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Mackenzie, Kristen; Kelly, Jaimon; So, Daniel; Coffey, Vernon G; Byrne, Nuala

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1 The effect of exercise interventions on resting metabolic rate: a systematic review and meta-
2 analysis.

3
4 MacKenzie-Shalders, K¹., Kelly, J.T.²., So, D³., Coffey, V.G.² & Byrne, N.M.³

5
6 1. Bond University, Bond Institute of Health and Sport, Faculty of Health Sciences
7 and Medicine (Gold Coast, Australia)

8 2. Bond University, Bond Institute of Health and Sport, Faculty of Health Sciences
9 and Medicine (Gold Coast, Australia) / The University of Queensland, School of
10 Public Health, Faculty of Medicine (Brisbane, Australia)

11 3. Bond University, Bond Institute of Health and Sport, Faculty of Health Sciences
12 and Medicine (Gold Coast, Australia)/ Monash University, Faculty of Medicine
13 Nursing and Health Sciences, Central Clinical School, Department of
14 Gastroenterology (Melbourne, Australia)

15 4. University of Tasmania, School of Health Sciences, College of Health and
16 Medicine (Launceston, Australia)

17
18 **Corresponding Author:** Dr Kristen MacKenzie-Shalders

19 c/o Bond Institute of Health & Sport

20 Faculty of Health Sciences & Medicine, Bond University.

21 2 Promethean Way, Robina.

22 4226 Australia

23 kmackenz@bond.edu.au

24 +61 7 55951018

25 Orcid ID: 0000-0003-4938-5362

26 **Co-author contact details**
27 Jaimon T. Kelly: jaimon.kelly@griffith.edu.au
28 Daniel So: daniel.so@monash.edu
29 Vernon G: Coffey vcoffey@bond.edu.au,
30 Nuala M Byrne: nuala.byrne@utas.edu.au

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36 1. ABSTRACT

37

38 *The systematic review and meta-analysis evaluated the effect of aerobic, resistance and*
39 *combined exercise on RMR (kCal/day) and performed a methodological assessment of*
40 *indirect calorimetry protocols within the included studies. Subgroup analyses included*
41 *energy/diet restriction and body composition changes. Randomized control trials (RCTs),*
42 *quasi – RCTs and cohort trials featuring a physical activity intervention of any form and*
43 *duration excluding single exercise bouts were included. Participant exclusions included*
44 *medical conditions impacting upon RMR, the elderly (≥ 65 years of age) or pregnant,*
45 *lactating or post-menopausal women. The review was registered in the International*
46 *Prospective Register of Systematic Reviews (CRD 42017058503). 1669 articles were*
47 *identified; 22 were included in the qualitative analysis and 18 were meta-analysed. Exercise*
48 *interventions (aerobic and resistance exercise combined) did not increase resting metabolic*
49 *rate (mean difference (MD): 74.6 kcal/d [95% CI: -13.01, 161.33], $P = 0.10$). While there*
50 *was no effect of aerobic exercise on RMR (MD: 81.65 kcal/d [95% CI: -57.81, 221.10], $P =$*
51 *0.25), resistance exercise increased RMR compared to controls (MD: 96.17 kcal/d [95% CI:*
52 *45.17, 147.16], $P = 0.0002$). This systematic review effectively synthesises the effect of*
53 *exercise interventions on RMR in comparison to controls; despite heterogenous*
54 *methodologies and high risk of bias within included studies.*

55

56 *Abstract Word Count – 200 words*

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58 2. KEYWORDS

59 Measurement, Metabolism, Nutrition, Physiology, Exercise.

60

61

62 3. INTRODUCTION

63

64 Human energy expenditure has three primary components: activity energy expenditure,
65 resting metabolic rate (RMR) and dietary induced thermogenesis (DIT) [1]. The accurate
66 measurement and interpretation of RMR is beneficial as it is a principal contributor to daily
67 energy expenditure. In practice, this is usually measured by Indirect Calorimetry, a method
68 that is 'indirect' as it measures airflow and the percentage of oxygen (O₂) and carbon dioxide
69 (CO₂) to generate the respiratory exchange ratio (RER) which is subsequently converted to
70 energy expended through known relationships [2, 3]. It is important for practitioners to
71 understand how behaviours and lifestyle can impact on components of energy expenditure, in
72 particular the effect of exercise on RMR is of interest as it has implications for health and
73 sports performance. Despite this, there is a lack of agreement in the literature regarding the
74 potential for exercise to modulate RMR in humans.

75

76 Previous studies have reported increases, decreases or no change in RMR as a result of
77 chronic adaptations to endurance or resistance exercise programs [4-9]. These differences
78 may be attributable to a range of factors. For example, changes in body composition directly
79 impact RMR due to the relative energy contribution of different body tissues; fat-free mass is
80 known to explain 25 - 70% of the variance in RMR and therefore gains and/or losses in
81 skeletal muscle due to resistance or aerobic exercise can impact on RMR [10, 11]. As well,
82 changes in dietary intake and/or energy expenditure with an exercise program will impact
83 RMR and its interpretation [12]. In addition to these primary factors, other physiological and
84 genetic factors contribute as exercise has the ability to impact thyroid status, protein turnover,
85 circulating leptin [13], thermogenesis [14], β -adrenergic stimulation [15] and mitochondrial
86 activity in the liver [16]. While understanding these factors is important for the interpretation
87 of changes in RMR, equivocal changes in RMR as a response to exercise have also been

88 attributed to sample size, differences in methodology - particularly the timing and technique
89 of measurement - and the intensity and duration of exercise programs [17].

90

91 While Indirect Calorimetry is widely accepted as a valid and reliable method of determining
92 RMR, high precision in the estimate of RMR is achieved when best-practice methodologies
93 are employed [18, 19]. In short, several aspects of measurement must be standardised
94 including familiarisation and/or acclimatisation with the measurement and the ventilated
95 hood, test conditions, stimulant intake, food intake and physical activity prior to
96 measurement, physiological state (e.g. illness, medications, altitude) and the method of
97 measurement and analysis [18, 19]. The method has been used successfully in the general
98 population and is regularly reported in studies examining the effects of exercise on whole
99 body metabolism [20, 21]. However, it is currently unclear whether publications that report
100 changes in RMR adhere to, and report, best practice protocols.

101

102 This systematic review synthesised evidence from experimental intervention studies that
103 assessed the effect of exercise programs including resistance exercise or endurance/aerobic
104 exercise on RMR to assess the primary research question ‘what is the effect of aerobic,
105 resistance and combined exercise training modalities on RMR (kCal/day) measured by
106 indirect calorimetry in comparison to a control group?. In addition, secondary aims for this
107 systematic review included 1) performing subgroup analyses assessing the impact of
108 energy/diet restriction, changes in body weight and body composition on changes in RMR
109 and 2) providing an overview of the methodologies reported in the included studies
110 measurement of RMR and how these align with best practice guidelines. It is hypothesised
111 that regular or prolonged exercise would have a measurable effect on RMR in accord with
112 changes in body composition.

113 **4. MATERIALS AND METHODS**

114

115 This systematic review was conducted in line with the guidelines of the Preferred Reporting
116 Items for Systematic Reviews and Meta-Analysis: The PRISMA statement [22], and the
117 guidelines of the Cochrane Handbook for Systematic Reviews and Interventions [23]. The
118 methods including the eligibility criteria, search strategy, extraction process and analysis
119 were pre-specified and documented in a protocol that was published in the International
120 Prospective Register of Systematic Reviews (CRD42017058503) available at
121 https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=58503.

122

123 **4.1. Literature search**

124

125 A literature search was performed in the electronic databases MEDLINE, EMBASE,
126 CENTRAL and SPORTSDISCUS (from inception to July 22, 2018), using a combination of
127 subject headings, free text terms and synonyms relevant to this review, in consultation with a
128 systematic review search librarian (**Supplemental Table 1**). There was no date or language
129 restriction in the search strategy non-English studies were translated and assessed against
130 inclusion criteria. A multi-step search approach was taken to retrieve relevant studies through
131 additional hand-searching. Two review authors (DS and JK) screened articles in a blinded,
132 standardized manner, with disagreements in judgement resolved by consensus or a third
133 reviewer (KMcKS).

134

135 **4.2. Study selection**

136

137 Search results were merged into reference management software Endnote (X8; Thomson
138 Reuters) and de-duplicated prior to screening. Studies were included if they met all of the
139 following criteria: 1) randomized controlled trial (RCT), cluster RCT, quasi-RCT,
140 prospective cohort and retrospective cohort trials; 2) inclusion of adult participants (≥ 18 years

141 of age); 3) intervention involving exercise and physical activity training; 4) inclusion of non-
142 exercising control group as a comparator; 5) assessed resting metabolic rate (RMR) at the
143 beginning and end of intervention using indirect calorimetry.

144

145 Studies involving populations with conditions impacting upon RMR - including medical
146 conditions such as sepsis and thyroid conditions the elderly (≥ 65 years of age), or pregnant,
147 lactating, or post-menopausal women were excluded. Studies involving the use of
148 medications or known stimulants known to elevate RMR were also excluded [18, 19].

149 Eligible interventions included physical activity or training of any form (e.g. aerobic exercise,
150 resistance training or concurrent training) of any duration, although studies involving a single
151 (acute) exercise bout were excluded. Studies involving multifactorial interventions involving
152 physical activity and dietary change were included if the dietary change delivered as the
153 intervention also served as the non-exercising comparator.

154

155 The primary outcome was between-group differences in either RMR, resting energy
156 expenditure or basal metabolic rate at the end of intervention, as well as changes from
157 baseline. Studies were included only if they reported on the primary study outcome, as either
158 between-group differences or changes from baseline.

159

160 **4.3. Data extraction and management**

161

162 Three reviewers (DS, JK and KMCKS) independently extracted the data from eligible studies,
163 and one reviewer (KMCKS) determined the final extraction when there were differences or
164 omissions. Data extracted included: study design (duration, location, details of 'run-in'
165 periods); participant characteristics, intervention details (type of physical activity, intensity,
166 duration and compliance); and other information including indirect calorimetry methodology
167 used, body composition assessment method and change in body composition analysis.

168

169 For all pre-specified primary, secondary and exploratory outcome data, the mean, standard
170 deviation (SD), standard error (SE) or 95% confidence intervals (CI) that were reported at
171 end of intervention were extracted for analysis. Where studies involved multiple intervention
172 groups involving different types of physical activity, data was extracted for each intervention
173 for separate analysis. Where multiple intervention arms reported the same type of activity (for
174 example two different aerobic activities) results were combined and compared against the
175 control in one analysis.

176

177 Risk of bias was independently assessed by two reviewers (DS and JK) using Cochrane
178 methodology [24] which assesses five domains of potential bias with each domain rated
179 either low, unclear or high risk of bias. Disagreements in risk of bias between the two
180 independent reviewers were resolved through discussion.

181

182 **4.4. Statistical analysis**

183

184 The overall treatment effect of physical activity on primary and secondary outcomes was
185 calculated using the difference between either the end of intervention values or change scores
186 for the intervention and comparator groups. Variance was calculated from the SD and SE of
187 end of intervention values or change scores, or from the confidence intervals (CI) where these
188 values were not available [25]. In crossover studies, the mean and SD, SE or CI of
189 intervention and control periods were extracted and analyzed separately [26]. Where
190 intervention endpoint data was unable to be obtained, the results were described narratively.

191

192 Meta-analysis was performed where outcomes were reported in at least two studies using
193 Revman (Version 5.3; Cochrane Collaboration). Outcome data was converted to the same
194 units prior to meta-analysis (kcal/day) and was reported as the mean difference (MD)[27]. A

195 random-effects model was used to produce a pooled estimate of the MD, and the fixed-effects
196 model was used to check for robustness and potential outliers. Inconsistencies between
197 studies were assessed using the I^2 statistic, where significant heterogeneity was defined as I^2
198 $\geq 50\%$.

199

200 Post hoc subgroup analyses were undertaken for primary and secondary outcomes that were
201 reported in at least two studies in each subgroup. Post hoc subgroup analyses included:
202 intervention types (aerobic and resistance training), exercise-alone versus combined diet-
203 exercise interventions, changes in total body mass (TBM) during the study period (increased;
204 decreased; stable; and not reported). These were categorised (decreased, versus stable, versus
205 increased) where a significant change in body composition was reported.

206

207 In studies including multiple, separate arms involving different exercise interventions, the
208 interventions were pooled together for the overall meta-analysis, with a weighted average of
209 the intervention arms and study variance calculated [28]. In the subgroup analyses exploring
210 the effect of different intervention types on RMR, the interventions were analysed separately
211 based on their respective intervention types

212

213 Significant outliers were determined by visual inspection as well as through a study-by-study
214 sensitivity analysis, where each study was sequentially omitted, and the remaining data re-
215 assessed. If a study contributed to over 30% heterogeneity (based on changes to the I^2
216 statistic) then it was removed from the analysis in the sensitivity analysis [27]. Funnel plots
217 were generated for outcomes where at least 10 studies were included in the meta-analysis
218 [29] and reporting bias detected by assessment of funnel plot asymmetry by visual inspection.

219 **5. RESULTS**

220

221 The literature search identified 1669 articles; the PRISMA Diagram in Figure 1 summarises
222 the results of the literature search. 22 studies were included in the qualitative analysis and 18
223 studies provided enough information to be included in the meta-analysis.

224

225 **5.1. Study characteristics**

226

227 The general characteristics of trials included in the systematic review are summarised in
228 Table 1. A total of 822 participants were captured in 22 studies; with most including less than
229 45 participants with the exception of Scharhag-Rosenberger et al. [30], Frey-Hewitt et al.
230 [31], Jennings et al. [32] and Gomersall et al. [33] which included 74, 85, 103 and 107
231 participants, respectively. One study by Hunter et al. [34] did not specify the exact number of
232 participants but reported the inclusion of at least 140 participants. The meta-analysis included
233 data from 392 participants and 270 controls. Most of the studies were a parallel study design
234 except for one cross-over study design [35]. The majority of studies were conducted in
235 overweight/obese populations that were predominantly sedentary [5, 31, 32, 34-44], two in
236 type-2 diabetic populations [32, 40], one in a population with metabolic syndrome [37],
237 several in predominantly normal-weight and/or healthy sedentary populations [17, 30, 33, 45-
238 48] and one in active, healthy populations [20]. All studies captured were in adult
239 populations, with several predominately focussing on females [5, 34, 36, 39, 42-44, 46, 48],
240 males [17, 20, 31, 38, 41, 47], a combination of both [30, 32, 33, 35, 40, 45] or gender was
241 not reported [37].

242

243 Several interventions were exercise only; with either a predominant focus on aerobic exercise
244 [17, 31, 40], resistance exercise [5, 30, 35, 38, 46, 48] or a combination of both exercise
245 modalities [32, 33]. Many studies used a combined dietary and exercise intervention; with
246 four studies using predominantly aerobic exercise [36, 37, 45, 47], two in resistance exercise
247 [20, 39] and five using a combination of both exercise modes [34, 41-44]. The shortest

248 intervention was 10 days [47]; while several studies were conducted over 2-6 weeks [20, 33,
249 39, 40, 43]. The majority of interventions were conducted over 12 weeks [17, 36, 37, 41, 42,
250 44-46] while several longer interventions spanned 20-24 weeks [5, 32, 35, 38] and the longest
251 study intervention was 12 months [31]. While some studies did not measure or report body
252 composition assessments [33, 37]; the majority of studies used Dual-Energy X-Ray
253 Absorptiometry (DEXA) [20, 34-36, 39, 40, 45, 48], anthropometry/skinfolds [30, 38, 43,
254 46], hydrostatic weighing, underwater weighing/air-displacement plethysmography [5, 17,
255 31, 41, 44, 47] or bio-electrical impedance (BIA) [32, 42].

256

257 **5.2. Meta-analysis**

258

259 Eighteen studies were able to be meta-analysed. Four studies were not included in the meta-
260 analysis as they only presented data in graphs or with no means/variance reported [37, 42],
261 did not contain specific participant numbers [34] or did not report outcome data in units that
262 were able to be reliably converted for meta-analysis [30].

263

264 Across the 18 intervention studies pooled into meta-analysis, exercise (aerobic and resistance
265 exercise combined) did not significantly increase RMR (MD: 74.16 kcal/day [95% CI: -
266 13.01, 161.33], $P=0.10$; Figure 2). There was high heterogeneity ($I^2 = 96\%$); with two
267 studies contributing as outliers [31, 36]. Neither study contributed over 30% toward the total
268 heterogeneity, with 7% (21) and 22% (26), respectively. However, removal of these two
269 studies from the analysis reduced the heterogeneity to 20%, and the overall finding became
270 significant (MD: 61.45 kcal/day [95% CI: 27.46, 95.44], $P=0.0004$).

271

272 Aerobic exercise did not significantly increase RMR compared to the control group (MD:
273 81.65 kcal/day [95% CI: -57.81, 221.10], $P = 0.25$, Figure 2), however there was high
274 heterogeneity ($I^2 = 98\%$) Resistance exercise significantly increased RMR compared to the

275 control group (MD: 96.17 kcal/day [95% CI: 45.17, 147.16], $P = 0.0002$; Figure 2) with
276 minimal statistical heterogeneity ($I^2 = 0\%$).

277

278 **5.3. Subgroup analyses**

279

280 Subgroup analysis comparing the effects of exercise-only interventions with combined
281 exercise and dietary interventions showed that both types of interventions led to
282 a similar effect, with neither exercise-only (MD: 46.79 kcal/day [95% CI: -9.52,103.09], $P =$
283 0.10, Figure 3) nor exercise and diet (MD: 74.16 kcal/day [95% CI: -13.01, 161.33], $P =$
284 0.12, Figure 3) subgroups having a significant effect on RMR.

285 Subgroup analysis comparing exercise intervention in individuals based on anthropometric
286 changes in TBM had a significant effect on RMR. Studies that reported a stable body mass
287 throughout the intervention period showed exercise increased RMR (MD: 66.17 kcal/day
288 [95% CI: 2.95, 129.38], $P = 0.04$, Figure 4). Studies that reported either an increase in body
289 mass or failed to report on body mass, showed RMR was not different as it was just outside
290 the $P < 0.05$ pre-determined criteria (MD: 70.61 kcal/day [95% CI: -3.58,144.81] , $P = 0.06$,
291 Figure IV and MD: 89.27 kcal/day [95% CI: -3.20,181.74], $P = 0.06$, Figure 4). There was no
292 effect of exercise on RMR in studies that reported a decreased body mass (MD:
293 84.59kcal/day [95% CI: -77.37, 246.54], $P = 0.31$, Figure 4).

294

295 **5.4. Comparison of study methods**

296

297 The methodologies that were used and reported for measuring RMR are summarised in
298 Supplementary File 2. Of the studies that reported RMR methodology; several studies
299 reported using a ventilated hood [17, 33, 40, 43-45, 47] and several used a mouthpiece with
300 one-way valve/nose clip [31, 39, 46, 48]. Most studies reported measuring RMR for 30 – 45
301 minutes [5, 17, 20, 30, 32-34, 36, 39, 41, 45, 46]; with some reporting shorter durations of 10

302 – 25 minutes [31, 40, 42-44, 48] while others did not report RMR measurement duration [35,
303 37, 38, 47]. Many studies did not report acclimation or familiarisation to the test protocol but
304 of the available data acclimation was undertaken between 15 - 30 minutes duration [5, 17, 31-
305 34, 39-44, 46] While many studies did not report a fasting duration prior to measurement of
306 RMR studies that provide detailed methods show participants were fasted 10 hours [41], 12
307 hours [17, 31-33, 39, 40, 43, 46] or overnight prior to commencing the test [20, 34, 48]. Some
308 studies reported time in recovery/rest following a previous exercise bout; either 12 hours [31,
309 33, 47], 24 hours [30, 42], 36 hours [5], 48 hours [17, 32, 48] or 72 hours [35] – however
310 most did not report the intensity or mode of the last exercise session. The RMR was typically
311 derived from measurements of resting oxygen uptake (VO_2), carbon dioxide production
312 (VCO_2) and RER (VCO_2/VO_2) using the Weir formula [49]. Some, but not all, studies
313 reported the test environment and conditions during which the measurement was undertaken
314 (e.g. thermo-neutral; low-light). RMR data was reported in a range of units e.g. mJ/d, kJ/d,
315 kJ/min and was generally reported as an absolute change.

316

317 The studies reported several methods of body composition assessment including Dual-Energy
318 X-Ray Absorptiometry [20, 35, 36, 39, 40, 45, 48], Hydrostatic weighing or Air-displacement
319 plethysmography [5, 17, 31, 41, 44, 47], Bio-electrical impedance [32, 42] or
320 skinfolds/anthropometry [30, 38, 43, 46]. Several studies reported TBM but did not report
321 FFM [30, 38, 43, 46] and several studies did not report TBM or FFM [33, 37, 47].

322

323 **5.5. Risk of Bias**

324

325 The risk of bias was unclear for many of the studies for random sequence generation,
326 allocation concealment, participant/personnel blinding and selective reporting
327 (Supplementary File 3). The risk of bias was low for blinding of outcome assessment,
328 moderate for incomplete outcome data and moderate-high for other bias.

329

330 22% of studies adequately reported random sequence generation to support a low risk of bias
331 assessment and allocation concealment [30, 32, 33, 35, 48]. For all studies, the risk of bias for
332 blinding of the participants to their condition was unclear and the risk of bias for blinding of
333 the outcome was low. For incomplete outcome data; 22% of studies had a high risk of bias
334 [34, 35, 38, 42, 43], 22% had an unclear risk of bias [5, 31, 36, 41, 45] and 55% had a low
335 risk of bias [17, 20, 30, 32, 33, 37, 39, 40, 44, 46-48]. For selective reporting, 9% had low
336 [30, 33], 86% had an unclear [5, 17, 20, 31, 32, 34-48]; while only one study had a high risk
337 of bias [36] . Only a single study was judged as high risk of bias for ‘other bias’ [34] because
338 it didn’t report on participant numbers, with 32% of studies judged as low risk of bias [30-33,
339 38, 40, 47], with the remainder judged to be unclear.

340 6. DISCUSSION

341

342 The primary findings from the review were 1) resistance exercise significantly increased
343 RMR in comparison to a control group as measured by indirect calorimetry, 2) aerobic
344 exercise and exercise-combined (i.e. resistance exercise and aerobic exercise) did not
345 significantly increase RMR in comparison to a control group, 3) a lack of comparable body
346 composition assessment data meant it was unclear how changes in body composition
347 interacted with changes in RMR and 4) while there were a large proportion of studies which
348 did not report key aspects of their methodology that would represent best practice and/or
349 there was inconsistency in methodology between studies, this meta-analysis only included
350 studies with a control group thus limiting the impact of their methodological differences on
351 the meta-analysis

352 The meta-analysis captured data from 392 participants and 270 controls (total 662
353 participants) and in large part addresses the inherent limitation of small-scale or single-arm

354 studies. This systematic review provides new information to show a resistance exercise
355 program has the capacity to increase RMR. A primary adaptation associated with resistance
356 training is upregulation of anabolic processes within skeletal muscle resulting in hypertrophy
357 and increased muscle cross sectional area [50]. It is generally well-accepted that increases in
358 fat-free/lean mass and total body mass may induce an increase in RMR due to greater volume
359 of metabolically active tissue, skeletal muscle remodelling and increasing the fat free-to-total
360 body mass ratio [51-53]. Moreover, fat-free mass has been shown to make a substantial
361 contribution (25– 70 %) to individual variations in RMR [10, 11]. While the findings of the
362 meta-analysis support such a contention, the sub-analyses did not support a clear association
363 between changes in body composition and RMR. Unfortunately, total body mass was not
364 reported on all occasions and while some studies used body composition assessment
365 measures that more accurately measure compartmental body mass (i.e. fat mass and fat-free
366 mass) others, such as DEXA, used derived or predicted values to determine reported
367 compartmental body mass. Moreover, there is an increasing awareness of the deficiencies in
368 the 2-compartment (FFM and FM) profile of body composition in explaining variance in
369 RMR and in RMR changes, and that the future may lie in an operational quantitative dynamic
370 organ-system RMR model [54].

371 While the data clearly show resistance exercise is effective for increasing RMR, a similar
372 outcome was not apparent for aerobic exercise. Interestingly, aerobic exercise has the
373 capacity to induce modest hypertrophy but the effect may be dependent on the mode and
374 intensity of aerobic exercise and the physical activity status of the participant [55]. In
375 addition, our meta-analysis showed the overall effect of aerobic and resistance exercise
376 combined on RMR was not significant. Therefore, we suggest the addition of higher quality,
377 methodologically sound studies are warranted to better determine the effects of different
378 exercise modalities on RMR. While no study contributed greater than 30% heterogeneity;
379 two clear outliers reported a significant increase in RMR following aerobic exercise

380 compared to a control group [31, 36]. As it was not explicitly stated - and the methodological
381 reporting was broad - it was not clear whether the studies adhered to best-practice protocols
382 for the measurement of RMR. Interestingly, when these studies were removed from the
383 analysis there was a significant, positive effect of combined exercise modalities on RMR.

384 A potential confounding factor within the literature that may influence this meta-analysis is
385 the effect of preceding exercise when study cohorts progress from sedentary to exercising
386 status. Specifically, baseline RMR testing may be undertaken without preceding exercise
387 while post-intervention testing may occur with limited recovery after the final exercise bout
388 which may artificially inflate the measurement of RMR. It is important that studies follow
389 best practice protocols which prescribe cessation from exercise or vigorous physical activity
390 for a standardized period prior to the measurement of RMR. Compher et al. [18] recommend
391 2 hours of abstention from moderate aerobic exercise (Grade II – fair) and 14 hours for
392 vigorous exercise (Grade III – limited) and Fullmer et al. [19] recommend 12-48 hours after
393 light to vigorous intensity physical activity. As many of the participants were untrained and
394 were potentially doing exercise that would generate post-exercise oxygen consumption
395 (EPOC) and due to the potential for micro-trauma and repair of muscle damage, it has also
396 been suggested that longer periods of abstinence up to 72 hours may be warranted [53]. Many
397 studies in the current meta-analysis did not report abstinence from physical activity prior to
398 the measurement of RMR. If exercise was performed in this time this could artificially inflate
399 the measurement and thus the authors could conclude an effect of the exercise intervention on
400 RMR; however as there was a methodologically-comparative control group in each study the
401 overall effect in this meta-analysis would not be impacted. In addition, while our inclusion
402 criteria allowed for interventions that both included or did not include dietary interventions,
403 and energy balance is one consideration that may influence RMR independent of training
404 [12], these were only included where the diet only intervention served as the control group.

405 The sub-analysis confirmed that the effect of exercise on RMR was similar between exercise-
406 only and combined dietary-exercise studies.

407 The methodology characteristics table (Supplementary File 2) highlighted several gaps in the
408 included study methodologies when compared to best practice guidelines. While many
409 studies reported a fasting period in-line with best-practice guidelines, other areas of
410 standardisation including familiarisation, time-of-day, room conditions, body position, the
411 control for stimulants or supplements and physiological conditions (illness, medications)
412 prior to measurement was minimal. Other key aspects of RMR methodology, including the
413 calculation of steady-state and calibration procedures were not routinely reported despite
414 being important aspects of evidence-based practice [18, 19]. The risk of bias was moderate-
415 high for some of the studies. While most studies did not report random sequence generation
416 or allocation concealment, this is difficult in small-scale studies that include an exercise
417 intervention.

418 This systematic review and meta-analysis clearly shows that resistance exercise
419 generates increases in resting metabolic rate while aerobic and combined resistance and
420 aerobic exercise fail to induce a robust effect on changes in RMR. While some limitations of
421 this systematic review have already been discussed, it should also be noted that number of
422 observations can impact statistical significance and there were less resistance exercise
423 studies. In addition, the overall effect had wide confidence intervals suggesting a high
424 variability in data. The systematic review included exercise interventions of any type and
425 duration, excluding single exercise bouts, and thus compared different study designs and
426 methodologies. For example, while there was a clear effect of resistance exercise on RMR,
427 differences in the type of resistance exercise and its' overarching aim (i.e. changes in power,
428 strength or muscular endurance) were beyond the scope of this review. As well, the effect of
429 exercise was most evident when total body mass remained stable during the intervention
430 period, but lack of comparable data means it was unclear how changes in body composition

431 interacted with changes in RMR. Despite this, a strength of this systematic review and meta-
432 analysis is that it addresses the inherent limitation of small-scale or single-arm studies as it
433 included a range of studies in comparison to control group. It is strongly recommended that
434 future studies to adhere to best-practice protocols in the measurement of RMR and body
435 composition assessment and to ensure that methodology is adequately reported to permit
436 replication and appropriate interpretation [18, 19].

437 **7. AUTHORSHIP CONTRIBUTION**

438 KMS, NB and VC contributed to the study design concept and protocol. KMS, DS and JK
439 contributed to the initial and updated literature search and screening, data extraction and risk
440 of bias. KMS drafted the manuscript with contribution from DS and JK. All authors
441 performed critical analysis and revision of manuscript and approved the final version.

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446 **9. CONFLICT OF INTEREST**

447 Authors K. MacKenzie-Shalders, J.T. Kelly, D, So, V.G, Coffey & N.M. Byrne declare they
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595 **Figure Legends**

596

597 Figure 1: Flow diagram of studies evaluated in the systematic review.

598

599 Figure 2: Forest plot of randomized controlled trials in adults comparing interventions
600 involving exercise and physical activity training with non-exercising control group
601 comparators. The overall effect of exercise and physical activity is presented (1.2.1).
602 Additionally, sub-group effects based on the specific type of exercise training are also
603 presented: aerobic (1.2.2) and resistance (1.2.3). Data are presented as means and SDs of
604 RMR at the end of intervention. Effects of trials are presented as kilocalorie per day and MD
605 (95% CI). CI, confidence interval; IV; inverse variance; MD, mean difference; RMR, resting
606 metabolic rate; SD, standard deviation.

607

608 Figure 3: Forest plot of randomized controlled trials in adults comparing interventions
609 involving exercise and physical activity training with non-exercising control group
610 comparators. Studies are sub-grouped by whether the exercise and physical activity training
611 was delivered alone (1.14.1) or in combination with dietary modifications (1.14.2). Data are
612 presented as means and SDs of RMR at the end of intervention. Effects of trials are presented
613 as kilocalorie per day and MD (95% CI). CI, confidence interval; IV; inverse variance; MD,
614 mean difference; RMR, resting metabolic rate; SD, standard deviation.

615

616 Figure 4: Forest plot of randomized controlled trials in adults comparing interventions
617 involving exercise and physical activity training with non-exercising control group
618 comparators. Studies are sub-grouped based on the mean reported changes in total body mass
619 of participants during the study period, categorised as: stable (1.6.1); increased (1.6.3);
620 decreased (1.6.4); and not reported (1.6.6). Effects of trials are presented as kilocalorie per
621 day and MD (95% CI). CI, confidence interval; IV; inverse variance; MD, mean difference;
622 RMR, resting metabolic rate; SD, standard deviation.

623