

1 **TITLE**

2 **Changes in cardiorespiratory fitness following exercise training prescribed relative to traditional**  
3 **intensity anchors and to physiological thresholds: a systematic review with meta-analysis of**  
4 **individual participant data**

5 **Running heading**

6 Cardiorespiratory Fitness and Exercise Intensity Prescription: Individual Participant Data Meta-analysis

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## 21 **ABSTRACT**

### 22 **Background**

23 It is unknown whether there are differences in maximal oxygen uptake ( $\text{VO}_{2\text{max}}$ ) response when  
24 prescribing intensity relative to traditional (TRAD) anchors or to physiological thresholds (THR).

### 25 **Objectives**

26 The present meta-analysis sought to compare: a) mean change in  $\text{VO}_{2\text{max}}$ ; b) proportion of individuals  
27 increasing  $\text{VO}_{2\text{max}}$  beyond a minimum important difference (MID); and c) response variability in  $\text{VO}_{2\text{max}}$   
28 between TRAD and THR.

### 29 **Methods**

30 Electronic databases were searched, yielding data for 1544 individuals from 42 studies. Two datasets  
31 were created, comprising studies with a control group ('controlled' studies), and without a control group  
32 ('non-controlled' studies). A Bayesian approach with multi-level distributional models was used to  
33 separately analyse  $\text{VO}_{2\text{max}}$  change scores from the two datasets and inferences were made using Bayes  
34 factors (BF). The MID was predefined as one metabolic equivalent (MET;  $3.5 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ).

### 35 **Results**

36 In controlled studies, mean  $\text{VO}_{2\text{max}}$  change was greater in THR compared to TRAD ( $4.1$  vs  $1.8 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ,  $\text{BF}>100$ ) with 64% of individuals in THR experiencing an increase in  $\text{VO}_{2\text{max}}>\text{MID}$ , compared  
37 to 16% of individuals taking part in TRAD. Evidence indicated no difference in standard deviation of  
38 change between THR and TRAD ( $1.5$  vs  $1.7 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ,  $\text{BF}=0.55$ ), and greater variation in exercise  
39 groups relative to non-exercising controls ( $1.9$  vs  $1.3 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ,  $\text{BF}=12.4$ ). In non-controlled  
40 studies, mean  $\text{VO}_{2\text{max}}$  change was greater in THR vs TRAD ( $4.4$  vs  $3.4 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ,  $\text{BF}=35.1$ ) with  
41 no difference in standard deviation of change ( $3.0$  vs  $3.2 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ,  $\text{BF}=0.41$ ).

### 43 **Conclusion**

44 Prescribing exercise intensity using THR approaches elicited superior mean changes in  $VO_{2max}$  and  
45 increased the likelihood of increasing  $VO_{2max}$  beyond the MID compared to TRAD. Future exercise  
46 training studies should thus consider the use of THR approaches to prescribe exercise intensity where  
47 possible. Analysis comparing interventions with controls suggested the existence of intervention  
48 response heterogeneity, however, evidence was not obtained for a difference in response variability  
49 between THR and TRAD. Future primary research should be conducted with adequate power to  
50 investigate the scope of inter-individual differences in  $VO_{2max}$  trainability, and if meaningful, the  
51 causative factors.

## 52 **Key Points**

- 53 • Prescribing exercise training relative to physiological thresholds rather than traditional intensity  
54 anchors, elicited superior changes in cardiorespiratory fitness and increased the proportion of  
55 individuals increasing cardiorespiratory fitness by at least one metabolic equivalent.
- 56 • No difference in cardiorespiratory response variability was observed between exercise groups.  
57 Comparisons with controls, however, provided evidence of inter-individual response variability  
58 that warrants further investigation.
- 59 • Considering the link between cardiorespiratory fitness and both health and performance  
60 outcomes, future studies should aim to prescribe exercise relative to physiological thresholds  
61 where possible.

62

63 **DECLARATIONS**

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65 No funding and financial assistance was used for this review.

66 **Conflicts of interest**

67 Authors Samuel J. R. Meyler, Paul A. Swinton, Lindsay Bottoms, Lance C. Dalleck, Ben Hunter, Mark  
68 A. Sarzynski, David Wellsted, Camilla J. Williams, Daniel Muniz-Pumares declare that they have no  
69 conflicts of interest relevant to the content of this review.

70 **Availability of data and material**

71 Datasets analysed in the current review are available upon reasonable request but are subject to  
72 permission from original authors.

73 **Ethics approval**

74 Each study received ethical approval from their respective institutions, conformed to the guidelines of  
75 the Declaration of Helsinki, and obtained written informed consent from each participant prior to  
76 commencing data collection.

77 **Author contributions**

78 All authors: (1) made substantial contributions to the conception or design of the work; or the  
79 acquisition, analysis, or interpretation of data; and (2) drafted the work or revised it critically for  
80 important intellectual content. All authors read and approved the final version of the manuscript.

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## 83 1 INTRODUCTION

84 Cardiorespiratory fitness, measured as maximum oxygen uptake ( $\dot{V}O_{2max}$ ), represents the upper limit of  
85 cardiopulmonary-muscle oxidative function [1], quantifying the body's ability to transport and utilise  
86 oxygen [2]. As such,  $\dot{V}O_{2max}$  is recognised as a key determinant of endurance performance, with elite  
87 endurance athletes demonstrating some of the highest  $\dot{V}O_{2max}$  values ever recorded [3,4]. Additionally,  
88  $\dot{V}O_{2max}$  is an important marker of cardiovascular health [5–7] and low levels of  $\dot{V}O_{2max}$  are a strong risk  
89 factor for all-cause and disease-specific mortality [5]. Despite being the only major risk factor not  
90 routinely assessed in clinical practice, growing epidemiological and clinical evidence suggests that  
91  $\dot{V}O_{2max}$  may be a stronger predictor of mortality than traditionally assessed risk factors such as smoking,  
92 type 2 diabetes mellitus, and obesity [7]. Increasing  $\dot{V}O_{2max}$  is thus a commonly sought-after phenotypic  
93 change across different populations. Evidence indicates that increasing  $\dot{V}O_{2max}$  by one metabolic  
94 equivalent (MET;  $3.5 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) can reduce mortality risk by ~10-30% [5,8] and health care costs  
95 by ~5% [9,10]. In turn, a value of one MET can be used as a minimum important difference (MID)  
96 when evaluating changes in  $\dot{V}O_{2max}$  following a period of exercise training [7,11].

97 Changes in  $\dot{V}O_{2max}$  can be explained by the Fick principle, where  $\dot{V}O_{2max}$  is the product of maximum  
98 cardiac output and arteriovenous oxygen difference [12,13]. Adaptations causing changes in cardiac  
99 output (i.e., the product of heart rate and stroke volume) represent 'central' adaptations whereby  
100 phenotypic modifications alter convective oxygen delivery, whereas adaptations causing changes in  
101 arteriovenous oxygen difference reflect 'peripheral' adaptations, comprised of changes in oxygen  
102 extraction and utilisation [14]. The most effective means of increasing  $\dot{V}O_{2max}$  is through endurance  
103 training, typically in the form of constant load continuous training and/or interval-based training, which  
104 are shown to increase  $\dot{V}O_{2max}$  by ~5.5 and ~4.9  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ , respectively [15]. On the other hand,  
105  $\dot{V}O_{2max}$  is markedly reduced by periods of inactivity (e.g., bed rest) [16]. Whilst both approaches of  
106 exercise training have been demonstrated to be efficacious at the group level [15], the individual effect  
107 of exercise training on  $\dot{V}O_{2max}$  appears to exhibit a heterogenous distribution [17,18], suggesting that  
108 some individuals do not attain some of the benefits of exercise.

109 Several biological and methodological factors underpin this apparent ‘response variability’ (for a review  
 110 see [19]), as well as measurement error and day-to-day biological variability [20]. To tackle response  
 111 variability, and specifically the number of individuals attaining a change in  $\dot{V}O_{2max}$  surpassing a  
 112 predefined threshold, interventions commonly adopt ‘additive’ approaches (for a review see [21]). For  
 113 example, augmenting the exercise stimulus (i.e., increasing training volume, frequency, and/or  
 114 intensity) often proves effective in increasing response rate as a result of greater group mean increases  
 115 in  $\dot{V}O_{2max}$  [22–25]. Aiming to elicit superior changes in  $\dot{V}O_{2max}$  and reduce response variability to the  
 116 initial stimulus, an example of a ‘subtractive’ approach [21], may be achieved through changing the  
 117 method used to prescribe exercise intensity [19]. However, the effect of using different means of  
 118 exercise prescription to do so are unclear.

119 Exercise intensity is commonly prescribed relative to traditional (TRAD) intensity anchors (Table 1)  
 120 [15] whereby recommended percentages of such values are used to prescribe exercise in a given  
 121 intensity domain. It is worth noting that whilst various nomenclature is used to describe the different  
 122 intensity domains in performance and health settings [26], the three-domain classification (moderate,  
 123 heavy, and severe intensity exercise) will be referred to in the present study. Notably, TRAD approaches  
 124 are evidenced to elicit marked variation in acute physiological responses and exercise tolerance [27–  
 125 33]. As changes in  $\dot{V}O_{2max}$  manifest in response to specific exercise-induced adaptive stimuli [34], when  
 126 different stimuli are experienced by individuals over time, it is plausible that this may contribute to a  
 127 portion of  $\dot{V}O_{2max}$  response variability [19,31,35].

128 **Table 1.** ‘Traditional’ anchors of exercise intensity

<b>Intensity Anchor</b>	<b>Abbreviation</b>	<b>Description</b>
<b>Maximum oxygen uptake</b>	$\dot{V}O_{2max}$	Maximum oxygen uptake attained during maximal exercise despite increases in external workload
<b>Oxygen uptake reserve</b>	$\dot{V}O_{2R}$	Difference between maximum and resting oxygen uptake
<b>Maximum heart rate</b>	$HR_{max}$	Maximum heart rate reached during maximal exercise despite increases in external workload

<b>Heart rate reserve</b>	HRR	Difference between maximum and resting heart rate
<b>Maximum work rate</b>	$WR_{max}$	Maximum work rate achieved during an incremental exercise test

129

130 Instead, using physiological thresholds that demarcate the intensity domains as intensity anchors (Table  
 131 2) has shown to elicit more homogenous acute physiological responses to an exercise bout  
 132 [29,32,33,36]. It is of interest to explore whether this has a positive impact on longer term responses  
 133 (i.e., training-induced changes in  $\dot{V}O_{2max}$ ) regarding their magnitude and variability. If the magnitude  
 134 of training-induced changes in  $\dot{V}O_{2max}$  can be increased among a larger proportion of individuals, and  
 135 the number of individuals experiencing negligible changes in their  $\dot{V}O_{2max}$  is reduced, this could have  
 136 profound implications for improving health outcomes and approaches to exercise prescription.

137 **Table 2.** Physiological thresholds delineating the boundary of the moderate and heavy intensity domain  
 138 and the heavy and severe intensity domain

<b>Physiological threshold</b>	<b>Description</b>
<b>Boundary between the moderate and heavy intensity domain</b>	
Lactate threshold (LT)	Blood lactate concentration rises above baseline levels
Gas exchange threshold (GET)	First breakpoint at which $\dot{V}CO_2$ increases disproportionately to $\dot{V}O_2$
First ventilatory threshold ( $VT_1$ )	An increase in $\dot{V}_E/\dot{V}O_2$ with no concurrent increase in $\dot{V}_E/\dot{V}CO_2$
<b>Boundary between the heavy and severe intensity domain</b>	
Maximum lactate steady-state (MLSS)	Highest constant workload that leads to a balance between lactate production and elimination
Respiratory compensation point (RCP)	Second breakpoint at which $\dot{V}_E$ increases disproportionately to $\dot{V}O_2$
Second ventilatory threshold ( $VT_2$ )	A simultaneous increase in both $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$
Critical power (CP)	Asymptote of the power–duration relationship

139  $\dot{V}CO_2$ : Carbon dioxide production,  $\dot{V}_E$ : minute ventilation,  $\dot{V}O_2$ : oxygen uptake

140 **1.1 Objectives**

141 Examining differences between THR and TRAD exercise programmes (and using non-exercising  
142 control groups [CON] where applicable), we sought to: a) compare the mean change scores in  $\dot{V}O_{2\max}$   
143 and the proportion of individuals expected to attain increases in  $\dot{V}O_{2\max}$  beyond a MID of one MET (3.5  
144  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) between THR and TRAD; and b) test the hypothesis that  $\dot{V}O_{2\max}$  response variability is  
145 lower in THR compared to TRAD.

146 **2 METHODS**

147 **2.1 Protocol and registration**

148 This review was pre-registered on PROSPERO (id: CRD42021226644) and the present protocol has  
149 been conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-  
150 analysis of Individual Participant Data guidelines [37] (Supplementary file).

151 **2.2 Eligibility criteria**

152 2.2.1 Type of study

153 Randomised controlled and non-controlled training studies, written in English, and published before  
154 October 2023.

155 2.2.2 Type of participants

156 Healthy males and females,  $\geq 18$  years of age,  $\text{BMI} \leq 30 \text{ kg}\cdot\text{m}^2$ , and were not suffering from any acute  
157 or chronic disease(s).

158 2.2.3 Type of interventions

159 Training interventions had to meet the following criteria: a) exercise training lasted  $\geq 3$  weeks; b)  
160 consisted of either continuous training, interval training, or a combination of both, c) exercise was either  
161 walking, running or cycling; d)  $\dot{V}O_{2\max}$  was directly measured pre- and post-intervention via indirect  
162 calorimetry during an incremental test to task failure; and e) individuals were either allocated to  
163 traditionally prescribed exercise training (TRAD), whereby exercise intensity was prescribed relative

164 to a physiological value, as outlined in Table 1; and/or to a physiological threshold (THR) as outlined  
165 in Table 2. The latter includes studies using the delta method ( $\Delta$ ) whereby intensity is prescribed using  
166 a physiological threshold and physiological value (i.e.,  $50\% \Delta = \text{gas exchange threshold} + [0.5 \times (\text{critical}$   
167  $\text{power-gas exchange threshold})]$ ). Exercise groups involving additional interventional manipulations,  
168 such as nutritional supplementation and/or environmental manipulation were excluded. Two datasets  
169 were created from eligible studies, one containing ‘controlled’ studies, where studies included volume-  
170 matched THR and TRAD exercise group and a non-exercising control group (CON); and ‘non-  
171 controlled’ studies, where data from any single THR and TRAD exercise group was included.

### 172 **2.3 Identifying studies for systematic review - information sources and search strategy**

173 Electronic databases PubMed and Scopus were searched initially in 2021 and updated in 2023 such that  
174 papers published before October 2023 were included. Databases were searched using the following  
175 terms: ‘high-intensity interval training’, ‘continuous training’, ‘endurance training’, ‘maximum oxygen  
176 uptake’, ‘peak oxygen uptake’, ‘ $\dot{V}O_{2\max}$ ’, ‘cardiorespiratory fitness’, ‘healthy adults’. Additional  
177 resources were sought via the scrutinisation of reference lists, review articles, and contact with research  
178 teams of relevant papers. The literature search and study selection process was carried out independently  
179 by two authors (SM and BH) using a systematic review software (Covidence, Veritas Health Innovation,  
180 Australia). A third reviewer (author DM) resolved any disagreements regarding study eligibility. The  
181 title and abstracts were extracted from the database searches and duplicates were removed automatically  
182 by the Covidence software. Papers that were not relevant based on the title were removed. Title and  
183 abstracts were screened to identify studies that appeared to meet the predefined eligibility criteria. Full  
184 texts of studies passing the title and abstract screening were then scrutinised to determine their eligibility  
185 for inclusion in the review.

### 186 **2.4 Data collection processes**

187 Corresponding authors of eligible studies were contacted via email or by other means of contact (e.g.,  
188 ResearchGate, social media). Authors were provided with a brief summary of the aims of the present  
189 study and invited to share anonymised individual participant data (IPD). Anonymised IPD included age,

190 sex, height (cm), pre- and post-intervention mass (kg),  $\dot{V}O_{2\max}$  ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  and  $\text{L}\cdot\text{min}^{-1}$ ), and BMI  
191 for all individuals. Lead authors were contacted in the same manner if corresponding authors were  
192 unreachable. A follow-up email containing a deadline for response was sent to authors in the absence  
193 of a reply.

## 194 **2.5 IPD integrity**

195 Once IPD was received, data were checked for consistency with the published report, at the individual  
196 level for inconsistencies and missing data. Only individuals with a complete data set were included in  
197 the review and individual data not meeting the participant eligibility criteria were excluded. Any  
198 discrepancies between IPD and published reports were discussed with the study authors.

## 199 **2.6 Risk of bias**

200 Risk of bias was assessed in each individual study by two reviewers (SM and DMP). For randomised  
201 trials, the Cochrane risk-of-bias tool for randomised trials (RoB2) was used [38]. The ROBINS-I tool  
202 was used for assessing risk of bias in non-randomised and uncontrolled intervention studies [39]. An  
203 inter-reviewer reliability analysis using the Kappa statistic ( $k$ ) was performed to determine consistency  
204 between reviewers (supplementary file).

## 205 **2.7 Specification of outcomes and effect measures**

206 All analyses were conducted using  $\dot{V}O_{2\max}$  ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) change scores, calculated for each individual  
207 as the post-intervention value minus the baseline value. Measures of effect were based on group  
208 differences according to this absolute scale and percentage expected to exceed the MID.

## 209 **2.8 Synthesis methods**

210 Across all analyses, one-stage IPD meta-analysis models were developed. All models were conducted  
211 within a Bayesian framework with random intercepts to account for systematic variation across  
212 individual studies. Change scores relative to baseline were calculated for each participant on an absolute  
213 scale ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) and distributional models were used to estimate both the mean difference and  
214 standard deviation of the difference. A group term (TRAD vs. THR, or Exercise vs. Control) was added

215 as a predictor for the mean and standard deviation, with a log link used for the latter. Posterior  
 216 distributions were summarised by reporting the median and 95% credible intervals (CrI) for the mean  
 217 and 75% CrIs for the standard deviation. Separate Bayes factors were estimated comparing models with  
 218 and without the group predictor for the mean and standard deviation. A Bayes factor greater than 1.0  
 219 provided evidence supporting a group difference, whereas values less than 1.0 provided evidence  
 220 supporting no group difference. The overall strength of evidence in favour of the different models was  
 221 evaluated according to a previously defined scale [40], with non-neutral descriptions ranging from  
 222 anecdotal to extreme evidential strength (Table 3).

**Table 3.** Category of evidence for Bayes Factor interpretation

Bayes Factor (BF)	Strength of Evidence
$\geq 100$	Extreme
30-100	Very strong
10-30	Strong
3-10	Moderate
1-3	Anecdotal
1	No evidence

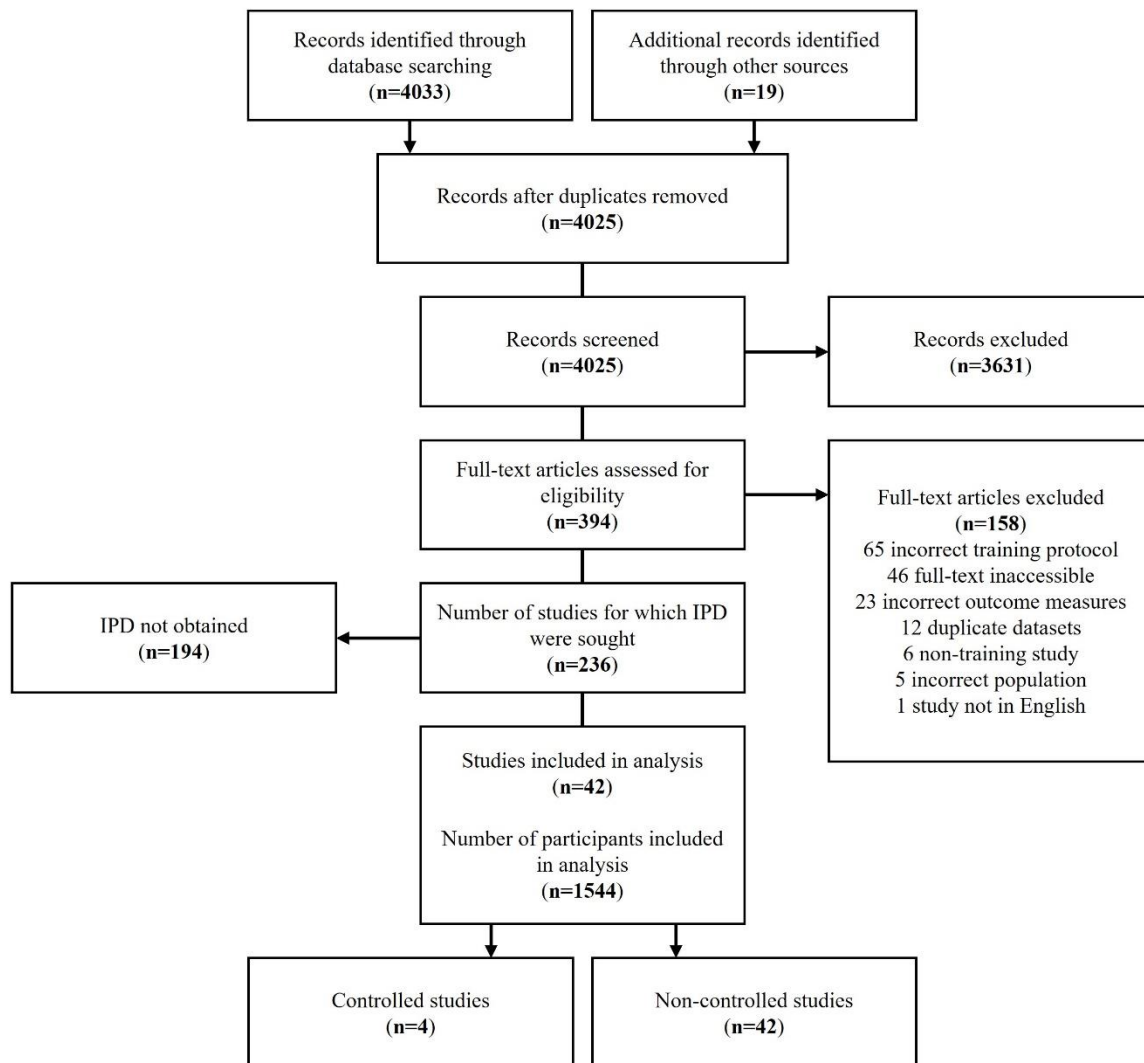
223

224 To investigate the proportion of individuals exceeding the MID, we used the posterior samples from  
 225 the distributional model to generate posterior predictions (n=10,000) and calculated the proportion that  
 226 exceeded the threshold in each group. Default weakly informative priors were used including Student-  
 227 t and half-t priors with 3 degrees of freedom. All analyses were performed using the R wrapper package  
 228 brms interfaced with Stan to perform sampling [41] and the R package bridgesampling to calculate  
 229 Bayes factors. Convergence of parameter estimates was obtained for all models with Gelman-Rubin  
 230 R-hat values below 1.1 [42].

## 231 **3 RESULTS**

### 232 **3.1 Study selection and IPD obtained**

233 See Figure 1 for the flow diagram pertaining to study identification and screening, and the amount of  
 234 IPD obtained.



**Figure 1.** Flow diagram of the study identification and screening process.

### 235 3.2 IPD integrity and risk of bias within studies

236 There were no issues that needed to be raised following the checking of IPD. Risk of bias assessments  
 237 for individual studies are included in the supplementary file. There was no need for any weighting  
 238 adjustments prior to the subsequent analyses. Domain 1: low risk 87%, some concerns 3%, high risk  
 239 10%; Domain 2: low risk 100%; Domain 3: low risk 100%; Domain 4: low risk 100%; Domain 5: low  
 240 risk 10%, high risk 90%; Overall: low risk 10%, some concerns 80%, high risk 10% (Supplementary  
 241 file). Of note, IPD from the HERITAGE study [17] was included in the current analyses. Due to the

242 large amount of HERITAGE IPD analysed (n=562) compared to that of the other eligible studies  
243 combined (n=953), the analyses were run with and without its inclusion. There was, however, no  
244 difference between the primary results in either case and thus the results are reported including the  
245 HERITAGE IPD.

### 246 **3.3 Study characteristics**

247 Individual study characteristics are presented in Table 4 and summary characteristics of THR and  
248 TRAD studies are presented in Table 5.

249 **Table 4.** Participant characteristics, sample size, training characteristics and  $\dot{V}O_{2max}$  change scores for studies included in the present individual participant data meta-  
 250 analysis

Study	Year	Participants (age)	Sex	n	Method	Type	Mode (sessions)	Protocol	$\dot{V}O_{2max}$ (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )		Change	Change
									Pre	Post	%	mL·kg <sup>-1</sup> ·min <sup>-1</sup>
									Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
<b>Arboleda et al.</b> [43]	2019	Sedentary (29±8)	M	18	TRAD	INT	Running (24)	15 x 30 s @ 90-95% HRmax	40.1 ± 6.2	43.7 ± 6.2	9.7 ± 9.8	3.6 ± 3.5
				20			TRAD	CT	Running (24)	40 min @ 65-75% HRmax	43.5 ± 8.6	44.9 ± 8.7
<b>Astorino et al.</b> [44]	2018	Active (27±8)	M/F	14	THR	INT	Cycling (9)	8-10 x 1 min @ 130% VT	38.8 ± 4.3	41 ± 4.6	5.7 ± 3.9	2.2 ± 1.6
<b>Astorino et al.</b> [45]	2013	Sedentary (24±7)	F	4	TRAD	INT	Cycling (33)	6-10 x 1 min @ 80-90% Wmax	31.7 ± 4.4	36.4 ± 4.2	15.4 ± 9.1	4.7 ± 2.5
				8			TRAD	INT	Cycling (33)	6-10 x 1 min @ 60-80% Wmax	30.6 ± 4.2	37.1 ± 3.4
<b>Berger et al.</b> [46]	2006	Active (23±4)	M	8	TRAD	CT	Cycling (18-24)	30 min @ 60% VO2max	33.7 ± 3.8	39.8 ± 6	18 ± 7.7	6.1 ± 3
				8			TRAD	INT	Cycling (18-24)	20 x 1 min @ 90% VO2max	34.6 ± 6.8	43 ± 8.3

<b>Bonafiglia et al.</b> [47]	2016	Active (20±1)	M/F	21	TRAD	CT	Cycling	30 min @ 65% VO2max (12)	42.2 ± 6.5	43.9 ± 6.5	4.4 ± 7.9	1.7 ± 3.2
<b>Bouchard et al.</b> [17]	1999	Sedentary (35±14)	M/F	562	TRAD	CT	Cycling	30-50 min @ 55-75% VO2max (60)	33.1 ± 8.6	38.7 ± 9.1	18 ± 9.9	5.6 ± 2.9
<b>Branch et al.</b> [48,49]	1997, 1999	Sedentary (32±5)	F	8	TRAD	CT	Running	150-375 kcal/session @ 80% HRmax (40)	36.2 ± 4.9	38.8 ± 7.5	6.8 ± 8.8	2.6 ± 3.8
				10	TRAD	CT	Cycling	150-375 kcal/session @ 80% HRmax (40)	29.2 ± 7.9	35.5 ± 7	24.6 ± 13.7	6.3 ± 2.6
				8	TRAD	CT	Cycling	150-375 kcal/session @ 40% HRmax (40)	29.8 ± 4.6	34.1 ± 6.6	16.5 ± 25.3	4.3 ± 7.9
<b>Byrd et al.</b> [50]	2019	Sedentary (32±9)	M/F	11	THR	INT + CT	Cycling + Running	CT: 30-50 min @ <VT1 to >VT2; INT: 8-12 x 60 s @ 100% $\dot{V}O_2$ max (30)	33.6 ± 4	38.4 ± 4.4	14.3 ± 3.6	4.8 ± 1.1
				11	TRAD	INT + CT	Cycling + Running	CT: 30-50 min @ 40-65% HRR (30)	30.4 ± 6.2	33 ± 7.2	8.1 ± 3.3	2.5 ± 1.2
<b>Casaburi et al.</b> [51]	1987	Sedentary (23±1)	M/F	9	THR	CT	Cycling	45 min @ 50-75% $\Delta$ (40)	34.5 ± 4.1	40.3 ± 4.1	17.3 ± 8	5.8 ± 2.5
<b>Dalleck et al.</b> [52]	2008	Sedentary (37±6)	F	13	TRAD	CT	Walking	(~180 min) 250-1000 kcal/wk @ 50% $\dot{V}O_2R$ (30-40)	35.5 ± 5.9	37.9 ± 4.5	7.8 ± 8	2.5 ± 2.3

<b>Dalleck et al.</b> [53]	2016	Sedentary (68±8)	M/F	10	THR	CT	Aerobic exercise (21)	25-50 min @ <VT1 to >VT2	25.9 ± 3.8	29.7 ± 4.9	14.7 ± 7.8	3.8 ± 2.2
				9	TRAD	CT	Aerobic exercise (21)	25-50 min @ 40-65% HRR	24.1 ± 12.3	26.3 ± 11.9	11.4 ± 9.5	2.2 ± 1.5
<b>Daussin et al.</b> [54]	2008	Sedentary (46±8)	M/F	13	THR	CT	Cycling (24)	20-35 min rep 5 min (4 min @ LT, 1 min @ 90% Pmax)	29.1 ± 5.9	31.9 ± 6.4	9.8 ± 8.7	2.8 ± 2.5
				13	THR	INT	Cycling (24)	Work matched with INT	27.5 ± 5.3	32.3 ± 6.5	18.5 ± 16.7	4.8 ± 4.9
<b>Fiorenza et al.</b> [55]	2019	Sedentary (57±8)	M	12	TRAD	INT	Cycling (18)	10-15 min of '10-20-30 training', 3 min rec between 5 min bouts @30%, 50%, 100% max intensity	36.6 ± 8.4	39.4 ± 4.8	7.8 ± 7.8	2.8 ± 2.7
<b>Ghiarone et al.</b> [56]	2019	Active (26±5)	M	8	THR	INT + CT	Cycling (18)	Train twice daily (3d/wk) CT: 5 min @ LT1 plus 100 min @ 50% Δ (LT1 and LT2), INT: 10 x 2 min @ 20% Δ (LT2 and PPO)	36 ± 4.3	39.3 ± 5.4	9 ± 7	3.3 ± 2.5

				7	THR	INT	Cycling	Train once daily (6d/wk)	37.9 ± 7.9	40.2 ± 6.6	8.6 ± 21.9	2.3 ± 5.8
						+ CT	(18)	CT: CT: 5 min @ LT1 plus 100 min @ 50% Δ (LT1 and LT2), INT: 10 x 2 min @ 20% Δ (LT2 and PPO)				
<b>Gormley et al.</b>	2008	Active	M/F	14	TRAD	CT	Cycling	30-40 min @ 50-75%	34.5 ± 8.6	39.1 ± 9	13.9 ± 10.3	4.6 ± 3.3
[57]		(22±3)					(22)	HRR				
				12	TRAD	INT	Cycling	Wk 1 and 2: 30-40 min @ 50-75% HRR, Wk 3-6: 5 x 5 min @ 95% HRR	36.5 ± 5.8	43 ± 7.6	17.7 ± 10.2	6.5 ± 3.8
				14	TRAD	CT	Cycling	30-60 min @ 50% HRR	35.5 ± 7.9	38.8 ± 9.1	10 ± 10.9	3.4 ± 4
							(23)					
<b>Granata et al.</b>	2016	Active	M	10	THR	INT	Cycling	4-7 x 4 min @ 35-75% Δ	45.1 ± 7.6	52.2 ± 7.8	16.2 ± 6.6	7.1 ± 2.8
[58]		(21±2)					(52)	(LT and WRpeak); 5-12 x 4 min @ 30-80% Δ; 8-20 x 2 min @ 50-80% Δ				
<b>Hov et al. [59]</b>	2022	Healthy	M	10	TRAD	INT	Running	4 x 4 min @ 90-95%	62.1 ± 4.8	66 ± 5	6.3 ± 2.4	3.9 ± 1.5
		(23±2)					(24)	HRmax				

<b>Jacques et al.</b> [60]	2021	Moderately trained (35±10)	M	15	THR	INT	Cycling (36)	6-14 x 2 min @ 40-70% Δ	52.3 ± 9.8	56.5 ± 10	8.8 ± 12.6	4.2 ± 6.2
<b>Landen et al.</b> [61]	2021	Moderately trained (35±7)	F	18	THR	INT	Cycling (12)	6-14 x 2 min @ 40-70% Δ	44.5 ± 9	45.9 ± 8.1	3.9 ± 5.2	1.5 ± 2.1
<b>Litleskare et al.</b> [62]	2020	Active (25±4)	M/F	12	TRAD	CT	Running (24)	30-60 min @ 70-80% HRpeak	47.9 ± 5.9	49.7 ± 6.2	3.9 ± 5.6	1.8 ± 2.6
<b>Maturana et al.</b> [63]	2021	Sedentary (27±6)	M/F	21	THR	CT	Cycling (18)	60 min @ LTP1	30.4 ± 4.3	32.7 ± 4.2	7.9 ± 8.6	2.3 ± 2.6
				21	TRAD	INT	Cycling (18)	4 x 4 min @ 90% HRmax	31.9 ± 4.1	37.2 ± 4.1	17 ± 7.9	5.3 ± 2.1
<b>Maunder et al.</b> [64]	2021	Active (32±7)	M	8	THR	INT + CT	Cycling (15)	4-6 x 8 min @ VT2; 90 min @ 95% VT1; 3 x 25 min @ 50% Δ (VT1 and VT2); 6-10 x 3 min	52.5 ± 6.4	53.4 ± 6.9	1.7 ± 3.5	0.9 ± 1.8
<b>McNicol et al.</b> [65]	2009	Active (21±5)	M/F	14	THR	CT	Running (18)	20 min @ 0.8 km/h less than LTv + 0.1 km/h per session	44 ± 5.5	47.6 ± 6.5	8.7 ± 12.2	3.6 ± 5.1
				13	THR	CT	Running (18)	20 min @ 0.8 km/h less than LTv	44 ± 6.9	45.3 ± 7	3 ± 2.4	1.3 ± 1

<b>Mendes et al.</b> [66]	2013	Untrained (23±2)	M	13	THR	CT	Cycling (18)	24-39 min @ MLSS	44.9 ± 4.8	49.8 ± 4.5	11.2 ± 7.2	4.9 ± 3.1
<b>Myrkos et al.</b> [67]	2023	Young adults (21±3)	M/F	13	TRAD	INT	Running (14)	Running bouts @ 90% PTV	57.7 ± 8	61.4 ± 9.23	6.5 ± 5.7	3.8 ± 3.4
				11	THR	CT	Running (14)	-2.5% of CV	58.2 ± 7.5	61.1 ± 6.4	5.6 ± 6.7	3 ± 3.7
<b>Nicolini et al.</b> [68]	2019	Sedentary (23±4)	M	15	TRAD	INT	Cycling (18)	5 x 1 min @ 105-135% WRpeak	35.5 ± 4.8	40 ± 5.1	12.9 ± 7	4.5 ± 2.2
<b>Nio et al.</b> [69]	2020	Untrained (52±4)	F	25	TRAD	INT	Cycling (36)	4 x 4 min @ 90-95% HRmax	29.4 ± 5.3	35.4 ± 5.4	21.6 ± 11.4	6.1 ± 2.9
<b>O'Leary et al.</b> [70]	2017	Untrained (26±5)	M/F	10	THR	CT	Cycling (18)	90% LT matched to work (KJ) done in INT	43.5 ± 5.9	47.4 ± 8	8.6 ± 8.4	3.9 ± 3.8
				8	THR	INT	Cycling (18)	6-8 x 5 min @ 50% Δ	44.8 ± 4.2	48.8 ± 5.4	8.8 ± 7.3	4 ± 3.1
<b>Pothier et al.</b> [71]	2021	Untrained (69±5)	M/F	21	TRAD	INT + CT	Cycling (36)	INT: 20 x 15s @ 100- 110% MAP, CT: 20 min @ 65-75% MAP	22.2 ± 6.2	24.3 ± 7	10.4 ± 16.6	2.1 ± 3.4
<b>Preobrazenski et al.</b> [72]	2019	Active (21±2)	M	14	TRAD	CT	Cycling (15)	30 min @ 65% WRpeak	46 ± 6.7	49.7 ± 5.2	8.7 ± 7.3	3.7 ± 3.1

				14	THR	CT	Cycling	30 min @ 'NEG' talk-test (15) stage	45.8 ± 5.9	51.2 ± 6.1	12.2 ± 7.1	5.4 ± 3
<b>Reuter et al.</b> [73]	2023	Untrained (46±8)	M/F	16	TRAD	CT	Running/ walking (78)	50 min @ 55% HRR	34.5 ± 3.8	35.3 ± 4	2.6 ± 9.1	0.8 ± 3.1
				15	TRAD	CT + INT	Running/ walking (78)	CT: 50 min @ 55% HRR, INT: 4 x 4 min @ 95% HRmax	33.9 ± 5.3	37.3 ± 4.9	10.7 ± 8	3.4 ± 2.7
<b>Schaun et al.</b> [74]	2018	Healthy (23±4)	M	14	TRAD	INT	Running (48)	8 x 20 s @ 130% v $\dot{V}O_2$ max	46.8 ± 7.1	57.7 ± 6.7	24.9 ± 15.6	11 ± 6.2
				14	THR	CT	Running (48)	30 min @ 90-95% HR at VT2	47.9 ± 7.5	56.6 ± 7.9	19.6 ± 15.6	8.8 ± 6
<b>Schubert et al.</b> [75]	2017	Active (30±9)	M/F	11	TRAD	INT	Cycling (12)	6-8 x 90% PPO	31.4 ± 9.7	33.1 ± 9.8	6.1 ± 5.2	1.8 ± 1.7
<b>Scharhag-Rosenberger et al.</b> [76]	2012	Untrained (41±6)	M/F	20	TRAD	CT	Running/ walking (156)	45 min @ 60% HRR	37.8 ± 5.3	43.1 ± 7.1	14.2 ± 11.7	5.3 ± 4.2
<b>Stensvold et al.</b> [77]	2015	(72±2)	M/F	77	TRAD	CT	Aerobic exercise (156)	50 min @ 70% HRpeak	31.1 ± 5.9	32.6 ± 6.1	5.5 ± 10.7	1.5 ± 3.4

			M/F	49	TRAD	INT	Aerobic exercise (156)	repetitions of 4 min intervals with 3 min recovery periods 85-95% HRpeak	31.8 ± 6.9	35.7 ± 6.7	13.7 ± 14.6	3.9 ± 4.3
<b>Tarumi et al.</b> [78]	2022	Older adults (70±6)	M/F	28	TRAD	CT + INT	Running/ walking (156)	CT: 25-40 min @ 75-85% and 85-90% HRmax	22.5 ± 4	25.1 ± 4.1	15 ± 28.4	2.6 ± 5.5
<b>Tjønnå et al.</b> [79]	2013	Inactive (42±3)	M	10	TRAD	INT	Running/ walking (30)	1 x 4 min @ 90% HRmax	39.2 ± 5.3	44.1 ± 5.6	12.9 ± 7.7	4.9 ± 2.7
				12	TRAD	INT	Running/ walking (30)	4 x 4 min @ 90% HRmax	44.8 ± 5.3	51 ± 4.6	14.4 ± 8.9	6.2 ± 3.6
<b>Vanhatalo et al.</b> [80]	2008	Habitually active (29±6)	M/F	9	THR	INT	Cycling (12)	2 x p/wk 6 x 5 min at 105% EP + 1 x p/wk 10 x 2 min @ 50% WEP expenditure during the first 2 min period	50.7 ± 5.4	56 ± 6	10.5 ± 5.3	5.3 ± 2.7
<b>Vollaard et al.</b> [81]	2009	Healthy (24±2)	M	23	TRAD	CT	Cycling (24)	45 min @70% VO2max	49.2 ± 5.2	55.6 ± 7.1	13.1 ± 10.8	6.4 ± 4.9

<b>Weatherwax et al. [82]</b>	2019	Sedentary (46±11)	M/F	16	THR	CT	Aerobic exercise (33)	Energy Expenditure of 5.6-15.4 kcal/kg/wk @ HR <VT1 to >VT2	30.5 ± 6.6	34 ± 7.7	11.4 ± 3.9	3.5 ± 1.5
				13	TRAD	CT	Aerobic exercise (33)	Energy Expenditure of 5.6-15.4 kcal/kg/wk @ 40-65% HRR	25.2 ± 4.7	26.5 ± 4.2	6.1 ± 7.7	1.4 ± 1.9
<b>Wolpern et al. [83]</b>	2015	Sedentary (33±10)	M/F	9	THR	CT	Running (31)	20-30 min @ HR <VT1 to >VT2	35.4 ± 8.8	39.5 ± 8.8	12.2 ± 5.2	4.1 ± 0.9
				11	TRAD	CT	Running (31)	20-30 min @ 40-65% HRR	35.1 ± 5.5	36.4 ± 5.7	4 ± 5.4	1.4 ± 1.8
<b>Yan et al. [84]</b>	2017	Moderately trained (32±8)	M	66	THR	INT	Cycling (12)	6-14 x 2 min @ 40-70% Δ	49.2 ± 8	50.5 ± 7.7	3.2 ± 9.4	1.3 ± 4.3

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251 THR: exercise prescribed relative to physiological thresholds, TRAD: exercise prescribed relative to a traditional intensity anchor, CT: continuous exercise, INT:

252 interval exercise, HR<sub>max</sub>: maximum heart rate, HR<sub>peak</sub>: peak heart rate, HRR: heart rate reserve,  $\dot{V}O_{2max}$ : maximum oxygen uptake,  $\dot{V}O_{2R}$ : oxygen uptake reserve, VT:

253 ventilatory threshold, WEP: work above end power during a 3 min all out test, PPO: peak power output,  $v\dot{V}O_{2max}$ : velocity at  $\dot{V}O_{2max}$ , WR<sub>peak</sub>: peak work rate, MAP:

254 maximum aerobic power, LT: lactate threshold, Δ: delta method, MLSS: maximum lactate steady state, LTv: velocity at LT, CV: critical velocity, PTV: peak treadmill

255 velocity, LTP: lactate turn point, Pmax: maximum power, M: males, F: females.

256 **Table 5.** Summary characteristics of controlled and non-controlled THR and TRAD studies included  
 257 in the present individual participant data meta-analysis

	<b>Study group</b>		
<b>Controlled Studies</b>	<b>THR</b>	<b>TRAD</b>	<b>CON</b>
Studies (n)	4	4	4
Individuals (n)	46	44	49
Sex (M, F)	18, 28	16, 28	20, 29
Age (y)	43±17	46±17	44±14
Body mass (kg)	72±11	73±11	75±10
Baseline $\dot{V}O_{2max}$ (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	31±7	29±5	29±6
Training duration (wks.)	13±1	13±1	
Training sessions (n)	29±5	29±5	
Continuous exercise	3	3	
Interval exercise	0	0	
Combination	1	1	
<b>Non-controlled Studies</b>	<b>THR</b>	<b>TRAD</b>	
Studies (n)	18	25	
Individuals (n)	354	1190	
Sex (M, F)	239, 115	565, 622	
Age (y)	31±12	38±18	
Body mass (kg)	75±13	71±13	
Baseline $\dot{V}O_{2max}$ (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	42±10	34±9	
Training duration (wks.)	7±4	14±14	
Training sessions (n)	23±11	43±39	
Continuous exercise	13	19	
Interval exercise	8	16	
Combination	4	4	

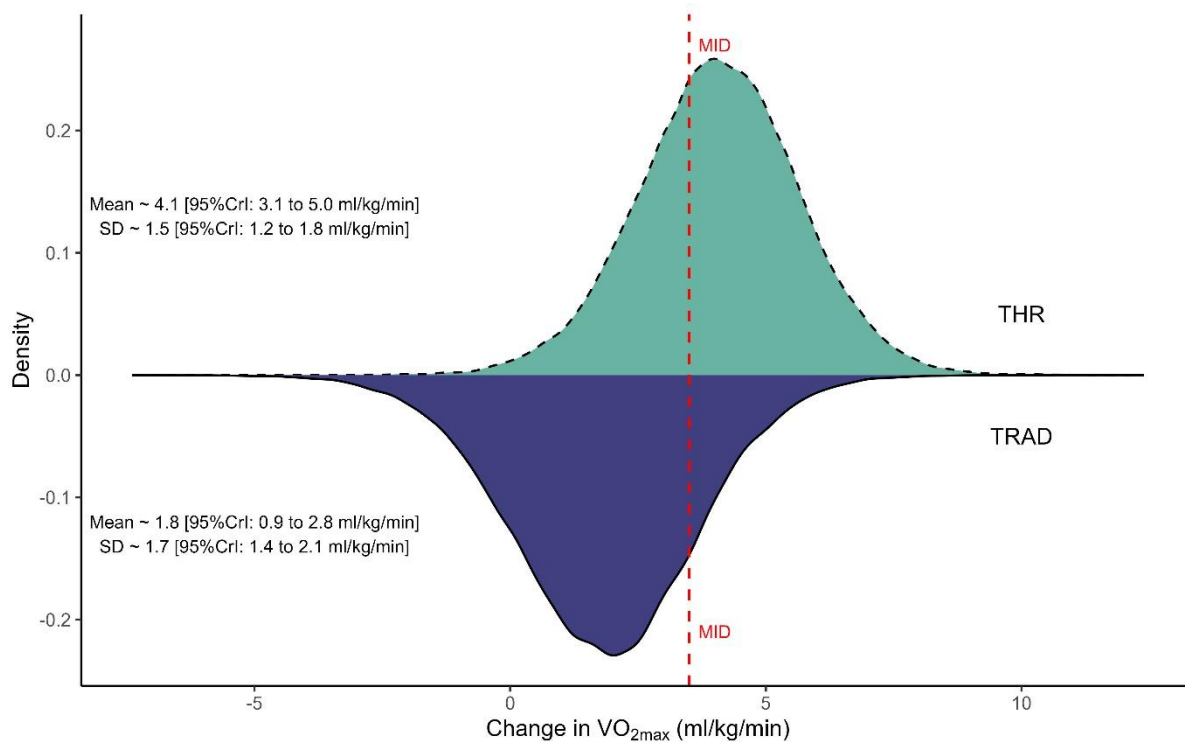
258  $\dot{V}O_{2max}$ : maximum oxygen uptake. Data are presented as means or mean ± standard deviation.

259 **3.4 Result of syntheses**

260 3.4.1 Changes in maximum oxygen uptake

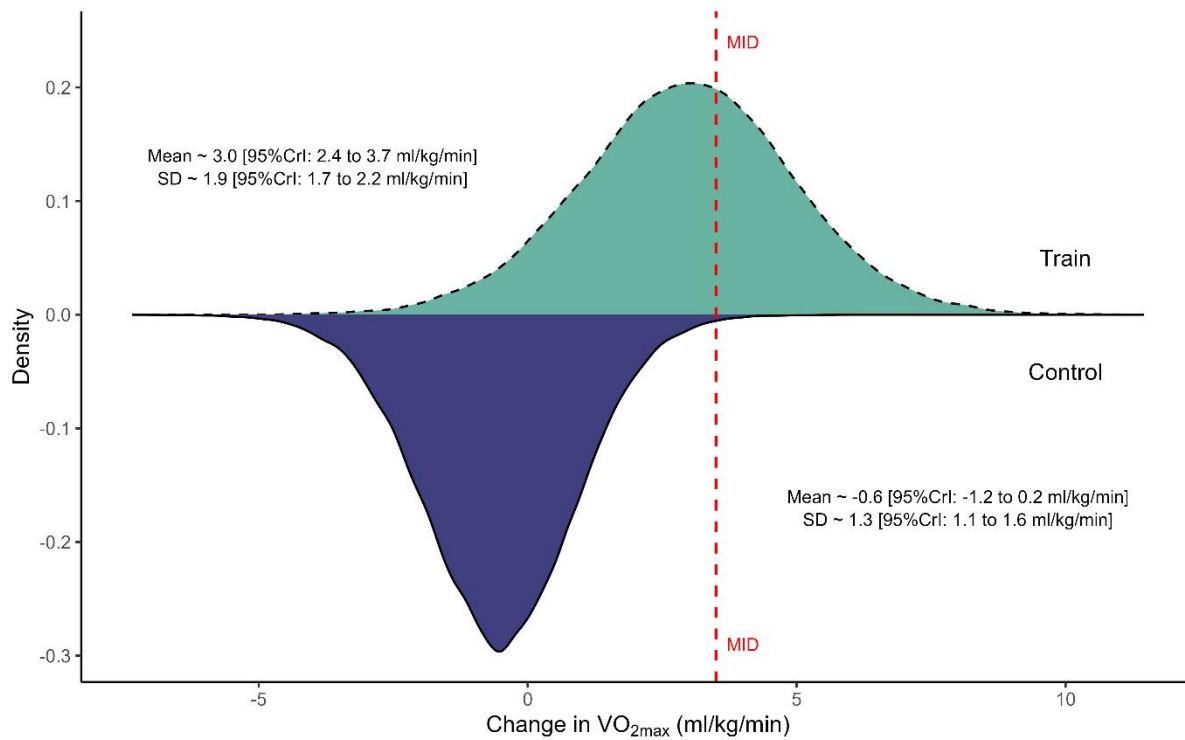
261 *Controlled studies*

262 ‘Extreme’ evidence ( $BF > 100$ ) was identified in support of a greater improvement in  $\dot{V}O_{2max}$  for THR  
263 ( $4.1$  [95%CrI:  $3.1$  to  $5.0$   $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]) compared to TRAD ( $1.8$  [95%CrI:  $0.9$  to  $2.8$   $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ];  
264 Figure 2). Individuals were estimated to be approximately four times more likely to experience an  
265 increase in  $\dot{V}O_{2max}$  greater than the MID in THR (64%) compared to TRAD (16%). There was  
266 ‘anecdotal’ evidence ( $BF = 0.55$ ) in support of no difference in variation of  $\dot{V}O_{2max}$  change scores  
267 between THR ( $1.5$  [75%CrI:  $1.2$  to  $1.8$   $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]) and TRAD ( $1.7$  [75%CrI:  $1.4$  to  $2.1$   $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ];  
268  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]; Figure 2). When THR and TRAD were combined, ‘strong’ evidence ( $BF = 12.4$ ) was identified  
269 in support of a greater variation in  $\dot{V}O_{2max}$  change scores in the training groups ( $1.9$  [75%CrI:  $1.7$  to  $2.2$   
270  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]) compared to CON ( $1.3$  [75%CrI:  $1.1$  to  $1.6$   $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]; Figure 3).



**Figure 2.** Modelled changes in  $\dot{V}O_{2max}$  ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) from controlled studies comparing exercise prescription using traditional intensity anchors or physiological thresholds. MID: minimum important difference, THR: exercise training prescribed relative to physiological thresholds ( $n = 46$ ),

TRAD: exercise training prescribed relative to traditional intensity anchors (n=44), SD: standard deviation; CrI: credible interval.

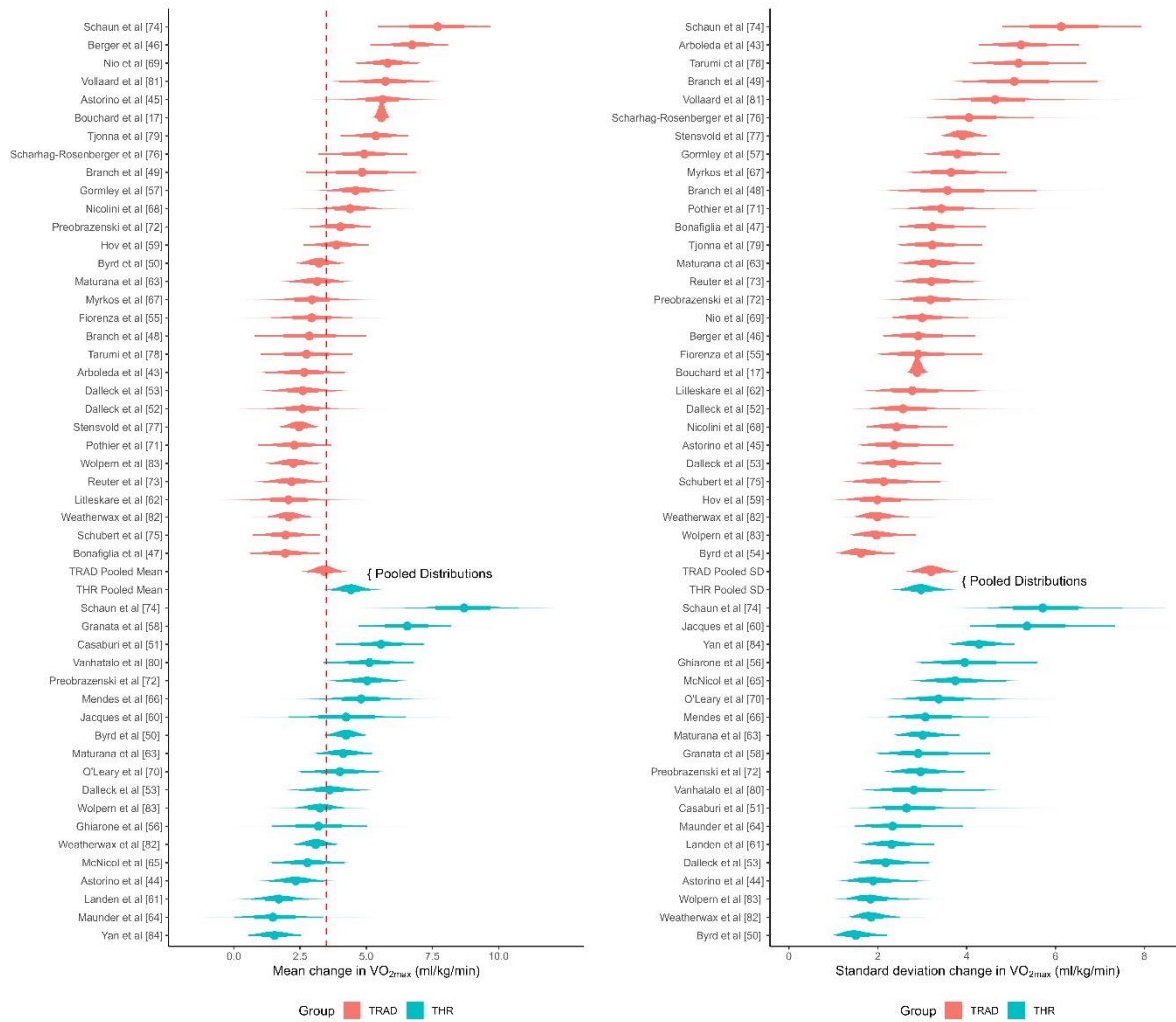


**Figure 3.** Modelled changes in  $\dot{V}O_{2max}$  ( $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) from controlled studies comparing pooled data from all training groups and control. MID: minimum important difference Train: comprises data from groups where exercise training is prescribed using either traditional intensity anchors or relative to physiological thresholds (n=90), Control: comprises data from non-exercising control groups (n=49), SD: standard deviation; CrI: credible interval.

271

272 *Non-controlled studies*

273 In general, similar findings to those obtained for controlled studies were observed in non-controlled  
 274 studies. ‘Very strong’ evidence (BF=35.1) was identified in support of a greater improvement in  $\dot{V}O_{2max}$   
 275 for THR (4.4 [95%CrI: 3.7 to 5.2  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]) compared to TRAD (3.4 [95%CrI: 2.8 to 4.1  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ];  
 276 Figure 4). Predictions using the fitted model estimated 60% of individuals in THR should be  
 277 expected to increase  $\dot{V}O_{2max}$  beyond the MID, with 47% expected in TRAD. ‘Anecdotal’ evidence  
 278 (BF=0.41) was identified in support of no difference in variation of  $\dot{V}O_{2max}$  change scores between THR  
 279 (3.0 [75%CrI: 2.7 to 3.3  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]) and TRAD (3.2 [75%CrI: 2.9 to 3.5  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ]; Figure 4).



**Figure 4.** Forest plot of modelled mean (left) and standard deviation (right) change in  $\dot{V}O_{2max}$  ( $mL \cdot kg^{-1} \cdot min^{-1}$ ) across non-controlled studies comprising exercise prescription using either traditional intensity anchors or physiological thresholds. Distributions represent “shrunk estimates” based on all relevant effect sizes, the random effects model fitted, and borrowing of information across studies to reduce uncertainty. Circles and connected intervals represent the median value and 95% credible intervals for the shrunk estimates. Pooled estimates across conditions are presented in the centre of the plot. Red line illustrates the minimum important difference threshold. THR: exercise training prescribed relative to physiological thresholds, TRAD: exercise training prescribed relative to traditional intensity anchors.

282 This is the first IPD meta-analysis to explore the magnitude and variation in  $\dot{V}O_{2max}$  change scores  
283 elicited by training programmes using THR and TRAD approaches. The main findings were: 1)  
284 prescribing exercise intensity using THR approaches elicited superior mean changes in  $\dot{V}O_{2max}$  and  
285 increased the likelihood of an individual increasing  $\dot{V}O_{2max}$  beyond the MID; and 2) there appeared to  
286 be no difference in response variability between THR and TRAD.

#### 287 *4.1 Mean changes in $\dot{V}O_{2max}$*

288 Superior increases in  $\dot{V}O_{2max}$  were observed in THR compared to TRAD in both the controlled and non-  
289 controlled analyses. In the controlled studies, it was estimated that individuals were approximately four  
290 times as likely to experience an increase in  $\dot{V}O_{2max}$  beyond the MID. This estimate was based on the  
291 statistical model indicating 64% of participants undergoing THR would experience an increase of  $\geq 3.5$   
292 mL·kg<sup>-1</sup>·min<sup>-1</sup> compared with 16% of participants undergoing TRAD. In the non-controlled studies,  
293 greater variability was observed across the larger data set, however, it was estimated that on average,  
294 60% and 47% of individuals would experience changes beyond the MID in THR and TRAD,  
295 respectively.

296 Regarding the notion of increasing ‘response rates’, herein defined as the proportion of individuals  
297 improving a given parameter beyond a predefined threshold, the present findings agree with previous  
298 literature whereby increased  $\dot{V}O_{2max}$  response rates are typically explained by greater mean change  
299 scores as opposed to reductions in inter-individual variability [25]. In turn, using THR approaches  
300 represents a viable approach in increasing response rates, and thus, increasing the likelihood of  
301 individuals attaining the health- and performance-related benefits of exercise training. Importantly,  
302 instead of requiring increases in training dose following TRAD (i.e., by increasing training intensity,  
303 frequency, and/or duration), using THR approaches appears to be an effective method to increase the  
304 proportion of individuals attaining increases in  $\dot{V}O_{2max}$  beyond a predefined threshold in response to the  
305 initial exercise stimulus.

#### 306 *4.2 Variability in $\dot{V}O_{2max}$ change scores*

307 An interesting finding of the current analysis was that greater variability in  $\dot{V}O_{2max}$  change scores were  
308 observed in exercising groups compared with the non-exercising control group (Figure 3). Whilst the  
309 magnitude of this evidence was small, this provides evidence of inter-individual differences in  $\dot{V}O_{2max}$   
310 trainability [18,19,85–87]. This warrants further investigation as currently, differences in inter-  
311 individual variability are often found to be attributable to measurement error and biological variability  
312 as opposed to differences in trainability [20,88,89].

313 However, contrary to our hypothesis, weak evidence was obtained in support of no difference in the  
314 variability of  $\dot{V}O_{2max}$  change scores between THR and TRAD in both analyses. It has been shown that  
315 using THR approaches better normalises exercise intensity among individuals compared to when using  
316 TRAD anchors, reducing the variability in exercise tolerance and eliciting more homogenous acute  
317 physiological responses [29,32,33,36]. Based on the acute data presented in these studies, it was  
318 hypothesised that repeated performance of THR would manifest in a more consistent chronic stimulus  
319 across participants, resulting in reduced variation in change scores. Previous studies have reported  
320 increased  $\dot{V}O_{2max}$  response rates following exercise training prescribed using THR compared to TRAD  
321 [50,53,82,90], however, in such studies it was unclear whether the increased response rates were the  
322 product of a reduction in response variability or simply increased group mean changes in  $\dot{V}O_{2max}$ , or  
323 both. Based on the present findings and a lack of evidence supporting a difference in the variability in  
324  $\dot{V}O_{2max}$  change scores following THR, it appears that increased response rates are primarily explained  
325 by greater mean  $\dot{V}O_{2max}$  change scores.

326 Typically, THR studies implemented continuous training [53,66,67,70,72,82,90–94]. It is plausible that  
327 the prescribed intensities were low enough such that acute metabolic responses to THR and TRAD  
328 exercise were not markedly different, despite what may have been large differences in external work  
329 rate among individuals [33]. Notably, when intensities approach or exceed the boundary between the  
330 heavy- and severe-intensity domain, marked differences in exercise durations and responses can be  
331 observed despite only minimal differences in external work rate [33,95–97]. Using physiological  
332 thresholds to prescribe and control exercise around this transition may be where such approaches hold  
333 their value. Furthermore, the activation of signalling pathways associated with key physiological

334 changes promoting increases in  $\dot{V}O_{2\max}$  (e.g., mitochondrial biogenesis) are shown to increase at  
335 intensities within the severe intensity domain compared to the moderate and heavy intensity domains  
336 [98]. Thus, having the ability to prescribe exercise accurately both above and below the boundary  
337 between the heavy and severe intensity domain, as is shown when using THR approached, might have  
338 beneficial implications on the manifestation of subsequent adaptation.

339 Various approaches are used to determine and apply physiological thresholds for training purposes  
340 [99,100]. Whilst they all aim to approximate the transition between the moderate and heavy intensity  
341 domain or the heavy and severe intensity domain, they are not identical [101]. Critical power is often  
342 considered the most accurate representation of the latter boundary [96] and as aforementioned is shown  
343 to better control exercise intensity than when using TRAD approaches. This is likely explained by the  
344 fact that using TRAD approaches do not account for the relative positioning of an individual's critical  
345 power relative to a maximum physiological value, such as  $\dot{V}O_{2\max}$  or  $HR_{\max}$  [33]. Using critical power  
346 as a tool for exercise prescription, however, appears to be limited in exercise-related research with only  
347 one study in the present dataset [80] using the concept for training purposes. An advantage of using  
348 critical power is that a given work rate can be used to define the exercise session(s), negating the need  
349 to adjust exercise intensity to match a given heart rate or  $\dot{V}O_2$  response. In the HERITAGE study, the  
350 fluctuation in the training work rate was the third most impactful factor (6%) on  $\dot{V}O_{2\max}$  response  
351 variability, despite overall adherence being greater than 95% [102]. It would thus be interesting to  
352 investigate whether a reduction in response variability is observed to a higher degree were critical power  
353 used as an intensity anchor, particularly when comparing studies prescribing heavy- and/or severe-  
354 intensity exercise using a traditional intensity anchor, as this is where we may expect to see a more  
355 profound difference in response variability.

356 It is worth noting that the relative intensity of exercise is consistently shown to influence the magnitude  
357 of training-induced adaptations [15,54,57,65,103–105] and that similar adaptations can be observed  
358 following a small volume of exercise performed at very high intensities and a large volume of exercise  
359 performed at lower intensities [106–110]. In a recent study by Inglis et al. [105], eighty-four healthy  
360 participants performed moderate, heavy, severe, or extreme intensity exercise training where exercise

361 intensity was prescribed using a ‘domain-based’ approach (i.e., THR) using the LT and the maximum  
362 metabolic steady state (based on blood lactate and  $\dot{V}O_2$  responses) to determine the boundaries between  
363 the moderate-heavy and heavy-severe intensity domains, respectively. Interestingly, all exercise groups  
364 bar the moderate intensity exercise group increased  $\dot{V}O_{2max}$ , the power output at the LT, and the power  
365 output at the maximum metabolic steady state. Such results further support the notion that that exercise  
366 intensity is a key determinant of training-induced changes in training-induced adaptations. All in all,  
367 exercise intensity demonstrates a clear influence on the magnitude of subsequent changes in markers  
368 such as  $\dot{V}O_{2max}$ .

369 Such findings incite the argument that the method used to prescribe exercise intensity is in fact  
370 irrelevant, and that irrespective of whether a THR or TRAD approach is used, whichever approach  
371 elicits the highest relative exercise intensity will likely induce the largest increases in  $\dot{V}O_{2max}$  thereafter.  
372 On this, it is important to consider the findings of Collins et al. [104] who conducted a training  
373 intervention comprised of CT prescribed at 44% of the maximum power output achieved in a GXT  
374 ( $P_{GXT}$ ) and INT prescribed at 80%  $P_{GXT}$ . Of note, there were instances where exercise intensity, when  
375 expressed relative to critical power, was higher in the CT group compared to the INT group, and as a  
376 result, these individuals experienced superior changes in critical power post-training. At first glance,  
377 this contradicts the argument that high intensity INT is superior to lower intensity CT [15,54,57,65,103–  
378 105]; however, it instead supports the notion that when prescribing exercise intensity, whether that be  
379 for CT or INT, anchoring intensity relative to a maximum physiological value such as  $\dot{V}O_{2max}$  is not  
380 appropriate [31,33,35,111]. Overall, the authors concluded that the higher the training intensity is when  
381 expressed relative to critical power, instead of relative to  $\dot{V}O_{2max}$ , the greater the training-induced  
382 changes thereafter [104]. Therefore, whilst the argument may be presented that the method used to  
383 prescribe exercise intensity is inconsequential so long as high intensity exercise is prescribed, a THR  
384 based approach should be used to ensure that exercise intensity is in fact ‘high’ for a given individual  
385 based on their unique intensity domains and not just *intended* to be ‘high’ based on a generalised  
386 approach to exercise intensity prescription. Additionally, in the instance that an individual has not  
387 achieved a change in  $\dot{V}O_{2max}$ , for example, above a given ‘response’ threshold, the possibility exists that

388 the intensity elicited when using a TRAD based approach was simply too low when expressed relative  
389 to critical power [19,33,104,112]. Using critical power, or an alternative threshold, would negate this  
390 issue of heterogeneity in the prescribed exercise intensity; however, further studies are warranted to  
391 confirm this notion [104].

#### 392 *4.4 Limitations*

393 A limitation of the present study was the limited amount of IPD obtained from those meeting the  
394 inclusion criteria. Whilst 236 studies met the predefined criteria (Figure 1), the response rate of IPD  
395 obtained was 18% (N=42). Additionally, THR IPD (n=354) was limited compared to that of TRAD  
396 IPD (n=1190). Exercise training programmes are still routinely prescribed at intensities anchored  
397 relative to traditional parameters (i.e.,  $\dot{V}O_{2max}$  and  $HR_{max}$ ) [15,18,85,113,114]. Understandably, using  
398 HR-based parameters can negate the need for laboratory or field testing, making this an attractive  
399 approach, albeit not the most accurate. However, the continued use of  $\dot{V}O_{2max}$  as an intensity anchor is  
400 surprising given its known inaccuracy in controlling exercise intensity among individuals  
401 [29,31,33,36,115,116]. Moreover, if measuring  $\dot{V}O_{2max}$ , data used to determine given physiological  
402 thresholds (e.g., gas exchange threshold) is readily available. Alternatively, self-assessed threshold tools  
403 such as rating of perceived exertion (RPE) can be used as surrogates for physiological thresholds and  
404 provide an easily accessible means of prescribing and controlling exercise intensity based off a  
405 threshold-based approach [117–119]. For example, using the 6-20 Borg scale, moderate, heavy, and  
406 severe intensity exercise can be prescribed at approximately  $\leq 13$ , 14-16, and  $\geq 17$ , respectively [118].  
407 Lehtonen et al. [118] also note that pairing RPE with external work (e.g., running pace or power output)  
408 and internal physiological response (e.g., heart rate) would add a further element of sophistication to  
409 the prescription and monitoring of exercise training. There is also evidence demonstrating that critical  
410 power and the running equivalent critical speed, can be derived from habitual training data and/or a  
411 series of time trials [120–122]. This allows for a more accessible means of critical speed and/or critical  
412 power determination, negating the need for laboratory-based testing [122]. The results presented herein  
413 will hopefully encourage greater consideration of using THR approaches, where possible, when  
414 designing future exercise research studies.

415 Another limitation of the present study is that compared to the controlled dataset, the non-controlled  
416 dataset contained IPD from studies with marked differences in study characteristics. For example,  
417 studies adopted various training doses, populations, modes of exercise and training types (Table 3).  
418 Effects of these differences were easily observed when comparing the range in mean  $\dot{V}O_{2max}$   
419 improvements estimated across the different studies (Figure 4). Despite differences in study  
420 characteristics, overall findings from both analyses were consistent. As such, the two datasets and  
421 analyses complement each other and help account for their individual limitations; for example, the  
422 controlled studies comprise similar study characteristics but are small in sample size, whereas the non-  
423 controlled studies express a much larger sample size but marked differences in study characteristics. If  
424 enough data were available, stricter eligibility criteria could have been used such that a more  
425 homogenous non-controlled dataset could have been analysed. This would have allowed a more robust  
426 comparison between THR and TRAD studies regarding the magnitude and variability in  $\dot{V}O_{2max}$  change  
427 scores, as was done in the controlled study analysis. However, more THR studies are needed for this to  
428 occur. Additionally, information regarding adherence to training at the individual level in each  
429 independent study was not sought. Thus, conclusions concerning the impact of training adherence on  
430 subsequent  $\dot{V}O_{2max}$  change scores cannot be elucidated.

## 431 **5 CONCLUSION**

432 The current IPD meta-analysis found no difference in  $\dot{V}O_{2max}$  response variability between training  
433 programmes utilising THR and TRAD approaches. However, using THR approaches appears to be a  
434 more effective means of increasing the likelihood of an individual attaining meaningful increases in  
435  $\dot{V}O_{2max}$ , and thus, increased response rates may be more commonly observed using such approaches.  
436 The current analysis also provides some evidence supporting the existence of inter-individual  
437 differences in  $\dot{V}O_{2max}$  trainability based on greater variation in change scores between exercise and  
438 control groups. Future primary research should be conducted with adequate power to investigate the  
439 scope of inter-individual differences in  $\dot{V}O_{2max}$  trainability, and if meaningful, the causative factors.

440

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