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1 **A systematic review and meta-analysis comparing cardiopulmonary exercise test values**
2 **obtained from the arm cycle and the leg cycle respectively in healthy adults**

3

4 **Key words:** aerobic capacity, exercise testing, oxygen uptake, leg cycle, arm cycle, ergometer,
5 systematic review, meta-analysis.

6 *Word Count: 2.738*

7 **Abstract (200 words)**

8 **Introduction:** The cardiopulmonary exercise test (CPET) assesses maximal oxygen uptake
9 (VO₂max) and is commonly performed on a leg cycle ergometer (LC). However, some individuals
10 will rather perform the CPET on an arm cycle ergometer (AC).

11 **Objective:** To compare VO₂max values obtained by the AC test and the LC test in healthy adults.

12 **Methods:** MEDLINE, EMBASE, CINAHL, and PEDro were searched in April 2015. Studies were
13 included if they reported within comparison VO₂max values obtained from CPET using AC and
14 LC in healthy adults. The differences in VO₂max (ACL_{C_{diff}}) were pooled across studies using
15 random effects meta-analysis and three different methods were used to estimate the ratio between
16 the values obtained from the tests (ACL_{C_{ratio}}).

17 **Results:** We included 41 studies with a total of 581 participants. The mean ACL_{C_{diff}} across studies
18 was 12.5 ml/kg/min and 0.89 l/min with a mean ACL_{C_{ratio}} of 0.70. The ACL_{C_{diff}} was lower in
19 studies with higher mean age and lower aerobic capacity.

20 **Conclusion:** There is linear association between the AC and LC values in healthy non-athletic
21 individuals. The AC obtained values were on average 70% of the LC values. The magnitude of this
22 difference appeared to be reduced in studies on older and less active populations.

23

24 **1. Introduction**

25 The cardiopulmonary exercise test (CPET) is the gold standard for the direct assessment of
26 maximal oxygen uptake (VO_{2max})¹⁻⁵. VO_{2max} determines the maximal ability for the human body to
27 deliver, obtain and consume oxygen during maximal exercise and is a measure of maximum aerobic
28 capacity⁴. Assessments of aerobic capacity are used by physicians and healthcare professionals to
29 evaluate exercise capacity⁵, exercise intolerance⁶ and functional aerobic impairment⁷, which all
30 provide important information on health status and prognosis in various populations^{2,8-11}.

31 CPET is commonly performed on a treadmill or on a leg cycle ergometer (LC)^{3,5}. However, due to
32 disability, co-morbidity, preference or athletic discipline there is a need to investigate alternatives to
33 LC¹². In some cases, it could be more important to assess arm fitness when leg exercise is not
34 feasible or possible¹³⁻¹⁵. A potential alternative is to perform the test with the upper body using an
35 arm cycle ergometer (AC)¹³. The AC test is however challenged as studies have shown that
36 untrained individuals will achieve a lower level of VO_{2max} on the AC, due to a reduced stress on the
37 cardiovascular system, compared to LC^{12,15,16}. Having a smaller amount of muscle mass being active
38 during the test, AC is likely to result in an earlier termination of the CPET due to peripheral factors
39 such as an earlier onset of lactate threshold, rather than central cardiovascular limitations^{12,17}.

40 Whilst individual studies have directly assessed the difference in VO_{2max} of a CPET conducted
41 using AC compared to LC in healthy adults, we know of no previous systematic review of these
42 studies.

43 The objectives of this study were to undertake a systematic review and meta-analysis of the VO_{2max}
44 achieved by AC compared to LC in healthy adults and to explore factors that may be predictive of
45 this difference. The determination of this factor would allow the direct comparison of data obtained
46 on the two tests.

47 **2. Methods**

48 This review was conducted and reported according to the Preferred Reporting Items for Systematic
49 Reviews and Meta-Analyses ([PRISMA](#)) guidelines¹⁸.

50

51 **2.1 Data sources and searches**

52 Preliminary searches were conducted and relevant search terms identified. A formal search of the
53 databases MEDLINE, EMBASE, CINAHL, and PEDro was undertaken in April 2015. References
54 of the identified studies in the preliminary searches were screened and relevant search terms were
55 added to the search strategy. The search strategy consisted of a combination of relevant keywords
56 and MeSH/Thesaurus terms for: 1) direct assessment of VO_{2max} , 2) a CPET performed on an AC
57 and 3) a CPET performed on an LC. No language or publication limits were applied. The reference
58 lists of identified studies were checked and we contacted the authors of unobtainable studies and
59 evaluated papers suggested by experts in the field. Search strategies specified for MEDLINE is
60 presented in appendix.

61 **2.3 Study selection**

62 Study selection was undertaken based on a priori defined criteria. Only original research papers
63 reporting within comparison maximum or peak VO_2 , as litres per minute (l/min) or as millilitre
64 oxygen per kilogram per minute (ml/min/kg), were considered eligible for inclusion in this
65 systematic review. The CPET had to be non-assisted on AC and LC. We included studies in groups
66 of healthy adults (age >18 years) with a reported level of physical activity < 300 minutes per week.
67 People with higher physical activity levels were considered athletes and where therefore excluded
68¹⁹.

69 Two authors (RTL, CK) independently screened titles and abstracts and assessed eligible articles in

70 full-text. Any inconsistencies between authors were discussed and disagreement was solved by
71 consultation of a third author (JC).

72 **2.4 Data extraction and risk of bias assessment**

73 The following information was extracted: sample size, gender distribution, mean age, mean height,
74 body mass index (BMI) together with the $VO_{2\max}$ values, peak respiratory exchange ratio (RER),
75 CPET starting Watt, and Watt increment for both the AC and LC test.

76 *The Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies*²⁰ was used to
77 assess the methodological quality of all included studies. Six items (6-10 and 13) were considered
78 not applicable for the studies included in this review and thus did not contribute to the quality rating
79 total score (SumQAT). Two authors (RTL and CK) independently extracted data and undertook the
80 quality assessment. Inconsistencies between reviewers were discussed and in cases of disagreement,
81 a third reviewer (JC) was consulted.

82

83 **2.5 Data analysis**

84 The mean $VO_{2\max}$ difference between AC and LC ($ACL_{C_{diff}}$) was calculated for each study. Given
85 the within subject nature of these comparisons we adjusted the standard deviation of this difference
86 for the within subject correlation using the method described in chapter 16.4.6.1 of the Cochrane
87 Handbook²¹. The level of statistical heterogeneity was assessed using the I^2 score. The $ACL_{C_{diff}}$,
88 for ml/kg/min and l/min, were pooled across studies using a conservative random effects meta-
89 analysis given the variation participant characteristics across included studies. Summary of the
90 characteristics of included studies are expressed as median values and interquartile range (IQR).

91

92 We used meta-regressions to perform sub-group analyses to clarify, which variables were affecting
93 the main analysis on the $ACL_{C_{diff}}$. The sub-groups included were: aerobic capacity (as a categorical

94 variable based the Aastrand classification -“low”, “fair”, “average”, “good” or “high”) ²²,
95 participant mean age (in years), participant gender (percentage of males), study risk of bias
96 (SumQAT), and the difference in peak RER values during test.
97 Three different approaches were used to find the ratio between AC and LC (ACL_{ratio}). First a
98 meta-analysis of the ACL_{ratio} was undertaken using the studies presenting the group mean \pm
99 standard deviation of the within comparison ratio (%). Second a linear regression model was
100 determined using the group mean values. The linear regression analysis was weighted by sample
101 size. Third the reported AC values were divided with the reported LC values, giving an estimate of
102 the ratio in each study, which are expressed as a total mean ratio.
103 All analyses were performed using Review Manager 5.3 (Cochrane collaboration) software and
104 Stata 14.0 software (StataCorp. 2013. *Stata Statistical Software: Release 14.9* College Station, TX:
105 StataCorp LP). A p-value ≤ 0.05 was considered statistically significant.

106

107

108 **3. Results**

109 **3.1 Study selection**

110 Our database searches identified 3,300 records. After removing 617 duplicates, 2,683 unique
111 studies remained. We excluded 2,510 studies by screening their title and abstract and 173 studies
112 were considered eligible for full text review. Of these, 131 did not meet the inclusion criteria. Thus,
113 41 studies (published between 1973 and 2014) were included in the review^{12,15,17,23-60}. Citations and
114 reasons for full text exclusion are listed in appendix. The study selection process is summarised as a
115 flow chart in [Figure 1](#).

116

117 **3.2 Description of studies**

118 A summary of the characteristics of the included studies is provided in [Table 1](#). The full
119 characteristics of included studies are listed in appendix.

120

121 **3.3 Risk of bias in included studies**

122 [Figure 2](#) presents a summary of the risk of bias in the included studies. The median SumQAT was 4
123 points, (IQR: 3 to 5). A detailed risk of bias of each study is listed in appendix.

124

125 *3.3.1 Research question and study population*

126 Although all included studies were judged to have a well-defined research question (item 1), 13
127 groups^{15,17,25,30,34-38,44,47,52,53} had insufficient description of the study population (item 2). One study
128⁴³ described the participation rate of eligible subjects (item 3) and 13^{15,24,26,29,32,33,35,36,41,43,46,55,57}
129 studies had a subject-recruitment within the same population (item 4). Four studies^{15,38,39,46}
130 included sample size justification (item 5).

131 *3.3.2 Outcome measures*

132 Five studies^{17,34,40,45,53} did not report the VO_{2max} as ml/kg/min but as l/min (item 11) and therefore
133 not adjusting their outcome for subject weight.

134 *3.3.3 Blinding and statistical analysis*

135 One study¹² blinded the outcome assessor (item 12) and 12 studies^{25,34,37,38,40,42,43,45,48,51,52,55} did not
136 provide report a description of their statistical analysis methods (item 14).

137 **3.4 Meta-analysis of VO_{2max} difference between AC and LC**

138 A total of 36 groups (413 participants) reported data on the ACLC_{diff} measured in ml/kg/min. The
139 meta-analysis for the ACLC_{diff} is shown in [Figure 3](#). The pooled mean VO_{2max} was 12.5 ml/kg/min,
140 (95% CI: 10.3 to 14.7, I² = 59.9%, p > 0.001) higher for LC than AC. A total of 37 comparisons
141 (415 participants) presented data of the ACLC_{diff} in l/min with pooled mean VO_{2max} of 0.89 l/min,
142 (95% CI: 0.78 to 1.00, I² = 30.5%, p=0.043) higher for LC than AC as shown in figure 4.

143 **3.5 Subgroup analyses**

144 In univariable meta-regression and multivariable meta-regression, lower participant mean age and
145 higher aerobic capacity were found to be significantly associated an increased ACLC_{diff}. The meta-
146 regressions are shown in Table 2.

147 **3.6 Analyses of the AC/LC ratio**

148 The mean ratio between the AC and LC for the 37 groups (n=413 participants) reporting VO_{2max} in
149 ml/kg/min was 0.70 (95% CI: 0.66 to 0.73) in favour of the LC. The corresponding value of the 37
150 groups (n=415 participants) reporting VO_{2max} in l/min, the mean ACLC_{ratio} was 0.71 (95% CI: 0.66
151 to 0.75). The meta-analysis (n=46 studies) for the ACLC_{ratio} across studies as 71%, (95% CI: 68 to
152 74, I² = 0%, p=0.530) ([Figure 5](#)). The coefficient for the linear regression between AC and LC
153 mean VO_{2max} was 0.65 ml/kg/min (95% CI: 0.48 to 0.81) with an r² of 0.689 (Figure 6).

154 **4. Discussion**

155 This systematic review and meta-analysis brings together data from 41 studies in 581 healthy
156 individuals directly comparing VO_{2max} values obtained from the AC compared to LC. We found the
157 LC to have substantively higher VO_{2max} value (mean difference: 12.5 ml/kg/min and 0.89 l/min)
158 than AC. But with an I^2 value of 59.9% for the $ACLCL_{diff}$ in ml/kg/min these results could be
159 affected by substantial heterogeneity. Our results support the belief that the AC test achieves lower
160 oxygen uptake values as it involves a smaller amount of muscle mass and places less stress on the
161 cardiovascular system^{12,15,16}.

162 Both age and the aerobic capacity appear to be associated with the $ACLCL_{diff}$. The
163 difference is decreased with increasing age and increased with better aerobic capacity. This was
164 somehow expected, due to the fact that aerobic capacity decreases with age²².

165 The RER represent the relationship between the volume of carbon dioxide and the
166 volume of oxygen in every breath and it is recommended to continue VO_{2max} tests until RER values
167 above 1.1 are reached in order to obtain a valid CPET²³. The majority of studies reporting RER
168 values reported values in both tests to be above 1.1^{23,24,26-29,32,36,38,46,60}. Only one study reported
169 RER values for the AC to be above 1.1 and RER values for the LC to be below 1.1²³, and three
170 studies reported RER for both test to be below 1.1^{33,39,49}. We expected the difference in the
171 obtained RER values to affect the $ACLCL_{diff}$. However, we did not find this relationship, which could
172 be due to by a lack of power, as only 24 and 16 studies are included in the meta-regressions. The
173 level of aerobic capacity is somehow affected by gender²². However, we did not find a correlation
174 between gender distribution and the $ACLCL_{diff}$. This makes our results applicable for future research
175 and clinical use in single gender groups as well as mixed gender groups.

176 The $ACLCL_{diff}$ does not seem to be affected by the risk of bias in the studies as low
177 quality studies are reporting the same $ACLCL_{diff}$ as high quality studies. This may be explained by

178 the precise and accurate equipment used in CPET⁶¹, and thereby the possibility of precise testing in
179 different settings, which increases the clinical applicability.

180 The most accurate estimate of the ratio is the meta-analysis of the reported ratios, but
181 only four studies^{33,39,46,54} reported mean \pm SD (%) values for the ratio between the tests. The meta-
182 analysis revealed a linear relationship between the AC values and LC values with an ACLC_{ratio} of
183 70%. This analysis should be seen as the main expression for the ratio between the values of the AC
184 and the LC, where no important heterogeneity were found⁶². Three different methods were used to
185 estimate the ACLC_{ratio} due to the number of studies reporting values to incorporate in the meta-
186 analysis for the ratio. The calculation and the linear regression of the ACLC_{ratio} should only be used
187 as a prediction, since they do not incorporate standard deviations. Despite different approaches to
188 estimate the ratio, the results are very similar and the ACLC_{ratio} of 70% is similar to the ones
189 described in the literature^{33,39,46,54}. To increase the power of this and investigate if the 70% is a
190 valid estimate for the population mean ACLC_{ratio}, future research should report within comparison
191 ratios between the AC and the LC, making them applicable for inclusion in meta-analysis.

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196 This is the first systematic review and meta-analysis of literature comparing arm and leg exercise,
197 and it is thus important to stress that our study has a number of limitations. First, some studies did
198 not report ACL_{diff} standard deviation which meant we had to impute the value based on an
199 assumed within participant correlation coefficient (r-value) between AC and LC VO_{2max} . This
200 method is recommended by the Cochrane Handbook²¹ but we acknowledge that it may influence
201 the accuracy of our findings. The only way to avoid these limitations in a meta-analysis is for future
202 research to report the correlation coefficients between the two tests. However, we undertook
203 sensitivity analyses to assess the impact of this estimation on our findings. A small number of
204 studies have reported a range of correlation coefficients between the AC test and the LC test (0.78,
205 0.94, 0.77, 0.32, 0.70)^{12,17,31,37,54}. The pooled ACL_{diff} was found to be 12.52 ml/kg/min (95% CI:
206 10.2 to 14.6) based on the lowest of these r-values (0.32) and 12.6 ml/kg/min (95% CI: 10.6 to
207 14.7) with the highest reported r-value (0.94). In other words, this imputation method made little or
208 no difference to the pooled results. Future studies need to report the standard deviation (or
209 equivalent) of the mean difference between AC and LC VO_{2max} or the within person correlation
210 coefficient.

211 Secondly, the quality of the included studies was variable. In this review, we sought to
212 assess study risk of bias using the QAT, tool as it can be applied to cross-sectional studies²⁰.
213 However, to make this tool relevant to this review we had to adapt it by dropping some of the
214 original QAT elements (items 6-10 and item 13)

215 Thirdly, this review was limited to non-athlete healthy adults and limits
216 generalizability of our findings. Non-athlete healthy adults are expected to have a larger aerobic
217 capacity when doing CPET using the legs compared to the arms due to everyday use and large
218 lower limb muscle mass²⁹. However, in athletic populations, particularly arm-trained populations,
219 the ACL_{diff} is expected to be smaller than shown in this review⁶³. To avoid systematic bias we

220 excluded 18 comparisons in individuals performing more than 300 minutes per week of physical
221 activity or involved in competitive exercise ¹⁹. The groups contained ‘well trained subjects’,
222 ‘triathletes’, ‘swimmers’, ‘cross-country skiers’ or ‘highly arm-trained’. However, we did not
223 exclude studies in sedentary individuals. Two of the studies included extremely sedentary or
224 sedentary subjects ^{39,47}. But having an ACLC_{ratio} of 76% and 64% these studies are not likely to
225 have had a systematic affect on our results. A sensitivity analysis was performed without the two
226 studies and showed only minor impact on the result. The pooled ACLC_{diff} was found to be 12.7
227 ml/kg/min (95% CI: 10.4 to 15.0). Future well conducted studies are needed that directly compare
228 AC and LC in other populations, especially in disease populations with limitations by lower limb
229 disability such as peripheral vascular disease or osteoarthritis.

230 **5. Conclusion**

231 This systematic review and meta-analysis showed that in studies on healthy non-athletic individuals
232 although there was a linear association between the VO_{2max} for AC and LC tests, the VO_{2max}
233 achieved by AC tests were on average 70% lower than compared to the LC. This magnitude of this
234 difference appeared to be reduced in studies with older and less active populations.

235

236

237 **6. Conflicts of interest**

238 All authors declare that they have no conflict of interest.

239

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378

3,300 of records identified through database searching 10th of April 2015
Medline (n=1138)
Embase (n=1512)
CINAHL (n=354)
Pedro (n=296)

No additional records identified through other sources

2683 of records after duplicates removed

617 of duplicates removed

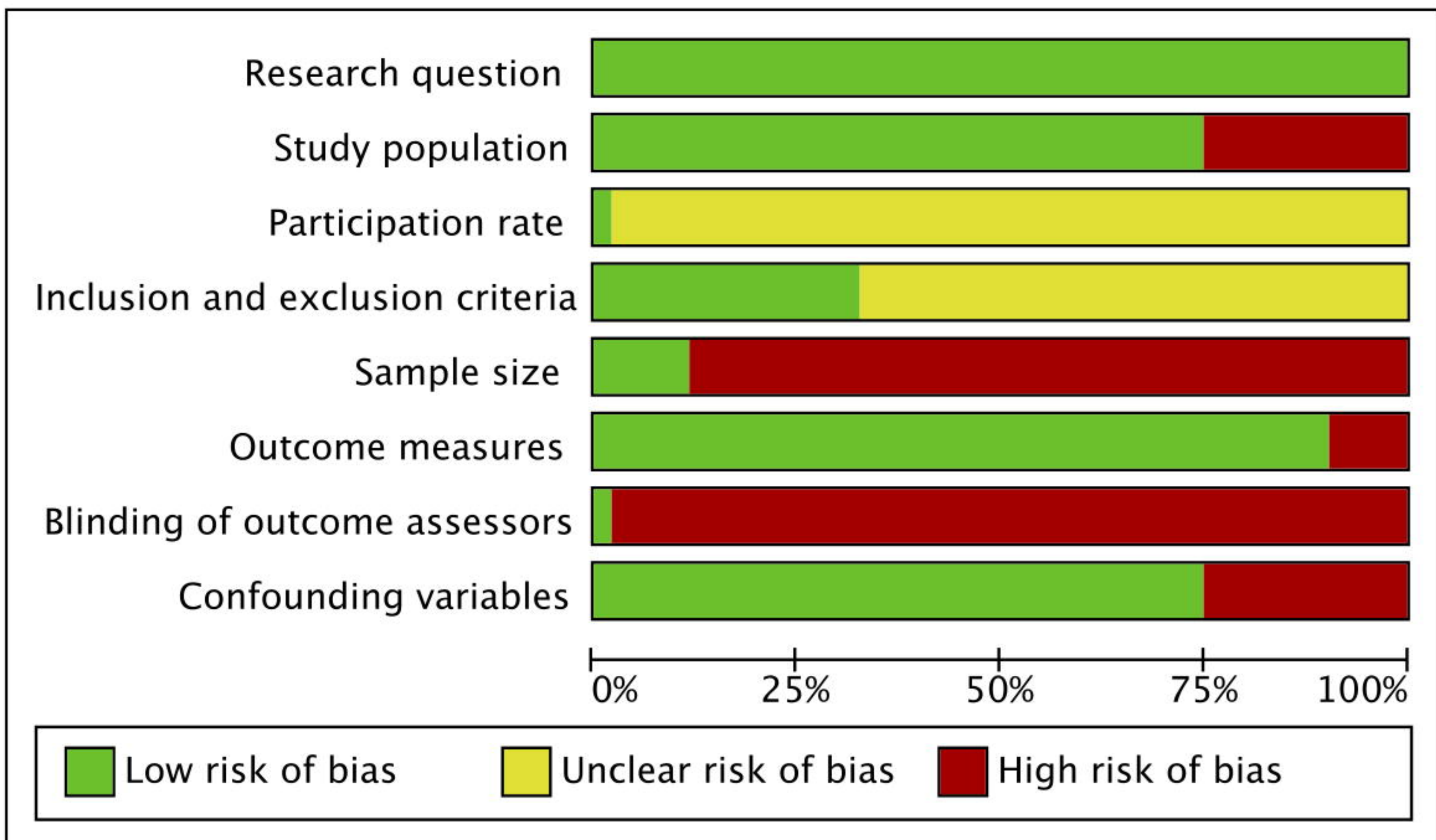
2683 of records screened

2510 of records excluded due to:
Lack of AC test (n=672)
Lack of LC test (n=476)
Lack of outcome (n=1362)

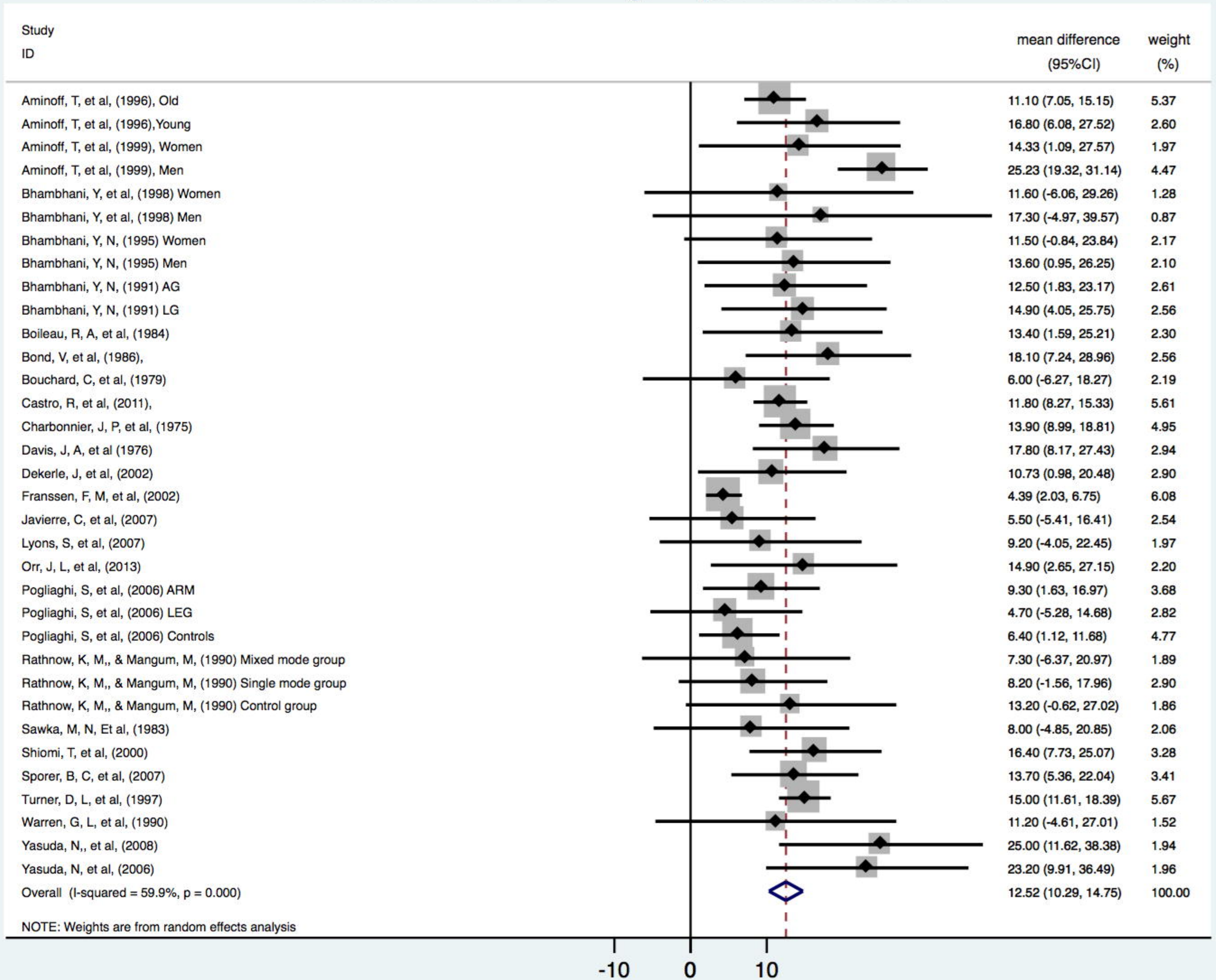
173 of full-text articles assessed for eligibility

131 of full-text articles excluded due to:
Study design (n=9)
Age (n=18)
Lack of AC test (n=40)
Lack of LC test (n=6)
Lack of outcome (n=13)
No within comparison data (n=1)
Assisted testing (n=1)
Athlete population (n=18)
Patient population (n=14)
Unobtainable study (n=9)
Lack of data (n=1)

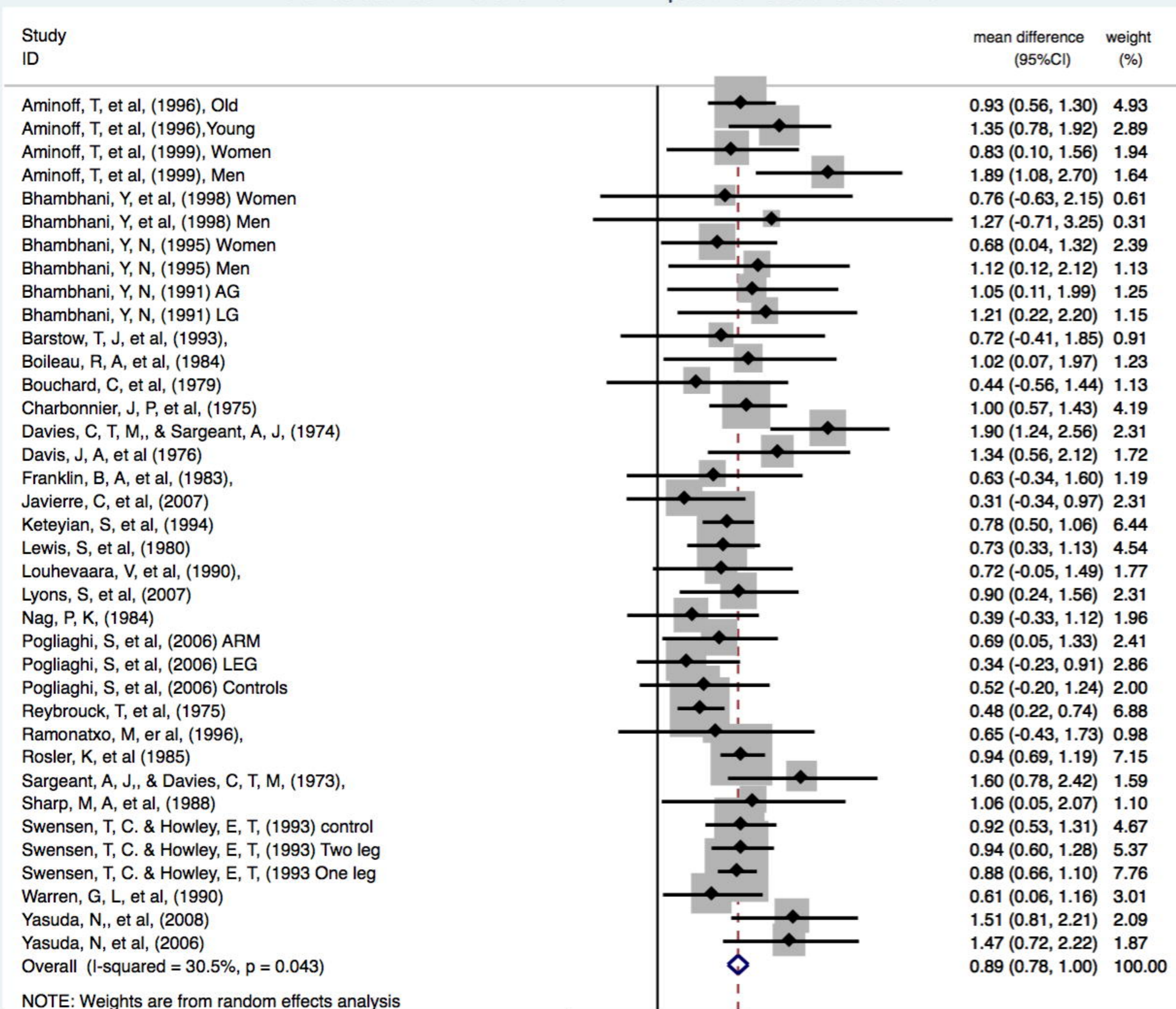
41 of studies included in the systematic review and meta-analysis



Difference between AC and LC in ml/kg/min - positive values favours LC



Difference between AC and LC in l/min - positive values favours LC



NOTE: Weights are from random effects analysis

Ratio (%) between AC and LC - values < 100% favours LC

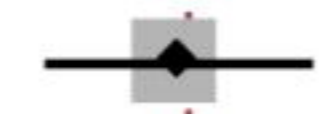
Study

ID

mean ratio (%)
(95%CI)

weight
(%)

Charbonnier, J, P, et al, (1975)



70.10 (58.54, 81.66)

8.11

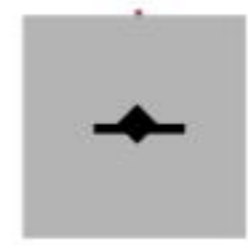
Javierre, C, et al, (2007)



75.20 (49.72, 100.68)

1.67

Pogliaghi, S, et al, (2006) ARM



71.00 (67.08, 74.92)

70.60

Pogliaghi, S, et al, (2006) LEG



83.00 (67.91, 98.09)

4.76

Pogliaghi, S, et al, (2006) Controls



72.00 (56.32, 87.68)

4.41

Shiomi, T, et al, (2000)



64.50 (54.31, 74.69)

10.44

Overall (I-squared = 0.0%, p = 0.530)



70.93 (67.64, 74.23)

100.00

NOTE: Weights are from random effects analysis

-101

0

101

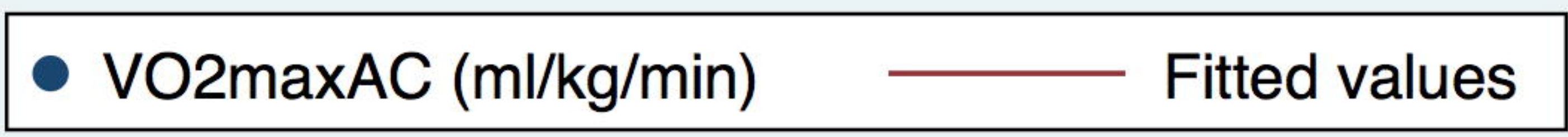
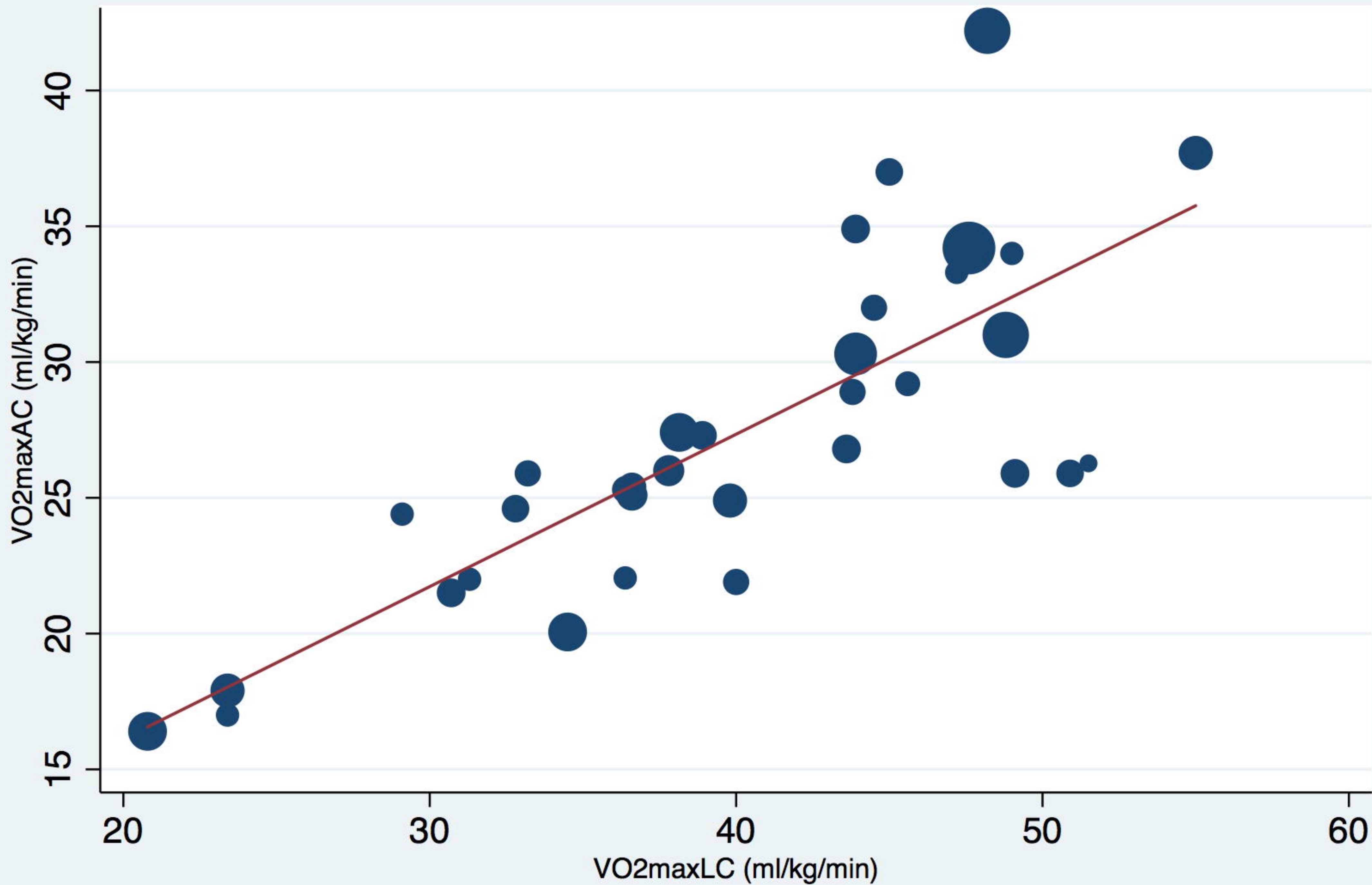


Table 1 - Study Characteristics of the 53 groups from the 41 included studies

Continent of publication	(%)
North America	56.6 %
Europe	35.8 %
South America	3.8 %
Asia	3.8 %
Study Design	
RCT	17.0 %
Non-RCT	3.8 %
Cross-sectional	79.2 %
Study risk of bias	Median (IQR)
SumQAT	4 points (3 to 5)
Participant characteristics	
Gender	(%)
Male only	66 %
Female only	15.1 %
Mixed	15.1 %
Not reported	3.8 %
	Median (IQR)
Mean age years	28.4 years (25 to 32.3)
Mean BMI, kg/m ²	23.65 kg/m ² (22.7 to 25)
Aerobic capacity	(%)
Low	3.8 %
Average	28.7 %
Good	5.6 %
High	3.8 %
Did not report	58.1 %
Test characteristics	
Order on AC/LC test	(%)
AC first	3.8 %
LC first	18.9 %
Random order	45.3 %
Not reported	32 %
	Median (IQR)
Time between tests (hours)	72 (24 to 168)
AC start level (watts)	25 (15 to 40)
LC start levels (watts)	50 (30 to 50)
AC increase/min (watt)	10.7 (5 to 17)
LC increase/min (watt)	30 (20.7 to 30)
IQR: Interquartile range, SumQAT: sum of quality assessment tool score, AC: Arm cycle, LC: Leg cycle	

Table 2 – Meta-regression analyses performed on each variable (univariable) and adjusted for all variables (multivariable)

Univariable meta-regression on ACL_{diff}	Groups included in analysis	Mean coefficient (95% CI)	p-value
Aerobic capacity	27	4.1 (95% CI: 1.5 to 6.6)	p=0.003
Gender distribution (% male)	33	-1.25 (95% CI: -7.4 to 4.9)	p=0.684
Mean age	29	-2.1 (95% CI: -0.3 to -0.1)	p<0.001
Mean difference in peak RER values	24	-12.1 (95% CI: -68.8 to 44.6)	p=0.663
Risk of bias (SumQAT score)	34	-0.19 (95% CI: -2.6 to 2.2)	p=0.875
Multivariable meta-regression on ACL_{diff}			
Aerobic capacity	16	4.0 (95% CI: 0.81 to 7.2)	p=0.019
Gender distribution (% male)	16	4.5 (95% CI: -4.1 to 13.2)	p=0.268
Mean age (years)	16	-0.25 (95% CI: -0.4 to -0.06)	p=0.014
Mean difference in peak RER values	16	7.9 (95% CI: -59.0 to 74.8)	p=0.797
Risk of bias (SumQAT score)	16	0.9 (95% CI: -3.8 to 5.6)	p=0.682
ACL_{diff} : difference between obtained AC VO_{2max} and obtained LC VO_{2max} , 95% CI: 95% confidence intervals, RER: respiratory exchange ratio, SumQAT: sum of quality assessment tool score			