1613	1.4500	1.0000	23,375.9143	13,177.0820
Age (yr)	-0.0155	0.0066	-0.0286	-0.0025	1.0004	20,275.4224	15,245.7925
Duration	0.0487	0.0210	0.0076	0.0899	1.0001	20,379.1630	14,317.3501
Baseline VO2	-0.0066	0.0097	-0.0257	0.0125	1.0005	19,584.7270	15,104.6339



Supplementary Figure 4a - Risk of Bias assessment summary. RoB2.0 tool for randomised trials (v22.8.2019).



Supplementary Figure 4b - Risk of Bias assessment summary. ROBINS-I tool for non-randomised trials (ROBINS-I V2, 2024).



Supplementary Figure 4c - Risk of Bias assessment summary. RoB 2 tool for crossover trials (RoB 2, v18.3.2021).

Matthew Hutchinson: PhD Thesis

Study ID	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall	
Allemeier 1994	Intervention	Control	VO2max	1	!	+	+	!	!	!	+
Metcalfe 2012	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Ijichi 2015	Intervention	Exercise Control	VO2max	1	+	+	+	!	!	!	
Gillen 2016	Intervention	Control	VO2max	1	+	+	+	!	!	+	
Harris 2014	Intervention	Exercise Control	VO2max	1	+	+	+	!	!	!	D1
Bayati 2011	Intervention	Control	VO2max	1	+	+	+	!	!	!	D2
Barnett 2014	Intervention	Control	VO2max	1	+	+	+	!	!	!	D3
Burgomaster 2008	Intervention	Exercise Control	VO2max	1	+	+	+	!	!	!	D4
Hazell 2010	Intervention	Control	VO2max	1	+	+	+	!	!	!	D5
Hazell 2010	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Hazell 2010	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Astorino 2011	Intervention	Control	VO2max	1	+	+	+	+	!	!	
Shepherd 2013	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Ijichi 2015	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Kiviniemi 2015	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
McGarr 2014	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Nalcakan 2014	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Zelt 2014	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Zelt 2014	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Burgomaster 2005	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Burgomaster 2006	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Bailey 2009	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Trilk 2011	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Richardson 2014	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Harmer 2006	Intervention	Clinical Exercise	VO2max	1	+	+	+	!	!	!	
Skleryk 2013	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Hellsten-Westing 15	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Schubert 2017	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Naves 2018	Intervention	Exercise	VO2max	1	!	+	+	+	!	!	
Haines 2020	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Higgins 2016	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Yamagishi 2017	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Yamagishi 2017	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Cuddy 2019	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Metcalfe 2020	Intervention	Control	VO2max	1	+	+	+	!	+	!	
Thomas 2020	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Thomas 2020	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Thomas 2020	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Nalcakan 2018	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Nalcakan 2018	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Aslankeser 2017	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Allen 2017	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Allen 2017	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Kavaliuskas 2018	Intervention	Control	VO2max	1	!	+	+	!	!	!	
Richardson 2016	Intervention	Control	VO2max	1	!	+	+	!	!	!	
De Sousa 2018	Intervention	Control	VO2max	1	!	+	!	+	!	!	!
De Sousa 2018	Intervention	Control	VO2max	1	!	+	!	+	!	!	!
Tan 2021	Intervention	Nutritional	VO2max	1	+	+	+	!	!	!	
Olek 2018	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Olek 2018	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Camacho-Cardenosa	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Broatch 2017	Intervention	Ergogenic Aid + Interventic	VO2max	1	!	+	+	!	!	!	
Thompson 2018	Intervention	Ergogenic Aid + Interventic	VO2max	1	+	+	+	!	!	!	
De Smet 2016	Intervention	Ergogenic Aid + Interventic	VO2max	1	+	+	+	!	!	!	
Little 2019	Intervention	Exercise	VO2max	1	+	+	+	!	+	!	
Muggeridge 2017	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Wyckelsma 2020	Intervention	Ergogenic Aid + Interventic	VO2max	1	!	+	+	!	!	!	
Yamagishi 2019	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Yamagishi 2019	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Oliveira 2022	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Digby 2020	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Bostad 2023	Intervention	Exercise	VO2max	1	!	+	+	!	+	!	
Bostad 2023	Intervention	Exercise	VO2max	1	!	+	+	!	+	!	
Opazo-Diaz 2023	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Inglis 2024	Intervention	Control	VO2max	1	+	+	+	!	!	!	
De Poli 2024	Intervention	Control	VO2max	1	+	+	+	!	!	!	
Colpitts 2021	Intervention	Exercise	VO2max	1	!	+	+	!	+	!	
Colpitts 2021	Intervention	Exercise	VO2max	1	!	+	+	!	+	!	
Leahy 2022	Intervention	Exercise	VO2max	1	+	+	+	!	!	!	
Juskeviciute 2024	Intervention	Exercise	VO2max	1	!	+	+	!	!	!	
Hebisz 2024	Intervention	Control	VO2max	1	+	+	+	!	!	!	

- Low risk
- Some concerns
- High risk
- D1 Randomisation process
- D2 Deviations from the intended interventions
- D3 Missing outcome data
- D4 Measurement of the outcome
- D5 Selection of the reported result

Supplementary Figure 4d - Risk of Bias domain-level risk assessment summary (RoB2.0 v22.8.2019).

		Risk of bias domains							
		D1	D2	D3	D4	D5	D6	D7	Overall
Study	Metcalfe 2016	+	+	+	+	+	-	-	-
	Gillen 2014	+	+	+	+	+	-	-	-
	Whyte 2010	+	+	+	+	+	-	-	-
	Larsen 2013	+	+	+	+	+	-	-	-
	Katz 1984	+	+	+	+	+	-	-	-
	Scalzo 2014	+	+	+	+	+	-	-	-
	Stathis 1994	+	+	+	+	+	-	-	-
	McKenna 1997	+	+	+	+	+	-	-	-
	MacDougall 1998	+	+	+	+	+	-	-	-
	Harmer 2000	+	+	+	+	+	-	-	-
	Bostad 2021	+	+	+	+	+	-	-	-
	Mandic 2022	+	+	+	+	+	-	-	-
	Krusnauskas 2020	+	+	+	+	+	-	-	-
	Denham 2018	+	+	+	+	+	-	-	-
	Jurimae 2022	+	+	+	+	+	-	-	-
Lloria-Varella 2024	+	+	+	+	+	-	+	-	
Mandic 2023	+	+	+	+	+	-	-	-	
Domains:		Judgement							
D1: Bias due to confounding.		- Moderate							
D2: Bias due to selection of participants.		+ Low							
D3: Bias in classification of interventions.									
D4: Bias due to deviations from intended interventions.									
D5: Bias due to missing data.									
D6: Bias in measurement of outcomes.									
D7: Bias in selection of the reported result.									

Chapter 3 - The effect of training frequency on changes in aerobic power following reduced-exertion high-intensity interval training (REHIT)

INTRODUCTION

SIT is characterised by repeated, brief, intermittent bursts of ‘all-out’ exercise, interspersed with periods of active or passive recovery (Hardcastle et al., 2014). As outlined in Chapters 1 and 2, reductions in sprint duration and sprint repetitions can substantially reduce the volume of SIT without necessarily attenuating improvements in $\dot{V}O_{2\max}$. REHIT represents one of the lowest-volume variants of SIT, typically involving 2×20 s all-out sprints within a 10-min cycling session (Metcalf et al., 2012). However, while considerable attention has been given to reducing sprint volume within individual sessions, comparatively little research has examined whether the weekly frequency of REHIT sessions can also be reduced without compromising adaptation.

There is a lack of studies investigating the impact of weekly training frequency on the changes in $\dot{V}O_{2\max}$ in comparison to the influence of intensity (Tripp et al., 2025), especially studies incorporating SIT (Thomas et al., 2020), where a training frequency of 3 sessions/week is the most commonly studied SIT protocol in the literature (Vollaard et al., 2017). Thomas et al. (2020) state that no papers have justified why three sessions per week should be used as the ‘optimal’ training frequency; Thomas et al. (2020) therefore compared 2, 3 and 4 REHIT sessions (2×20 -sec sprints) per week for 6 weeks. Interestingly, their research demonstrated that performing two sessions of REHIT induced significant improvements in $\dot{V}O_{2\max}$ (+10.2%), whereas performing 3 (+8.1%) or 4 (+7.3%) sessions did not confer additional benefit. Other SIT studies (Adamson et al., 2019, Camacho-Cardenosa et al., 2017, Yamagishi and Babraj, 2017) have also reported improvements in $\dot{V}O_{2\max}$ using a training frequency of two sessions per week. However, the independent effect of training frequency is difficult to isolate because these studies differ in sprint duration, sprint repetitions, intervention length and participant characteristics.

Evidence regarding once-weekly training is limited and inconsistent. For example, Chin et al. (2020) reported significant improvements in $\dot{V}O_{2\max}$ after 8 weeks of once-weekly HIIT (12×1 min intervals at 90% HRR with 1-min active recovery at 70% HRR). Conversely, Lenk et al. (2025) observed no significant changes following 6 weeks of a once-weekly 4×4 -min HIIT protocol at 90-95% HRmax. However, this group had a relatively high baseline $\dot{V}O_{2\max}$ (53 ± 7 mL $\cdot$ kg $^{-1}\cdot$ min $^{-1}$), which may have limited the potential for adaptation with such a low stimulus. The authors reported significant improvements in $\dot{V}O_{2\max}$ in the two- and three-session-per-week groups (Lenk et al., 2025). Additional evidence suggests that low-frequency training (≤ 2 sessions per week) can maintain clinically meaningful improvements in $\dot{V}O_{2\max}$. For example, Nakahara et al. (2015) demonstrated that a severe-intensity protocol (80% Wmax to volitional fatigue) performed once per week for 3 months was sufficient to improve $\dot{V}O_{2\max}$ significantly. However,

given that such protocols are neither time-efficient nor easily tolerated, it is unlikely to be practically relevant or scalable beyond a lab-based study.

Currently, establishing the most effective and/or easiest exercise interventions to improve cardiorespiratory fitness is a matter of trial and error (Nalcakan et al., 2018). Therefore, it remains to be seen whether a training frequency as low as one session/week, combined with the low exercise volume of REHIT (2×20 s ‘all-out’ sprints; 3 min active recovery), will elicit similar health improvements. Thomas et al. (2020) provides the rationale for the present study as they demonstrated the efficacy of REHIT to improve $\dot{V}O_{2\max}$ after just two sessions/week, this findings is significant in context to combatting the well documented ‘lack of time’ barrier to exercise participation (Trost et al., 2002) as reducing the number of training sessions per week from 3, to 2, substantially reduces the weekly time commitment to exercise, while maintaining clinically meaningful improvements in $\dot{V}O_{2\max}$. They also concluded that future research should investigate whether an even lower training frequency (1 session/week) would be sufficient to elicit similar improvements in $\dot{V}O_{2\max}$.

This research would be of significance as reducing the training frequency would have a large effect on the weekly time commitment to exercise (10 min/week) and since a perceived ‘lack of time’ is a major barrier to exercise participation, it is possible that lowering the training frequency would increase the uptake and subsequent adherence to exercise (Thomas et al., 2020). Thus, the present study aims to determine the effect of training frequency (1 vs. 2 sessions/week) on changes in $\dot{V}O_{2\max}$ in response to 6 weeks of REHIT in physically inactive individuals.

METHODS

Participants

Apparently healthy, inactive participants were recruited from the University of Stirling and randomised into one of three groups: either performing the REHIT protocol (Metcalf et al., 2012) once per week (REHIT1), twice per week (REHIT2), or a non-exercise control group. Participants were randomised using the sealed envelope method. Exclusion criteria were age <18 or >40 years of age, classified as highly physically active according to the International Physical Activity Questionnaire (IPAQ), answering “yes” to one or more questions on the standard Physical Activity Readiness Questionnaire (PAR-Q), clinically significant hypertension (>140/>90 mmHg), resting heart rate of ≥ 100 bpm, BMI >35 kg/m², individuals reporting a positive test for COVID-19, or pregnancy. Nineteen participants volunteered to take part, but 2 participants withdrew from the study (Control: n=2) after completing their first incremental cycling test to exhaustion. Participant characteristics are shown in **Table 3.1**. All participants voluntarily agreed to participate in the study after reading the Participant Information Sheet and signing a consent form. Ethical approval was granted (NICR - 2022 4056 5055) from the University of Stirling Ethics Committee for Research Involving Human Participants in accordance with the Code of Ethics.

Experimental Procedure

Participants completed an incremental cycling test to exhaustion on an electronically braked cycle ergometer (Lode, Excalibur Sport) to determine baseline $\dot{V}O_{2\max}$ one week before commencing the exercise intervention. Oxygen uptake was measured breath-by-breath using an online gas analyser (Cosmed, Quark CPET). The test started at an intensity of 50 W. Intensity was increased by 1 W every 3 seconds until volitional exhaustion was reached. $\dot{V}O_{2\max}$ was determined using a 15-breath rolling average and accepted if ≥ 2 of the following criteria were met: a respiratory exchange ratio >1.15 , volitional exhaustion, a plateau in oxygen uptake despite increased intensity, and/or a heart rate within 10 beats of the age-predicted maximum ($220 - \text{age}$). Participants were asked to refrain from strenuous exercise and/or consuming caffeine or alcohol within 24 hours before testing. Due to issues encountered with the online gas analyser where it systematically under-estimated $\dot{V}O_{2\max}$ values. After testing repeatedly at different submaximal values, the online gas analyser was sent to Italy for repair. Since the direct measurement of $\dot{V}O_{2\max}$ was affected, maximal aerobic power ($W_{\max}$) attained during the incremental cycling test to exhaustion was used as the outcome measure to determine changes in maximal aerobic power. $W_{\max}$ was defined as the highest work rate achieved during the incremental ramp test. $W_{\max}$ was recorded directly from the electronically braked ergometer as the highest work rate attained before participants were unable to maintain the minimum required cadence of 60 rpm despite verbal encouragement.

Participants completed a 6-week exercise intervention of the REHIT exercise protocol. Participants were randomly allocated to one of three groups (Control, REHIT1, REHIT2) using the sealed envelope method. Although the current study began with a control group, recruitment had to be adjusted to the randomisation strategy in response to poor volunteer numbers. To maintain sufficient numbers for meaningful comparisons between the REHIT intervention groups, allocation to the control group was discontinued, and participants were then randomised between REHIT1 and REHIT2. Participants either performed 1 (REHIT1) or 2 (REHIT2) REHIT sessions per week, while participants in the Control group were asked to maintain their regular lifestyle for 6 weeks. The REHIT exercise protocol involved 10 min of unloaded cycling on a mechanically braked cycle ergometer (Monark, Ergomedic 894e), interspersed with 2×20 s 'all-out' sprints against a resistance of 7.5% of participants' body mass. The first sprint began at 1 minute 40 seconds and finished at 2 minutes, and the second sprint began at 5 minutes 40 seconds and finished at 6 minutes. Participants were asked to cycle as fast as they could in the immediate lead-up (2-3 s) to each sprint. 'All-out' sprint durations started at 10 s in week 1, increased to 15 s in week 2, and further increased to 20 s for weeks 3-6. Participants in REHIT2 had at least 1 day of recovery in between the two weekly sessions. Verbal encouragement was given during each sprint.

A post-intervention $\dot{V}O_{2\max}$ incremental cycling test was performed 3-5 days after the final exercise session (REHIT1; 3 ± 1 days, REHIT2; 4 ± 2 days). RPE (15-point Borg scale) (Borg, 1982), affect (11-point feeling scale (Hardy and Rejeski, 1989)) and felt arousal (Svebak and Murgatroyd, 1985) were recorded every minute during each exercise session to monitor the relevant psychological changes of the participants in response to REHIT. All psychological questionnaire data were collected for analysis as part of a separate PhD project.

Statistical Analysis

Results are expressed as mean values $\pm$ SD. Statistical analysis was performed using R, and tables and figures were created in R. A two-way mixed model ANOVA group (REHIT1/REHIT2) $\times$ time (pre-/post-intervention) was used to determine differences between the groups for $\Delta W_{\max}$.

Significance was accepted at $p < 0.05$.

A sensitivity power analysis was performed using G*Power 3.1 (Faul et al., 2007) for a repeated-measures, within-between interaction. Based on the final sample of 14 participants, two groups, two time points, $\alpha = 0.05$, 80% power, a pre-post correlation of $r = .964$, and a nonsphericity correction of $\epsilon = 1$, the minimum detectable interaction effect was Cohen's $f = 0.109$ ($\lambda = 9.32$).

The practical relevance of the changes in $W_{\max}$ was assessed using the smallest worthwhile change (SWC). In accordance with Marocolo et al. (2019), the SWC was calculated as $0.6 \times$ between-participant $W_{\max}$ SD_{baseline} because the participants had a low fitness level. The baseline SD across the REHIT1 and REHIT2 groups was 45.2 W, producing an SWC of 27.1 W.

RESULTS

No significant differences were observed between groups at baseline for body mass, BMI, or Pre $W_{\max}$ (**Table 3.1**). Overall mean adherence was not significantly different between the two groups (98% for REHIT1, 93% for REHIT2). 1 participant missed 1 session from REHIT1 (47/48 sessions completed), 3 participants missed 1 session, and 1 participant missed 2 sessions from REHIT2 (67/72 sessions completed). There was a significant main effect of time for $W_{\max}$, $F(1,12) = 12.38$, $p = 0.004$, $\eta^2 = .508$, indicating that $W_{\max}$ increased from pre- to post-intervention when both REHIT groups were considered together. However, there was no significant group $\times$ time interaction, $F(1, 12) = 0.32$, $p = 0.580$, $\eta^2 = .026$, indicating no clear evidence that the change in $W_{\max}$ differed between REHIT1 and REHIT2. **Figure 3.1** shows the changes in $W_{\max}$ from pre- to post-intervention, which were 9.6 ± 14.6 W ($5.8 \pm 8.5\%$) in REHIT1 and 13.3 ± 7.3 W ($7.5 \pm 4.9\%$) in REHIT2. The difference between the mean changes in REHIT2 and REHIT1 was 3.7 W (95% CI: -10.5 to 17.9 W). The mean increases in $W_{\max}$ in REHIT1 and REHIT2 did not exceed the smallest worthwhile change of 27.1 W.

Table 3.1 – Participant characteristics

	REHIT1	REHIT2	Control
	N = 8	N = 6	N = 3
Age (y)	23 ± 4	23 ± 4	20 ± 1
Height (m)	1.69 ± 0.10	1.72 ± 0.15	1.78 ± 0.15
Body Mass (kg)	67.4 ± 9.1	75.4 ± 27.9	79.7 ± 6.7
BMI (kg·m⁻²)	23.6 ± 2.9	24.8 ± 6.1	25.4 ± 4.2
Wmax (W)	167 ± 27	197 ± 61	204 ± 43

Values shown are mean ± SD.

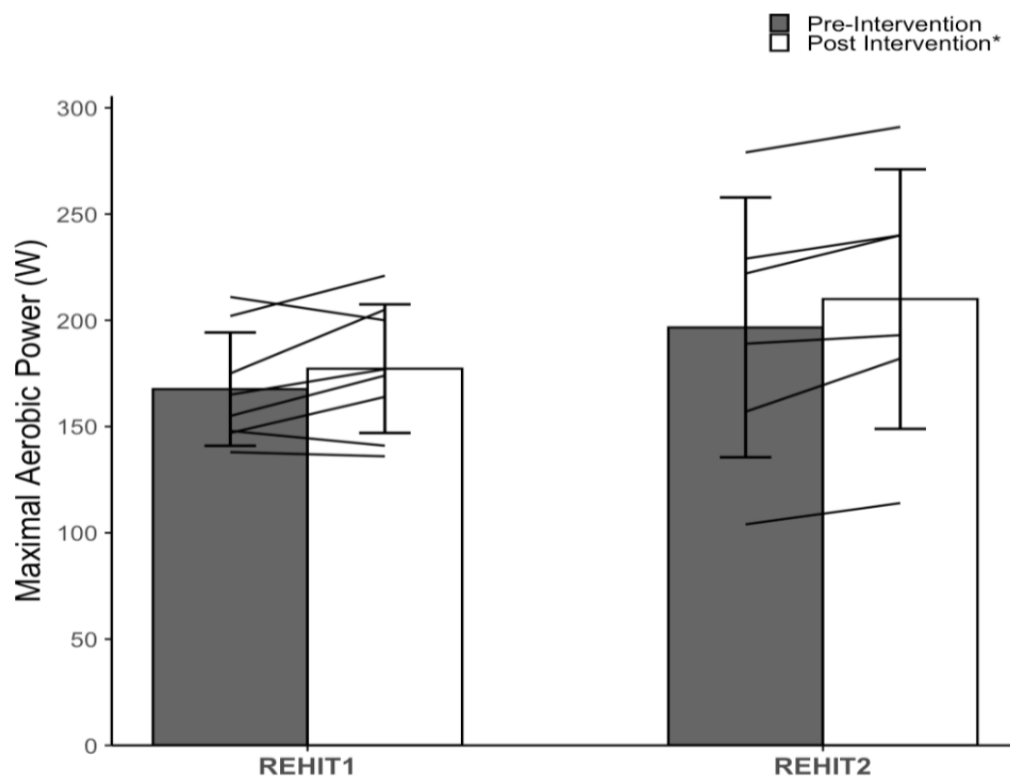


Figure 3.1 - Group mean and individual data with directional changes in Wmax in response to 6 weeks of REHIT performed at a training frequency of either once- (REHIT1) or twice (REHIT2) weekly. * $p < 0.01$ for the main effect of time.

DISCUSSION

The present study aimed to compare changes in $W_{\max}$ following six weeks of once- and twice-weekly REHIT sessions in physically inactive individuals. $W_{\max}$ was used as the primary outcome as unforeseen issues with the online gas analyser prevented the reliable direct measurement of $\dot{V}O_{2\max}$. $W_{\max}$ represents the highest external workload that can be sustained during an incremental exercise test (Kuipers et al., 1987) and is strongly associated with $\dot{V}O_{2\max}$ (Storer et al., 1990). Nevertheless, it should be interpreted as a measure of maximal aerobic performance rather a direct measurement of cardiorespiratory fitness.

$W_{\max}$ increased from pre- to post-intervention when the two REHIT groups were considered together, as indicated by the significant main effect of time. The mean changes were 9.6 ± 14.6 W in REHIT1 and 13.3 ± 7.3 W in REHIT2. However, there was no significant group $\times$ time interaction, and the interaction effect was small ($\eta p^2 = .026$). Therefore, there was no clear evidence that the change in $W_{\max}$ differed between participants completing REHIT once or twice per week. The non-significant group $\times$ time interaction does not demonstrate equivalence between the two training frequencies, as a non-significant conventional interaction test cannot provide evidence that an interaction is absent or negligible (Jabbari and Cribbie, 2022, Altman and Bland, 1995).

The practical importance of the changes was also assessed using the SWC. Following the approach recommended by Marocolo et al. (2019) for participants with a low fitness level, the SWC was calculated to be at a threshold of 27.1 W. The mean increases in REHIT1 and REHIT2 groups did not exceed this threshold. Therefore, although $W_{\max}$ increased significantly over time, the magnitude of the mean change within either group did not reach the threshold for what would be considered a worthwhile improvement.

The finding of no significant group $\times$ time interaction in the present study is in contrast to work by Dalleck et al. (2010), which showed a significant interaction between the frequency of sessions and peak workload values following 6 weeks of interval training (6-8 $\times$ 30 s sprints at $\sim$ 110-120% of peak workload). They showed that the magnitude of $W_{\max}$ improvements was significantly greater in the group training twice per week (14.4 ± 8.8 W) compared to once (9.5 ± 14.7 W) per week. The present study demonstrated comparable improvements in $W_{\max}$ to those reported by Dalleck et al. (2010), although no significant difference was observed between groups in the current study. The mean changes in $W_{\max}$ were numerically similar to those reported by Dalleck et al. (2010), although the present study did not identify a significant group-by-time interaction. The smaller sample in the present study (REHIT1, $n=8$; REHIT2, $n=6$), compared with Dalleck et al. (2010) (once-weekly, $n = 11$; twice-weekly, $n = 9$), may have contributed to uncertainty in the estimated between-group difference. However, the differing statistical significance of the findings cannot be attributed to sample size alone. The sensitivity analysis and confidence interval reported below provide further context for interpreting this uncertainty.

Numerically similar mean increases in $W_{\max}$ were observed following the REHIT intervention despite a lower weekly exercise time commitment than in Dalleck et al. (2010) (10 and 20 min/week vs. ~30 and ~60 min/week, respectively). However, this descriptive comparison does not establish equivalent effects between protocols. Furthermore, without an adequately sized non-exercise control group, the increases observed in the present study cannot be attributed conclusively to REHIT.

Additionally, differences in baseline $W_{\max}$ between the two studies complicate comparisons further, for example, in the present study, the sample population were physically inactive with substantially lower baseline $W_{\max}$ values across both groups (167 ± 27 W; REHIT1, 197 ± 61 W; REHIT2) compared to the active cohort (279 ± 65 W; 1 day/wk, 276 ± 42 W; 2 days/wk) studied by Dalleck et al. (2010). Therefore, the similar improvements observed following a lower total weekly commitment to exercise in the current study may partly be explained by the fact that individuals with lower baseline fitness levels typically demonstrate larger proportional gains following training (Milanovic et al., 2015).

It is well established that exercise intensity strongly influences the increase in $\dot{V}O_{2\max}$ induced by exercise (MacInnis and Gibala, 2017). The REHIT exercise protocol used in the present study involved sprints at an 'all-out' intensity, which equates to approximately 350% of $\dot{V}O_{2\max}$ (Ito, 2019). In contrast, Dalleck et al. (2010) implemented intervals at ~110-120% of peak workload. This difference in exercise intensity may partly explain why the current cohort demonstrated similar improvements in $W_{\max}$ despite a substantially lower total training volume.

Although a significant improvement in $W_{\max}$ was observed in the current study across both groups, this does not always translate into meaningful $\dot{V}O_{2\max}$ gains as evidenced in other SIT studies (Burgomaster et al., 2005, Dalleck et al., 2010, Kavaliuskas et al., 2017, MacDougall et al., 1998). This may be due to SIT improving endurance performance, potentially through peripheral muscular mechanisms such as enhanced metabolic efficiency (Burgomaster et al., 2006) or increased glycolytic flux (MacDougall et al., 1998), rather than central cardiovascular mechanisms, which would lead to an improved $\dot{V}O_{2\max}$.

A sensitivity power analysis provided further context for the non-significant interaction. Based on the final sample of 14 participants and the observed pre-post correlation, the study had 80% power at $\alpha = .05$ to detect a group x time interaction of Cohen's $f = 0.109$ or greater. Effects below this sensitivity threshold may not have been detected. The estimated difference in mean $W_{\max}$ change between REHIT2 and REHIT1 was 3.7 W (95% CI: -10.5 to 17.9 W). As the confidence interval included zero and values favouring either training frequency, there is considerable uncertainty around the true between-group difference. Therefore, the absence of a significant interaction should be interpreted as an absence of clear evidence of a difference between the training frequencies, rather than evidence that once- and twice-weekly REHIT produce equivalent outcomes.

A central limitation was the absence of an adequately sized non-exercise control group. Although a control condition was included initially, recruitment difficulties meant that randomisation to the

control group was halted at $n=3$, and any new volunteers were randomised to either REHIT1 or REHIT2 to ensure there were enough participants in the intervention groups for analysis. This meant the data was insufficient for a reliable inferential comparison. It is therefore impossible to determine how much of the observed pre to post increase in W_{max} was attributable to REHIT. Alternative explanations include normal day-to-day variations between tests, familiarisation with the testing protocol, and changes in participant effort or motivation. Therefore, the findings should be interpreted only as a comparison of the W_{max} changes observed following once- and twice-weekly REHIT, rather than evidence that either frequency was effective relative to no exercise. There are several other limitations to the present study. Firstly, W_{max} was used as the primary outcome measure, serving as an indirect indicator of maximal aerobic capacity, rather than directly measured $\dot{V}O_{2max}$ using an online gas analyser. Although W_{max} is highly correlated with $\dot{V}O_{2max}$, particularly during cycle ergometry (Storer et al., 1990), and has been reported to have acceptable test-retest reliability at the group level (Sorensen et al., 2007), it does not fully capture all the determinants of aerobic fitness measured directly. Secondly, assessors were non-blinded during testing, which may have introduced unconscious bias during assessments. For example, assessors may have been less motivating or unintentionally influenced participants' efforts during testing. Given that motivation is a key factor influencing performance during maximal aerobic capacity testing (Midgley et al., 2018), this could have affected the reliability of W_{max} values achieved during testing. Third, a potential learning effect can't be ruled out, as none of the participants had previously experienced a maximal incremental cycling test to exhaustion, which may have contributed to improved performance during the post-intervention test, independent of physiological adaptations. There is evidence for such practice effects between the first two maximal incremental tests (Hopkins et al., 2001), in which non-athletes are less reliable than athletes. However, others have found no learning effects in healthy, recreationally active adults (Dideriksen and Mikkelsen, 2017). Without an adequately sized control group or repeated baseline measurements, the extent to which familiarisation contributed to the observed changes cannot be established.

The findings of the current study contribute to the body of research aimed at identifying the minimal amount of exercise required to elicit meaningful health improvements in the ever-growing physically inactive population. Establishing the lowest dose of exercise that provides sufficient stimulus for such improvements has important real-world implications for promoting physical activity in the general population, particularly for those who perceive a lack of time as a major barrier to regular exercise participation. Demonstrating that performing a single 10-minute REHIT session per week can significantly improve maximal aerobic capacity – the best predictor of overall health and disease risk – would provide further support for the recommendation of very low-volume, time-efficient exercise in public health and real-world interventions aimed at improving health and long-term adherence to exercise.

Future research should address the methodological limitations encountered in the present study. First, the required sample size should be determined prospectively, with an additional allowance for dropouts. Participants should be allocated using a prespecified stratified randomisation procedure to improve balance in important baseline characteristics across REHIT1, REHIT2 and control. Baseline $\dot{V}O_{2\max}$ should be used as the stratification variable. The allocation procedure and planned response to recruitment difficulties should be specified before recruitment and should not be altered in response to emerging group sizes.

If recruitment of an adequately sized control group is not feasible, future research should consider incorporating a no-exercise control period before the intervention so that each participant can act as their own control. Participants could complete a familiarisation test followed by two baseline assessments separated by a period in which they maintain their usual lifestyle. They could then be stratified according to baseline $\dot{V}O_{2\max}$ and randomised to REHIT1 or REHIT2. Comparing each participant's change during the control period with their change during the intervention would help distinguish changes related to the intervention from test-retest variability and familiarisation.

Furthermore, direct measurement of $\dot{V}O_{2\max}$ should be used to assess changes in cardiorespiratory fitness reliably with contingency arrangements in place before data collection commences in case of equipment failure. Additionally, future research should incorporate assessor-blinding during testing procedures to minimise potential bias and include familiarisation sessions prior to baseline testing to potentially reduce any learning effect of the maximal incremental tests, which may be more important for physically inactive cohorts with no previous experience of maximal testing.

In conclusion, $W_{\max}$ increased over time in participants allocated to once- and twice-weekly REHIT, but there was no clear evidence that the magnitude of change differed between the training frequencies. The mean change in neither group exceeded the SWC calculated as 27.1 W.

Furthermore, because an adequately sized control group was not available, the observed changes cannot be attributed conclusively to REHIT. These findings should therefore be regarded as preliminary and do not provide sufficient evidence to recommend once-weekly REHIT as equivalent or superior to twice-weekly REHIT sessions.

Chapter 4 - Improvements in aerobic fitness with exercise training: the role of myokines

INTRODUCTION

Considerable interindividual variability exists in the magnitude of improvement in $\dot{V}O_{2\max}$ following a standardised exercise intervention, as discussed in **Chapter 1**. Although genetic factors contribute substantially to this variability, the molecular mechanisms through which these differences translate into physiological adaptations remain poorly understood (Bouchard et al., 1999, Keller et al., 2011). Improvements in $\dot{V}O_{2\max}$ are considered to be primarily limited by central adaptations that increase oxygen delivery, including increases in blood volume and maximal cardiac output (Lundby et al., 2017). However, peripheral adaptations that improve the extraction and utilisation of oxygen within skeletal muscle also contribute substantially to the improvement in $\dot{V}O_{2\max}$ following training (Joyner and Lundby, 2018, Skattebo et al., 2020). Despite extensive knowledge of the training adaptations that underpin improvements in $\dot{V}O_{2\max}$ following standardised exercise interventions, there remains a lack of understanding of the mechanisms/pathways that mediate the $\dot{V}O_{2\max}$ -enhancing adaptations, whether central or peripheral. Differences in molecular signalling within skeletal muscle may contribute to the regulation of both central and peripheral adaptations and identifying signals that differ according to the degree of $\dot{V}O_{2\max}$ responsiveness may provide insight into why some individuals demonstrate substantially greater improvements following the same training stimulus.

One potential mechanism linking skeletal muscle activity with exercise-induced adaptations is the production and release of myokines. Steensberg et al. (2000) were the first to demonstrate that skeletal muscle is a secretory organ with endocrine functions, building on this work, they later defined any such protein that is released from the skeletal muscle and exerts either endocrine, paracrine, or autocrine effects, as a “myokine” (Pedersen et al., 2003, Severinsen and Pedersen, 2020). Myokines have also been shown to mediate crosstalk between active and inactive muscle, as Catoire et al. (2012) reported changes in gene expression in the exercising and non-exercising legs following one-legged endurance exercise. This supports the idea that myokines may modulate $\dot{V}O_{2\max}$. Efforts have been made to identify all myokines that are secreted from skeletal muscle, along with details of their specific functions (Catoire et al., 2014, Hartwig et al., 2014, Norheim et al., 2011, Pourteymour et al., 2017, Raschke et al., 2013), giving the term “myokinome”, which now contains information on over 650 myokines (Khan and Ghafoor, 2019). However, there is still work to be done in determining each myokine’s specific function(s).

The rationale for the selection of the candidate myokines in the current study was derived primarily from the findings of Keller et al. (2011) and Catoire et al. (2014). Keller et al. (2011) used gene ontology analysis to identify a training response transcriptome associated with the magnitude of improvement in $\dot{V}O_{2\max}$ following endurance training. A total of 86 genes were regulated differently between individuals demonstrating smaller and larger improvements in $\dot{V}O_{2\max}$, with

the genes more strongly regulated in the high-response group being associated with cardiovascular and tissue development. Catoire et al. (2014) used secretome analysis to identify approximately 70 putative myokines that were regulated in skeletal muscle following 12 weeks of combined endurance and resistance training. When the findings of the two studies were compared, 13 genes that differed according to the magnitude of $\dot{V}O_{2\max}$ improvement also encoded putative myokines that were responsive to exercise training. This overlap was greater than expected by chance and provided the primary rationale that the regulation and release of specific myokines may contribute to differences in $\dot{V}O_{2\max}$ adaptation.

Several of the candidate myokines selected for investigation have known or proposed functions associated with the extracellular matrix and vascular remodelling. COL4A1, COL4A2 and COLIV α represent components of extracellular matrix, while LAMA4 encoded laminin- α 4, which is involved in micro vessel maturation (Catoire et al., 2014, Thyboll et al., 2002). CTHRC1 has been implicated in vascular remodelling (Wang et al., 2023), while SPARC is an extracellular matrix associated protein which has also been implicated in the development of erythroid progenitor cells (Luo et al., 2012, Hartwig et al., 2014). Furthermore, KDR encodes VEGFR2, a major receptor involved in VEGF signalling and therefore provides a potential link with exercise-induced angiogenesis (Holmes et al., 2007). These processes are relevant to $\dot{V}O_{2\max}$ because capillarisation and vascular remodelling may improve oxygen delivery and utilisation within skeletal muscle, although the direct involvement of these myokines in determining $\dot{V}O_{2\max}$ adaptation has not been established. Keller et al. (2011) identified MHCC to provide a possible connection with the wider training-response network as it has been proposed to modify insulin and IGF2 receptor activity (Naranda et al., 1997). Whereby IGF2 has been shown to be a key regulator of human satellite cell proliferation, differentiation, and mitochondrial bioenergetics (Voshtani et al., 2025). BDNF is a recognised exercise associated protein and appears to play a role in the activation of AMPK and increased fat oxidation (Matthews et al., 2009), along with mitochondrial biogenesis (Wood et al., 2018).

Three additional exercise-responsive proteins, CCL21, VEGF-C and THBS4, were included as comparator myokines. These proteins have previously been identified as being regulated by skeletal muscle contraction and/or exercise training, but were not among the 13 myokines identified from the overlap between the $\dot{V}O_{2\max}$ response transcriptome and exercise-responsive secretome described above (Catoire et al., 2014). Their inclusion therefore allowed the current study to investigate whether any associations with the magnitude of $\dot{V}O_{2\max}$ adaptation were specific to the candidate myokines, rather than reflecting a general response among exercise-regulated proteins.

Taken together, these findings provide a plausible basis for myokines contributing to interindividual variability in $\dot{V}O_{2\max}$ adaptation. Individuals demonstrating greater improvements in $\dot{V}O_{2\max}$ may exhibit greater regulation and/or release of specific exercise-responsive myokines, which could provide a stronger stimulus for vascular, metabolic or structural adaptation. Therefore,

the present study aimed to investigate whether training-induced changes in the plasma concentrations of selected myokines were associated with differences in the magnitude of improvement in $\dot{V}O_{2\max}$ following exercise training. Identifying the factors that determine heterogeneity in response to training is important for overall public health and further establishing the not-yet-fully-understood molecular links between exercise and disease prevention via improved $\dot{V}O_{2\max}$ can only strengthen the public health message that exercise is medicine (Whitham and Febbraio, 2016).

METHODS

Participants

Apparently healthy, untrained male participants were recruited from the University of Stirling (n=22). Two participants withdrew from the study due to illness, leaving 20 participants in the final sample. Exclusion criteria were <18 or >40 years of age, classification as highly physically active on the International Physical Activity Questionnaire (IPAQ), answering “yes” to one or more questions on the standard Physical Activity Readiness Questionnaire (PAR-Q), resting blood pressure >140/>90 mmHg, resting heart rate of ≥ 100 bpm, BMI >35 kg/m², a personal history of metabolic or cardiovascular disease, or female participants due to the unknown effects of the menstrual cycle on the levels of measured myokines. Participant characteristics are shown in **Table 4.1**. All participants voluntarily agreed to participate in the study after reading the Participant Information Sheet and signing an informed consent form. Ethical approval was granted (NICR - 2023 14437 11229) from the University of Stirling Ethics Committee for Research Involving Human Participants in accordance with the Code of Ethics.

Experimental Procedure

$\dot{V}O_{2\max}$ assessment

All participants completed an incremental cycling test to exhaustion on an electronically braked cycle ergometer (Lode, Excalibur Sport) to determine baseline $\dot{V}O_{2\max}$. Oxygen uptake was measured breath-by-breath using an online gas analyser (K5, Cosmed, Banbury, UK). The test started at an intensity of 50 W; intensity was increased by 1 W every 3 seconds until either volitional exhaustion or inability to maintain a pedalling frequency of >60 rpm was reached. $\dot{V}O_{2\max}$ was determined using a 15-breath rolling average and accepted if ≥ 2 of the following criteria were met: a respiratory exchange ratio >1.15, volitional exhaustion, a plateau in oxygen uptake despite increasing intensity, and/or a heart rate within 10 beats of the age-predicted maximum (220-age). Participants were asked to refrain from strenuous exercise and from consuming caffeine or alcohol within 24 hours of testing. Verbal encouragement was given throughout.

Blood samples were collected twenty-four hours after the pre- and post-intervention $\dot{V}O_{2\max}$ tests, following an overnight fast, during which only water was permitted. The post-intervention $\dot{V}O_{2\max}$ test was completed, where possible, 3 days after the final REHIT session, meaning that the post-intervention blood sample was collected ~4 days after the final training session. The blood sampling timeline was chosen to determine whether the REHIT intervention resulted in sustained changes in circulating myokine concentrations, rather than measuring the transient response to an individual training session. A 10 mL venous blood sample was collected from an antecubital vein into a 10 mL lavender Vacutainer tube (Becton Dickinson, BD, UK) containing K2EDTA anticoagulant. Blood samples were immediately placed into ice and taken to the lab for analysis. Haemoglobin concentration was measured by depositing 10 μ L of venous blood into a microcuvette which was then placed into a portable analyser (HemoCue Hb 201+, HemoCue Ltd, Angelholm, Sweden). Haematocrit was determined in triplicate using the microhematocrit packed cell volume method. EDTA-anticoagulated whole blood was drawn into three microhematocrit capillary tubes, which were sealed at one end and centrifuged at 12,000 g for 5 minutes. The packed cell volume was measured using a microhematocrit reader (Hawksley & Sons Ltd, Sussex, UK), and the modal value was used in the subsequent analysis. The remaining blood was centrifuged at 1500 g for 10 min at 4°C. Samples were stored at -80°C until all participants had completed the study.

The percentage change in plasma volume between the pre-and post-training samples was estimated from haemoglobin and haematocrit values using the equation of Dill and Costill (1974).

$$\Delta PV(\%) = 100 \times \left[\left(\text{Hb}_{\text{pre}} / \text{Hb}_{\text{post}} \right) \times \left(100 - \text{Hct}_{\text{post}} \right) / \left(100 - \text{Hct}_{\text{pre}} \right) - 1 \right]$$

Where Hb represents haemoglobin concentration and Hct represents haematocrit.

Post-intervention myokine concentrations were corrected for changes in plasma volume using the calculated percentage change in plasma volume.

Myokine selection

The candidate myokines were selected based primarily on the findings of Keller et al. (2011) and Catoire et al. (2014). Keller et al. (2011) identified a training-responsive skeletal muscle transcriptome associated with improvements in aerobic capacity. These data were compared with exercise-regulated putative skeletal muscle secretome reported by Catoire et al. (2014), resulting in 13 overlapping candidate genes. The myokines selected for analysis were COL4A1, COL4A2, COLIV α , CTHRC1, LAMA4, MHCC, SPARCL1, VEGFR2, and BDNF. Three additional exercise-responsive myokines, CCL21, VEGF-C and THBS4, were included as comparator controls. CCL21 has previously been identified as a contraction regulated protein released by cultured human skeletal muscle cells, while THBS4 and VEGF-C have been identified as exercise-regulated candidate secretory proteins (Raschke et al., 2013, Catoire et al., 2014, Pourteymour et

al., 2017). Unlike the primary candidate myokines, these three proteins were not identified from the $\dot{V}O_2\text{max}$ -response transcriptome and the exercise-training secretome. They were therefore included to determine whether associations with $\dot{V}O_2\text{max}$ responsiveness were specific to the selected candidate myokines.

Myokine analysis

Plasma concentrations of the selected myokines were quantified using two magnetic bead-based multiplex immunoassays on a Luminex platform running xPONENT software (version 4.2.1509.0). BDNF, CCL21, COLIV α , VEGF-C and VEGFR2 were analysed using a customised five-analyte Human Luminex Discovery Assay (LXSAHM-05; lot L152628; R&D Systems, Minneapolis, USA). A sample volume of 70 μL was used and concentrations were expressed in pg/mL. COL4A1, COL4A2, CTHRC1, LAMA4, MHCC, SPARCL1 and THBS4 were analysed using a Cloud-Clone magnetic bead-based multiplex assay (IS135; lot L2; Cloud-Clone Corp., Wuhan, China). A sample volume of 70 μL was used and concentrations were expressed in ng/mL. Both assays were carried out in 96-well plates according to the manufacturers' instructions. Before analysis, the plasma samples were thawed at room temperature and mixed gently by inversion. Each plasma sample was prepared and analysed in duplicate, the average value being used for each participant, with a minimum count of 50 beads per analyte. NID was also selected for analysis but had to be excluded due to a technical error.

REHIT intervention

Participants completed 6 weeks of reduced-exertion high-intensity interval training (REHIT), performing three sessions per week. The exercise sessions involved 10 minutes of unloaded cycling interspersed with 2 'all-out' sprints. During week 1, the sprint duration was 10 seconds, increasing to 15 seconds in week 2 and to 20 seconds in weeks 3-6. The all-out sprints were performed against a resistance of 7.5% of the participant's body mass. Sprints finished at 2 minutes and 6 minutes into the 10-minute session. Participants who missed more than three training sessions were excluded from the data analyses. After the 6 weeks, participants were asked to perform a second $\dot{V}O_2\text{max}$ test 2-5 days after the last REHIT session (2.9 ± 0.4 days) to determine the effect of training under the same conditions as the baseline $\dot{V}O_2\text{max}$ test. Twenty-four hours after the $\dot{V}O_2\text{max}$ test and following an overnight fast, a post-training venous blood sample was taken and analysed as described above. Participants were ranked from low to high based on their improvement in $\dot{V}O_2\text{max}$ and designated to either the high, medium, or low responder group.

Power output and cadence were recorded during each REHIT session. Peak power relative to body mass ($\text{W}\cdot\text{kg}^{-1}$) and maximum cadence (rpm) were obtained for each of the two sprints. For the comparison between the first and final training sessions, the values from the two sprints were averaged to provide one value per participant for each session. Peak power relative to body mass was selected as the primary power measure to account for differences in body mass between participants, while maximum cadence was examined to determine whether participants were able to

generate a sufficient sprint effort. Cadence was examined as a secondary measure of sprint performance. Missing power or cadence values were not imputed. Training heart rate data were unavailable and therefore could not be included in the analysis.

To provide a measure of the training stimulus achieved across the intervention, mean training peak power relative to body mass was calculated for each participant. Peak power values from the available sprints were initially averaged within each training session, after which the session values were averaged across the intervention to provide one mean training peak power value per participant.

Statistical Analysis

Results are expressed as mean values $\pm$ SD. Statistical analyses were performed using R and Jamovi, while tables and figures were created in R. Differences between pre- and post-training $\dot{V}O_2\text{max}$ and W_{max} were initially examined using paired sample t-tests. Participants were divided into three groups based on individual $\dot{V}O_2\text{max}$ response to training (low/medium/high responders). A two-way mixed model ANOVA with group (High/Medium/Low) $\times$ time (pre-/post-intervention) was used to determine differences between groups in changes in each myokine. To determine whether any differences in the myokine response were influenced by the training stimulus achieved during the intervention, the analysis was repeated as a two-way mixed ANCOVA with mean training peak power relative to body mass included as a covariate.

Changes in peak power relative to body mass and maximum cadence were examined using separate two-way mixed ANOVAs, with session as the within-participant factor and responder group as the between-participant factor. The session-by-responder-group interaction was used to determine whether changes in training performance differed between the low, medium and high responders. Pearson's correlation coefficient was used to assess bivariate correlations between $\Delta\dot{V}O_2\text{max}$ and myokine responses. Significance was accepted at $p < 0.05$.

An a priori power calculation was performed for the planned comparison between the low- and high-responder tertiles. In the absence of directly comparable estimates for changes in circulating concentrations of the selected myokines, the calculation assumed a large standardised mean difference of 1.5 pooled within-tertile SDs between the low- and high-responder groups. This assumption was informed by the substantial differences in training-responsive skeletal muscle gene expression previously reported between extreme $\dot{V}O_2\text{max}$ response groups (Keller et al., 2011), rather than by established estimates of circulating myokine responses. Using a two-sided significance level of $\alpha = 0.05$, eight participants in each extreme tertile (low vs high responder groups) provided 80% power to detect an effect of this magnitude. Equal allocation across the low-, medium- and high-responder tertiles therefore produced a planned total sample size of 24 participants.

RESULTS

Overall mean adherence for the REHIT sessions was 97% (348/360 sessions completed). Across the full sample, $\dot{V}O_2\text{max}$ increased significantly by $6.6 \pm 9.3\%$ ($p = 0.007$; **Table 4.2**). W_{max} increased from 245.8 ± 64.6 W before training to 268.1 ± 61.6 W, representing a mean increase of 22.3 ± 16.8 W ($10.3 \pm 9.4\%$; $p < 0.001$). No significant overall changes were observed for any of the myokines (**Table 4.2**). After designation to a group based on $\Delta\%\dot{V}O_2\text{max}$ response, the mean $\Delta\%\dot{V}O_2\text{max}$ for each group was as follows: high responder group $14.6 \pm 5.7\%$; medium responder group $5.8 \pm 2.0\%$; low responder group $-3.2 \pm 4.5\%$. The mean W_{max} changes according to $\dot{V}O_2\text{max}$ response groups were as follows: high responder group 28.6 ± 17.6 W; medium responder group 19.0 ± 8.8 W; low responder group 16.1 ± 18.1 W. There was no significant difference in W_{max} change between the responder groups. A significant group-by-time interaction effect was observed for LAMA4 ($p = 0.029$); however, post hoc comparisons did not reveal any significant pairwise differences between groups. After mean training peak power relative to body mass was included as a covariate, the time-by-responder-group interaction for LAMA4 remained significant ($p = .041$). There was no significant time-by-mean-training-peak-power interaction for LAMA4 ($p = .902$), indicating that the change in LAMA4 was not associated with the power produced during training.

No significant interactions were found for any other myokine (**Figure 4.1**). **Supplementary Table 1** shows the relationships between changes in $\dot{V}O_2\text{max}$ and each myokine; none were statistically significant.

Complete peak power and cadence data from the first and final training sessions were available for 18 participants (low responders, $n=6$; medium responders, $n=3$; high responders, $n=9$). Peak power relative to body mass was 9.47 ± 1.13 $\text{W} \cdot \text{kg}^{-1}$ during the first session and 9.55 ± 1.04 $\text{W} \cdot \text{kg}^{-1}$ during the final session. There was no significant effect of session ($F(1,15)=0.33$, $p=.571$), responder group ($F(2,15)=0.02$, $p=.982$), or session-by-responder-group interaction ($F(2,15)=0.19$, $p=.826$). The change in peak power was -0.03 ± 0.41 $\text{W} \cdot \text{kg}^{-1}$ in the low responders, 0.31 ± 0.69 $\text{W} \cdot \text{kg}^{-1}$ in the medium responders and 0.07 ± 0.95 $\text{W} \cdot \text{kg}^{-1}$ in the high responders.

Maximum cadence increased from 157.8 ± 17.1 rpm during the first session to 166.3 ± 13.3 rpm during the final session, with a significant main effect of session ($F(1,15)=4.97$, $p=.041$). There was no significant main effect of responder group ($F(2,15)=1.25$, $p=.316$) or session-by-responder-group interaction ($F(2,15)=0.04$, $p=.958$). The increase in maximum cadence was 8.7 ± 15.9 rpm in the low responders, 6.4 ± 5.6 rpm in the medium responders and 9.0 ± 13.9 rpm in the high responders. These findings provide no evidence that the low responders produced a lower relative peak power or were unable to generate a sufficient sprint cadence. However, this analysis was limited by the absence of final-session data for two participants (low responder $n=1$, medium responder $n=1$).

Table 4.1 - Participant Characteristics (n=20)

Age (y)	25 ± 5
Height (m)	1.76 ± 0.07
Body Mass (kg)	77.1 ± 12.6
BMI (kg·m²)	24.7 ± 3.4
VO₂max (L·min⁻¹)	3.10 ± 0.80
VO₂max (mL·kg⁻¹·min⁻¹)	40.3 ± 7.1
Wmax (W)	246 ± 65

Values shown are Mean ± SD

Table 4.2 - pre-to post-intervention changes in $\dot{V}O_2$ max and plasma myokine concentrations.

Variable	Pre Post	P value
Pre VO₂max (L·min⁻¹) Post VO₂max (L·min⁻¹)	3.10 ± 0.80 3.28 ± 0.73	0.007*
Pre VO₂max (mL·kg⁻¹·min⁻¹) Post VO₂max (mL·kg⁻¹·min⁻¹)	40.3 ± 7.1 42.6 ± 6.9	0.001*
Pre COL4a1 (ng/mL) Post COL4a1 (ng/mL)	7.60 ± 8.57 8.57 ± 2.82	0.328
Pre COL4a2 (ng/mL) Post COL4a2 (ng/mL)	13.64 ± 14.98 9.86 ± 4.83	0.255
Pre CTHRC1 (ng/mL) Post CTHRC1 (ng/mL)	1.26 ± 2.17 0.77 ± 0.41	0.303
Pre LAMa4 (ng/mL) Post LAMa4 (ng/mL)	6.05 ± 2.57 6.35 ± 1.67	0.624
Pre MHCC (ng/mL) Post MHCC (ng/mL)	0.12 ± 0.21 0.08 ± 0.06	0.361
Pre SPARCL1 (ng/mL) Post SPARCL1 (ng/mL)	1.30 ± 2.65 0.64 ± 0.44	0.269
Pre THBS4 (ng/mL) Post THBS4 (ng/mL)	0.18 ± 0.30 0.11 ± 0.06	0.318

Pre BDNF (pg/mL)	496.9 ± 697.2	0.495
Post BDNF (pg/mL)	657.4 ± 873.8	
Pre CCL21 (pg/mL)	353.4 ± 106.6	0.147
Post CCL21 (pg/mL)	340.3 ± 102.7	
Pre COLIVa (pg/mL)	557.8 ± 294.3	0.989
Post COLIVa (pg/mL)	557.6 ± 267.7	
Pre VEGF-C (pg/mL)	193.5 ± 165.6	0.226
Post VEGF-C (pg/mL)	230.8 ± 193.5	
Pre VEGFR2 (pg/mL)	8958.8 ± 2974.5	0.129
Post VEGFR2 (pg/mL)	8625.9 ± 2989.2	
Values shown are Mean ± SD. *Denotes significance.		

Table 4.3 - Peak power relative to body mass and maximum cadence during the first and final REHIT sessions.

Measure	Group	n	1st Session	Final Session	Change
Peak power (W·kg⁻¹)	Overall	18	9.47 ± 1.13	9.55 ± 1.04	0.08 ± 0.74
	Low	6	9.46 ± 1.23	9.43 ± 1.32	-0.03 ± 0.41
	Medium	3	9.34 ± 0.97	9.65 ± 0.27	0.31 ± 0.69
	High	9	9.52 ± 1.24	9.59 ± 1.07	0.07 ± 0.95
Maximum cadence (rpm)	Overall	18	157.8 ± 17.1	166.3 ± 13.3	8.5 ± 13.0
	Low	6	164.8 ± 23.1	173.5 ± 18.3	8.7 ± 15.9
	Medium	3	154.4 ± 16.1	160.8 ± 13.6	6.4 ± 5.6
	High	9	154.2 ± 13.0	163.2 ± 7.5	9.0 ± 13.9

Values shown are mean ± SD.

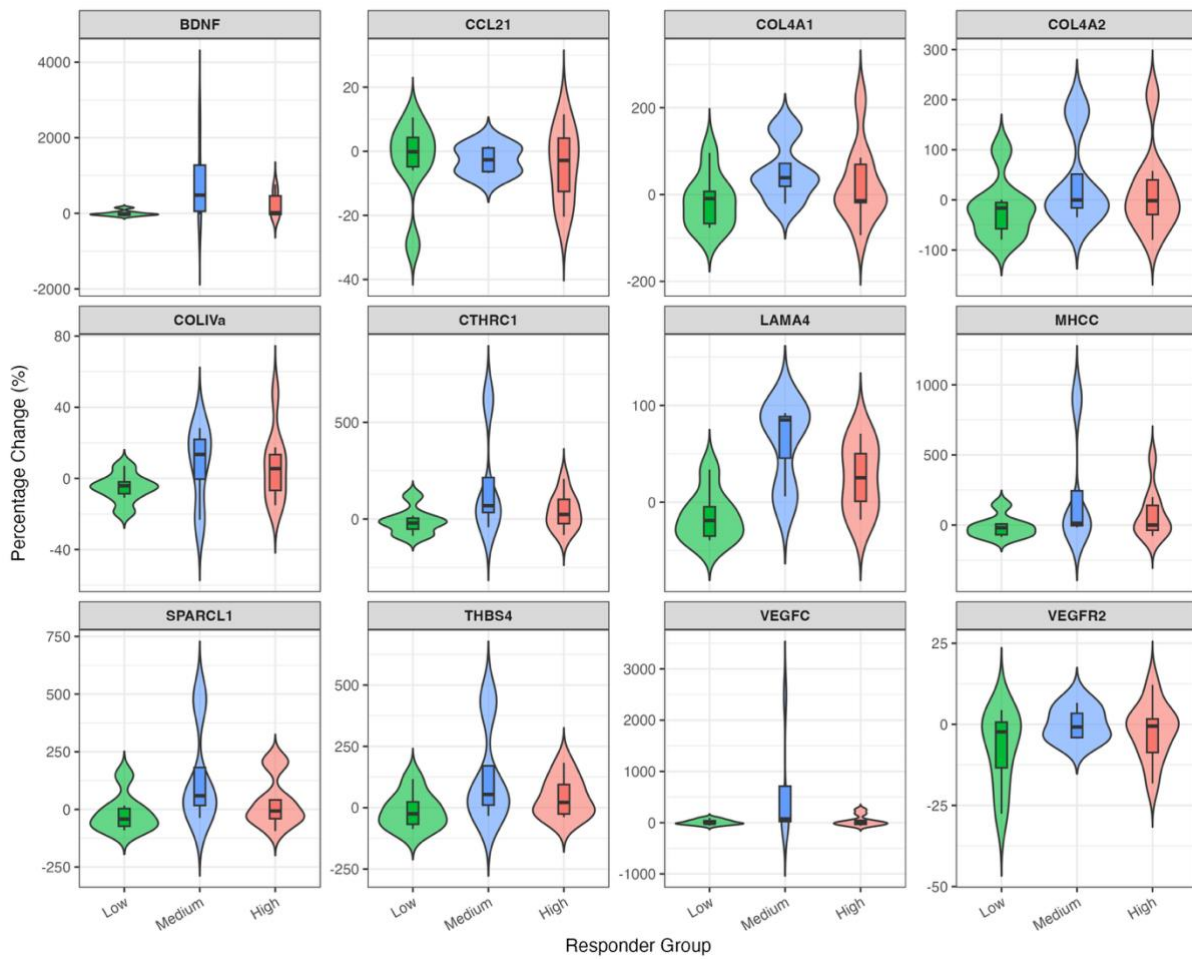


Figure 4.1 - Percentage change in blood myokines across high, medium and low $\dot{V}O_{2\max}$ responder groups. Each shape represents the group distribution, and each box displays the median and interquartile range. LAMA4 High: $n=8$; LAMA4 Medium: $n=3$. THBS4 High: $n=8$. CCL21 High: $n=8$. COL1A High: $n=8$.

DISCUSSION

The present study aimed to determine whether there were differences in the responses of specific exercise-induced myokines between low- and high- $\dot{V}O_2\text{max}$ responders. The main finding of this study is that there is no effect on the association between the magnitude of the response for $\dot{V}O_2\text{max}$ and changes in any of the exercise-induced myokines. The lack of a significant finding in the current study may be due to several factors. First, the myokines selected for investigation in the current study may not play a role in changes in $\dot{V}O_2\text{max}$ with SIT. Second, the myokines chosen for analysis were selected because their encoding genes are differentially regulated between high- and low-responders to exercise (Catoire et al., 2014, Keller et al., 2011). However, it has been shown that an increase in mRNA expression does not always correspond with a concomitant rise in plasma myokine levels (Geiger et al., 2013). This discordance may exist because many myokines have been noted to exert autocrine or paracrine effects within the muscle environment, whereby the muscle cells uptake the myokines rather than being released in sufficient amounts to influence circulatory plasma levels (Garneau et al., 2024, Matthews et al., 2009, Pedersen and Febbraio, 2012, Safdar et al., 2016).

Furthermore, the pattern of myokine release is highly dependent on exercise modality and intensity, as evidenced by Little et al. (2018), who showed greater overlap in myokine profiles between a single bout of endurance exercise and chronic wheel running than between an exhaustive sprint and either condition in rats. As the myokines examined in the current study were selected based on findings from endurance exercise protocols (Catoire et al., 2014, Keller et al., 2011), while the current study implemented an ‘all-out’ sprint interval training protocol, differences in exercise mode may have contributed to the absence of significant changes in plasma myokine concentrations. Further evidence to support this point comes from research that has shown BDNF to be significantly elevated following higher intensity exercise (Dinoff et al., 2017, Szuhany et al., 2015), highlighting a positive correlation between exercise intensity and the magnitude of increases, which is in contrast to research implementing endurance exercise (Catoire et al., 2014), where no significant changes were found. Similarly, no significant change in serum SPARC was detected following acute supramaximal exercise (Songsorn et al., 2017). However, a meta-analysis (Bettariga et al., 2024) reported increased SPARC plasma concentrations following acute endurance exercise (50-70% $\dot{V}O_2\text{max}$). Future studies should examine the association between changes in $\dot{V}O_2\text{max}$ and changes in myokine levels in response to endurance training, as this was the exercise modality in the original studies (Catoire et al., 2014, Keller et al., 2011) that identified the myokines to be explored in the current study.

The absence of change in any of the myokines in the current study may be explained by the timing of blood sample collection. Given that many myokines exhibit transient increases in circulating plasma during / immediately after exercise, they typically return to baseline levels between 180 min and 24 h post-exercise (Bettariga et al., 2024, Garneau et al., 2020, Szuhany et al., 2015). Since the current study collected blood samples 24 hours after an incremental test to exhaustion but

~4 days after their final SIT bout, any significant changes that may have existed may have remained undetected. It is important to note that the detectability of these responses depends on the specific half-life of each myokine and on how long their mRNA expression remains elevated post-exercise, both of which can vary considerably between myokines (Garneau et al., 2020, Kuang et al., 2022).

Nevertheless, this does not mean the selected myokines played no role in mediating adaptations that may have led to improvements in $\dot{V}O_{2\max}$. It may be that SIT does not result in chronic adaptations that alter the resting levels of plasma myokines but instead increases the magnitude of each myokine's responsiveness. For example, in a meta-analysis investigating the effects of exercise on BDNF (Szuhany et al., 2015), the authors found that each episode of exercise results in a 'dose' of BDNF activity, with the magnitude of this 'dose' enhanced by regular exercise but not maintained at a chronically elevated level. As the magnitude of exercise-induced myokine release is stated to be highly variable between individuals (Bettariga et al., 2024), it is plausible that high responders for $\dot{V}O_{2\max}$ release larger amounts of specific myokines – potentially those measured in the current study - as part of an adaptive response to training, compared with low responders. For example, if high responders exhibit a greater post-exercise increase in LAMA4, a protein thought to play a role in vascular and basement-membrane remodelling (Knoll et al., 2007, Stenzel et al., 2011, Thyboll et al., 2002), a higher uptake of this protein within the muscles could increase the stimulation of the mechanisms responsible for adaptations such as angiogenesis (Thyboll et al., 2002), which may then lead to greater improvements in $\dot{V}O_{2\max}$ compared to low responders. Taken together, the proposed mechanisms by which the selected myokines might contribute to training adaptations remain speculative, given that no significant between-group differences were observed for any of the myokines.

Several methodological considerations may have influenced the results of this study. First, the selection of myokines was based on transcriptomic differences observed in endurance exercise protocols (Catoire et al., 2014, Keller et al., 2011), whereas the present study intervention used an 'all-out' REHIT intervention. Since myokine release varies across exercise modalities and intensities (Little et al., 2018), the chosen panel may not have captured the most responsive proteins for this type of training.

Second, the timing of blood sampling was selected to investigate whether REHIT resulted in a sustained elevation in circulating myokine concentrations, rather than the short-lived response to an individual exercise session. A strength of this approach was that the post-intervention samples were collected ~4 days after the final REHIT session, which reduced the likelihood that the results were determined by the immediate response to the final training bout. Collecting both samples 24 hours after the same $\dot{V}O_{2\max}$ test and following an overnight fast also provided some standardisation between the pre- and post-intervention measurements. However, many myokines reported in the literature exhibit rapid elevations immediately after exercise, returning to baseline within hours (Bettariga et al., 2024, Garneau et al., 2020, Szuhany et al., 2015). Therefore, any transient

differences in circulating concentrations may have been missed. The use of a single sampling timepoint also means that the absence of significant changes does not rule out a role for the selected myokines in training adaptation, it only indicates that sustained differences were not detected at the selected sampling time.

Third, the use of resting plasma concentrations may not adequately reflect the physiological processes by which the selected myokines underpin training adaptations. Several myokines exert autocrine or paracrine effects locally within the muscle environment (Pedersen and Febbraio, 2012, Safdar et al., 2016), meaning that measuring systemic levels may not accurately reflect their influence on adaptation. This limitation is compounded by the fact that, to our knowledge, the circulatory responses of several of the selected myokines to SIT have not yet been investigated, making it unclear whether they are released in sufficient quantities to be detected in plasma. Finally, inter-individual variability in both myokine responsiveness (Bettariga et al., 2024, Whitham and Febbraio, 2016) and $\dot{V}O_2\text{max}$ adaptations may require larger sample sizes to detect differences and reveal associations between the two.

Although the current study indicates that a 6-week SIT intervention does not lead to chronic changes in resting circulatory levels of the selected myokines, even in high responders to exercise, this does not rule out their role in driving adaptations that mediate improvements in $\dot{V}O_2\text{max}$. Since maximal exercise capacity is the most powerful predictor of mortality (Imboden et al., 2019), and the role of these myokines in response to exercise remains poorly understood, further investigation is warranted. Improving our understanding of their role in adaptations to $\dot{V}O_2\text{max}$ with exercise may enable improved personalised lifestyle advice and the development of novel drug targets. Therefore, future studies should use a repeated acute-exercise sampling design to distinguish chronic changes in the acute myokine response to exercise. Before the intervention, a resting blood sample should be collected immediately before the baseline $\dot{V}O_2\text{max}$ test, followed by samples immediately after the test and during recovery, for example at 1, 3 and 24 hours. The same sampling schedule should then be repeated around the post-intervention $\dot{V}O_2\text{max}$ test, using the same time of day and fasting conditions. The post-intervention test should also remain separated from the final training session to prevent the acute response to the final REHIT session influencing the resting measurement. This design would allow resting concentrations to be compared before and after training, while also determining whether training altered the magnitude or time course of the acute myokine response. It would therefore be possible to examine whether high $\dot{V}O_2\text{max}$ responders exhibit a greater exercise-induced release of specific myokines than low responders, even if their resting concentrations remain unchanged. Additionally, where feasible, muscle biopsies collected alongside selected blood samples would also help determine whether changes in circulating concentrations reflect altered expression or uptake in skeletal muscle.

Female participants should also be included in future research rather than being excluded because of uncertainty surrounding the effects of the menstrual cycle. A direct extension of the present study could initially recruit naturally menstruating women, where cycles could be tracked for at

least two months before testing to assist with scheduling, the cycle phase should also be confirmed retrospectively using circulating oestradiol and progesterone (Janse De Jonge et al., 2019). The pre- and post-intervention $\dot{V}O_2\text{max}$ tests and blood sampling should be completed during the same menstrual-cycle phase where possible (Elliott-Sale et al., 2021). For example, participants could complete baseline $\dot{V}O_2\text{max}$ testing and blood sampling during the early follicular phase of one cycle. The start of the intervention would then be individually scheduled so that the participant completed 18 sessions over six weeks, with the final session occurring 2-5 days before the equivalent phase two cycles later. For participants using hormonal contraception, the type and formulation should be recorded, and testing should occur during the same active or inactive phase of contraceptive use at baseline and follow-up (Elliott-Sale et al., 2021). If matching menstrual or contraceptive phase is not possible, hormone concentrations could be measured and included in the statistical analysis. The sample size should be sufficient to examine whether sex or ovarian hormone status modifies the myokine response to exercise.

In conclusion, the present study found no evidence that differences in $\dot{V}O_2\text{max}$ responsiveness are associated with changes in select resting plasma myokine concentrations following 6 weeks of REHIT. This finding may reflect the choice of specific myokines analysed, the exercise modality used, and limitations related to the timing of blood sampling and the assay's sensitivity in detecting changes. The study highlights the complexity of attributing molecular signalling pathways to tangible aerobic adaptations. Importantly, the results reinforce the need for future research to classify modality-specific myokines further, establish the nature of the function of exercise-induced myokines, i.e., autocrine, paracrine, or endocrine, and combine plasma and muscle assessments to examine whether the magnitude of acute myokine response contributes to inter-individual variation in training-induced improvements in $\dot{V}O_2\text{max}$. Understanding these relationships will be essential for advancing personalised exercise prescription and identifying potential molecular targets that underpin aerobic fitness adaptations.

SUPPLEMENTARY DATA

Supplementary Table 1 – Relationship between exercise-induced changes in individual myokines and changes in $\dot{V}O_2\text{max}$

Myokine	<i>r</i>	p value
COLIVa	0.44	0.062
COL4A1	0.40	0.084
LAMA4	0.38	0.120
COL4A2	0.38	0.096
THBS4	0.25	0.310
SPARCL1	0.23	0.340
CTHRC1	0.19	0.430
MHCC	0.14	0.560
VEGFR2	0.12	0.620
BDNF	0.05	0.820
VEGF.C	-0.04	0.870
CCL21	-0.13	0.590

Chapter 5 – General Discussion

Physical inactivity remains a major global health concern, with recent estimates indicating that nearly one-third of adults (31.3%; 1.8 billion) fail to achieve recommended PA levels (Strain et al., 2024). Low cardiorespiratory fitness is also associated with an increased risk of all-cause mortality and several chronic conditions, including heart failure, stroke, hypertension, dementia, and depression (Lang et al., 2024). Given this, the development of time-efficient exercise interventions that improve $\dot{V}O_2\text{max}$ may be valuable for individuals who perceive a lack of time as a barrier to regular exercise. However, reducing the time required to complete an exercise session does not, by itself, establish whether individuals will take up and maintain that exercise long-term.

REHIT has emerged as a promising approach, with protocols incorporating two brief all-out cycling sprints shown to improve $\dot{V}O_2\text{max}$ following six weeks of training (Metcalf et al., 2012, Thomas et al., 2020). These findings raise questions around how much exercise is required to produce an effective training stimulus, how frequently that stimulus needs to be repeated, and which physiological processes contribute to the resulting adaptations. Establishing the minimum effective dose therefore requires consideration of sprint repetitions, weekly training frequency and intervention duration, alongside the outcome being measured. It also requires an understanding of whether reducing the exercise dose affects the magnitude and consistency of adaptation.

The three studies presented in this thesis addressed different aspects of these questions. **Chapter 2** used an updated meta-analysis and a Bayesian approach to examine the relationship between sprint repetitions and changes in $\dot{V}O_2\text{max}$. **Chapter 3** investigated the effects of reducing REHIT training frequency, using changes in W_{max} to assess maximal cycling performance. **Chapter 4** examined whether changes in the plasma concentrations of selected candidate myokines differed between groups with different magnitudes of $\dot{V}O_2\text{max}$ improvement. This general discussion brings these findings together to consider how they advance the understanding of REHIT in inactive populations. Particular attention is given to what can be concluded about the minimum effective dose, the limitations of the evidence concerning mechanisms and individual responses, and the further research needed to inform practical exercise prescription.

Time-efficient exercise and the “minimal dose”

Using data from 78 studies with 93 trials ($n=1188$), **Chapter 2** found that increasing the number of sprint repetitions within a SIT session was not associated with meaningfully greater improvements in $\dot{V}O_2\text{max}$. This supports the use of protocols involving as few as two sprints but does not necessarily mean that sprint volume can be reduced further without affecting the response to training. An important distinction is therefore whether additional sprints provide further benefit once a sufficient training stimulus has been achieved, or whether reducing the number of sprints below this level attenuates adaptation. **Chapter 2** mainly addresses the former question.

Studies investigating single-sprint training provide some insight into the latter. Songsorn et al. (2016) found no significant improvement in $\dot{V}O_{2\max}$ relative to a control group following four weeks of a single 20 s sprint performed three times per week. A subsequent study also found no significant change following a similar intervention (Songsorn et al., 2017). Wong et al. (2024) found no significant improvement in aerobic fitness following single 30 s sprints performed five times per week for six weeks, although participants were physically active. More recently, Chatlaong et al. (2026) reported no improvement in $\dot{V}O_{2\max}$ relative to a control group following four weeks of single 20 s sprints in sedentary adults. Together, these findings suggest that regularly performing a standalone all-out effort does not guarantee an improvement in $\dot{V}O_{2\max}$.

However, sprint number cannot be considered independently of the duration and distribution of the efforts. Nalcakan et al. (2018) observed greater improvements in $\dot{V}O_{2\max}$ with two 20 s sprints than with two 10 s sprints, indicating that retaining two repetitions does not necessarily preserve the training response when their duration is reduced. Improvements in $\dot{V}O_{2\max}$ have also been reported with three individual sprints distributed across the day, a protocol termed “sprint exercise snacks” (Little et al., 2019, Wun et al., 2020). These protocols should not be interpreted as evidence that one sprint per training day is sufficient, because participants completed several daily sprints. Nevertheless, they suggest that the efforts do not always need to be completed within the same short exercise session.

When considered alongside the findings of **Chapter 2**, this evidence is consistent with a possible threshold-based stimulus, whereby a small number of sufficiently demanding sprints provides a stimulus for improving $\dot{V}O_{2\max}$, with additional repetitions providing limited further benefit. This contrasts with the expectation that increasing training volume produces progressively greater adaptations, informed by evidence from endurance and resistance training. For example, greater volumes of aerobic exercise have produced graded improvements in cardiorespiratory fitness, while higher weekly resistance-training volumes have been associated with greater strength gains (Church et al., 2007, Ralston et al., 2017). However, these relationships depend on the outcome and exercise dose being examined and should not automatically be applied to the number of sprint repetitions within a SIT session. These findings do not establish two sprints as a universal threshold, particularly because the single-sprint studies mentioned did not directly compare one and two sprints under otherwise matched conditions.

Beyond the characteristics of individual exercise sessions, the duration of the training intervention may also influence the response. **Chapter 2** identified a positive association between intervention duration and improvements in $\dot{V}O_{2\max}$. Although this between-study association does not establish causality, it suggests that extending the training period may offer greater scope for further improvement than adding repetitions to individual sessions. A longer-term controlled study would help investigate this relationship by maintaining a consistent REHIT prescription and assessing $\dot{V}O_{2\max}$ at several time points, for example, at baseline and after 6, 12 and 24 weeks. This would help determine whether improvements continue to accumulate or eventually plateau, rather than

assuming that the association observed in **Chapter 2** continues indefinitely. Recording training attendance and completed exercise would also help distinguish the influence of intervention duration from changes in adherence over time.

Chapter 3 addressed another component of the exercise dose by reducing weekly training frequency. The improvement in $W_{\max}$ following once-weekly REHIT provides evidence of improved maximal cycling performance, but cannot confirm a corresponding improvement in $\dot{V}O_{2\max}$. This distinction is illustrated by Songsorn et al. (2016), who observed an improvement in $W_{\max}$ without a significant $\dot{V}O_{2\max}$ training effect. Therefore, the absence of a significant difference between the once- and twice-weekly groups in **Chapter 3** does not establish equivalent improvements in $W_{\max}$ and cannot demonstrate equivalent aerobic adaptations. These findings support further investigation of once-weekly REHIT but directly measured $\dot{V}O_{2\max}$ is needed to determine whether reducing training frequency preserves the benefit to cardiorespiratory fitness. For physically inactive adults, the practical aim should therefore be to minimise the demands of training while retaining a worthwhile benefit, rather than simply prescribing the smallest possible amount of exercise.

Mechanistic considerations and inter-individual variability

The findings of **Chapter 2** raise questions about why a small number of sprints can provide an effective training stimulus, while additional repetitions appear to offer little further benefit for $\dot{V}O_{2\max}$. One possible explanation is that the responses contributing to adaptation are sufficiently stimulated by a small number of sprints, rather than increasing proportionally with each additional repetition. However, this should not be interpreted as meaning that a single sprint fails to activate exercise-responsive signalling. Chen et al. (2000) demonstrated increased AMPK activity following a single 30 s sprint, while Metcalfe et al. (2015) observed increased ACC phosphorylation and PGC-1 α gene expression following REHIT involving two 20 s sprints. These studies show that signalling occurs following both single- and repeated-sprint exercise, but do not establish whether adding a second sprint produces a disproportionately greater response. Acute signalling pathway activation therefore cannot, on its own, explain the apparent difference in training adaptations between these protocols.

Any proposed signalling mechanism must also be linked to the physiological adaptations responsible for increasing whole-body oxygen uptake. Mandic et al. (2022) reported increases in blood volume, haemoglobin mass and maximal cardiac output alongside improved $\dot{V}O_{2\max}$, while Bostad et al. (2021) observed increased peak cardiac output following low-volume SIT. Stronger evidence for a contribution from blood-volume expansion was provided by Mandic et al. (2023), who found that removing the training-induced expansion through phlebotomy reduced maximal cardiac output and $\dot{V}O_{2\max}$. In contrast, Bostad et al. (2023) reported improved $\dot{V}O_{2\text{peak}}$ without a significant change in peak cardiac output. These contrasting findings leave uncertainty about the relative contributions of central and peripheral adaptations, particularly given the acknowledged

limitations of non-invasive cardiac output measurement. Importantly, these studies used three sprints per session and cannot establish whether two sprints stimulate the same adaptations. This distinction between the stimulus within a session and its repetition across the training period is also relevant to **Chapter 3**. Reducing training frequency retained the two-sprint structure of each session but reduced how often participants were exposed to it. Even if two sprints provide a sufficient acute stimulus, this does not establish how frequently that stimulus must be repeated to improve $\dot{V}O_{2\max}$.

Myokines provide one possible link between the response of exercising muscle and adaptations occurring locally or in other tissues. Recent work by Olsen et al. (2026) identified exercise-intensity dependent changes in circulating proteins and metabolites, alongside evidence of altered secretory responses in muscle cells. This supports investigating muscle-to-organ communication following sprint exercise, although it does not establish that particular myokines cause cardiovascular adaptation or explain a sprint number threshold. **Chapter 4** addresses a related question by examining whether changes in the circulating concentrations of selected candidate myokines differed between participants with different magnitudes of $\dot{V}O_{2\max}$ improvement. The magnitude of $\dot{V}O_{2\max}$ improvement varied between participants in **Chapter 4**. **Chapter 4** built on previous evidence (Keller et al., 2011), in which 86 genes were identified as being differentially regulated between low- and high-responders to exercise. 13 of these genes encoded myokines previously shown to be responsive to exercise training (Catoire et al., 2014). This observed overlap between the two studies provided the reason for selecting the myokines targeted in this chapter.

Although a significant group-by-time interaction was observed for LAMA4, which remained significant after adjustment for training peak power, post-hoc comparisons did not identify significant differences between specific responder groups. No significant interactions were detected for the other myokines. These findings therefore provide limited evidence that changes in the selected circulating myokines differ according to the magnitude of $\dot{V}O_{2\max}$ improvement, and do not establish a role for these proteins in mediating training adaptation. This could be because the selected myokines are not key contributors to the mechanism by which $\dot{V}O_{2\max}$ is modulated. Alternatively, several methodological and physiological considerations may explain these findings. The small responder groups limit the conclusions that can be drawn. The original sample-size calculation was based on detecting a very large difference of 1.5 SD between the lowest and highest responder groups, with 24 participants planned compared with 20 completing the intervention. The study therefore had limited ability to detect smaller between-group differences. Although the findings did not clearly identify changes in these circulating measurements as an explanation for the observed differences in $\dot{V}O_{2\max}$ improvement, they do not exclude smaller associations or establish that the selected myokines have no role in adaptation.

The timing of blood sampling provides a further consideration. The intention was to investigate persistent changes in circulating concentrations following the intervention, rather than the

immediate response to the final training session. However, blood samples were collected after the $\dot{V}O_{2\max}$ tests, meaning that residual responses to these tests could not be excluded. Exercise-related myokine responses vary over time, making the interval between exercise and sampling important when interpreting circulating measurements (Bettariga et al., 2024). Consequently, these samples should not automatically be considered measurements of resting concentrations unaffected by recent exercise.

Furthermore, a single sampling point before and after the intervention cannot characterise transient myokine responses during exercise and recovery. Myokines may also exert local autocrine or paracrine actions within skeletal muscle, which circulating measurements may not adequately reflect (Pedersen and Febbraio, 2012). **Chapter 4** demonstrated a mean increase in $\dot{V}O_{2\max}$ of $14.6 \pm 5.7\%$ in the high responder group compared to $-3.2 \pm 4.5\%$ in the low responder group but the selected plasma measurements and sampling strategy did not provide a clear explanation for the differences in improvement between responder groups. The findings leave open the possibility that acute responses or local muscle actions are more informative than changes measured at these particular sampling points.

Implications for public health and exercise prescription

The findings of this thesis suggest that some aspects of the exercise dose could be reduced while retaining improvements in cardiorespiratory fitness or maximal cycling performance. However, the practical value of these findings depends on whether inactive adults choose to undertake REHIT and continue training outside a research setting.

Participation depends on more than the duration of the exercise session. Although reducing sprint repetitions may limit the decline in affect during sprint exercise (Metcalf et al., 2022), this does not mean that all-out exercise will be acceptable to everyone. Familiarisation, appropriate initial support and a clear explanation of what the sprints involve may be important for adults unfamiliar with such vigorous exercise. Access to a suitable cycle ergometer, its cost, location, and the time required for travel also need consideration. Taken together, a 10-minute cycling session does not necessarily represent a 10-minute time commitment.

The workplace study by Metcalfe et al. (2020) provides an example of how some delivery barriers might be addressed. Computer-guided REHIT delivered in the workplace improved $\dot{V}O_{2\max}$ over six weeks, and participants generally considered the programme acceptable. However, interviews also identified difficulties when sprint duration increased to 20 s, demonstrating that participants could view the programme positively while still finding the sprints uncomfortable. Its short duration cannot establish whether attendance would continue over several months or whether fitness improvements would be maintained. It also remains important to determine whether REHIT adds to participants' habitual activity or replaces other exercise. Maintaining a short exercise programme would have different implications if it encouraged additional activity than if participants used it to justify reducing other movement.

REHIT may therefore expand the exercise options available to some inactive adults, particularly where lack of time is an important barrier. However, this thesis does not establish that it increases habitual PA, replaces the wider benefits of recommended aerobic and muscle-strengthening activity (World Health, 2020), or produces a particular reduction in mortality. Its public health value will depend on whether achievable improvements in fitness can be combined with accessible delivery and sustained participation.

Future directions

The priority following **Chapter 2** is to establish whether reducing the number of sprint repetitions from two to one attenuates improvements in $\dot{V}O_{2\max}$. A randomised controlled study in physically inactive adults could compare one versus two 20 s all-out sprints, performed three times per week for six weeks, alongside a non-training control group. The study should be designed to detect a prespecified worthwhile difference between the training groups, rather than interpreting a significant improvement in one group and a nonsignificant improvement in the other as evidence that their responses differ. This would help establish the minimum effective number of sprints within that particular prescription, rather than a universal minimum dose applicable to all SIT protocols.

If two sprints produced a greater improvement than one, this finding, considered alongside the limited additional benefit associated with further repetitions in **Chapter 2**, would strengthen the case for a threshold-like training response. Subsequent research should then investigate which physiological or molecular responses might account for this pattern. An acute crossover study comparing one, two and three sprints could examine whether adding a second sprint changes the magnitude, timing or nature of the response, and whether a third sprint provides a further stimulus. Muscle sampling and repeated blood sampling could investigate intracellular signalling and candidate myokine responses, alongside measurements of the metabolic disturbance and mechanical work performed.

However, identifying a different acute response would not establish that it mediates the improvement in $\dot{V}O_{2\max}$. These responses would also need to be related to subsequent training-induced changes in oxygen delivery and utilisation, with further direct experimental tests required to establish causality. This would move the research beyond identifying a minimal effective dose and towards explaining why particular combinations of sprint number and duration are effective. A further priority following the work of **Chapter 3** is to determine whether once-weekly REHIT improves directly measured $\dot{V}O_{2\max}$, and whether its effects depend on the number of sessions completed or the period over which they are distributed. A randomised study could compare once-weekly training for twelve weeks with twice-weekly training for six weeks, alongside a non-exercise control group maintaining its usual activity/lifestyle. Both training groups would complete 12 prescribed sessions, with assessments taken at baseline, week six and week twelve. However, the equal-session comparison would still involve different intervention durations and would not completely isolate training frequency from time spent training. Key protocol parameters should be

comparable, with sprint duration progressed by session number rather than calendar week.

Attendance, sprint power and total mechanical work should be recorded because equal numbers of prescribed sessions do not guarantee equal training loads. $\dot{V}O_{2\max}$ should be measured directly alongside $W_{\max}$, with a standardised familiarisation session for the REHIT training intervention and a test-retest protocol for the baseline $\dot{V}O_{2\max}$ assessment. The addition of a verification bout directly after the completion of the $\dot{V}O_{2\max}$ assessments may also help to establish a true $\dot{V}O_{2\max}$. Alongside the training comparison, physiological measurements could investigate whether improvements in $\dot{V}O_{2\max}$ arise predominantly through increased oxygen delivery, increased tissue oxygen extraction, or contributions from both. Mandic et al. (2022) reported increases in cardiac output, blood volume and haemoglobin mass following training involving three 30 s sprints. These findings provide a rationale for examining central adaptation during lower-volume REHIT, rather than demonstrating that the same changes occur with two sprints or once-weekly training.

Measuring oxygen uptake alongside PhysioFlow-derived estimates of cardiac output and stroke volume before and after training would help address this question. Responses should be compared at matched absolute workloads as well as maximal exercise, because post-training maximal tests may involve higher workloads. Combining measured oxygen uptake with estimated cardiac output would permit an indirect estimate of the systemic $a-vO_2$ diff, rather than a direct measurement of oxygen extraction.

Near-infrared spectroscopy (NIRS) could complement these measurements by assessing oxygenation in the working muscles during cycling. However, this signal reflects the local balance between oxygen delivery and utilisation and does not directly isolate muscle oxygen consumption. Additionally, the reliability of these measurements also need consideration. For example, Schoch et al. (2025) identified substantial individual measurement variability in PhysioFlow estimates despite favourable group-level reliability in trained adults. Implementing repeat assessments and signal-quality checks would therefore be important before interpreting individual changes as evidence of predominantly central or peripheral adaptation. These combined measurements could help distinguish likely contributions and would provide useful input into the physiological mechanisms contributing to $\dot{V}O_{2\max}$ improvements following lower-volume SIT (≤ 3 sprints) but measurement error would still limit the interpretation of these changes.

Some of these questions are already being addressed in the developing REHIT literature. Astorino et al. (2026) have recently published a protocol for a trial involving 120 inactive adults, addressing the small sample size issues. The protocol will compare twice-weekly REHIT over 12 weeks with a non-exercise control while incorporating cardiac-output via PhysioFlow which provides further suggestions for the recommendations made above. However, this design does not include a once-weekly group, leaving the proposed comparison of training schedules described above as a clear next step in the developing REHIT literature, as long as the major limitations discussed in the current thesis are addressed.

Longer-term studies are also needed to determine whether improvements in fitness are maintained and whether participants continue REHIT beyond a short intervention. Workplace or community settings would allow recruitment, attendance, retention and participants' experiences to be assessed alongside changes in $\dot{V}O_2\text{max}$. Measuring PA outside of the intervention as a follow-up would help determine whether REHIT adds to participants' usual activity or replaces other exercise.

Following **Chapter 4**, future studies should distinguish changes in resting myokine concentrations from changes in the acute response to exercise. A resting sample should be collected before the $\dot{V}O_2\text{max}$ test following a standardised period without exercise, with additional samples collected during recovery. Repeating this procedure before and after training would allow changes in resting concentrations and the size and time course of the acute response to be examined separately.

Muscle biopsies could also investigate local changes that may not be reflected in plasma. Larger samples would allow these relationships to be examined more precisely, using continuous changes in $\dot{V}O_2\text{max}$ rather than relying solely on responder groups.

Overall conclusions

This thesis advances understanding of low-volume SIT and REHIT by examining which aspects of the exercise dose can be reduced and what remains uncertain about the resulting adaptations.

Chapter 2 found limited additional $\dot{V}O_2\text{max}$ benefit from increasing sprint repetitions within the protocols studied, supporting low-volume approaches without establishing a universal minimum dose. **Chapter 3** provided preliminary evidence of improved maximal cycling performance following once-weekly REHIT, while leaving its effect on $\dot{V}O_2\text{max}$ unresolved. **Chapter 4** did not identify clear differences between responder groups in changes in the selected circulating myokines, but its sample size and sampling strategy limit conclusions about their involvement in adaptation.

For inactive adults, these findings support the development of time-efficient exercise options rather than a single optimal prescription. The next steps are to establish the aerobic effects of reduced training frequency, investigate the physiological processes contributing to adaptation, and determine whether accessible delivery produces sustained participation. REHIT may offer a useful option for some adults, but its wider public health contribution depends on evidence extending beyond short-term laboratory improvements.

References

- ADAMSON, S., KAVALIAUSKAS, M., YAMAGISHI, T., PHILLIPS, S., LORIMER, R. & BABRAJ, J. 2019. Extremely short duration sprint interval training improves vascular health in older adults. *Sport Sciences for Health*, 15.
- ALEKSOVSKA, K., PUGGINA, A., GIRALDI, L., BUCK, C., BURNS, C., CARDON, G., CARLIN, A., CHANTAL, S., CIARAPICA, D., COLOTTO, M., CONDELLO, G., COPPINGER, T., CORTIS, C., D'HAESE, S., DE CRAEMER, M., DI BLASIO, A., HANSEN, S., IACOVIELLO, L., ISSARTEL, J., IZZICUPO, P., JAESCHKE, L., KANNING, M., KENNEDY, A., LING, F., LUZAK, A., NAPOLITANO, G., NAZARE, J. A., PERCHOUX, C., PISCHON, T., POLITO, A., SANNELLA, A., SCHULZ, H., SOHUN, R., STEINBRECHER, A., SCHLICHT, W., RICCIARDI, W., MACDONNCHA, C., CAPRANICA, L. & BOCCIA, S. 2019. Biological determinants of physical activity across the life course: a "Determinants of Diet and Physical Activity" (DEDIPAC) umbrella systematic literature review. *Sports Med Open*, 5, 2.
- ALLEMEIER, C. A., FRY, A. C., JOHNSON, P., HIKIDA, R. S., HAGERMAN, F. C. & STARON, R. S. 1994. Effects of sprint cycle training on human skeletal muscle. *J Appl Physiol* (1985), 77, 2385-90.
- ALLEN, N. G., HIGHAM, S. M., MENDHAM, A. E., KASTELEIN, T. E., LARSEN, P. S. & DUFFIELD, R. 2017. The effect of high-intensity aerobic interval training on markers of systemic inflammation in sedentary populations. *Eur J Appl Physiol*, 117, 1249-1256.
- ALLENDER, S., COWBURN, G. & FOSTER, C. 2006. Understanding participation in sport and physical activity among children and adults: a review of qualitative studies. *Health Educ Res*, 21, 826-35.
- ALMENDRO, V., BUSQUETS, S., AMETLLER, E., CARBÓ, N., FIGUERAS, M., FUSTER, G., ARGILÉS, J. M. & LÓPEZ-SORIANO, F. J. 2006. Effects of interleukin-15 on lipid oxidation: disposal of an oral [(14)C]-triolein load. *Biochim Biophys Acta*, 1761, 37-42.
- ALTMAN, D. G. & BLAND, J. M. 1995. Statistics notes: Absence of evidence is not evidence of absence. *BMJ*, 311, 485.
- AMERICAN COLLEGE OF SPORTS MEDICINE 2021. *ACSM's Guidelines for Exercise Testing and Prescription*, Philadelphia, Wolters Kluwer.
- AMINI, H., HABIBI, S., ISLAMOGLU, A. H., ISANEJAD, E., UZ, C. & DANIYARI, H. 2021. COVID-19 pandemic-induced physical inactivity: the necessity of updating the Global Action Plan on Physical Activity 2018-2030. *Environ Health Prev Med*, 26, 32.
- ARAUJO BONETTI, D. E. P. R., MURIAS, J. M., ANTUNES, B. M., MARINARI, G., DUTRA, Y. M., MILIONI, F. & ZAGATTO, A. M. 2024. Five Weeks of Sprint Interval Training Improve Muscle Glycolytic Content and Activity But Not Time to Task Failure in Severe-Intensity Exercise. *Med Sci Sports Exerc*, 56, 1355-1367.
- ASLANKESER, Z. & BALCI, S. 2017. Substrate oxidation during incremental exercise in young women: the effects of 2-week high intensity interval training. *Med Sport*, 70, 137-49.
- ASTORINO, T. A., ALLEN, R. P., ROBERSON, D. W., JURANCICH, M., LEWIS, R., MCCARTHY, K. & TROST, E. 2011. Adaptations to high-intensity training are independent of gender. *Eur J Appl Physiol*, 111, 1279-86.

- ASTORINO, T. A., CAUSER, E., HAZELL, T. J., ARHEN, B. B. & GURD, B. J. 2022. Change in Central Cardiovascular Function in Response to Intense Interval Training: A Systematic Review and Meta-analysis. *Med Sci Sports Exerc*, 54, 1991-2004.
- ASTORINO, T. A., EDMUNDS, R. M., CLARK, A., KING, L., GALLANT, R. A., NAMM, S., FISCHER, A. & WOOD, K. M. 2017. High-Intensity Interval Training Increases Cardiac Output and V O₂max. *Med Sci Sports Exerc*, 49, 265-273.
- ASTORINO, T. A., METCALFE, R. S. & VOLLAARD, N. B. J. 2026. The effect of low volume sprint interval training on cardiorespiratory fitness: study protocol for a definitive randomized controlled trial. *Trials*, 27, 340.
- ASTORINO, T. A. & SCHUBERT, M. M. 2014. Individual responses to completion of short-term and chronic interval training: a retrospective study. *PLoS One*, 9, e97638.
- BAILEY, S. J., WILKERSON, D. P., DIMENNA, F. J. & JONES, A. M. 2009. Influence of repeated sprint training on pulmonary O₂ uptake and muscle deoxygenation kinetics in humans. *J Appl Physiol (1985)*, 106, 1875-87.
- BARNETT, C., CAREY, M., PROIETTO, J., CERIN, E., FEBBRAIO, M. A. & JENKINS, D. 2004. Muscle metabolism during sprint exercise in man: influence of sprint training. *J Sci Med Sport*, 7, 314-22.
- BARRY, V. W., BARUTH, M., BEETS, M. W., DURSTINE, J. L., LIU, J. & BLAIR, S. N. 2014. Fitness vs. fatness on all-cause mortality: a meta-analysis. *Prog Cardiovasc Dis*, 56, 382-90.
- BASSETT, D. R., JR. & HOWLEY, E. T. 2000. Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Med Sci Sports Exerc*, 32, 70-84.
- BATRAKOULIS, A. & FATOUROS, I. G. 2022. Psychological Adaptations to High-Intensity Interval Training in Overweight and Obese Adults: A Topical Review. *Sports (Basel)*, 10.
- BAUMAN, A., MEROM, D., BULL, F. C., BUCHNER, D. M. & FIATARONE SINGH, M. A. 2016. Updating the Evidence for Physical Activity: Summative Reviews of the Epidemiological Evidence, Prevalence, and Interventions to Promote "Active Aging". *Gerontologist*, 56 Suppl 2, S268-80.
- BAUMAN, A. E., REIS, R. S., SALLIS, J. F., WELLS, J. C., LOOS, R. J., MARTIN, B. W. & LANCET PHYSICAL ACTIVITY SERIES WORKING, G. 2012. Correlates of physical activity: why are some people physically active and others not? *Lancet*, 380, 258-71.
- BAYATI, M., FARZAD, B., GHARAKHANLOU, R. & AGHA-ALINEJAD, H. 2011. A practical model of low-volume high-intensity interval training induces performance and metabolic adaptations that resemble 'all-out' sprint interval training. *J Sports Sci Med*, 10, 571-6.
- BEERE, P. A., RUSSELL, S. D., MOREY, M. C., KITZMAN, D. W. & HIGGINBOTHAM, M. B. 1999. Aerobic Exercise Training Can Reverse Age-Related Peripheral Circulatory Changes in Healthy Older Men. *Circulation*, 100, 1085-1094.
- BEN ABDERRAHMAN, A., PRIOUX, J., CHAMARI, K., BEN OUNIS, O., TABKA, Z. & ZOUHAL, H. 2013. Running interval training and estimated plasma-volume variation. *Int J Sports Physiol Perform*, 8, 358-65.
- BENTLEY, D. J. & MCNAUGHTON, L. R. 2003. Comparison of W(peak), VO₂(peak) and the ventilation threshold from two different incremental exercise tests: relationship to endurance performance. *J Sci Med Sport*, 6, 422-35.
- BETTARIGA, F., TAAFFE, D. R., GALVAO, D. A., LOPEZ, P., BISHOP, C., MARKARIAN, A. M., NATALUCCI, V., KIM, J. S. & NEWTON, R. U. 2024. Exercise training mode effects on myokine expression in healthy adults: A systematic review with meta-analysis. *J Sport Health Sci*, 13, 764-779.

- BHAMBHANI, Y. 2004. Muscle Oxygenation Trends During Dynamic Exercise Measured by Near Infrared Spectroscopy. *Canadian Journal of Applied Physiology*, 29, 504-523.
- BHAMBHANI, Y., MAIKALA, R. & ESMAIL, S. 2001. Oxygenation trends in vastus lateralis muscle during incremental and intense anaerobic cycle exercise in young men and women. *European journal of applied physiology*, 84, 547-56.
- BIDDLE, S. J. & BATTERHAM, A. M. 2015. High-intensity interval exercise training for public health: a big HIT or shall we HIT it on the head? *Int J Behav Nutr Phys Act*, 12, 95.
- BISHOP, D. J., BECK, B., BIDDLE, S. J. H., DENAY, K. L., FERRI, A., GIBALA, M. J., HEADLEY, S., JONES, A. M., JUNG, M., LEE, M. J., MOHOLDT, T., NEWTON, R. U., NIMPHIUS, S., PESCATELLO, L. S., SANER, N. J. & TZARIMAS, C. 2025. Physical Activity and Exercise Intensity Terminology: A Joint American College of Sports Medicine (ACSM) Expert Statement and Exercise and Sport Science Australia (ESSA) Consensus Statement. *J Sci Med Sport*, 28, 980-991.
- BONAFIGLIA, J. T., ROTUNDO, M. P., WHITTALL, J. P., SCRIBBANS, T. D., GRAHAM, R. B. & GURD, B. J. 2016. Inter-Individual Variability in the Adaptive Responses to Endurance and Sprint Interval Training: A Randomized Crossover Study. *PLoS One*, 11, e0167790.
- BONET, J. B., MAGALHAES, J., VISCOR, G., PAGES, T., VENTURA, J. L., TORRELLA, J. R. & JAVIERRE, C. 2020. Inter-Individual Different Responses to Continuous and Interval Training in Recreational Middle-Aged Women Runners. *Front Physiol*, 11, 579835.
- BONNE, T. C., DOUCENDE, G., FLUCK, D., JACOBS, R. A., NORDSBORG, N. B., ROBACH, P., WALTHER, G. & LUNDBY, C. 2014. Phlebotomy eliminates the maximal cardiac output response to six weeks of exercise training. *Am J Physiol Regul Integr Comp Physiol*, 306, R752-60.
- BORG, G. A. 1982. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*, 14, 377-81.
- BOSTAD, W., VALENTINO, S. E., MCCARTHY, D. G., RICHARDS, D. L., MACINNIS, M. J., MACDONALD, M. J. & GIBALA, M. J. 2021. Twelve weeks of sprint interval training increases peak cardiac output in previously untrained individuals. *Eur J Appl Physiol*, 121, 2449-2458.
- BOSTAD, W., WILLIAMS, J. S., VAN BERKEL, E. K., RICHARDS, D. L., MACDONALD, M. J. & GIBALA, M. J. 2023. Biological sex does not influence the peak cardiac output response to twelve weeks of sprint interval training. *Sci Rep*, 13, 22995.
- BOUCHARD, C. Human adaptability may have a genetic basis. Health risk estimation, risk reduction and health promotion. Proceedings for the 18th annual meeting of the society of prospective medicine. Ottawa: Canadian Public Health Institution, 1983. 443-76.
- BOUCHARD, C., AN, P., RICE, T., SKINNER, J. S., WILMORE, J. H., GAGNON, J., PERUSSE, L., LEON, A. S. & RAO, D. C. 1999. Familial aggregation of VO₂max response to exercise training: results from the HERITAGE Family Study. *J Appl Physiol (1985)*, 87, 1003-8.
- BOUCHARD, C., LESAGE, R., LORTIE, G., SIMONEAU, J.-A., HAMEL, P., BOULAY, M. R., PERUSSE, L., THERIAULT, G. & LEBLANC, C. 1986. Aerobic performance in brothers, dizygotic and monozygotic twins. *Medicine & Science in Sports & Exercise*, 18, 639-646.
- BOUCHARD, C., SARZYNSKI, M. A., RICE, T. K., KRAUS, W. E., CHURCH, T. S., SUNG, Y. J., RAO, D. C. & RANKINEN, T. 2011. Genomic predictors of the maximal O₂ uptake

- response to standardized exercise training programs. *J Appl Physiol* (1985), 110, 1160-70.
- BROATCH, J. R., PETERSEN, A. & BISHOP, D. J. 2017. Cold-water immersion following sprint interval training does not alter endurance signaling pathways or training adaptations in human skeletal muscle. *Am J Physiol Regul Integr Comp Physiol*, 313, R372-R384.
- BROEKHUIZEN, L. N., BOEKHOLDT, S. M., ARSENAULT, B. J., DESPRES, J. P., STROES, E. S., KASTELEIN, J. J., KHAW, K. T. & WAREHAM, N. J. 2011. Physical activity, metabolic syndrome, and coronary risk: the EPIC-Norfolk prospective population study. *Eur J Cardiovasc Prev Rehabil*, 18, 209-17.
- BURGOMASTER, K. A., HEIGENHAUSER, G. J. & GIBALA, M. J. 2006. Effect of short-term sprint interval training on human skeletal muscle carbohydrate metabolism during exercise and time-trial performance. *J Appl Physiol* (1985), 100, 2041-7.
- BURGOMASTER, K. A., HOWARTH, K. R., PHILLIPS, S. M., RAKOBOWCHUK, M., MACDONALD, M. J., MCGEE, S. L. & GIBALA, M. J. 2008. Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. *J Physiol*, 586, 151-60.
- BURGOMASTER, K. A., HUGHES, S. C., HEIGENHAUSER, G. J., BRADWELL, S. N. & GIBALA, M. J. 2005. Six sessions of sprint interval training increases muscle oxidative potential and cycle endurance capacity in humans. *J Appl Physiol* (1985), 98, 1985-90.
- BURKNER, P.-C. 2017. brms : An R Package for Bayesian Multilevel Models Using Stan. *Journal of Statistical Software*, 80, 1-28.
- BURTSCHER, J., STRASSER, B., BURTSCHER, M. & MILLET, G. P. 2022. The Impact of Training on the Loss of Cardiorespiratory Fitness in Aging Masters Endurance Athletes. *Int J Environ Res Public Health*, 19.
- BUSQUETS, S., FIGUERAS, M., ALMENDRO, V., LÓPEZ-SORIANO, F. J. & ARGILÉS, J. M. 2006. Interleukin-15 increases glucose uptake in skeletal muscle An antidiabetogenic effect of the cytokine. *Biochimica et Biophysica Acta (BBA) - General Subjects*, 1760, 1613-1617.
- CAMACHO-CARDENOSA, M., CAMACHO-CARDENOSA, A., MARTINEZ GUARDADO, I., MARCOS-SERRANO, M., TIMON, R. & OLCINA, G. 2017. A new dose of maximal-intensity interval training in hypoxia to improve body composition and hemoglobin and hematocrit levels: a pilot study. *J Sports Med Phys Fitness*, 57, 60-69.
- CAMPOREZ, J. P., JORNAYVAZ, F. R., PETERSEN, M. C., PESTA, D., GUIGNI, B. A., SERR, J., ZHANG, D., KAHN, M., SAMUEL, V. T., JURCZAK, M. J. & SHULMAN, G. I. 2013. Cellular mechanisms by which FGF21 improves insulin sensitivity in male mice. *Endocrinology*, 154, 3099-109.
- CAREY, A. L., STEINBERG, G. R., MACAULAY, S. L., THOMAS, W. G., HOLMES, A. G., RAMM, G., PRELOVSEK, O., HOHNEN-BEHRENS, C., WATT, M. J., JAMES, D. E., KEMP, B. E., PEDERSEN, B. K. & FEBBRAIO, M. A. 2006. Interleukin-6 increases insulin-stimulated glucose disposal in humans and glucose uptake and fatty acid oxidation in vitro via AMP-activated protein kinase. *Diabetes*, 55, 2688-97.
- CARPENTER, B., GELMAN, A., HOFFMAN, M. D., LEE, D., GOODRICH, B., BETANCOURT, M., BRUBAKER, M. A., GUO, J., LI, P. & RIDDELL, A. 2017. Stan: A Probabilistic Programming Language. *J Stat Softw*, 76.
- CARRICK-RANSON, G., HASTINGS, J. L., BHELLA, P. S., SHIBATA, S., FUJIMOTO, N., PALMER, D., BOYD, K. & LEVINE, B. D. 2012. The Effect of Age-related Differences in Body

- Size and Composition on Cardiovascular Determinants of VO₂max. *The Journals of Gerontology: Series A*, 68, 608-616.
- CATOIRE, M., MENSINK, M., BOEKSCHOTEN, M. V., HANGELBROEK, R., MULLER, M., SCHRAUWEN, P. & KERSTEN, S. 2012. Pronounced effects of acute endurance exercise on gene expression in resting and exercising human skeletal muscle. *PLoS One*, 7, e51066.
- CATOIRE, M., MENSINK, M., KALKHOVEN, E., SCHRAUWEN, P. & KERSTEN, S. 2014. Identification of human exercise-induced myokines using secretome analysis. *Physiol Genomics*, 46, 256-67.
- CHAN, W. S., NG, C. F., PANG, B. P. S., HANG, M., TSE, M. C. L., IU, E. C. Y., OOI, X. C., YANG, X., KIM, J. K., LEE, C. W. & CHAN, C. B. 2024. Exercise-induced BDNF promotes PPAR δ -dependent reprogramming of lipid metabolism in skeletal muscle during exercise recovery. *Science Signaling*, 17, eadh2783.
- CHATLAONG, M. A., BENTLEY, J. P., DOWELL, H. C., SMITH, O. J. & JESSEE, M. B. 2026. Cardiorespiratory and vascular function outcomes following 4 weeks of single-sprint training. *Frontiers in Physiology*, Volume 17 - 2026.
- CHEN, Z.-P., MCCONELL, G. K., MICHELL, B. J., SNOW, R. J., CANNY, B. J. & KEMP, B. E. 2000. AMPK signaling in contracting human skeletal muscle: acetyl-CoA carboxylase and NO synthase phosphorylation. *American Journal of Physiology-Endocrinology and Metabolism*, 279, E1202-E1206.
- CHIDNOK, W., DIMENNA, F. J., BAILEY, S. J., BURNLEY, M., WILKERSON, D. P., VANHATALO, A. & JONES, A. M. 2013. .VO₂max is not altered by self-pacing during incremental exercise: reply to the letter of Alexis R. Mauger. *Eur J Appl Physiol*, 113, 543-4.
- CHIN, E. C., YU, A. P., LAI, C. W., FONG, D. Y., CHAN, D. K., WONG, S. H., SUN, F., NGAI, H. H., YUNG, P. S. H. & SIU, P. M. 2020. Low-Frequency HIIT Improves Body Composition and Aerobic Capacity in Overweight Men. *Med Sci Sports Exerc*, 52, 56-66.
- CHURCH, T. S., CHENG, Y. J., EARNEST, C. P., BARLOW, C. E., GIBBONS, L. W., PRIEST, E. L. & BLAIR, S. N. 2004. Exercise capacity and body composition as predictors of mortality among men with diabetes. *Diabetes Care*, 27, 83-8.
- CHURCH, T. S., EARNEST, C. P., SKINNER, J. S. & BLAIR, S. N. 2007. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *Jama*, 297, 2081-91.
- CHURCH, T. S., THOMAS, D. M., TUDOR-LOCKE, C., KATZMARZYK, P. T., EARNEST, C. P., RODARTE, R. Q., MARTIN, C. K., BLAIR, S. N. & BOUCHARD, C. 2011. Trends over 5 decades in U.S. occupation-related physical activity and their associations with obesity. *PLoS One*, 6, e19657.
- COATES, A. M., JOYNER, M. J., LITTLE, J. P., JONES, A. M. & GIBALA, M. J. 2023. A Perspective on High-Intensity Interval Training for Performance and Health. *Sports Med*, 53, 85-96.
- COCHRAN, A. J., PERCIVAL, M. E., TRICARICO, S., LITTLE, J. P., CERMAK, N., GILLEN, J. B., TARNOPOLSKY, M. A. & GIBALA, M. J. 2014. Intermittent and continuous high-intensity exercise training induce similar acute but different chronic muscle adaptations. *Exp Physiol*, 99, 782-91.
- COCKS, M., SHAW, C. S., SHEPHERD, S. O., FISHER, J. P., RANASINGHE, A., BARKER, T. A. & WAGENMAKERS, A. J. 2016. Sprint interval and moderate-intensity continuous training have equal benefits on aerobic capacity, insulin sensitivity, muscle

- capillarisation and endothelial eNOS/NAD(P)H oxidase protein ratio in obese men. *J Physiol*, 594, 2307-21.
- COCKS, M., SHAW, C. S., SHEPHERD, S. O., FISHER, J. P., RANASINGHE, A. M., BARKER, T. A., TIPTON, K. D. & WAGENMAKERS, A. J. M. 2013. Sprint interval and endurance training are equally effective in increasing muscle microvascular density and eNOS content in sedentary males. *The Journal of Physiology*, 591, 641-656.
- COLPITTS, B. H., SEAMAN, K., EADIE, A. L., BRUNT, K. R., BOUCHARD, D. R. & SENECHAL, M. 2021. Effects of sprint interval training on substrate oxidation in adults living with and without obesity: The i-FLEX study. *Physiol Rep*, 9, e14916.
- CUDDY, T. F., RAMOS, J. S. & DALLECK, L. C. 2019. Reduced Exertion High-Intensity Interval Training is More Effective at Improving Cardiorespiratory Fitness and Cardiometabolic Health than Traditional Moderate-Intensity Continuous Training. *Int J Environ Res Public Health*, 16.
- D'AMORE, C., SAUNDERS, S., BHATNAGAR, N., GRIFFITH, L. E., RICHARDSON, J. & BEAUCHAMP, M. K. 2023. Determinants of physical activity in community-dwelling older adults: an umbrella review. *Int J Behav Nutr Phys Act*, 20, 135.
- DALLECK, L., BUSHMAN, T. T., CRAIN, R. D., GAJDA, M. M., KOGER, E. M. & DERKSEN, L. A. 2010. Dose-response relationship between interval training frequency and magnitude of improvement in lactate threshold. *Int J Sports Med*, 31, 567-71.
- DARKHAL, P., GAO, M., MA, Y. & LIU, D. 2015. Blocking high-fat diet-induced obesity, insulin resistance and fatty liver by overexpression of IL-13 gene in mice. *Int J Obes (Lond)*, 39, 1292-9.
- DAUSSIN, F. N., PONSOT, E., DUFOUR, S. P., LONSDORFER-WOLF, E., DOUTRELEAU, S., GENY, B., PIQUARD, F. & RICHARD, R. 2007. Improvement of VO₂max by cardiac output and oxygen extraction adaptation during intermittent versus continuous endurance training. *Eur J Appl Physiol*, 101, 377-83.
- DAUSSIN, F. N., ZOLL, J., DUFOUR, S. P., PONSOT, E., LONSDORFER-WOLF, E., DOUTRELEAU, S., METTAUER, B., PIQUARD, F., GENY, B. & RICHARD, R. 2008. Effect of interval versus continuous training on cardiorespiratory and mitochondrial functions: relationship to aerobic performance improvements in sedentary subjects. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 295, R264-R272.
- DAVIS, J. A., WHIPP, B. J., LAMARRA, N., HUNTSMAN, D. J., FRANK, M. H. & WASSERMAN, K. 1982. Effect of ramp slope on determination of aerobic parameters from the ramp exercise test. *Med Sci Sports Exerc*, 14, 339-43.
- DE SMET, S., VAN THIENEN, R., DELDICQUE, L., JAMES, R., SALE, C., BISHOP, D. J. & HESPEL, P. 2016. Nitrate Intake Promotes Shift in Muscle Fiber Type Composition during Sprint Interval Training in Hypoxia. *Front Physiol*, 7, 233.
- DE SOUSA, A. F. M., MEDEIROS, A. R., BENITEZ-FLORES, S., DEL ROSSO, S., STULTS-KOLEHMAINEN, M. & BOULLOSA, D. A. 2018. Improvements in Attention and Cardiac Autonomic Modulation After a 2-Weeks Sprint Interval Training Program: A Fidelity Approach. *Front Physiol*, 9, 241.
- DENHAM, J., GRAY, A. J., SCOTT-HAMILTON, J., HAGSTROM, A. D. & MURPHY, A. J. 2018. Small non-coding RNAs are altered by short-term sprint interval training in men. *Physiol Rep*, 6, e13653.
- DENHAM, J., SCOTT-HAMILTON, J., HAGSTROM, A. D. & GRAY, A. J. 2020. Cycling Power Outputs Predict Functional Threshold Power and Maximum Oxygen Uptake. *J Strength Cond Res*, 34, 3489-3497.

- DEPAOLI, S., WINTER, S. D. & VISSER, M. 2020. The Importance of Prior Sensitivity Analysis in Bayesian Statistics: Demonstrations Using an Interactive Shiny App. *Front Psychol*, 11, 608045.
- DI RAIMONDO, D., MICELI, G., MUSIARI, G., TUTTOLOMONDO, A. & PINTO, A. 2017. New insights about the putative role of myokines in the context of cardiac rehabilitation and secondary cardiovascular prevention. *Ann Transl Med*, 5, 300.
- DIDERIKSEN, K. & MIKKELSEN, U. R. 2017. Reproducibility of incremental maximal cycle ergometer tests in healthy recreationally active subjects. *Clin Physiol Funct Imaging*, 37, 173-182.
- DIGBY, L., MCCARTHY, S. F., BORNATH, D. P. B., COPELAND, J. L. & HAZELL, T. J. 2023. Individual and Group Responses of Cardiorespiratory Fitness to Running and Cycling Sprint Interval Training. *J Strength Cond Res*, 37, e313-e316.
- DILL, D. B. & COSTILL, D. L. 1974. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol*, 37, 247-8.
- DINOFF, A., HERRMANN, N., SWARDFAGER, W. & LANCTOT, K. L. 2017. The effect of acute exercise on blood concentrations of brain-derived neurotrophic factor in healthy adults: a meta-analysis. *Eur J Neurosci*, 46, 1635-1646.
- DUNHAM, C. & HARMS, C. A. 2012. Effects of high-intensity interval training on pulmonary function. *Eur J Appl Physiol*, 112, 3061-8.
- DUNSTON, E. R. & TAYLOR, K. 2023. Psychological and Physiological Responses Across Six Weeks of HIIT and MICT in Previously Inactive, Young Adults. *Int J Exerc Sci*, 16, 756-769.
- EDVARSEN, E., HEM, E. & ANDERSEN, S. A. 2014. End criteria for reaching maximal oxygen uptake must be strict and adjusted to sex and age: a cross-sectional study. *PLoS One*, 9, e85276.
- EGAN, B. & SHARPLES, A. P. 2023. Molecular responses to acute exercise and their relevance for adaptations in skeletal muscle to exercise training. *Physiological Reviews*, 103, 2057-2170.
- EGAN, B. & ZIERATH, J. R. 2013. Exercise metabolism and the molecular regulation of skeletal muscle adaptation. *Cell Metab*, 17, 162-84.
- EKKEKAKIS, P., HALL, E. E. & PETRUZZELLO, S. J. 2004. Practical markers of the transition from aerobic to anaerobic metabolism during exercise: rationale and a case for affect-based exercise prescription. *Prev Med*, 38, 149-59.
- EKKEKAKIS, P., PARFITT, G. & PETRUZZELLO, S. J. 2011. The pleasure and displeasure people feel when they exercise at different intensities: decennial update and progress towards a tripartite rationale for exercise intensity prescription. *Sports Med*, 41, 641-71.
- ELLIOTT-SALE, K. J., MINAHAN, C. L., DE JONGE, X., ACKERMAN, K. E., SIPILÄ, S., CONSTANTINI, N. W., LEBRUN, C. M. & HACKNEY, A. C. 2021. Methodological Considerations for Studies in Sport and Exercise Science with Women as Participants: A Working Guide for Standards of Practice for Research on Women. *Sports Med*, 51, 843-861.
- ESBJÖRNSSON, M., RUNDQVIST, H. C., MASCHER, H., ÖSTERLUND, T., ROOYACKERS, O., BLOMSTRAND, E. & JANSSON, E. 2012. Sprint exercise enhances skeletal muscle p70S6k phosphorylation and more so in women than in men. *Acta Physiologica*, 205, 411-422.
- ESBJÖRNSSON-LILJEDAHL, M., BODIN, K. & JANSSON, E. 2002. Smaller muscle ATP reduction in women than in men by repeated bouts of sprint exercise. *Journal of Applied Physiology*, 93, 1075-1083.

- ESBJÖRNSSON-LILJEDAHL, M., SUNDBERG, C. J., NORMAN, B. & JANSSON, E. 1999. Metabolic response in type I and type II muscle fibers during a 30-s cycle sprint in men and women. *Journal of Applied Physiology*, 87, 1326-1332.
- FAGARD, R., BIELEN, E. & AMERY, A. 1991. Heritability of aerobic power and anaerobic energy generation during exercise. *Journal of Applied Physiology*, 70, 357-362.
- FAUL, F., ERDFELDER, E., LANG, A.-G. & BUCHNER, A. 2007. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39, 175-191.
- FITZGERALD, M. D., TANAKA, H., TRAN, Z. V. & SEALS, D. R. 1997. Age-related declines in maximal aerobic capacity in regularly exercising vs. sedentary women: a meta-analysis. *J Appl Physiol* (1985), 83, 160-5.
- FLEG, J. L., MORRELL, C. H., BOS, A. G., BRANT, L. J., TALBOT, L. A., WRIGHT, J. G. & LAKATTA, E. G. 2005. Accelerated longitudinal decline of aerobic capacity in healthy older adults. *Circulation*, 112, 674-82.
- FLORIN, A., LAMBERT, C., SANCHEZ, C., ZAPPIA, J., DURIEUX, N., TIEPPO, A. M., MOBASHERI, A. & HENROTIN, Y. 2020. The secretome of skeletal muscle cells: A systematic review. *Osteoarthritis Cartilage*, 2, 100019.
- FOGELHOLM, M. 2010. Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review. *Obes Rev*, 11, 202-21.
- FOSTER, C., FARLAND, C. V., GUIDOTTI, F., HARBIN, M., ROBERTS, B., SCHUETTE, J., TUURI, A., DOBERSTEIN, S. T. & PORCARI, J. P. 2015. The Effects of High Intensity Interval Training vs Steady State Training on Aerobic and Anaerobic Capacity. *J Sports Sci Med*, 14, 747-55.
- FRAZAO, D. T., DE FARIAS JUNIOR, L. F., DANTAS, T. C., KRINSKI, K., ELSANGEDY, H. M., PRESTES, J., HARDCASTLE, S. J. & COSTA, E. C. 2016. Correction: Feeling of Pleasure to High-Intensity Interval Exercise Is Dependent of the Number of Work Bouts and Physical Activity Status. *PLoS One*, 11, e0153986.
- FUKUSHIMA, N., MACHIDA, M., KIKUCHI, H., AMAGASA, S., HAYASHI, T., ODAGIRI, Y., TAKAMIYA, T. & INOUE, S. 2021. Associations of working from home with occupational physical activity and sedentary behavior under the COVID-19 pandemic. *J Occup Health*, 63, e12212.
- FULLER, A., OKWOSE, N., SCRAGG, J., EGGETT, C., LUKE, P., BANDALI, A., VELICKI, R., GREAVES, L., MACGOWAN, G. A. & JAKOVljeVIC, D. G. 2021. The effect of age on mechanisms of exercise tolerance: Reduced arteriovenous oxygen difference causes lower oxygen consumption in older people. *Experimental Gerontology*, 149, 111340.
- GABRY, J., SIMPSON, D., VEHTARI, A., BETANCOURT, M. & GELMAN, A. 2019. Visualization in Bayesian Workflow. *Journal of the Royal Statistical Society Series A: Statistics in Society*, 182, 389-402.
- GARNEAU, L., MULVIHILL, E. E., SMITH, S. R., SPARKS, L. M. & AGUER, C. 2024. Myokine Secretion following an Aerobic Exercise Intervention in Individuals with Type 2 Diabetes with or without Exercise Resistance. *Int J Mol Sci*, 25.
- GARNEAU, L., PARSONS, S. A., SMITH, S. R., MULVIHILL, E. E., SPARKS, L. M. & AGUER, C. 2020. Plasma Myokine Concentrations After Acute Exercise in Non-obese and Obese Sedentary Women. *Front Physiol*, 11, 18.
- GAUTHIER, A. P., LARIVIERE, M. & YOUNG, N. 2009. Psychometric properties of the IPAQ: a validation study in a sample of northern Franco-Ontarians. *J Phys Act Health*, 6 Suppl 1, S54-60.

- GEIGER, T., VELIC, A., MACEK, B., LUNDBERG, E., KAMPF, C., NAGARAJ, N., UHLEN, M., COX, J. & MANN, M. 2013. Initial quantitative proteomic map of 28 mouse tissues using the SILAC mouse. *Mol Cell Proteomics*, 12, 1709-22.
- GELMAN, A. & RUBIN, D. B. 1992. Inference from Iterative Simulation Using Multiple Sequences. *Statistical Science*, 7, 457-472, 16.
- GIBALA, M. 2009. Molecular responses to high-intensity interval exercise. *Appl Physiol Nutr Metab*, 34, 428-32.
- GIBALA, M. J., LITTLE, J. P., VAN ESSEN, M., WILKIN, G. P., BURGOMASTER, K. A., SAFDAR, A., RAHA, S. & TARNOPOLSKY, M. A. 2006. Short-term sprint interval versus traditional endurance training: similar initial adaptations in human skeletal muscle and exercise performance. *J Physiol*, 575, 901-11.
- GILLEN, J. B., MARTIN, B. J., MACINNIS, M. J., SKELLY, L. E., TARNOPOLSKY, M. A. & GIBALA, M. J. 2016. Twelve Weeks of Sprint Interval Training Improves Indices of Cardiometabolic Health Similar to Traditional Endurance Training despite a Five-Fold Lower Exercise Volume and Time Commitment. *PLoS One*, 11, e0154075.
- GILLEN, J. B., PERCIVAL, M. E., SKELLY, L. E., MARTIN, B. J., TAN, R. B., TARNOPOLSKY, M. A. & GIBALA, M. J. 2014. Three minutes of all-out intermittent exercise per week increases skeletal muscle oxidative capacity and improves cardiometabolic health. *PLoS One*, 9, e111489.
- GIST, N. H., FEDEWA, M. V., DISHMAN, R. K. & CURETON, K. J. 2014. Sprint interval training effects on aerobic capacity: a systematic review and meta-analysis. *Sports Med*, 44, 269-79.
- GOLDSTEIN, M. S. 1961. Humoral nature of the hypoglycemic factor of muscular work. *Diabetes*, 10, 232-4.
- GRANATA, C., OLIVEIRA, R. S., LITTLE, J. P., RENNER, K. & BISHOP, D. J. 2016. Training intensity modulates changes in PGC-1 α and p53 protein content and mitochondrial respiration, but not markers of mitochondrial content in human skeletal muscle. *FASEB J*, 30, 959-70.
- GURD, B. J., GILES, M. D., BONAFIGLIA, J. T., RALEIGH, J. P., BOYD, J. C., MA, J. K., ZELT, J. G. & SCRIBBANS, T. D. 2016. Incidence of nonresponse and individual patterns of response following sprint interval training. *Appl Physiol Nutr Metab*, 41, 229-34.
- GUTHOLD, R., STEVENS, G. A., RILEY, L. M. & BULL, F. C. 2018. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1.9 million participants. *Lancet Glob Health*, 6, e1077-e1086.
- HAGSTROMER, M., AINSWORTH, B. E., OJA, P. & SJOSTROM, M. 2010. Comparison of a subjective and an objective measure of physical activity in a population sample. *J Phys Act Health*, 7, 541-50.
- HAINES, M., BROOM, D., STEPHENSON, J. & GILLIBRAND, W. 2021. Influence of Sprint Duration during Minimal Volume Exercise on Aerobic Capacity and Affect. *Int J Sports Med*, 42, 357-364.
- HAKOLA, L. 2015. *Cardiorespiratory fitness and physical activity in older adults: a population-based study in men and women*.
- HARDCASTLE, S. J., RAY, H., BEALE, L. & HAGGER, M. S. 2014. Why sprint interval training is inappropriate for a largely sedentary population. *Front Psychol*, 5, 1505.
- HARDY, C. J. & REJESKI, W. J. 1989. Not What, but How One Feels: The Measurement of Affect during Exercise. *Journal of Sport and Exercise Psychology*, 11, 304-317.
- HARMER, A. R., MCKENNA, M. J., SUTTON, J. R., SNOW, R. J., RUELL, P. A., BOOTH, J., THOMPSON, M. W., MACKAY, N. A., STATHIS, C. G., CRAMERI, R. M., CAREY, M. F.

- & EAGER, D. M. 2000. Skeletal muscle metabolic and ionic adaptations during intense exercise following sprint training in humans. *J Appl Physiol* (1985), 89, 1793-803.
- HARMER, A. R., RUELL, P. A., MCKENNA, M. J., CHISHOLM, D. J., HUNTER, S. K., THOM, J. M., MORRIS, N. R. & FLACK, J. R. 2006. Effects of sprint training on extrarenal potassium regulation with intense exercise in Type 1 diabetes. *J Appl Physiol* (1985), 100, 26-34.
- HARRER, M., CUIJPERS, P., FURUKAWA, T. & EBERT, D. 2021. *Doing Meta-Analysis with R*, New York, Chapman and Hall/CRC.
- HARRIS, E., RAKOBOWCHUK, M. & BIRCH, K. M. 2014. Sprint interval and sprint continuous training increases circulating CD34+ cells and cardio-respiratory fitness in young healthy women. *PLoS One*, 9, e108720.
- HARTWIG, S., RASCHKE, S., KNEBEL, B., SCHELER, M., IRMLER, M., PASSLACK, W., MULLER, S., HANISCH, F. G., FRANZ, T., LI, X., DICKEN, H. D., ECKARDT, K., BECKERS, J., DE ANGELIS, M. H., WEIGERT, C., HARING, H. U., AL-HASANI, H., OUWENS, D. M., ECKEL, J., KOTZKA, J. & LEHR, S. 2014. Secretome profiling of primary human skeletal muscle cells. *Biochim Biophys Acta*, 1844, 1011-7.
- HAWLEY, J. A., HARGREAVES, M., JOYNER, M. J. & ZIERATH, J. R. 2014. Integrative biology of exercise. *Cell*, 159, 738-49.
- HAZELL, T. J., MACPHERSON, R. E., GRAVELLE, B. M. & LEMON, P. W. 2010. 10 or 30-s sprint interval training bouts enhance both aerobic and anaerobic performance. *Eur J Appl Physiol*, 110, 153-60.
- HEBISZ, R., CORTIS, C., HEBISZ, P., BORKOWSKI, J. & JASTRZEBSKA, A. 2024. Effects of polarised, sprint interval, high-intensity interval, and low-intensity training programs on aerobic fitness and cardiovascular health markers in active individuals. *Human Movement*, 25, 86-96.
- HELLSTEN-WESTING, Y., NORMAN, B., BALSOM, P. D. & SJODIN, B. 1993. Decreased resting levels of adenine nucleotides in human skeletal muscle after high-intensity training. *J Appl Physiol* (1985), 74, 2523-8.
- HESPANHOL, L., VALLIO, C. S., COSTA, L. M. & SARAGIOTTO, B. T. 2019. Understanding and interpreting confidence and credible intervals around effect estimates. *Braz J Phys Ther*, 23, 290-301.
- HIGGINS, J. P. T., LI, T. & DEEKS, J. J. 2024. Choosing effect measures and computing estimates of effect. In: HIGGINS, J. P. T., THOMAS, J., CHANDLER, J., CUMPSTON, M., LI, T., PAGE, M. J. & WELCH, V. A. (eds.) *Cochrane Handbook for Systematic Reviews of Interventions version 6.5*. Cochrane.
- HIGGINS, J. P. T., LI, T. & STERNE, J. 2021. Revised Cochrane risk of bias tool for randomized trials (RoB 2): Additional considerations for crossover trials (supplement).
- HIGGINS, S., FEDEWA, M. V., HATHAWAY, E. D., SCHMIDT, M. D. & EVANS, E. M. 2016. Sprint interval and moderate-intensity cycling training differentially affect adiposity and aerobic capacity in overweight young-adult women. *Appl Physiol Nutr Metab*, 41, 1177-1183.
- HILL, A. V. & LUPTON, H. 1923. Muscular Exercise, Lactic Acid, and the Supply and Utilization of Oxygen. *QJM: An International Journal of Medicine*, os-16, 135-171.
- HO, M.-Y., WEN, M.-S., YEH, J.-K., HSIEH, I. C., CHEN, C.-C., HSIEH, M.-J., TSAI, M.-L., YANG, C.-H., WU, V. C.-C., HUNG, K.-C., WANG, C.-C. & WANG, C.-Y. 2018. Excessive irisin increases oxidative stress and apoptosis in murine heart. *Biochemical and Biophysical Research Communications*, 503, 2493-2498.

- HOFFMANN, C. & WEIGERT, C. 2017. Skeletal Muscle as an Endocrine Organ: The Role of Myokines in Exercise Adaptations. *Cold Spring Harb Perspect Med*, 7.
- HOLMES, K., ROBERTS, O. L., THOMAS, A. M. & CROSS, M. J. 2007. Vascular endothelial growth factor receptor-2: structure, function, intracellular signalling and therapeutic inhibition. *Cell Signal*, 19, 2003-12.
- HOPKINS, W. G., SCHABORT, E. J. & HAWLEY, J. A. 2001. Reliability of power in physical performance tests. *Sports Med*, 31, 211-34.
- HUTTON, C. P., DÉRY, N., ROSA, E., LEMON, J. A., ROLLO, C. D., BOREHAM, D. R., FAHNESTOCK, M., DECATANZARO, D., WOJTOWICZ, J. M. & BECKER, S. 2015. Synergistic effects of diet and exercise on hippocampal function in chronically stressed mice. *Neuroscience*, 308, 180-193.
- IJICHI, T., HASEGAWA, Y., MORISHIMA, T., KURIHARA, T., HAMAOKA, T. & GOTO, K. 2015. Effect of sprint training: training once daily versus twice every second day. *Eur J Sport Sci*, 15, 143-50.
- IMBODEN, M. T., HARBER, M. P., WHALEY, M. H., FINCH, W. H., BISHOP, D. L., FLEENOR, B. S. & KAMINSKY, L. A. 2019. The Association between the Change in Directly Measured Cardiorespiratory Fitness across Time and Mortality Risk. *Prog Cardiovasc Dis*, 62, 157-162.
- INGLIS, E. C., IANNETTA, D., RASICA, L., MACKIE, M. Z., KEIR, D. A., MACINNIS, M. J. & MURIAS, J. M. 2024. Heavy-, Severe-, and Extreme-, but Not Moderate-Intensity Exercise Increase $\dot{V}O_{2max}$ and Thresholds after 6 wk of Training. *Med Sci Sports Exerc*, 56, 1307-1316.
- ITO, S. 2019. High-intensity interval training for health benefits and care of cardiac diseases - The key to an efficient exercise protocol. *World J Cardiol*, 11, 171-188.
- JABBARI, Y. & CRIBBIE, R. 2022. Negligible interaction test for continuous predictors. *J Appl Stat*, 49, 2001-2015.
- JACOBS, R. A., FLUCK, D., BONNE, T. C., BURGI, S., CHRISTENSEN, P. M., TOIGO, M. & LUNDBY, C. 2013. Improvements in exercise performance with high-intensity interval training coincide with an increase in skeletal muscle mitochondrial content and function. *J Appl Physiol (1985)*, 115, 785-93.
- JANSE DE JONGE, X., THOMPSON, B. & HAN, A. 2019. Methodological Recommendations for Menstrual Cycle Research in Sports and Exercise. *Medicine & Science in Sports & Exercise*, 51, 2610-2617.
- JIANG, L. Q., FRANCK, N., EGAN, B., SJÖGREN, R. J., KATAYAMA, M., DUQUE-GUIMARAES, D., ARNER, P., ZIERATH, J. R. & KROOK, A. 2013. Autocrine role of interleukin-13 on skeletal muscle glucose metabolism in type 2 diabetic patients involves microRNA let-7. *Am J Physiol Endocrinol Metab*, 305, E1359-66.
- JOYNER, M. J. & LUNDBY, C. 2018. Concepts About $\dot{V}O_{2max}$ and Trainability Are Context Dependent. *Exerc Sport Sci Rev*, 46, 138-143.
- JUNG, M. E., BOURNE, J. E. & LITTLE, J. P. 2014. Where does HIT fit? An examination of the affective response to high-intensity intervals in comparison to continuous moderate- and continuous vigorous-intensity exercise in the exercise intensity-affect continuum. *PLoS One*, 9, e114541.
- JURIMAE, J., PURGE, P., REMMEL, L., ERELINE, J., KUMS, T., KAMANDULIS, S., BRAZAITIS, M., VENCKUNAS, T. & PAASUKE, M. 2023. Changes in irisin, inflammatory cytokines and aerobic capacity in response to three weeks of supervised sprint interval training in older men. *J Sports Med Phys Fitness*, 63, 162-169.
- JUSKEVICIUTE, E., NEUBERGER, E., EIMANTAS, N., VENCKUNAS, T., KAMANDULIS, S., SIMON, P. & BRAZAITIS, M. 2024. Three-week sprint interval training (SIT) reduces

- cell-free DNA and low-frequency fatigue but does not induce VO₂max improvement in older men. *Eur J Appl Physiol*, 124, 1297-1309.
- KALLIOINEN, N., PAANANEN, T., BÜRKNER, P.-C. & VEHTARI, A. 2023. Detecting and diagnosing prior and likelihood sensitivity with power-scaling. *Statistics and Computing*, 34, 57.
- KATZ, A., SHARP, R. L., KING, D. S., COSTILL, D. L. & FINK, W. J. 1984. Effect of high intensity interval training on 2,3-diphosphoglycerate at rest and after maximal exercise. *Eur J Appl Physiol Occup Physiol*, 52, 331-5.
- KATZEL, L. I., SORKIN, J. D. & FLEG, J. L. 2001. A comparison of longitudinal changes in aerobic fitness in older endurance athletes and sedentary men. *J Am Geriatr Soc*, 49, 1657-64.
- KATZMARZYK, P. T., FRIEDENREICH, C., SHIROMA, E. J. & LEE, I. M. 2022. Physical inactivity and non-communicable disease burden in low-income, middle-income and high-income countries. *Br J Sports Med*, 56, 101-106.
- KAVALIAUSKAS, M., JAKEMAN, J. & BABRAJ, J. 2018. Early Adaptations to a Two-Week Uphill Run Sprint Interval Training and Cycle Sprint Interval Training. *Sports (Basel)*, 6.
- KAVALIAUSKAS, M., STEER, T. P. & BABRAJ, J. A. 2017. Cardiorespiratory fitness and aerobic performance adaptations to a 4-week sprint interval training in young healthy untrained females. *Sport Sci Health*, 13, 17-23.
- KELLER, P., VOLLAARD, N. B., GUSTAFSSON, T., GALLAGHER, I. J., SUNDBERG, C. J., RANKINEN, T., BRITTON, S. L., BOUCHARD, C., KOCH, L. G. & TIMMONS, J. A. 2011. A transcriptional map of the impact of endurance exercise training on skeletal muscle phenotype. *J Appl Physiol (1985)*, 110, 46-59.
- KHAN, S. U. & GHAFOR, S. 2019. Myokines: Discovery Challenges and Therapeutic Impediments. *J Pak Med Assoc*, 69, 1014-1017.
- KITZMAN, D. W., SCHOLZ, D. G., HAGEN, P. T., ILSTRUP, D. M. & EDWARDS, W. D. 1988. Age-Related Changes in Normal Human Hearts During the First 10 Decades of Life. Part II (Maturity): A Quantitative Anatomic Study of 765 Specimens From Subjects 20 to 99 Years Old. *Mayo Clinic Proceedings*, 63, 137-146.
- KIVINIEMI, A. M., TULPPO, M. P., ESKELINEN, J. J., SAVOLAINEN, A. M., KAPANEN, J., HEINONEN, I. H., HAUTALA, A. J., HANNUKAINEN, J. C. & KALLIOKOSKI, K. K. 2015. Autonomic Function Predicts Fitness Response to Short-Term High-Intensity Interval Training. *Int J Sports Med*, 36, 915-21.
- KLISSOURAS, V. 1971. Heritability of adaptive variation. *Journal of Applied Physiology*, 31, 338-344.
- KLISSOURAS, V., PIRNAY, F. & PETIT, J. M. 1973. Adaptation to maximal effort: genetics and age. *J Appl Physiol*, 35, 288-93.
- KNIGHT, D. R., SCHAFFARTZIK, W., POOLE, D. C., HOGAN, M. C., BEBOUT, D. E. & WAGNER, P. D. 1993. Effects of hyperoxia on maximal leg O₂ supply and utilization in men. *J Appl Physiol (1985)*, 75, 2586-94.
- KNOLL, R., POSTEL, R., WANG, J., KRATZNER, R., HENNECKE, G., VACARU, A. M., VAKEEL, P., SCHUBERT, C., MURTHY, K., RANA, B. K., KUBE, D., KNOLL, G., SCHAFER, K., HAYASHI, T., HOLM, T., KIMURA, A., SCHORK, N., TOLIAT, M. R., NURNBERG, P., SCHULTHEISS, H. P., SCHAPER, W., SCHAPER, J., BOS, E., DEN HERTOOG, J., VAN EEDEN, F. J., PETERS, P. J., HASENFUSS, G., CHIEN, K. R. & BAKKERS, J. 2007. Laminin- α 4 and integrin-linked kinase mutations cause human cardiomyopathy via simultaneous defects in cardiomyocytes and endothelial cells. *Circulation*, 116, 515-25.

- KOKKINOS, P., FASELIS, C., MYERS, J., KOKKINOS, J. P., DOUMAS, M., PITTARAS, A., KHEIRBEK, R., MANOLIS, A., PANAGIOTAKOS, D., PAPADEMETRIOU, V. & FLETCHER, R. 2014. Statin therapy, fitness, and mortality risk in middle-aged hypertensive male veterans. *Am J Hypertens*, 27, 422-30.
- KOKKINOS, P., MYERS, J., KOKKINOS, J. P., PITTARAS, A., NARAYAN, P., MANOLIS, A., KARASIK, P., GREENBERG, M., PAPADEMETRIOU, V. & SINGH, S. 2008. Exercise capacity and mortality in black and white men. *Circulation*, 117, 614-22.
- KOKKINOS, P., MYERS, J., NYLEN, E., PANAGIOTAKOS, D. B., MANOLIS, A., PITTARAS, A., BLACKMAN, M. R., JACOB-ISSAC, R., FASELIS, C., ABELLA, J. & SINGH, S. 2009. Exercise capacity and all-cause mortality in African American and Caucasian men with type 2 diabetes. *Diabetes Care*, 32, 623-8.
- KOSTKA, M., MORYS, J., MALECKI, A. & NOWACKA-CHMIELEWSKA, M. 2024. Muscle-brain crosstalk mediated by exercise-induced myokines - insights from experimental studies. *Front Physiol*, 15, 1488375.
- KOULMANN, N. & BIGARD, A. X. 2006. Interaction between signalling pathways involved in skeletal muscle responses to endurance exercise. *Pflugers Arch*, 452, 125-39.
- KRIP, B., GLEDHILL, N., JAMNIK, V. & WARBURTON, D. 1997. Effect of alterations in blood volume on cardiac function during maximal exercise. *Medicine & Science in Sports & Exercise*, 29, 1469-1476.
- KRUSCHKE, J. K. 2013. Posterior predictive checks can and should be Bayesian: comment on Gelman and Shalizi, 'Philosophy and the practice of Bayesian statistics'. *Br J Math Stat Psychol*, 66, 45-56.
- KRUSCHKE, J. K. 2021. Bayesian Analysis Reporting Guidelines. *Nat Hum Behav*, 5, 1282-1291.
- KRUSNAUSKAS, R., EIMANTAS, N., BARANAUSKIENE, N., VENCKUNAS, T., SNIECKUS, A., BRAZAITIS, M., WESTERBLAD, H. & KAMANDULIS, S. 2020. Response to Three Weeks of Sprint Interval Training Cannot Be Explained by the Exertional Level. *Medicina (Kaunas)*, 56.
- KUANG, J., MCGINLEY, C., LEE, M. J., SANER, N. J., GARNHAM, A. & BISHOP, D. J. 2022. Interpretation of exercise-induced changes in human skeletal muscle mRNA expression depends on the timing of the post-exercise biopsies. *PeerJ*, 10, e12856.
- KUIPERS, H., KEIZER, H. A., BROUNS, F. & SARIS, W. H. 1987. Carbohydrate feeding and glycogen synthesis during exercise in man. *Pflugers Arch*, 410, 652-6.
- LAMBERT, P. C., SUTTON, A. J., BURTON, P. R., ABRAMS, K. R. & JONES, D. R. 2005. How vague is vague? A simulation study of the impact of the use of vague prior distributions in MCMC using WinBUGS. *Stat Med*, 24, 2401-28.
- LANG, J. J., PRINCE, S. A., MERUCCI, K., CADENAS-SANCHEZ, C., CHAPUT, J. P., FRASER, B. J., MANYANGA, T., MCGRATH, R., ORTEGA, F. B., SINGH, B. & TOMKINSON, G. R. 2024. Cardiorespiratory fitness is a strong and consistent predictor of morbidity and mortality among adults: an overview of meta-analyses representing over 20.9 million observations from 199 unique cohort studies. *Br J Sports Med*, 58, 556-566.
- LARSEN, R. G., BEFROY, D. E. & KENT-BRAUN, J. A. 2013. High-intensity interval training increases in vivo oxidative capacity with no effect on P(i)-->ATP rate in resting human muscle. *Am J Physiol Regul Integr Comp Physiol*, 304, R333-42.
- LAWLER, P. R., FILION, K. B. & EISENBERG, M. J. 2011. Efficacy of exercise-based cardiac rehabilitation post-myocardial infarction: a systematic review and meta-analysis of randomized controlled trials. *Am Heart J*, 162, 571-584.e2.
- LEAHY, D. J., DALLECK, L. C. & RAMOS, J. S. 2022. Changes in the Fitness Fatness Index following reduced exertion high-intensity interval training versus moderate-

- intensity continuous training in physically inactive adults. *Front Sports Act Living*, 4, 961957.
- LEE, D. C., ARTERO, E. G., SUI, X. & BLAIR, S. N. 2010. Mortality trends in the general population: the importance of cardiorespiratory fitness. *J Psychopharmacol*, 24, 27-35.
- LEE, D. C., PATE, R. R., LAVIE, C. J., SUI, X., CHURCH, T. S. & BLAIR, S. N. 2014. Leisure-time running reduces all-cause and cardiovascular mortality risk. *J Am Coll Cardiol*, 64, 472-81.
- LEE, D. C., SUI, X., ARTERO, E. G., LEE, I. M., CHURCH, T. S., MCAULEY, P. A., STANFORD, F. C., KOHL, H. W., 3RD & BLAIR, S. N. 2011. Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular disease mortality in men: the Aerobics Center Longitudinal Study. *Circulation*, 124, 2483-90.
- LEE, D. C., SUI, X., CHURCH, T. S., LAVIE, C. J., JACKSON, A. S. & BLAIR, S. N. 2012a. Changes in fitness and fatness on the development of cardiovascular disease risk factors hypertension, metabolic syndrome, and hypercholesterolemia. *J Am Coll Cardiol*, 59, 665-72.
- LEE, I. M., SHIROMA, E. J., LOBELO, F., PUSKA, P., BLAIR, S. N., KATZMARZYK, P. T. & LANCET PHYSICAL ACTIVITY SERIES WORKING, G. 2012b. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet*, 380, 219-29.
- LENK, M., MATZKA, M., LAUBER, L., KUNZ, P. & SPERLICH, B. 2025. Impact of weekly frequency of high-intensity interval training on cardiorespiratory, metabolic, and performance measures in recreational runners - An exploratory study. *Physiol Rep*, 13, e70573.
- LEUCHTMANN, A. B., ADAK, V., DILBAZ, S. & HANDSCHIN, C. 2021. The Role of the Skeletal Muscle Secretome in Mediating Endurance and Resistance Training Adaptations. *Front Physiol*, 12, 709807.
- LIND, E., JOENS-MATRE, R. R. & EKKEKAKIS, P. 2005. What intensity of physical activity do previously sedentary middle-aged women select? Evidence of a coherent pattern from physiological, perceptual, and affective markers. *Prev Med*, 40, 407-19.
- LITTLE, H. C., TAN, S. Y., CALI, F. M., RODRIGUEZ, S., LEI, X., WOLFE, A., HUG, C. & WONG, G. W. 2018. Multiplex Quantification Identifies Novel Exercise-regulated Myokines/Cytokines in Plasma and in Glycolytic and Oxidative Skeletal Muscle. *Mol Cell Proteomics*, 17, 1546-1563.
- LITTLE, J. P., LANGLEY, J., LEE, M., MYETTE-COTE, E., JACKSON, G., DURRER, C., GIBALA, M. J. & JUNG, M. E. 2019. Sprint exercise snacks: a novel approach to increase aerobic fitness. *Eur J Appl Physiol*, 119, 1203-1212.
- LLORIA-VARELLA, J., KORAL, J., RAVEL, A., MURIAS, J. M., FEASSON, L. & BUSSO, T. 2024. Cardiorespiratory and Neuromuscular Improvements Plateau after 2 wk of Sprint Interval Training in Sedentary Individuals. *Med Sci Sports Exerc*, 56, 876-884.
- LLOYD JONES, M. C., MORRIS, M. G. & JAKEMAN, J. R. 2019. Effect of Work: Rest Ratio on Cycling Performance Following Sprint Interval Training: A Randomized Control Trial. *J Strength Cond Res*, 33, 3263-3268.
- LOE, H., ROGNMO, O., SALTIN, B. & WISLOFF, U. 2013. Aerobic capacity reference data in 3816 healthy men and women 20-90 years. *PLoS One*, 8, e64319.
- LOHSE, K. R., SAINANI, K. L., TAYLOR, J. A., BUTSON, M. L., KNIGHT, E. J. & VICKERS, A. J. 2020. Systematic review of the use of "magnitude-based inference" in sports science and medicine. *PLoS One*, 15, e0235318.

- LORTIE, G., SIMONEAU, J. A., HAMEL, P., BOULAY, M. R., LANDRY, F. & BOUCHARD, C. 1984. Responses of maximal aerobic power and capacity to aerobic training. *Int J Sports Med*, 5, 232-6.
- LUNDBY, C., MONTERO, D. & JOYNER, M. 2017. Biology of VO₂max: looking under the physiology lamp. *Acta Physiologica*, 220, 218-228.
- LUO, Z., LUO, P., YU, Y., ZHAO, Q., ZHAO, X. & CHENG, L. 2012. SPARC promotes the development of erythroid progenitors. *Experimental Hematology*, 40, 828-836.
- MA, J., SCRIBBANS, T., EDGETT, B., BOYD, J., SIMPSON, C., LITTLE, J. & GURD, B. 2013. Extremely low-volume, high-intensity interval training improves exercise capacity and increases mitochondrial protein content in human skeletal muscle. *Open Journal of Molecular and Integrative Physiology*, 3, 202.
- MACDOUGALL, J. D., HICKS, A. L., MACDONALD, J. R., MCKELVIE, R. S., GREEN, H. J. & SMITH, K. M. 1998. Muscle performance and enzymatic adaptations to sprint interval training. *J Appl Physiol (1985)*, 84, 2138-42.
- MACINNIS, M. J. & GIBALA, M. J. 2017. Physiological adaptations to interval training and the role of exercise intensity. *J Physiol*, 595, 2915-2930.
- MACPHERSON, R. E., HAZELL, T. J., OLVER, T. D., PATERSON, D. H. & LEMON, P. W. 2011. Run sprint interval training improves aerobic performance but not maximal cardiac output. *Med Sci Sports Exerc*, 43, 115-22.
- MAES, H. H. M., BEUNEN, G. P., VLIETINCK, R. F., NEALE, M. C., THOMIS, M., EYNDE, B. V., LYSSENS, R., SIMONS, J., DEROM, C. & DEROM, R. 1996. Inheritance of physical fitness in 10-yr-old twins and their parents. *Medicine & Science in Sports & Exercise*, 28, 1479-1491.
- MAHUTTE, C. K. & JAFFE, M. B. 1995. Effect of measurement errors on cardiac output calculated with O₂ and modified CO₂ Fick methods. *J Clin Monit*, 11, 99-108.
- MAKRIDES, L., HEIGENHAUSER, G. J. & JONES, N. L. 1990. High-intensity endurance training in 20- to 30- and 60- to 70-yr-old healthy men. *J Appl Physiol (1985)*, 69, 1792-8.
- MANDIC, M., ERIKSSON, L. M. J., MELIN, M., SKOTT, V., SUNDBLAD, P., GUSTAFSSON, T. & RULLMAN, E. 2023. Increased maximal oxygen uptake after sprint-interval training is mediated by central haemodynamic factors as determined by right heart catheterization. *J Physiol*, 601, 2359-2370.
- MANDIĆ, M., FORSGREN, M. F., ROMU, T., WIDHOLM, P., SUNDBLAD, P., GUSTAFSSON, T. & RULLMAN, E. 2021. Interval-induced metabolic perturbation determines tissue fluid shifts into skeletal muscle. *Physiological Reports*, 9, e14841.
- MANDIC, M., HANSSON, B., LOVRIC, A., SUNDBLAD, P., VOLLAARD, N. B. J., LUNDBERG, T. R., GUSTAFSSON, T. & RULLMAN, E. 2022. Improvements in Maximal Oxygen Uptake After Sprint-Interval Training Coincide with Increases in Central Hemodynamic Factors. *Medicine & Science in Sports & Exercise*, 54, 944-952.
- MANTHOU, E., GILL, J. M. & MALKOVA, D. 2015. Effect of exercise programs with aerobic exercise sessions of similar intensity but different frequency and duration on health-related measures in overweight women. *J Phys Act Health*, 12, 80-6.
- MAROCOLO, M., SIMIM, M. A. M., BERNARDINO, A., MONTEIRO, I. R., PATTERSON, S. D. & DA MOTA, G. R. 2019. Ischemic preconditioning and exercise performance: shedding light through smallest worthwhile change. *European Journal of Applied Physiology*, 119, 2123-2149.
- MATSUO, T., SATOME, K., SEINO, S., SHIMOJO, N., MATSUSHITA, A., IEMITSU, M., OHSHIMA, H., TANAKA, K. & MUKAI, C. 2014. Effects of a Low-Volume Aerobic-

- Type Interval Exercise on $\dot{V}O_2\text{max}$ and Cardiac Mass. *Medicine & Science in Sports & Exercise*, 46, 42-50.
- MATTHEWS, V. B., ASTRÖM, M. B., CHAN, M. H., BRUCE, C. R., KRABBE, K. S., PRELOVSEK, O., AKERSTRÖM, T., YFANTI, C., BROHOLM, C., MORTENSEN, O. H., PENKOWA, M., HOJMAN, P., ZANKARI, A., WATT, M. J., BRUUNSGAARD, H., PEDERSEN, B. K. & FEBBRAIO, M. A. 2009. Brain-derived neurotrophic factor is produced by skeletal muscle cells in response to contraction and enhances fat oxidation via activation of AMP-activated protein kinase. *Diabetologia*, 52, 1409-18.
- MATTIONI MATURANA, F., MARTUS, P., ZIPFEL, S. & AM, N. I. 2021. Effectiveness of HIIE versus MICT in Improving Cardiometabolic Risk Factors in Health and Disease: A Meta-analysis. *Med Sci Sports Exerc*, 53, 559-573.
- MCCORMACK, G. R. & VIRK, J. S. 2014. Driving towards obesity: a systematized literature review on the association between motor vehicle travel time and distance and weight status in adults. *Prev Med*, 66, 49-55.
- MCGARR, G., HARTLEY, G. & CHEUNG, S. 2014. Neither short-term sprint nor endurance training enhances thermal response to exercise in a hot environment. *Journal of Occupational and Environmental Hygiene*, 11, 47-53.
- MCKENNA, M., HEIGENHAUSER, G. J., MCKELVIE, R., OBMINSKI, G., MACDOUGALL, J. & JONES, N. 1997. Rapid increases in ATP turnover during intense, short-term exercise result from both anaerobic and aerobic metabolism: Enhanced pulmonary and active skeletal muscle gas exchange during intense exercise after sprint training in men.
- MENDEZ-VILLANUEVA, A., EDGE, J., SURIANO, R., HAMER, P. & BISHOP, D. 2012. The Recovery of Repeated-Sprint Exercise Is Associated with PCr Resynthesis, while Muscle pH and EMG Amplitude Remain Depressed. *PLOS ONE*, 7, e51977.
- METCALFE, R. & VOLLAARD, N. 2024. Reduced-exertion high-intensity interval training (REHIT): a feasible approach for improving health and fitness? *Appl Physiol Nutr Metab*, 49, 984-992.
- METCALFE, R. S., ATEF, H., MACKINTOSH, K., MCNARRY, M., RYDE, G., HILL, D. M. & VOLLAARD, N. B. J. 2020. Time-efficient and computer-guided sprint interval exercise training for improving health in the workplace: a randomised mixed-methods feasibility study in office-based employees. *BMC Public Health*, 20, 313.
- METCALFE, R. S., BABRAJ, J. A., FAWKNER, S. G. & VOLLAARD, N. B. 2012. Towards the minimal amount of exercise for improving metabolic health: beneficial effects of reduced-exertion high-intensity interval training. *Eur J Appl Physiol*, 112, 2767-75.
- METCALFE, R. S., KOUMANOV, F., RUFFINO, J. S., STOKES, K. A., HOLMAN, G. D., THOMPSON, D. & VOLLAARD, N. B. 2015. Physiological and molecular responses to an acute bout of reduced-exertion high-intensity interval training (REHIT). *Eur J Appl Physiol*, 115, 2321-34.
- METCALFE, R. S., TARDIF, N., THOMPSON, D. & VOLLAARD, N. B. 2016. Changes in aerobic capacity and glycaemic control in response to reduced-exertion high-intensity interval training (REHIT) are not different between sedentary men and women. *Appl Physiol Nutr Metab*, 41, 1117-1123.
- METCALFE, R. S. & VOLLAARD, N. B. J. 2021. Heterogeneity and incidence of non-response for changes in cardiorespiratory fitness following time-efficient sprint interval exercise training. *Appl Physiol Nutr Metab*, 46, 735-742.
- METCALFE, R. S., WILLIAMS, S., FERNANDES, G. S., ASTORINO, T. A., STORK, M. J., PHILLIPS, S. M., NIVEN, A. & VOLLAARD, N. B. J. 2022. Affecting Effects on Affect: The Impact of Protocol Permutations on Affective Responses to Sprint Interval

- Exercise; A Systematic Review and Meta-Analysis of Pooled Individual Participant Data. *Front Sports Act Living*, 4, 815555.
- MEYER, T., AURACHER, M., HEEG, K., URHAUSEN, A. & KINDERMANN, W. 2006. Does cumulating endurance training at the weekends impair training effectiveness? *Eur J Cardiovasc Prev Rehabil*, 13, 578-84.
- MIDGLEY, A. W., MARCHANT, D. C. & LEVY, A. R. 2018. A call to action towards an evidence-based approach to using verbal encouragement during maximal exercise testing. *Clin Physiol Funct Imaging*, 38, 547-553.
- MIDGLEY, A. W., MCNAUGHTON, L. R. & CARROLL, S. 2006. Verification phase as a useful tool in the determination of the maximal oxygen uptake of distance runners. *Applied Physiology, Nutrition, and Metabolism*, 31, 541-548.
- MIDGLEY, A. W., MCNAUGHTON, L. R., POLMAN, R. & MARCHANT, D. 2007. Criteria for determination of maximal oxygen uptake: a brief critique and recommendations for future research. *Sports Med*, 37, 1019-28.
- MILANOVIC, Z., SPORIS, G. & WESTON, M. 2015. Effectiveness of High-Intensity Interval Training (HIT) and Continuous Endurance Training for VO₂max Improvements: A Systematic Review and Meta-Analysis of Controlled Trials. *Sports Med*, 45, 1469-81.
- MIYAMOTO-MIKAMI, E., ZEMPO, H., FUKU, N., KIKUCHI, N., MIYACHI, M. & MURAKAMI, H. 2018. Heritability estimates of endurance-related phenotypes: A systematic review and meta-analysis. *Scand J Med Sci Sports*, 28, 834-845.
- MONTERO, D. & LUNDBY, C. 2017. Refuting the myth of non-response to exercise training: 'non-responders' do respond to higher dose of training. *J Physiol*, 595, 3377-3387.
- MOUNIER, R., THÉRET, M., LANTIER, L., FORETZ, M. & VIOLLET, B. 2015. Expanding roles for AMPK in skeletal muscle plasticity. *Trends Endocrinol Metab*, 26, 275-86.
- MUGGERIDGE, D. J., SCULTHORPE, N., JAMES, P. E. & EASTON, C. 2017. The effects of dietary nitrate supplementation on the adaptations to sprint interval training in previously untrained males. *J Sci Med Sport*, 20, 92-97.
- MURIAS, J. M., KOWALCHUK, J. M. & PATERSON, D. H. 2010. Time course and mechanisms of adaptations in cardiorespiratory fitness with endurance training in older and young men. *J Appl Physiol (1985)*, 108, 621-7.
- MUSTELIN, L., LATVALA, A., PIETILÄINEN, K. H., PIIRILÄ, P., SOVIJÄRVI, A. R., KUJALA, U. M., RISSANEN, A. & KAPRIO, J. 2011. Associations between sports participation, cardiorespiratory fitness, and adiposity in young adult twins. *Journal of Applied Physiology*, 110, 681-686.
- MYERS, J., MCAULEY, P., LAVIE, C. J., DESPRES, J. P., ARENA, R. & KOKKINOS, P. 2015. Physical activity and cardiorespiratory fitness as major markers of cardiovascular risk: their independent and interwoven importance to health status. *Prog Cardiovasc Dis*, 57, 306-14.
- NAKAHARA, H., UEDA, S. Y. & MIYAMOTO, T. 2015. Low-frequency severe-intensity interval training improves cardiorespiratory functions. *Med Sci Sports Exerc*, 47, 789-98.
- NAKAJIMA, S., OHSAWA, I., OHTA, S., OHNO, M. & MIKAMI, T. 2010. Regular voluntary exercise cures stress-induced impairment of cognitive function and cell proliferation accompanied by increases in cerebral IGF-1 and GST activity in mice. *Behavioural Brain Research*, 211, 178-184.

- NALCAKAN, G. R. 2014. The Effects of Sprint Interval vs. Continuous Endurance Training on Physiological And Metabolic Adaptations in Young Healthy Adults. *J Hum Kinet*, 44, 97-109.
- NALCAKAN, G. R., SONGSORN, P., FITZPATRICK, B. L., YUZBASIOGLU, Y., BRICK, N. E., METCALFE, R. S. & VOLLAARD, N. B. J. 2018. Decreasing sprint duration from 20 to 10 s during reduced-exertion high-intensity interval training (REHIT) attenuates the increase in maximal aerobic capacity but has no effect on affective and perceptual responses. *Appl Physiol Nutr Metab*, 43, 338-344.
- NARANDA, T., GOLDSTEIN, A. & OLSSON, L. 1997. A peptide derived from an extracellular domain selectively inhibits receptor internalization: target sequences on insulin and insulin-like growth factor 1 receptors. *Proc Natl Acad Sci U S A*, 94, 11692-7.
- NAVES, J. P. A., VIANA, R. B., REBELO, A. C. S., DE LIRA, C. A. B., PIMENTEL, G. D., LOBO, P. C. B., DE OLIVEIRA, J. C., RAMIREZ-CAMPILLO, R. & GENTIL, P. 2018. Effects of High-Intensity Interval Training vs. Sprint Interval Training on Anthropometric Measures and Cardiorespiratory Fitness in Healthy Young Women. *Front Physiol*, 9, 1738.
- NOONE, J., MUCINSKI, J. M., DELANY, J. P., SPARKS, L. M. & GOODPASTER, B. H. 2024. Understanding the variation in exercise responses to guide personalized physical activity prescriptions. *Cell Metab*, 36, 702-724.
- NORHEIM, F., RAASTAD, T., THIEDE, B., RUSTAN, A. C., DREVON, C. A. & HAUGEN, F. 2011. Proteomic identification of secreted proteins from human skeletal muscle cells and expression in response to strength training. *Am J Physiol Endocrinol Metab*, 301, E1013-21.
- O'DRISCOLL, J. M., WRIGHT, S. M., TAYLOR, K. A., COLEMAN, D. A., SHARMA, R. & WILES, J. D. 2018. Cardiac autonomic and left ventricular mechanics following high intensity interval training: a randomized crossover controlled study. *J Appl Physiol* (1985), 125, 1030-1040.
- OGAWA, T., SPINA, R. J., MARTIN, W. H., KOHRT, W. M., SCHECHTMAN, K. B., HOLLOSZY, J. O. & EHSANI, A. A. 1992. Effects of aging, sex, and physical training on cardiovascular responses to exercise. *Circulation*, 86, 494-503.
- OLEK, R. A., KUJACH, S., ZIEMANN, E., ZIOLKOWSKI, W., WAZ, P. & LASKOWSKI, R. 2018. Adaptive Changes After 2 Weeks of 10-s Sprint Interval Training With Various Recovery Times. *Front Physiol*, 9, 392.
- OLIVEIRA, J., GENTIL, P., NAVES, J. P., SOUZA FILHO, L. F., SILVA, L., ZAMUNER, A. R., DE LIRA, C. A. & REBELO, A. 2022. Effects of High Intensity Interval Training versus Sprint Interval Training on Cardiac Autonomic Modulation in Healthy Women. *International Journal of Environmental Research and Public Health*, 19, 12863.
- OLSEN, L., BOTELLA, J., BARROWS, D., ROMERO, E., BAIRD, K., KATAYAMA, M., KILIC, E., PERALTA, C., ZANOUE, N., SANFORD, H., FARRELL, L., AXELROD, C. L., PLUCIŃSKA, K., WALKER, J., YAN, L., FREDRICKSON, K., POURQUIE, O., ROBBINS, J. M., VINOGRADOVA, E. V., MOLINA, H., PLACE, N., KIRWAN, J. P., ZIERATH, J. R., KROOK, A., GERSZTEN, R. E., BISHOP, D. J. & COHEN, P. 2026. Exercise intensity modulates interorgan communication and is associated with cardiometabolic health outcomes in humans. *Cell Rep Med*, 7, 102988.
- OMINYI, J., CLIFTON, A. & NWEDU, A. 2025. Understanding physical activity participation among underserved women: a mixed-methods cross sectional study using an ecological framework. *BMC Public Health*, 25, 2178.
- OPAZO-DIAZ, E. A., ACEITUNO, H. F., DIAZ, A. A., BAES, M. I., FUENTES, J. P. & PEREZ-BEY, A. 2023. Training response and time course adaptations to sprint interval training

- and moderate intensity continuous training in sedentary young people. *Gazz Med Ital - Arch Sci Med*, 182, 126-133.
- OSTROWSKI, K., ROHDE, T., ASP, S., SCHJERLING, P. & PEDERSEN, B. K. 2001. Chemokines are elevated in plasma after strenuous exercise in humans. *Eur J Appl Physiol*, 84, 244-5.
- OSTROWSKI, K., ROHDE, T., ZACHO, M., ASP, S. & PEDERSEN, B. K. 1998. Evidence that interleukin-6 is produced in human skeletal muscle during prolonged running. *J Physiol*, 508 (Pt 3), 949-53.
- OUZZANI, M., HAMMADY, H., FEDOROWICZ, Z. & ELMAGARMID, A. 2016. Rayyan-a web and mobile app for systematic reviews. *Syst Rev*, 5, 210.
- PAGE, M. J., MCKENZIE, J. E., BOSSUYT, P. M., BOUTRON, I., HOFFMANN, T. C., MULROW, C. D., SHAMSEER, L., TETZLAFF, J. M., AKL, E. A., BRENNAN, S. E., CHOU, R., GLANVILLE, J., GRIMSHAW, J. M., HROBJARTSSON, A., LALU, M. M., LI, T., LODER, E. W., MAYO-WILSON, E., MCDONALD, S., MCGUINNESS, L. A., STEWART, L. A., THOMAS, J., TRICCO, A. C., WELCH, V. A., WHITING, P. & MOHER, D. 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Rev Esp Cardiol (Engl Ed)*, 74, 790-799.
- PANDEY, A., KRAUS, W. E., BRUBAKER, P. H. & KITZMAN, D. W. 2020. Healthy Aging and Cardiovascular Function: Invasive Hemodynamics During Rest and Exercise in 104 Healthy Volunteers. *JACC Heart Fail*, 8, 111-121.
- PANDEY, A., SWIFT, D. L., MCGUIRE, D. K., AYERS, C. R., NEELAND, I. J., BLAIR, S. N., JOHANNSEN, N., EARNEST, C. P., BERRY, J. D. & CHURCH, T. S. 2015. Metabolic Effects of Exercise Training Among Fitness-Nonresponsive Patients With Type 2 Diabetes: The HART-D Study. *Diabetes Care*, 38, 1494-501.
- PANG, B. P. S., CHAN, W. S. & CHAN, C. B. 2021. Mitochondria Homeostasis and Oxidant/Antioxidant Balance in Skeletal Muscle-Do Myokines Play a Role? *Antioxidants (Basel)*, 10.
- PAROLIN, M. L., CHESLEY, A., MATSOS, M. P., SPRIET, L. L., JONES, N. L. & HEIGENHAUSER, G. J. 1999. Regulation of skeletal muscle glycogen phosphorylase and PDH during maximal intermittent exercise. *Am J Physiol*, 277, E890-900.
- PEDERSEN, B. K. 2011. Muscles and their myokines. *J Exp Biol*, 214, 337-46.
- PEDERSEN, B. K. & FEBBRAIO, M. A. 2008. Muscle as an Endocrine Organ: Focus on Muscle-Derived Interleukin-6. *Physiological Reviews*, 88, 1379-1406.
- PEDERSEN, B. K. & FEBBRAIO, M. A. 2012. Muscles, exercise and obesity: skeletal muscle as a secretory organ. *Nat Rev Endocrinol*, 8, 457-65.
- PEDERSEN, B. K., STEENBERG, A., FISCHER, C., KELLER, C., KELLER, P., PLOMGAARD, P., FEBBRAIO, M. & SALTIN, B. 2003. Searching for the exercise factor: is IL-6 a candidate? *J Muscle Res Cell Motil*, 24, 113-9.
- PEDERSEN, L. & HOJMAN, P. 2012. Muscle-to-organ cross talk mediated by myokines. *Adipocyte*, 1, 164-167.
- PERRY, C. G. R., LALLY, J., HOLLOWAY, G. P., HEIGENHAUSER, G. J. F., BONEN, A. & SPRIET, L. L. 2010. Repeated transient mRNA bursts precede increases in transcriptional and mitochondrial proteins during training in human skeletal muscle. *The Journal of Physiology*, 588, 4795-4810.
- PESERICO, C., MEZZAROBBA, P., SILVA, D., KRAVCHYCHYN, A., ALVES, J. & MACHADO, F. 2018. Blood lactate concentrations following maximal incremental test in male runners with different ages. *Revista Brasileira de Educação Física e Esporte*, 32, 5-16.

- PETERSEN, E. W., CAREY, A. L., SACCHETTI, M., STEINBERG, G. R., MACAULAY, S. L., FEBBRAIO, M. A. & PEDERSEN, B. K. 2005. Acute IL-6 treatment increases fatty acid turnover in elderly humans in vivo and in tissue culture in vitro. *Am J Physiol Endocrinol Metab*, 288, E155-62.
- PETERSEN, J. A., NAISH, C., GHONEIM, D., CABAJ, J. L., DOYLE-BAKER, P. K. & MCCORMACK, G. R. 2021. Impact of the COVID-19 Pandemic on Physical Activity and Sedentary Behaviour: A Qualitative Study in a Canadian City. *Int J Environ Res Public Health*, 18.
- PIERCE, S. J., HAHN, A. G., DAVIE, A. & LAWTON, E. W. 1999. Prolonged incremental tests do not necessarily compromise VO₂max in well-trained athletes. *J Sci Med Sport*, 2, 356-63.
- PIMENTEL, A. E., GENTILE, C. L., TANAKA, H., SEALS, D. R. & GATES, P. E. 2003. Greater rate of decline in maximal aerobic capacity with age in endurance-trained than in sedentary men. *J Appl Physiol (1985)*, 94, 2406-13.
- POLLOCK, M. L., MENGELKOCH, L. J., GRAVES, J. E., LOWENTHAL, D. T., LIMACHER, M. C., FOSTER, C. & WILMORE, J. H. 1997. Twenty-year follow-up of aerobic power and body composition of older track athletes. *J Appl Physiol (1985)*, 82, 1508-16.
- POOLE, D. C. & JONES, A. M. 2017. Measurement of the maximum oxygen uptake $\dot{V}O_{2\text{max}}$: $\dot{V}O_{2\text{peak}}$ is no longer acceptable. *J Appl Physiol (1985)*, 122, 997-1002.
- POON, E. T., WONGPIPIT, W., HO, R. S. & WONG, S. H. 2021. Interval training versus moderate-intensity continuous training for cardiorespiratory fitness improvements in middle-aged and older adults: a systematic review and meta-analysis. *J Sports Sci*, 39, 1996-2005.
- POURTEYMOUR, S., ECKARDT, K., HOLEN, T., LANGLEITE, T., LEE, S., JENSEN, J., BIRKELAND, K. I., DREVON, C. A. & HJORTH, M. 2017. Global mRNA sequencing of human skeletal muscle: Search for novel exercise-regulated myokines. *Mol Metab*, 6, 352-365.
- PROCTOR, D. N. & JOYNER, M. J. 1997. Skeletal muscle mass and the reduction of VO₂max in trained older subjects. *J Appl Physiol (1985)*, 82, 1411-5.
- R CORE TEAM 2023. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing.
- RALEIGH, J. P., GILES, M. D., ISLAM, H., NELMS, M., BENTLEY, R. F., JONES, J. H., NEDER, J. A., BOONSTRA, K., QUADRILATERO, J., SIMPSON, C. A., TSCHAKOVSKY, M. E. & GURD, B. J. 2018. Contribution of central and peripheral adaptations to changes in maximal oxygen uptake following 4 weeks of sprint interval training. *Appl Physiol Nutr Metab*, 43, 1059-1068.
- RALSTON, G. W., KILGORE, L., WYATT, F. B. & BAKER, J. S. 2017. The Effect of Weekly Set Volume on Strength Gain: A Meta-Analysis. *Sports Med*, 47, 2585-2601.
- RASCHKE, S., ECKARDT, K., BJORKLUND HOLVEN, K., JENSEN, J. & ECKEL, J. 2013. Identification and validation of novel contraction-regulated myokines released from primary human skeletal muscle cells. *PLoS One*, 8, e62008.
- REICHERT, F. F., BARROS, A. J., DOMINGUES, M. R. & HALLAL, P. C. 2007. The role of perceived personal barriers to engagement in leisure-time physical activity. *Am J Public Health*, 97, 515-9.
- RELJIC, D., LAMPE, D., WOLF, F., ZOPF, Y., HERRMANN, H. J. & FISCHER, J. 2019. Prevalence and predictors of dropout from high-intensity interval training in sedentary individuals: A meta-analysis. *Scand J Med Sci Sports*, 29, 1288-1304.
- RICHARDS, J. C., JOHNSON, T. K., KUZMA, J. N., LONAC, M. C., SCHWEDER, M. M., VOYLES, W. F. & BELL, C. 2010. Short-term sprint interval training increases insulin

- sensitivity in healthy adults but does not affect the thermogenic response to β -adrenergic stimulation. *The Journal of Physiology*, 588, 2961-2972.
- RICHARDSON, A. J. & GIBSON, O. R. 2015. Simulated hypoxia does not further improve aerobic capacity during sprint interval training. *J Sports Med Phys Fitness*, 55, 1099-106.
- RICHARDSON, A. J., RELF, R. L., SAUNDERS, A. & GIBSON, O. R. 2016. Similar Inflammatory Responses following Sprint Interval Training Performed in Hypoxia and Normoxia. *Front Physiol*, 7, 332.
- RICHARDSON, R. S., GRASSI, B., GAVIN, T. P., HASELER, L. J., TAGORE, K., ROCA, J. & WAGNER, P. D. 1999. Evidence of O₂ supply-dependent V_{O₂ max in the exercise-trained human quadriceps. *Journal of Applied Physiology*, 86, 1048-1053.}
- RINDSKOPF, D. 2020. Reporting Bayesian Results. *Eval Rev*, 44, 354-375.
- ROBERGS, R. & LANDWEHR, R. 2002. The surprising history of the "HRmax=220-age" equation. *International Journal of Online Engineering - iJOE*, 5.
- ROSENBLAT, M. A., GRANATA, C. & THOMAS, S. G. 2022. Effect of Interval Training on the Factors Influencing Maximal Oxygen Consumption: A Systematic Review and Meta-Analysis. *Sports Med*, 52, 1329-1352.
- ROSS, R., BLAIR, S. N., ARENA, R., CHURCH, T. S., DESPRES, J. P., FRANKLIN, B. A., HASKELL, W. L., KAMINSKY, L. A., LEVINE, B. D., LAVIE, C. J., MYERS, J., NIEBAUER, J., SALLIS, R., SAWADA, S. S., SUI, X., WISLOFF, U., AMERICAN HEART ASSOCIATION PHYSICAL ACTIVITY COMMITTEE OF THE COUNCIL ON, L., CARDIOMETABOLIC, H., COUNCIL ON CLINICAL, C., COUNCIL ON, E., PREVENTION, COUNCIL ON, C., STROKE, N., COUNCIL ON FUNCTIONAL, G., TRANSLATIONAL, B. & STROKE, C. 2016. Importance of Assessing Cardiorespiratory Fitness in Clinical Practice: A Case for Fitness as a Clinical Vital Sign: A Scientific Statement From the American Heart Association. *Circulation*, 134, e653-e699.
- ROSS, R., DE LANNOY, L. & STOTZ, P. J. 2015. Separate Effects of Intensity and Amount of Exercise on Interindividual Cardiorespiratory Fitness Response. *Mayo Clin Proc*, 90, 1506-14.
- ROSS, R., GOODPASTER, B. H., KOCH, L. G., SARZYNSKI, M. A., KOHRT, W. M., JOHANNSEN, N. M., SKINNER, J. S., CASTRO, A., IRVING, B. A., NOLAND, R. C., SPARKS, L. M., SPIELMANN, G., DAY, A. G., PITSCH, W., HOPKINS, W. G. & BOUCHARD, C. 2019. Precision exercise medicine: understanding exercise response variability. *Br J Sports Med*, 53, 1141-1153.
- ROSS, R. & MYERS, J. 2023. Cardiorespiratory Fitness and Its Place in Medicine. *Rev Cardiovasc Med*, 24, 14.
- ROSSITER, H. B., KOWALCHUK, J. M. & WHIPP, B. J. 2006. A test to establish maximum O₂ uptake despite no plateau in the O₂ uptake response to ramp incremental exercise. *J Appl Physiol (1985)*, 100, 764-70.
- RUFFINO, J. S., SONGSORN, P., HAGGETT, M., EDMONDS, D., ROBINSON, A. M., THOMPSON, D. & VOLLAARD, N. B. 2017. A comparison of the health benefits of reduced-exertion high-intensity interval training (REHIT) and moderate-intensity walking in type 2 diabetes patients. *Appl Physiol Nutr Metab*, 42, 202-208.
- SAFDAR, A., SALEEM, A. & TARNOPOLSKY, M. A. 2016. The potential of endurance exercise-derived exosomes to treat metabolic diseases. *Nat Rev Endocrinol*, 12, 504-17.
- SAINANI, K. L. 2018. The Problem with "Magnitude-based Inference". *Med Sci Sports Exerc*, 50, 2166-2176.

- SAINANI, K. L., LOHSE, K. R., JONES, P. R. & VICKERS, A. 2019. Magnitude-based Inference is not Bayesian and is not a valid method of inference. *Scand J Med Sci Sports*, 29, 1428-1436.
- SARZYNSKI, M. A., GHOSH, S. & BOUCHARD, C. 2017. Genomic and transcriptomic predictors of response levels to endurance exercise training. *J Physiol*, 595, 2931-2939.
- SAWKA, M. N., CONVERTINO, V. A., EICHNER, E. R., SCHNIEDER, S. M. & YOUNG, A. J. 2000. Blood volume: importance and adaptations to exercise training, environmental stresses, and trauma/sickness. *Med Sci Sports Exerc*, 32, 332-48.
- SCALZO, R. L., PELTONEN, G. L., BINNS, S. E., SHANKARAN, M., GIORDANO, G. R., HARTLEY, D. A., KLOCHAK, A. L., LONAC, M. C., PARIS, H. L., SZALLAR, S. E., WOOD, L. M., PEELOR, F. F., 3RD, HOLMES, W. E., HELLERSTEIN, M. K., BELL, C., HAMILTON, K. L. & MILLER, B. F. 2014. Greater muscle protein synthesis and mitochondrial biogenesis in males compared with females during sprint interval training. *FASEB J*, 28, 2705-14.
- SCHARHAG-ROSENBERGER, F., WALITZEK, S., KINDERMANN, W. & MEYER, T. 2012. Differences in adaptations to 1 year of aerobic endurance training: individual patterns of nonresponse. *Scand J Med Sci Sports*, 22, 113-8.
- SCHOCH, R., WAGNER, J., NIEMEYER, M., BRUGGISSER, F., INFANGER, D., CARRARD, J., GASSER, B., SCHMIDT-TRUCKSÄSS, A. & KNAIER, R. 2025. Reliability of hemodynamic parameters measured by bioimpedance cardiography at different intensities during incremental exercise testing. *Front Cardiovasc Med*, 12, 1531027.
- SCHUBERT, M. M., CLARKE, H. E., SEAY, R. F. & SPAIN, K. K. 2017. Impact of 4 weeks of interval training on resting metabolic rate, fitness, and health-related outcomes. *Appl Physiol Nutr Metab*, 42, 1073-1081.
- SCHUTTE, N. M., NEDEREND, I., HUDZIAK, J. J., BARTELS, M. & DE GEUS, E. J. 2016. Twin-sibling study and meta-analysis on the heritability of maximal oxygen consumption. *Physiol Genomics*, 48, 210-9.
- SCHWARZER, G., CARPENTER, J. R. & RUCKER, G. 2015. *Meta-Analysis with R*, Cham, Springer.
- SCRIBBANS, T. D., EDGETT, B. A., VOROBJ, K., MITCHELL, A. S., JOANISSE, S. D., MATUSIAK, J. B., PARISE, G., QUADRILATERO, J. & GURD, B. J. 2014. Fibre-specific responses to endurance and low volume high intensity interval training: striking similarities in acute and chronic adaptation. *PLoS One*, 9, e98119.
- SEVERINSEN, M. C. K. & PEDERSEN, B. K. 2020. Muscle-Organ Crosstalk: The Emerging Roles of Myokines. *Endocr Rev*, 41, 594-609.
- SHAHABI, S., ESFARJANI, F., REISI, J., MOMENZADEH, S., JAMI, M.-S. & ZAMANI, S. 2021. The Effects of 8-Week Resistance and Endurance Trainings on Bone Strength Compared to Irisin Injection Protocol in Mice. *Advanced Biomedical Research*, 10, 40.
- SHEPHERD, S. O., COCKS, M., TIPTON, K. D., RANASINGHE, A. M., BARKER, T. A., BURNISTON, J. G., WAGENMAKERS, A. J. & SHAW, C. S. 2013. Sprint interval and traditional endurance training increase net intramuscular triglyceride breakdown and expression of perilipin 2 and 5. *J Physiol*, 591, 657-75.
- SISSON, S. B., KATZMARZYK, P. T., EARNEST, C. P., BOUCHARD, C., BLAIR, S. N. & CHURCH, T. S. 2009. Volume of exercise and fitness nonresponse in sedentary, postmenopausal women. *Med Sci Sports Exerc*, 41, 539-45.

- SKATTEBO, O., BJERRING, A. W., AUENSEN, M., SARVARI, S. I., CUMMING, K. T., CAPELLI, C. & HALLEN, J. 2020. Blood volume expansion does not explain the increase in peak oxygen uptake induced by 10 weeks of endurance training. *Eur J Appl Physiol*, 120, 985-999.
- SKLERYK, J. R., KARAGOUNIS, L. G., HAWLEY, J. A., SHARMAN, M. J., LAURSEN, P. B. & WATSON, G. 2013. Two weeks of reduced-volume sprint interval or traditional exercise training does not improve metabolic functioning in sedentary obese men. *Diabetes Obes Metab*, 15, 1146-53.
- SLOTH, M., SLOTH, D., OVERGAARD, K. & DALGAS, U. 2013. Effects of sprint interval training on VO₂max and aerobic exercise performance: A systematic review and meta-analysis. *Scand J Med Sci Sports*, 23, e341-52.
- SONG, H., GUAN, Y., ZHANG, L., LI, K. & DONG, C. 2010. SPARC interacts with AMPK and regulates GLUT4 expression. *Biochem Biophys Res Commun*, 396, 961-6.
- SONG, Y. & LAN, H. 2024. The Effects of High-Intensity Interval Training on Cardiometabolic Health in Children and Adolescents: A Systematic Review and Meta-Analysis. *J Sports Sci Med*, 23, 690-706.
- SONGSORN, P., BRICK, N., FITZPATRICK, B., FITZPATRICK, S., MCDERMOTT, G., MCCLEAN, C., DAVISON, G. W., VOLLAARD, N. B. J. & METCALFE, R. S. 2019. Affective and Perceptual Responses during Reduced-Exertion High-Intensity Interval Training (REHIT). *International Journal of Sport and Exercise Physiology*, 18, 717-732.
- SONGSORN, P., LAMBETH-MANSELL, A., MAIR, J. L., HAGGETT, M., FITZPATRICK, B. L., RUFFINO, J., HOLLIDAY, A., METCALFE, R. S. & VOLLAARD, N. B. 2016. Exercise training comprising of single 20-s cycle sprints does not provide a sufficient stimulus for improving maximal aerobic capacity in sedentary individuals. *Eur J Appl Physiol*, 116, 1511-7.
- SONGSORN, P., RUFFINO, J. & VOLLAARD, N. B. 2017. No effect of acute and chronic supramaximal exercise on circulating levels of the myokine SPARC. *Eur J Sport Sci*, 17, 447-452.
- SORENSEN, J. B., KRAGSTRUP, J., KJAER, K. & PUGGAARD, L. 2007. Exercise on prescription: trial protocol and evaluation of outcomes. *BMC Health Serv Res*, 7, 36.
- STAN DEVELOPMENT TEAM. 2025. *Prior choice recommendations* [Online]. Stan Project Wiki. Available: <https://github.com/stan-dev/stan/wiki/Prior-Choice-Recommendations> [Accessed].
- STATHIS, C. G., FEBBRAIO, M. A., CAREY, M. F. & SNOW, R. J. 1994. Influence of sprint training on human skeletal muscle purine nucleotide metabolism. *J Appl Physiol* (1985), 76, 1802-9.
- STEELE, J., PLOTKIN, D., VAN EVERY, D., ROSA, A., ZAMBRANO, H., MENDELOVITS, B., CARRASQUILLO-MERCADO, M., GRGIC, J. & SCHOENFELD, B. J. 2021. Slow and Steady, or Hard and Fast? A Systematic Review and Meta-Analysis of Studies Comparing Body Composition Changes between Interval Training and Moderate Intensity Continuous Training. *Sports (Basel)*, 9.
- STEENSBERG, A., VAN HALL, G., OSADA, T., SACCHETTI, M., SALTIN, B. & KLARLUND PEDERSEN, B. 2000. Production of interleukin-6 in contracting human skeletal muscles can account for the exercise-induced increase in plasma interleukin-6. *J Physiol*, 529 Pt 1, 237-42.
- STENZEL, D., FRANCO, C. A., ESTRACH, S., METTOUCHI, A., SAUVAGET, D., ROSEWELL, I., SCHERTEL, A., ARMER, H., DOMOGATSKAYA, A., RODIN, S., TRYGGVASON, K., COLLINSON, L., SOROKIN, L. & GERHARDT, H. 2011. Endothelial basement

- membrane limits tip cell formation by inducing Dll4/Notch signalling in vivo. *EMBO Rep*, 12, 1135-43.
- STEPHENS, N. A., XIE, H., JOHANNSEN, N. M., CHURCH, T. S., SMITH, S. R. & SPARKS, L. M. 2015. A transcriptional signature of "exercise resistance" in skeletal muscle of individuals with type 2 diabetes mellitus. *Metabolism*, 64, 999-1004.
- STERNE, J. & HIGGINS, J. 2024. The Risk Of Bias In Non-randomized Studies-of Interventions, Version 2 (ROBINS-I V2) assessment tool (for follow-up studies). Cochrane Methods Bias.
- STERNE, J. A., GAVAGHAN, D. & EGGER, M. 2000. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *J Clin Epidemiol*, 53, 1119-29.
- STERNE, J. A. C., SAVOVIC, J., PAGE, M. J., ELBERS, R. G., BLENCOWE, N. S., BOUTRON, I., CATES, C. J., CHENG, H. Y., CORBETT, M. S., ELDRIDGE, S. M., EMBERSON, J. R., HERNAN, M. A., HOPEWELL, S., HROBJARTSSON, A., JUNQUEIRA, D. R., JUNI, P., KIRKHAM, J. J., LASSERSON, T., LI, T., MCALEENAN, A., REEVES, B. C., SHEPPERD, S., SHRIER, I., STEWART, L. A., TILLING, K., WHITE, I. R., WHITING, P. F. & HIGGINS, J. P. T. 2019. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*, 366, l4898.
- STOREN, O., HELGERUD, J., SAEBO, M., STOA, E. M., BRATLAND-SANDA, S., UNHJEM, R. J., HOFF, J. & WANG, E. 2017. The Effect of Age on the V O₂max Response to High-Intensity Interval Training. *Med Sci Sports Exerc*, 49, 78-85.
- STORER, T. W., DAVIS, J. A. & CAIOZZO, V. J. 1990. Accurate prediction of VO₂max in cycle ergometry. *Med Sci Sports Exerc*, 22, 704-12.
- STRAIN, T., FLAXMAN, S., GUTHOLD, R., SEMENOVA, E., COWAN, M., RILEY, L. M., BULL, F. C., STEVENS, G. A. & COUNTRY DATA AUTHOR, G. 2024. National, regional, and global trends in insufficient physical activity among adults from 2000 to 2022: a pooled analysis of 507 population-based surveys with 5.7 million participants. *Lancet Glob Health*, 12, e1232-e1243.
- SU, L., FU, J., SUN, S., ZHAO, G., CHENG, W., DOU, C. & QUAN, M. 2019. Effects of HIIT and MICT on cardiovascular risk factors in adults with overweight and/or obesity: A meta-analysis. *PLoS One*, 14, e0210644.
- SUBRAMANIAN, V., TUCKER, W. J., PETERS, A. E., UPADHYA, B., KITZMAN, D. W. & PANDEY, A. 2025. Cardiovascular Aging and Exercise: Implications for Heart Failure Prevention and Management. *Circ Res*, 137, 205-230.
- SUGIYAMA, T., CHANDRABOSE, M., HOMER, A. R., SUGIYAMA, M., DUNSTAN, D. W. & OWEN, N. 2020. Car use and cardiovascular disease risk: Systematic review and implications for transport research. *Journal of Transport & Health*, 19, 100930.
- SUNDET, J. M., MAGNUS, P. & TAMBS, K. 1994. The heritability of maximal aerobic power: a study of Norwegian twins. *Scandinavian Journal of Medicine & Science in Sports*, 4, 181-185.
- SVEBAK, S. & MURGATROYD, S. 1985. Metamotivational dominance: A multimethod validation of reversal theory constructs. *Journal of Personality and Social Psychology*, 48, 107-116.
- SZUHANY, K. L., BUGATTI, M. & OTTO, M. W. 2015. A meta-analytic review of the effects of exercise on brain-derived neurotrophic factor. *J Psychiatr Res*, 60, 56-64.
- TALBOT, L. A., METTER, E. J. & FLEG, J. L. 2000. Leisure-time physical activities and their relationship to cardiorespiratory fitness in healthy men and women 18-95 years old. *Med Sci Sports Exerc*, 32, 417-25.

- TAN, V., LIM, I., TAN, P. T., TAN, F. & AZIZ, A. R. 2021. Comparison of physiological and clinical markers for chronic sprint-interval training exercise performed either in the fasted or fed states among healthy adults. *Curr Res Physiol*, 4, 192-201.
- TANAKA, H. & SEALS, D. R. 2008. Endurance exercise performance in Masters athletes: age-associated changes and underlying physiological mechanisms. *J Physiol*, 586, 55-63.
- TANIMURA, R., KOBAYASHI, L., SHIRAI, T. & TAKEMASA, T. 2022. Effects of exercise intensity on white adipose tissue browning and its regulatory signals in mice. *Physiological Reports*, 10, e15205.
- THIVEL, D., TREMBLAY, A., GENIN, P. M., PANAHI, S., RIVIERE, D. & DUCLOS, M. 2018. Physical Activity, Inactivity, and Sedentary Behaviors: Definitions and Implications in Occupational Health. *Front Public Health*, 6, 288.
- THODEN, J. S., MACDOUGALL, J. & WILSON, B. 1991. Testing aerobic power. *Physiological testing of the high-performance athlete*, 2, 107-173.
- THOMAS, G., SONGSORN, P., GORMAN, A., BRACKENRIDGE, B., CULLEN, T., FITZPATRICK, B., METCALFE, R. S. & VOLLAARD, N. B. J. 2020. Reducing training frequency from 3 or 4 sessions/week to 2 sessions/week does not attenuate improvements in maximal aerobic capacity with reduced-exertion high-intensity interval training (REHIT). *Appl Physiol Nutr Metab*, 45, 683-685.
- THOMPSON, C., VANHATALO, A., KADACH, S., WYLIE, L. J., FULFORD, J., FERGUSON, S. K., BLACKWELL, J. R., BAILEY, S. J. & JONES, A. M. 2018. Discrete physiological effects of beetroot juice and potassium nitrate supplementation following 4-wk sprint interval training. *Journal of Applied Physiology*, 124, 1519-1528.
- THYBOLL, J., KORTESMAA, J., CAO, R., SOININEN, R., WANG, L., IIVANAINEN, A., SOROKIN, L., RISLING, M., CAO, Y. & TRYGGVASON, K. 2002. Deletion of the laminin alpha4 chain leads to impaired microvessel maturation. *Mol Cell Biol*, 22, 1194-202.
- TIMMONS, J. A., KNUDSEN, S., RANKINEN, T., KOCH, L. G., SARZYNSKI, M., JENSEN, T., KELLER, P., SCHEELE, C., VOLLAARD, N. B., NIELSEN, S., AKERSTROM, T., MACDOUGALL, O. A., JANSSON, E., GREENHAFF, P. L., TARNOPOLSKY, M. A., VAN LOON, L. J., PEDERSEN, B. K., SUNDBERG, C. J., WAHLESTEDT, C., BRITTON, S. L. & BOUCHARD, C. 2010. Using molecular classification to predict gains in maximal aerobic capacity following endurance exercise training in humans. *J Appl Physiol* (1985), 108, 1487-96.
- TRANSPORT, D. F. 2023. *Transport statistics Great Britain: 2022 domestic travel*. [Online]. Great Britain: Department for Transport. Available: <https://www.gov.uk/government/statistics/transport-statistics-great-britain-2023/transport-statistics-great-britain-2022-domestic-travel>? [Accessed].
- TRAPP, E. G., CHISHOLM, D. J., FREUND, J. & BOUTCHER, S. H. 2008. The effects of high-intensity intermittent exercise training on fat loss and fasting insulin levels of young women. *International Journal of Obesity*, 32, 684-691.
- TRAPPE, S. W., COSTILL, D. L., VUKOVICH, M. D., JONES, J. & MELHAM, T. 1996. Aging among elite distance runners: a 22-yr longitudinal study. *J Appl Physiol* (1985), 80, 285-90.
- TREMBLAY, M. S., AUBERT, S., BARNES, J. D., SAUNDERS, T. J., CARSON, V., LATIMER-CHEUNG, A. E., CHASTIN, S. F. M., ALTENBURG, T. M. & CHINAPAW, M. J. M. 2017. Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act*, 14, 75.

- TRILK, J. L., SINGHAL, A., BIGELMAN, K. A. & CURETON, K. J. 2011. Effect of sprint interval training on circulatory function during exercise in sedentary, overweight/obese women. *Eur J Appl Physiol*, 111, 1591-7.
- TRIPP, T. R., GHITTER, R. S., KONTRO, H., HARGRAVE, S. J., GIBALA, M. J., ABOODARDA, S. J. & MACINNIS, M. J. 2025. Cardiorespiratory Fitness Improvements Following Low-Frequency Training Are Not Inferior to High-Frequency Training Matched for Intensity and Volume. *Scand J Med Sci Sports*, 35, e70024.
- TROST, S. G., OWEN, N., BAUMAN, A. E., SALLIS, J. F. & BROWN, W. 2002. Correlates of adults' participation in physical activity: review and update. *Med Sci Sports Exerc*, 34, 1996-2001.
- TURK, Y., THEEL, W., KASTELEYN, M. J., FRANSSEN, F. M. E., HIEMSTRA, P. S., RUDOLPHUS, A., TAUBE, C. & BRAUNSTAHL, G. J. 2017. High intensity training in obesity: a Meta-analysis. *Obes Sci Pract*, 3, 258-271.
- VAN BAAK, M. A., PRAMONO, A., BATTISTA, F., BEAULIEU, K., BLUNDELL, J. E., Busetto, L., CARRACA, E. V., DICKER, D., ENCANTADO, J., ERMOLAO, A., FARPOUR-LAMBERT, N., WOODWARD, E., BELLIHA, A. & OPPERT, J. M. 2021. Effect of different types of regular exercise on physical fitness in adults with overweight or obesity: Systematic review and meta-analyses. *Obes Rev*, 22 Suppl 4, e13239.
- VAN DE SCHOOT, R., SIJBRANDIJ, M., DEPAOLI, S., WINTER, S. D., OLFF, M. & VAN LOEY, N. E. 2018. Bayesian PTSD-Trajectory Analysis with Informed Priors Based on a Systematic Literature Search and Expert Elicitation. *Multivariate Behav Res*, 53, 267-291.
- VEHTARI, A., GELMAN, A., SIMPSON, D., CARPENTER, B. & BURKNER, P.-C. 2019. Rank-Normalization, Folding, and Localization: An Improved $R^{\hat{}}$ for Assessing Convergence of MCMC (with Discussion). *Bayesian Analysis*, 16, 667-718.
- VINCENT, G., LAMON, S., GANT, N., VINCENT, P. J., MACDONALD, J. R., MARKWORTH, J. F., EDGE, J. A. & HICKEY, A. J. 2015. Changes in mitochondrial function and mitochondria associated protein expression in response to 2-weeks of high intensity interval training. *Front Physiol*, 6, 51.
- VOLLAARD, N. B. J. & METCALFE, R. S. 2017. Research into the Health Benefits of Sprint Interval Training Should Focus on Protocols with Fewer and Shorter Sprints. *Sports Med*, 47, 2443-2451.
- VOLLAARD, N. B. J., METCALFE, R. S. & WILLIAMS, S. 2017. Effect of Number of Sprints in an SIT Session on Change in $\dot{V}O_{2\max}$: A Meta-analysis. *Med Sci Sports Exerc*, 49, 1147-1156.
- VOSHTANI, R., HOU, P., LIU, Z., CAO, L., FENG, C., SHAO, C., SHI, Y. & FANG, J. 2025. IGF2 regulates proliferation, differentiation, and mitochondrial bioenergetics in human satellite cells. *Biol Direct*, 20, 115.
- WANG, D., ZHANG, Y., YE, T., ZHANG, R., ZHANG, L., SHI, D., LI, T., XIA, G., NIU, K., ZHAO, Z., CHEN, Y., PAN, W., LIU, L., JIN, X. & SHEN, C. 2023. Cthrc1 deficiency aggravates wound healing and promotes cardiac rupture after myocardial infarction via non-canonical WNT5A signaling pathway. *Int J Biol Sci*, 19, 1299-1315.
- WANNER, M., PROBST-HENSCH, N., KRIEMLER, S., MEIER, F., AUTENRIETH, C. & MARTIN, B. W. 2016. Validation of the long international physical activity questionnaire: Influence of age and language region. *Prev Med Rep*, 3, 250-6.
- WARBURTON, D. E., HAYKOWSKY, M. J., QUINNEY, H. A., BLACKMORE, D., TEO, K. K., TAYLOR, D. A., MCGAVOCK, J. & HUMEN, D. P. 2004. Blood volume expansion and cardiorespiratory function: effects of training modality. *Med Sci Sports Exerc*, 36, 991-1000.

- WEATHERWAX, R. M., HARRIS, N. K., KILDING, A. E. & DALLECK, L. C. 2019. Incidence of V O₂max Responders to Personalized versus Standardized Exercise Prescription. *Med Sci Sports Exerc*, 51, 681-691.
- WEN, D., UTESCH, T., WU, J., ROBERTSON, S., LIU, J., HU, G. & CHEN, H. 2019. Effects of different protocols of high intensity interval training for VO(2)max improvements in adults: A meta-analysis of randomised controlled trials. *J Sci Med Sport*, 22, 941-947.
- WESTON, K. S., WISLOFF, U. & COOMBES, J. S. 2014. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. *Br J Sports Med*, 48, 1227-34.
- WHIPP, B. J., DAVIS, J. A., TORRES, F. & WASSERMAN, K. 1981. A test to determine parameters of aerobic function during exercise. *J Appl Physiol Respir Environ Exerc Physiol*, 50, 217-21.
- WHITHAM, M. & FEBBRAIO, M. A. 2016. The ever-expanding myokinome: discovery challenges and therapeutic implications. *Nat Rev Drug Discov*, 15, 719-29.
- WHYTE, L. J., GILL, J. M. & CATHCART, A. J. 2010. Effect of 2 weeks of sprint interval training on health-related outcomes in sedentary overweight/obese men. *Metabolism*, 59, 1421-8.
- WILLIAMS, C. J., GURD, B. J., BONAFIGLIA, J. T., VOISIN, S., LI, Z., HARVEY, N., CROCI, I., TAYLOR, J. L., GAJANAND, T., RAMOS, J. S., FASSETT, R. G., LITTLE, J. P., FRANCOIS, M. E., HEARON, C. M., JR., SARMA, S., JANSSEN, S., VAN CRAENENBROECK, E. M., BECKERS, P., CORNELISSEN, V. A., PATTYN, N., HOWDEN, E. J., KEATING, S. E., BYE, A., STENSVOLD, D., WISLOFF, U., PAPADIMITRIOU, I., YAN, X., BISHOP, D. J., EYNON, N. & COOMBES, J. S. 2019. A Multi-Center Comparison of O(2peak) Trainability Between Interval Training and Moderate Intensity Continuous Training. *Front Physiol*, 10, 19.
- WILLIAMS, C. J., WILLIAMS, M. G., EYNON, N., ASHTON, K. J., LITTLE, J. P., WISLOFF, U. & COOMBES, J. S. 2017. Genes to predict VO(2max) trainability: a systematic review. *BMC Genomics*, 18, 831.
- WILLIAMS, D. M., DUNSIGER, S., CICCOLO, J. T., LEWIS, B. A., ALBRECHT, A. E. & MARCUS, B. H. 2008. Acute Affective Response to a Moderate-intensity Exercise Stimulus Predicts Physical Activity Participation 6 and 12 Months Later. *Psychol Sport Exerc*, 9, 231-245.
- WILSON, T. M. & TANAKA, H. 2000. Meta-analysis of the age-associated decline in maximal aerobic capacity in men: relation to training status. *Am J Physiol Heart Circ Physiol*, 278, H829-34.
- WONG, P. Y., SOH, S. M. M., CHU, W.-J. M., LIM, M. X. C., JONES, L. E., SELVARAJ, S., CHOW, K. M. S., CHOO, H. W. D. & AZIZ, A. R. 2024. A single all-out bout of 30-s sprint-cycle performed on 5 consecutive days per week over 6 weeks does not enhance cardiovascular fitness, maximal strength, and clinical health markers in physically active young adults. *European Journal of Applied Physiology*, 124, 1861-1874.
- WOOD, J., TSE, M. C. L., YANG, X., BROBST, D., LIU, Z., PANG, B. P. S., CHAN, W. S., ZAW, A. M., CHOW, B. K. C., YE, K., LEE, C. W. & CHAN, C. B. 2018. BDNF mimetic alleviates body weight gain in obese mice by enhancing mitochondrial biogenesis in skeletal muscle. *Metabolism*, 87, 113-122.
- WORLD HEALTH, O. 2020. *WHO GUIDELINES ON PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOUR: WEB ANNEX Evidence Profiles*, World Health Organization.

- WORLD HEALTH, O. 2024. *Physical Activity* [Online]. World Health Organization. Available: <https://www.who.int/news-room/fact-sheets/detail/physical-activity>? [Accessed].
- WUN, C. H., ZHANG, M. J., HO, B. H., MCGEOUGH, K., TAN, F. & AZIZ, A. R. 2020. Efficacy of a Six-Week Dispersed Wingate-Cycle Training Protocol on Peak Aerobic Power, Leg Strength, Insulin Sensitivity, Blood Lipids and Quality of Life in Healthy Adults. *Int J Environ Res Public Health*, 17.
- WYCKELSMAN, V. L., VENCKUNAS, T., BRAZAITIS, M., GASTALDELLO, S., SNIECKUS, A., EIMANTAS, N., BARANAUSKIENE, N., SUBOCIUS, A., SKURVYDAS, A., PAASUKE, M., GAPEYEVA, H., KAASIK, P., PAASUKE, R., JURIMAE, J., GRAF, B. A., KAYSER, B., PLACE, N., ANDERSSON, D. C., KAMANDULIS, S. & WESTERBLAD, H. 2020. Vitamin C and E Treatment Blunts Sprint Interval Training-Induced Changes in Inflammatory Mediator-, Calcium-, and Mitochondria-Related Signaling in Recreationally Active Elderly Humans. *Antioxidants (Basel)*, 9.
- YAMAGISHI, T. & BABRAJ, J. 2017. Effects of reduced-volume of sprint interval training and the time course of physiological and performance adaptations. *Scand J Med Sci Sports*, 27, 1662-1672.
- YAMAGISHI, T. & BABRAJ, J. 2019. Active Recovery Induces Greater Endurance Adaptations When Performing Sprint Interval Training. *J Strength Cond Res*, 33, 922-930.
- YAMANAKA, M., TSUCHIDA, A., NAKAGAWA, T., NONOMURA, T., ONO-KISHINO, M., SUGARU, E., NOGUCHI, H. & TAJI, M. 2007. Brain-derived neurotrophic factor enhances glucose utilization in peripheral tissues of diabetic mice. *Diabetes Obes Metab*, 9, 59-64.
- ZEIHER, J., OMBRELLARO, K. J., PERUMAL, N., KEIL, T., MENSINK, G. B. M. & FINGER, J. D. 2019. Correlates and Determinants of Cardiorespiratory Fitness in Adults: a Systematic Review. *Sports Med Open*, 5, 39.
- ZELT, J. G., HANKINSON, P. B., FOSTER, W. S., WILLIAMS, C. B., REYNOLDS, J., GARNEYS, E., TSCHAKOVSKY, M. E. & GURD, B. J. 2014. Reducing the volume of sprint interval training does not diminish maximal and submaximal performance gains in healthy men. *Eur J Appl Physiol*, 114, 2427-36.
- ZILE, M. R., BAICU, C. F. & GAASCH, W. H. 2004. Diastolic Heart Failure — Abnormalities in Active Relaxation and Passive Stiffness of the Left Ventricle. *New England Journal of Medicine*, 350, 1953-1959.