

1 **Tart cherry supplementation and recovery from strenuous exercise: a systematic review and**
2 **meta-analysis**

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10 **ABSTRACT**

11 The aim of this study was to determine the efficacy of tart cherry supplementation on recovery
12 following strenuous exercise. A systematic review and meta-analysis was conducted using studies
13 investigating tart cherry supplementation on measures of muscle soreness, muscular strength,
14 muscular power, creatine kinase (CK), C reactive protein (CRP), Interleukin-6 (IL-6) and tumour
15 necrosis factor alpha (TNF α). A literature search ending in July 2020 was conducted in 3 databases
16 (SPORTDiscus, Web of Science and Pubmed). Data from 14 studies was extracted and pooled for
17 analysis. Tart cherry supplementation had a small beneficial effect in reducing muscle soreness (ES
18 = -0.44, 95% CI [-0.87, -0.02]). A moderate beneficial effect was observed for recovery of muscular
19 strength (ES = -0.78, 95% CI [-1.11, -0.46]). A moderate effect was observed for muscular power
20 (ES = -0.53, 95% CI [-0.77, -0.29]), a further subgroup analysis on this variable indicated a large
21 effect of tart cherry supplementation on recovery of jump height (ES = -0.82, 95% CI [-1.18, -0.45])
22 and a small significant effect of supplementation on sprint time (ES = -0.32, 95% CI [-0.60, -0.04]).
23 A small effect was observed for both CRP (ES = -0.46, 95% CI [-0.93, -0.00]) and IL-6 (ES = -0.35,
24 95% CI [-0.68, -0.02]). No significant effects were observed for CK, and TNF α . These results indicate
25 that the consumption of a tart cherry supplement can aid aspects of recovery from strenuous
26 exercise.

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28 **Key Words:** Muscle damage, prunus cerasus, Montmorency cherry, muscle function,
29 inflammation, functional foods

30

31 INTRODUCTION

32 The use of tart cherry (TC) products to aid recovery from strenuous exercise is becoming increasingly
33 popular. Consumption of tart cherries is thought to enhance recovery and attenuate symptoms of
34 exercise induced muscle damage (EIMD), this is likely due to the potent antioxidant and anti-
35 inflammatory properties of the cherry (Connolly et al., 2006; Bowtell et al., 2010; Bongiovanni et al,
36 2020).

37

38 Strenuous exercise can cause structural damage to the muscle fibre, leading to an inflammatory
39 response that is characterised by the infiltration of neutrophils and macrophages to the affected area
40 (Clarkson and Sayers, 1999). The activity of these immune cells results in the production of reactive
41 oxygen and nitrogen species (RONS) which can lead to oxidative stress. Oxidative stress is
42 considered an imbalance between the natural antioxidant defence systems of the body and the
43 production of RONS (Betteridge, 2000), if the defence systems become overwhelmed there may be
44 an exacerbation in the damage to the muscle fibres (Halliwell & Chirico, 1993; Lowe et al., 1995;
45 Toumi & Best, 2003; Aoi et al., 2004). Montmorency tart cherries contain high levels of flavonoids
46 and anthocyanins, the anti-inflammatory and antioxidant properties of these phytonutrients are
47 purported to reduce inflammation and RONS production via inhibition of the cyclooxygenase (COX-
48 1 and COX-2) pathways (Marzocchella et al., 2011). Due to this the consumption of TC products is
49 thought to attenuate the inflammatory response and accelerate recovery from muscle damage,
50 however it is important to note that these observations have been in vitro or animal models, this has
51 been reviewed in detail by Marzochella et al (2011).

52

53

54 Research investigating the efficacy of TC products as a recovery strategy has been positive, with a
55 number of studies supporting its use (Connolly et al., 2006; Howatson et al., 2010; Bowtell et al.,
56 2011; Bell et al., 2014a), and a few studies finding no benefit (Beals et al., 2016; McCormick et al.,
57 2016). However, there is wide variation in the responses of the dependent variables that have been
58 measured throughout the research. For example, Connolly et al. (2006) observed reduced delayed

59 onset muscle soreness (DOMS) with the consumption of TC juice following an eccentric exercise
60 protocol involving maximal contractions of the elbow flexors, yet Beals et al. (2017) observed no
61 difference between groups following maximal eccentric contractions of the quadriceps.
62 Inconsistencies in findings could be related to differences in exercise modalities, exercise familiarity,
63 duration and type of supplementation, with some studies supplementing with a juice (Howatson et
64 al., 2008; Quinlan and Hill 2019) and others supplementing with a powder (Levers et al., 2015) or
65 tablet (Kastello et al., 2014).

66

67 Exercise modality is likely a factor influencing the effectiveness of TC supplementation, as the
68 underlying cause of symptoms associated with exercise induced muscle damage will vary depending
69 on exercise stimulus (Levers et al., 2015; Vitale et al., 2017). The majority of research on TC
70 supplementation following endurance activity supports the use of TC products to attenuate
71 inflammation (Howatson et al., 2010; Bell et al., 2014a; Levers et al., 2016) and oxidative stress
72 (Howatson et al., 2010; Bell et al., 2014a). However, there are inconsistencies in the response of
73 some markers across studies, for example, three studies observed a decrease in the inflammatory
74 marker CRP (Bell et al., 2014a; Bell et al 2014b; Howatson et al., 2008) and two observed no
75 differences (Bell et al., 2016; Quinlan and Hill., 2019). This makes it difficult to draw conclusions on
76 the effectiveness of TC as a strategy to reduce EIMD.

77

78 The efficacy of TC supplementation in improving recovery following exercise inducing only
79 mechanical stress i.e. resistance exercise, is conflicting with studies supporting the use of TC
80 supplementation (Connolly et al., 2006; Kastello et al., 2014) and others showing no benefit (Beals
81 et al., 2016; Lamb et al., 2019). As such, a systematic review and meta-analysis of the research
82 findings will clarify the efficacy of TC supplementation as a recovery strategy and help to identify the
83 variables most affected by supplementation. Therefore, the aim of this investigation was to conduct
84 a systematic review and meta-analysis on the efficacy of TC supplementation in recovery following
85 exercise.

86

87 MATERIALS AND METHODS

88 *Literature Search*

89 A systematic review and meta-analysis was conducted using guidelines outlined in the Preferred
90 Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Liberati et al.,
91 2009). An electronic search of the literature ending in July 2020 was conducted in PubMed,
92 SPORTDiscuss and Web of Science using combinations of the following search terms; cherry OR
93 Montmorency cherry OR sour cherry OR Prunus cerasus OR Anthocyanin AND recovery OR athlete
94 OR inflammation OR oxidative stress OR muscle damage OR muscle soreness OR muscle function
95 OR jump OR sprint OR strength OR exercise OR interleukin 6 OR C reactive protein OR tumor
96 necrosis factor alpha OR creatine kinase OR reactive oxygen species OR reactive nitrogen species.
97 The reference lists of all included studies were also examined to identify any further articles. A three-
98 stage search strategy was independently undertaken by two members of the review team
99 (Title/Abstract Screen; Full Text Screen/Full Text Appraisal) and results were filtered using the
100 population, intervention, comparator, outcomes and study design (PICOS) criteria described in Table
101 1.

102 *****Insert table 1 here*****

103

104 *Outcome Variables*

105 The literature was examined for the effects of cherry supplementation on indices of recovery
106 following exercise that induced muscle damage. The following outcome variables were selected as
107 they reflect the most commonly assessed indices in the EIMD literature: muscular soreness,
108 muscular strength, muscular power, creatine kinase (CK), C reactive protein (CRP), interleukin-6 (IL-
109 6) and tumor necrosis factor alpha (TNF α).

110

111 Measurements of muscle soreness were obtained from visual analogue or Likert scales.
112 Measurements of muscular strength were obtained from measurements of maximum isometric,

113 isokinetic or isotonic contraction of the muscle. Measurements of muscular power included any
114 activity that measured the power of the muscle; for example the counter movement jump (CMJ) or a
115 sprint. Measurements of CK, CRP, IL-6 and TNF α were obtained from capillary or venous sampling.

116

117

118 *Inclusion and Exclusion Criteria*

119 Studies were included if they met the following criteria; (1) participants were randomised into a cherry
120 supplement or a placebo group; (2) if at least one outcome variable was measured at baseline and
121 again at 1 and/or 24 and/or 48 and/or 72 h after exercise; (3) the study population could be male or
122 female, of any fitness level or training background; (4) the supplement could be administered before
123 or after the exercise session. Studies were excluded if: (1) the experimental group received multiple
124 treatments; (2) the control group undertook any practice which could have affected recovery; (3)
125 there was insufficient data, or studies did not yield change score data; (4) a crossover design was
126 used but not with a contralateral limb, this is due to the contralateral repeated bout effect (Howatson
127 and van Someren, 2007).

128

129 *Extraction of Data*

130 Mean, SD and sample size data were extracted from all included studies and used to calculate
131 change from baseline scores. Where SD change scores were not reported, values were calculated
132 using a correlation coefficient. When it was not possible to calculate change scores for SD imputed
133 SD was calculated in accordance with current guidelines (Higgins and Green, 2011). Where
134 necessary mean and SD data were extracted from figures using software ImageJ (NIH, USA). Risk
135 of bias (Figure 1a and 1b) was assessed following guidelines outlined by the Cochrane Collaboration
136 (Higgins and Altman, 2008). The risk of bias assessment was carried out by two authors (JH and
137 GH) and any discrepancies were reviewed by a third author (KK). Data were extracted and compared
138 by two authors (JH and GH), where there were differences data was reviewed by a third author (KK).

139

140 **** Insert Figure 1a and Figure 1b here ****

141

142 *Statistical Analysis*

143 Analysis on the overall effect of tart cherry supplementation was carried out using Review Manager
144 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, 2011). Data were
145 analysed using a random-effect model. Standardised mean effect sizes (ES) and 95% confidence
146 intervals (CI's) were reported as (ES [LCL, UCL]), with LCL and UCL representing lower and upper
147 95% confidence limits respectively. Where sufficient datapoints allowed, a subgroup analysis was
148 conducted. For measurement of muscular power, subgroup analysis was carried out on method of
149 assessing power. Studies were categorised based upon whether they assessed a measure of jump
150 height or a sprint. For DOMS, strength, CK and CRP subgroup analysis was conducted on type of
151 damaging protocol used. Studies were categorised as either mechanical or metabolic. Where
152 mechanical included studies utilising repetitive effort maximal contractions or maximal effort sprints
153 and metabolic included studies requiring prolonged engagement of the aerobic system such as a
154 marathon run or the Loughborough intermittent shuttle test (LIST). The classification for each study
155 (mechanical or metabolic) is indicated in table 2. The threshold values for effect sizes were set at:
156 ≤ 0.2 (trivial), > 0.2 (small), > 0.5 (moderate) and > 0.8 (large) (Batterham and Hopkins, 2006).
157 Heterogeneity was assessed using an I^2 statistic indicating the percentage of variability across the
158 studies that is due to heterogeneity (Higgins and Green et al., 2008). The significance level was set
159 as $P \leq 0.05$.

160

161 **RESULTS**

162 Database searches identified a total of 6608 records. The majority of these records were not relevant
163 to this analysis, with many studies relating to other aspects of health, disease and nutrition and thus
164 were excluded. Nineteen studies remained for assessment of eligibility. Five studies were further

165 excluded due to: outcome variables not consistent with the inclusion criteria; variables measured at
166 time points not consistent with the inclusion criteria; missing data; or if people were exposed to
167 another treatment in addition to cherry supplementation which may have influenced the results (see
168 Figure 2). Following this process 14 studies remained for inclusion in this meta-analysis (see Table
169 2).

170

171 **** Insert Figure 2 here ****

172 **** Insert Table 2 here ****

173 A total number of 303 male and female participants were included in the dataset with a mean and
174 SD age of 26.8 (5.8) years. The training status of the participants was varied ranging from untrained
175 to well-trained athletes in a range of sports. The risk of bias assessment is demonstrated in Figure
176 1. Adequate sequence generation and allocation concealment was unclear for the majority of the
177 included studies, with five of the fourteen studies reporting how participants were allocated to groups
178 and just one study reporting adequate allocation concealment. Adequate blinding occurred in all
179 included studies with the use of a placebo treatment, in addition outcome data appeared to be
180 addressed in all included studies. Selective outcome reporting was rated high for two studies as
181 outcome data was not fully reported or omitted completely. Six of the included studies were
182 considered at risk of other bias and so were rated high. Of these studies four implemented either a
183 low phenolic diet or a dietary wash out period and three studies used a cross over study design.

184

185 A total of 52 data points were extracted from original research papers and included in the analysis
186 for DOMS (see Figure 3). A significant difference between groups in favour of cherry
187 supplementation was evident ($P < 0.05$, $Z = 2.06$). Supplementation with cherry products appears to
188 have a small beneficial effect in attenuating soreness following strenuous exercise (ES = -0.44, 95%
189 CI [-0.87, -0.02]). The I^2 statistic indicated high heterogeneity in the results (90%, $\text{Chi}^2 = 530.19$)
190 (Higgins and Green, 2008). A subgroup analysis of exercise type revealed no meaningful reduction
191 in heterogeneity, with I^2 values of 90% ($\text{Chi}^2 = 255.90$) and 89% ($\text{Chi}^2 = 273.89$) for the metabolic

192 and mechanical groups, respectively. However, the subgroup analysis revealed that TC
193 supplementation had a significant effect on attenuation of soreness in the mechanical group ($P < 0.05$)
194 but not the metabolic group ($P > 0.05$).

195

196 Analysis of 39 data points from 11 studies were included in the analysis for muscle strength (Figure
197 4). Analysis indicated a significant and moderate effect with the use of TC supplementation on the
198 recovery of muscle strength ($P < 0.001$, $Z = 4.76$, $ES = -0.78$, 95% CI [-1.11, -0.46]). A large amount
199 of heterogeneity was observed across the studies ($I^2 = 80\%$, $Chi^2 = 186.10$) (Higgins and Green,
200 2008). Further subgroup analysis indicated heterogeneity was reduced to 59% ($Chi^2 = 26.65$) in the
201 metabolic exercise group indicating minor heterogeneity in this group, however remained high in the
202 mechanical exercise group (84%, $Chi^2 = 186.10$).

203

204 **** Insert Figure 3 here ****

205

206 **** Insert Figure 4 here ****

207

208 Twenty three data points were used in the analysis for power. When considering the overall results
209 for power recovery, TC supplementation had a significant and moderate benefit ($P < 0.001$, $Z = 4.39$,
210 $ES = -0.53$, 95% CI [-0.77, -0.29]) (Figure 5). A small amount of heterogeneity was observed across
211 the studies ($I^2 = 29\%$, $Chi^2 = 31.17$) (Higgins and Green, 2008). A subgroup analysis carried out on
212 the type of measure for power revealed that supplementation with TC has a significant and large
213 effect on recovery of jump height ($P < 0.001$, $Z = 4.41$, $ES = -0.82$, 95% CI [-1.18, -0.45]), with small
214 heterogeneity ($I^2 = 28\%$, $Chi^2 = 12.53$). The analysis on sprint data revealed a small significant effect
215 of TC supplementation ($P = 0.02$, $Z = 2.26$, $ES = -0.32$, 95% CI [-0.60, 0.04]). Heterogeneity was
216 also low ($I^2 = 10\%$, $Chi^2 = 13.33$).

217

218 **** Insert Figure 5 here ****

219

220 Consumption of TC had no significant effect on concentrations of CK between groups ($P=0.26$, Z
221 $=0.26$) (Figure 6). Analysis was conducted on a sample of 32 datapoints revealing small
222 heterogeneity ($I^2 = 17\%$, $\text{Chi}^2 = 6.87$) (Higgins and Green, 2008). Subgroup analysis showed no
223 significant benefit of TC supplementation on CK for metabolically induced ($P=0.79$) or mechanically
224 induced ($P=0.10$) muscle damage.

225 An overall small and significant effect in favour of TC supplementation was observed on
226 concentrations of CRP, conducted on a sample of 20 data points ($P=0.05$, $Z = 1.96$, $\text{ES} = -0.46$, 95%
227 $\text{CI} [-0.93, -0.00]$) (Figure 7). Considerable heterogeneity was observed across the data points ($I^2 =$
228 78% , $\text{Chi}^2 = 87.59$) (Higgins and Green, 2008). Further subgroup analysis on exercise reduced the
229 heterogeneity to nothing in the metabolic group ($I^2 = 0\%$, $\text{Chi}^2 = 9.98$) and indicated a large positive
230 effect of consuming TC on concentrations of CRP following metabolically induced muscle damage
231 ($P<0.001$, $Z = 5.62$, $\text{ES} = -0.84$, 95% $\text{CI} [-1.13, -0.54]$). Contrasting this, the subgroup analysis
232 revealed no significant group differences for CRP following mechanically induced muscle damage
233 ($P = 0.79$).

234 Analysis for IL-6, carried out on 21 data points across 6 studies revealed a small significant benefit
235 of TC supplementation on concentrations of IL-6 ($P<0.05$, $Z = 2.08$, $\text{ES} = -0.35$, 95% $\text{CI} [-1.68, -$
236 $0.02]$) (Figure 8). Moderate heterogeneity was evident in the data set ($I^2 = 56\%$, $\text{Chi}^2 = 40.95$),
237 however no subgroup analysis was carried out as only one study induced muscle damage using a
238 protocol categorised as mechanical. No significant effects of TC supplementation were observed for
239 $\text{TNF}\alpha$ ($P=0.27$, $Z = 1.09$) (Figure 9). The heterogeneity across 19 datapoints was low ($I^2 = 0\%$)
240 (Higgins and Green, 2008). Subgroup analysis was not conducted as only one study induced muscle
241 damage using a protocol categorised as mechanical.

242

243 **** Insert Figure 6 here ****

244

245 **** Insert Figure 7 here ****

246

247 **** Insert Figure 8 here ****

248

249 **** Insert Figure 9 here ****

250

251 **DISCUSSION**

252 There is an increasing body of literature investigating the effectiveness of TC supplementation as a
253 recovery strategy; however, the variation in methodological design, study population and exercise
254 stimulus have resulted in inconsistent findings throughout the literature, with the exception of CK for
255 which no between group difference has consistently been observed. To the authors knowledge this
256 is the first study that has used a meta-analysis approach to evaluate the effectiveness of consuming
257 TC as a recovery strategy. This analysis suggests that supplementation with TC can attenuate losses
258 in strength and power, reduce the severity of DOMS and attenuate concentrations of CRP and IL-6.
259 No significant benefits were observed on concentrations of CK and TNF α following TC
260 supplementation.

261

262 Both metabolic and mechanical factors contribute to the aetiology of EIMD, the contribution of which
263 will vary depending on the type of exercise (Howatson and van Someren, 2008). Exercise modalities
264 with a large endurance component are predominantly fuelled from aerobic pathways and are
265 associated with high metabolic costs (Vitale et al., 2017; Bell et al., 2014a). Conversely, modalities
266 with large eccentric components are typically fuelled via anaerobic pathways and are associated
267 with higher mechanical stress (Levers et al., 2015; Bell et al., 2014a). Differences in relative
268 contribution from the different energy systems is likely to impact the type and magnitude of stress

269 caused by the exercise protocol (Bell et al., 2014a). Research has suggested that cherry
270 supplementation is suited to facilitating recovery from exercise with a large metabolic component
271 (Bell et al., 2014a). Due to this a subgroup analysis was carried out on exercise type, mechanical or
272 metabolic.

273

274 A significant and large effect was observed for muscle strength indicating that TC supplementation
275 was able to accelerate the recovery of muscle strength. The subgroup analysis on exercise type
276 indicated this observation was consistent between the metabolic and mechanical exercise groups.
277 Overall analysis for muscular power revealed a significant and moderate benefit. For this variable
278 sub-group analysis was carried out on method of assessment, jump height or sprint test. Subgroup
279 analysis revealed a significant and large beneficial effect of TC supplementation on jump height and
280 a significant but small beneficial effect on sprint speed. These differences in effect size between
281 subgroups could be due to the mechanics of the different movements, with the CMJ utilizing the
282 stretch shortening cycle and containing both an eccentric and concentric phase within the movement.
283 In addition, previous research has indicated a large learning effect with sprint trials (Bell et al.,
284 2014a). This study observed an improvement in sprint performance over time throughout the 72h
285 post trial period, this increase in performance was attributed to a learning effect and could explain a
286 smaller effect size for this measure.

287

288 Muscle damaging exercise leads to a decrease in the force generating capacity of the affected
289 muscle, this is attributed to myofibrillar disruption and damage to the muscle fibre architecture
290 (Clarkson and Hubal., 2002). Previous research has indicated that supplementation with TC can
291 protect against the declines in muscle function that are observed following strenuous exercise (Bell
292 et al., 2016). This has been proposed to occur as a result of a reduced acute inflammatory response
293 (Bell et al., 2016). This is supported by attenuated inflammatory markers observed in this meta-
294 analysis.

295

296 Supplementation with TC resulted in an overall significant but small effect on both CRP and IL-6 with
297 lower concentrations observed following TC consumption. Interestingly the subgroup analysis
298 carried out for CRP revealed TC supplementation had no significant effect on exercise protocols
299 categorised as mechanical and a large and significant effect on exercise categorised as metabolic.
300 Reduced concentrations of CRP have previously been attributed to a reduction in cell damage that
301 occurs as a result of oxidative stress (Bell et al., 2014a). Thus, it might be that TC supplementation
302 is more beneficial to exercise that is more metabolically challenging. It is also possible that prolonged
303 endurance exercise such as Marathon running could induce a systemic inflammatory response,
304 enhancing the ability of the TC supplement to have a greater blunting effect on the secondary muscle
305 damage response (Bell et al., 2014b). A possible explanation for the reduced inflammatory response
306 is that anthocyanins contained in the TC are able to inhibit the activity of prostaglandin enzymes,
307 which has been shown to mediate inflammation (Lanier, 2003). It should also be noted that the
308 exercise modalities classified as metabolic are not all free of mechanical damage. For example,
309 Marathon running has huge metabolic consequences but the repetitive eccentric contractions
310 occurring as part of the gait cycle will also induce mechanical damage. No benefit of
311 supplementation with TC was observed for TNF α . A subgroup analysis was not carried out for TNF α
312 and IL-6 due to the limited number of studies that measured these variables.

313

314 Data from this study indicate that the consumption of TC can attenuate the severity of DOMS, with
315 the observation of a small beneficial effect in favour of TC. The subgroup analysis revealed there
316 was no significant effect of TC supplementation on soreness following exercise that is metabolic in
317 nature, however there was a significant and moderate reduction in soreness following exercise that
318 is mechanical in nature. Soreness following damaging exercise has been attributed to increased
319 oxidative stress and inflammation (Beals et al., 2017), increased sensitivity of nociceptors and
320 mechanoreceptors to noxious chemicals, including prostaglandins, released during muscle damage
321 (Clarkson and Hubal., 2002) and microinjury to surrounding tissues that is exacerbated by immune
322 mediated inflammation (Sonkodi et al., 2020). It is possible that supplementation with TC can inhibit
323 the cyclooxygenase pathway, reducing the synthesis of prostaglandins (Marzocchella et al., 2011),

324 and dampening the secondary muscle damage response (Levers et al., 2015), this could result in
325 reduced muscle soreness. Damage to the connective tissue and structures within the muscle fibres
326 is likely to be greater following exercise that is mechanical in nature giving rise to a greater
327 inflammatory response, this may explain why TC supplementation has a greater effect following
328 exercise of a mechanical nature.

329

330 No significant effect of TC supplementation was observed compared to placebo for creatine kinase.
331 This is not surprising given that none of the 11 studies included in the analysis observed a significant
332 difference between groups for CK. High variability exists in the CK response between individuals
333 and in response to different types of exercise (Brancaccio et al., 2007). In addition to this training
334 status of the participants greatly affects the CK response to exercise. The variability in population,
335 training status and exercise modalities used within the studies included in this meta-analysis may
336 explain why no significant effects were observed. In addition to high inter-individual variability, there
337 is wide variability in the magnitude of change in CK across studies, for example Levers et al. (2016)
338 observed peak values of 870 IU/L in the TC group compared to Howatson et al. (2010) who observed
339 peak values of 2227 IU/L in the TC group. Due to this CK may not be a good marker for exercise
340 recovery but is a good indicator of the presence of EIMD.

341

342 Supplementation with TC is thought to attenuate RONS induced membrane damage therefore
343 limiting muscle damage and facilitating recovery. The results from this meta-analysis provide some
344 evidence to suggest that supplementation with TC can enhance certain aspects associated with
345 exercise recovery. A limitation of the present study is that oxidative stress was not included in the
346 analysis due to a lack of studies measuring the same markers of oxidative stress, therefore it is
347 difficult to get a mechanistic understanding of the effects of TC. In addition, whilst we tried to classify
348 exercise modalities based upon exercise type, mechanical or metabolic, many exercise modalities
349 often incur both mechanical and metabolic stress. This is important to note. Further research should

350 investigate exercise modalities that isolate metabolic or mechanical stress to better identify whether
351 TC supplementation is more effective under specific conditions.

352

353 Finally it is important to note that meta-analyses are limited by the data available and there are
354 several limitations in the literature; (1) the participants of several studies were of mixed gender, there
355 is no indication of how the menstrual cycle was controlled for in these studies; (2) the mode of
356 exercise and muscle groups involved varies greatly between studies, this is likely to induce different
357 levels of muscle damage via different mechanistic pathways, there was also variation in the training
358 status of the participants, this will affect the severity of the muscle damage experienced; (3) the type
359 of TC supplement and supplementation protocol varies between studies, with studies administering
360 various brands of juice (Howatson et al 2008; Bell et al., 2016; Quinlan and Hill 2019) and some
361 using a powder that is mixed with water (Levers 2015; Levers 2016; Beals et al., 2017). In addition
362 to this several studies implemented dietary restrictions asking participants to follow a low phenolic
363 diet. This could lead to an over estimation of the intervention effect and has been acknowledged in
364 the risk of bias assessment. Limitations 1-3 could all have had an influence on the variability of the
365 data and may explain why there was large heterogeneity in some of the variables. Finally(4)
366 Independent variables were only included in the meta-analysis if three studies had measured and
367 reported them. Whilst some studies have assessed markers of oxidative stress, there is not one
368 marker that has been assessed by three separate studies.

369

370 *Conclusion*

371 The results of this systematic review and meta-analysis indicate the supplementation with TC can
372 aid the recovery of muscle function and attenuate soreness following strenuous exercise. It is
373 possible that this occurs via a mediated inflammatory response as indicated by attenuations in the
374 concentration of CRP and IL-6. Further research is needed that investigates the effects of TC
375 supplementation on markers of oxidative stress, whilst taking into consideration the limitations of

376 these markers. Although the physiological mechanisms are yet to be fully understood, this meta-
377 analysis provides support for the use of TC to facilitate recovery following strenuous exercise.

378

379 **ACKNOWLEDGMENT, AUTHORSHIPS, DECLARATIONS**

380 All authors had a role in study design, data analysis and manuscript preparation. All authors have
381 approved the final version of the paper.

382 Authors confirm there are no conflicts of interest.

383

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530 **TABLES**

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532 **Table 1: Review Inclusion Criteria**

<u>Population:</u>	Healthy males and females with no restriction on age, activity level or training status.
<u>Intervention:</u>	Supplementation with a tart cherry product before, or before and after a single bout of exercise.
<u>Comparator:</u>	The effectiveness of supplementation with a tart cherry product on indices of recovery from exercise induced muscle damage in comparison to a control or placebo group.
<u>Outcomes:</u>	Measurements of muscular soreness, muscular strength, muscular power and blood biomarkers creatine kinase, C reactive protein, interleukin-6 and tumour necrosis factor alpha.
<u>Study Design:</u>	Randomised controlled trials, non-randomised controlled trials and cross over studies using a contralateral limb design.

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538 **Table 2.** Summary of literature included in the meta-analysis

Author(s)	Participant cohort (training status, gender, number)	Exercise intervention	Supplement type	Supplementation protocol	Outcome variables and measurement times (h)
Beals <i>et al.</i> (2017) †	Recreationally active <i>n</i> =19 male, <i>n</i> =10 female	Repetitive maximal effort isokinetic eccentric contractions of the quadriceps to fatigue	TC -30g TartVitaCherry freeze-dried powder with 0.5% anthocyanins mixed with unsweetened Black-Cherry Kool-Aide. PL -Sweetened black cherry mixed with 4 g of nutribiotic plain rice protein powder.	Two servings per day for 12 days. Four days prior, the day of and 7 days following the exercise protocol.	↔ DOMS (24, 48, 96, 168) ↔ Peak concentric torque (24, 48, 96, 168)
Bell <i>et al.</i> (2014a) ‡	Male trained cyclists <i>n</i> =16	High intensity stochastic cycling trial lasting 109 minutes completed on 3 consecutive days	TC - 30ml Cherry Active mixed with 100ml water. PL mixed berry cordial with 100ml water and maltodextrin	Two servings per day for 7 consecutive days. Four days pre and on each trial day.	↔ CK (0, 24, 48) ↓ IL-6 (0, 24, 48) ↓ C-RP (0, 24, 48) ↔ TNF α (0, 24, 48)
Bell <i>et al.</i> (2014b) ‡	Male trained cyclists <i>n</i> =16	High intensity stochastic cycling trial lasting 109 minutes.	TC - 30ml Cherry Active mixed with 100ml water. PL mixed berry cordial with 100ml water and maltodextrin	Two servings per day for 8 consecutive days. Four days pre, the day of and 3 days post trial.	↔ DOMS (24, 48, 72) ↔ 6s sprint cycle (24, 48, 72) ↑ MVIC (24, 48, 72) ↔ CK (0, 1, 24, 48, 72) ↓ IL-6 (0, 1, 24, 48, 72) ↓ C-RP (0, 1, 24, 48, 72) ↔ TNF α (0, 1, 24, 48, 72)
Bell <i>et al.</i> (2016) ‡	Male semi-professional soccer players <i>n</i> =16	Adapted Loughborough Intermittent Shuttle Test	TC - 30ml Cherry Active mixed with 100ml water.	Two servings per day for 7 consecutive days. Four	↓ DOMS (24, 48, 72) ↑ MVIC (24, 48, 72)

			PL mixed berry cordial with 100ml water and maltodextrin	days pre, the day of and 2 days post trial.	↑ CMJ (24, 48, 72) ↓ 20m sprint (24, 48, 72) ↔ CK (0, 1, 24, 48, 72) ↓ IL-6 (0, 1, 24, 48, 72) ↔ C-RP (0, 1, 24, 48, 72) ↔ TNF α (0, 1, 24, 48, 72)
Bowtell <i>et al.</i> (2011) †	Well trained male participants from intermittent team sports $n=10$	Ten sets of 10 knee extensions at 80% 1RM with an elongated eccentric phase lasting 3 seconds.	TC - 30 ml Cherry Active concentrate. PL - 30 ml Iso-energetic synthetically derived fruit concentrate	Two servings per day for 10 days. Seven days before, the day of and 2 days after.	↑ MVIC (1, 24, 48) ↔ CK (1, 24, 48) ↔ C-RP (1, 24, 48)
Brown <i>et al.</i> (2019) †	Female dancers from a University team $n=20$	Repeated sprint protocol consisting of 15x30 m maximal sprints with a rapid 10 m deceleration phase, each separated by 60 s rest.	TC - 30ml Cherry Active mixed with 100ml water. PL - 25ml of a synthetically derived fruit concentrate with negligible phytochemical content diluted with 100ml of water and fortified with maltodextrin and whey protein powder	Two servings per day for 8 days. Four days pre, the day of and 3 days post exercise.	↔ DOMS (0, 24, 48, 72) ↔ MVC (0, 24, 48, 72) ↑ CMJ (0, 24, 48, 72) ↔ 30m sprint (0, 24, 48, 72) ↔ CK (0, 1, 24, 48, 72) ↔ C-RP (0, 1, 24, 48, 72)
Connolly <i>et al.</i> (2006) †	Male College students $n=14$	40 (2 X 20) maximal eccentric contractions of the elbow flexors	TC - 12oz bottle of Cherrypharm. PL - unsweetend black cherry Kool-aid mixed with water.	Two servings per day for 8 days. Three days prior, the day of and 4 days post.	↓ DOMS (24, 48, 72, 96) ↔ Proximal tenderness (24, 48, 72, 96) ↑ MVIC (24, 48, 72, 96)

Howatson <i>et al.</i> (2008) ‡	Marathon runners <i>n</i> =13 male, <i>n</i> =7 female	A marathon run	TC - 12oz bottle of Cherrypharm. PL - fruit flavoured concentrate mixed with 8 fl oz water.	Two servings per day for 8 days. Five days before, the day of and 2 days post.	↔ DOMS (1, 24, 48) ↑ MVIC (1, 24, 48) ↔ CK (1, 24, 48) ↓ IL-6 (1, 24, 48) ↓ C-RP (1, 24, 48)
Kastello <i>et al.</i> (2014) †	Untrained participants <i>n</i> =10 male, <i>n</i> =4 female	Eccentric contractions of the bicep. Ten submaximal contractions followed by 5 sets of 10 maximal contractions	TC - A tablet consisting of Cherry Flex paste. PL - tablet consisting of cooking oil and red food colouring	One tablet twice a day for 16 days prior to and for 3 days following exercise	↓ DOMS (12, 24, 48, 72) ↔ Peak torque (12, 24, 48, 72) ↔ CK (12, 24, 48, 72) ↓ C-RP (12, 24, 48, 72)
Kuehl <i>et al.</i> (2010) ‡	Marathon runners <i>n</i> =36 male, <i>n</i> =18 female	Hood to Coast relay. Average total running distance of 26.3±2.5km	TC - 10.5oz bottle of Cherrish. PL - unsweetened fruit punch mixed with water	Two servings per day. Seven days prior to and the day of the race.	↓ DOMS (24)
Lamb <i>et al.</i> (2019) †	Non-resistance trained males <i>n</i> =24	Five sets of 10 unilateral eccentric elbow flexions	TC – 30 ml of Cherry Active diluted with 220ml water PL – 250ml of blackcurrant flavoured maltodextrin sports drink	Two servings per day.. Four days prior to the day of and 4 days post exercise.	↔ DOMS (1, 24, 48, 72, 96) ↔ MVIC (1, 24, 48, 72, 96) ↔ CK (1, 24, 48, 72, 96)
Levers <i>et al.</i> (2015) †	Resistance trained males <i>n</i> =23	Ten sets of 10 repetitions of a bar bell back squat at 70% 1RM with 3 min recovery between sets	TC - 480 mg Powdered tart cherry. PL - 480 mg rice flour mixed with water	One serving per day for 10 days. Seven days before, the day of and 2 days post exercise.	↓ DOMS (1, 24, 48) ↔ MVIC (1, 24, 48) ↔ CK (1, 24, 48) ↔ IL-6 (1, 24, 48)

					↔ TNFα (1, 24, 48)
Levers <i>et al.</i> (2016) ‡	Triathletes n=18 male	21.1km run under simulated race conditions	TC - 480 mg Powdered tart cherry. PL - 480 mg rice flour mixed with water	One serving per day for 10 days. Seven days before, the day of and 2 days post exercise.	↓ DOMS (1, 24, 48) ↔ CK (1, 24, 48) ↓ IL-6 (1, 24, 48) ↔ TNFα (1, 24, 48)
Quinlan <i>et al.</i> (2019) ‡	Team sport players n=8 male, n=12 female	Adapted LIST test	TC – 30ml of Montmorency tart cherry concentrate Holland and Barrett own brand mixed with 70ml water PL – 25ml of Robinsons summer fruit squash mixed with water	Two servings per day. Five days before the day of and 2 days post exercise.	↔ DOMS (1, 24, 48) ↑ MVIC (1, 24, 48) ↑ CMJ (1, 24, 48) ↓ 20m sprint (1, 24, 48) ↔ CK (1, 24, 48) ↔ C-RP (1, 24, 48)

539 CMJ, counter-movement jump; CK, creatine kinase; DOMS, delayed-onset muscle soreness; IL-6, interleukin-6; MVIC, maximum voluntary isometric contraction; PPT, pressure pain threshold; TNFα, tumor

540 necrosis factor alpha.

541 Increases or decreases represent improved performance or attenuations in a variable.

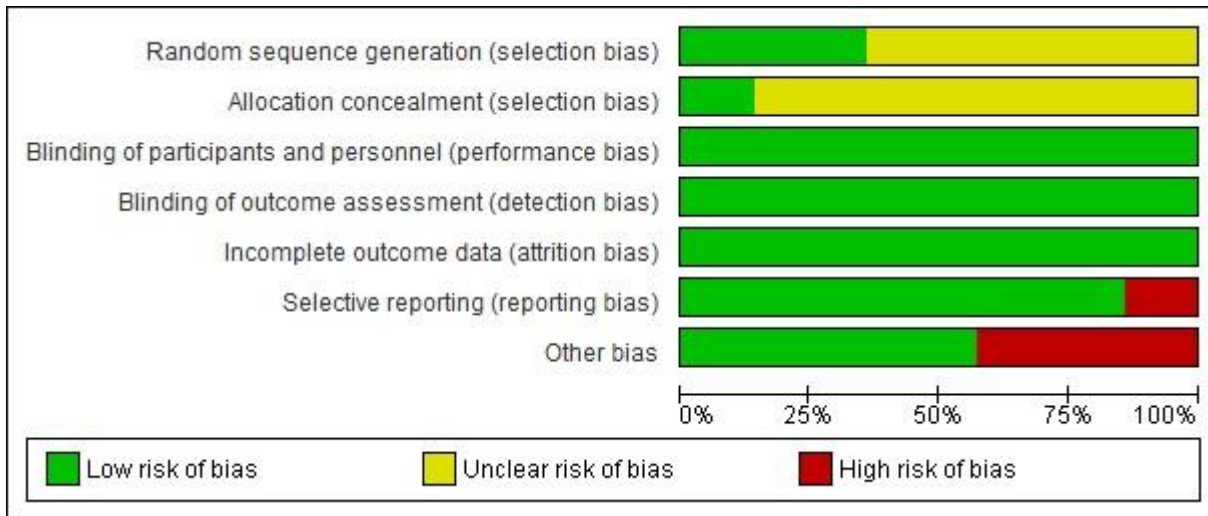
542 TC = tart cherry juice, PL = placebo

543 † denotes a study with an exercise protocol considered mechanical, ‡ denotes a study with an exercise protocol considered metabolic.

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545 **FIGURE CAPTIONS**

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548 **Figure 1a.** Risk of bias percentile chart, in accordance with the Cochrane Collaboration (Higgins

549 and Altman, 2008).

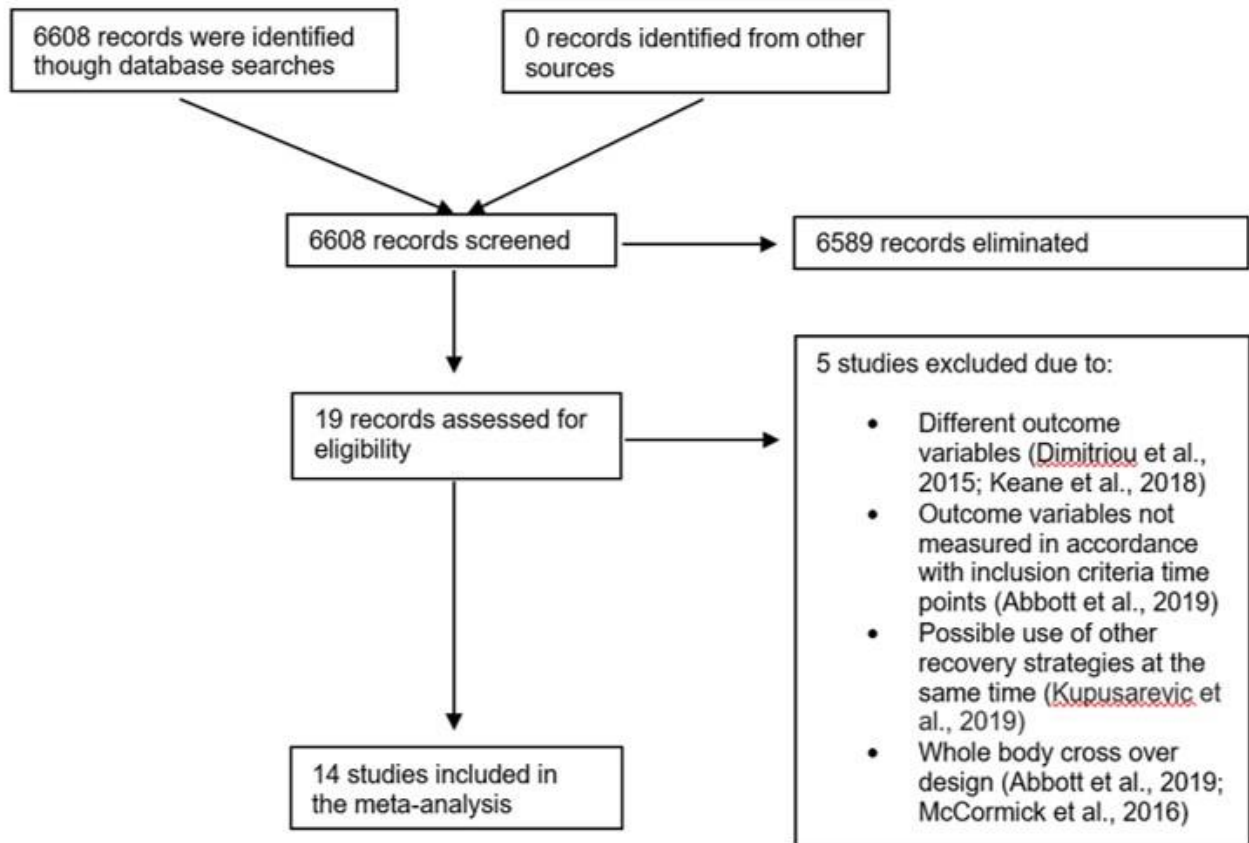
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	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Beals 2017	+	?	+	+	+	-	+
Bell 2014i	?	?	+	+	+	+	-
Bell 2014ii	?	?	+	+	+	+	-
Bell 2016	?	?	+	+	+	+	-
Bowtell 2011	+	?	+	+	+	+	-
Brown 2018	?	?	+	+	+	+	+
Connolly 2006	?	?	+	+	+	+	-
Howatson 2010	+	+	+	+	+	+	+
Kastello 2014	?	?	+	+	+	-	-
Kuehl 2010	?	?	+	+	+	+	+
Lamb 2019	+	?	+	+	+	+	+
Levers 2015	?	?	+	+	+	+	+
Levers 2016	?	?	+	+	+	+	+
Quinlan 2019	+	+	+	+	+	+	+

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552 **Figure 1b.** Risk of bias summary for each included study.

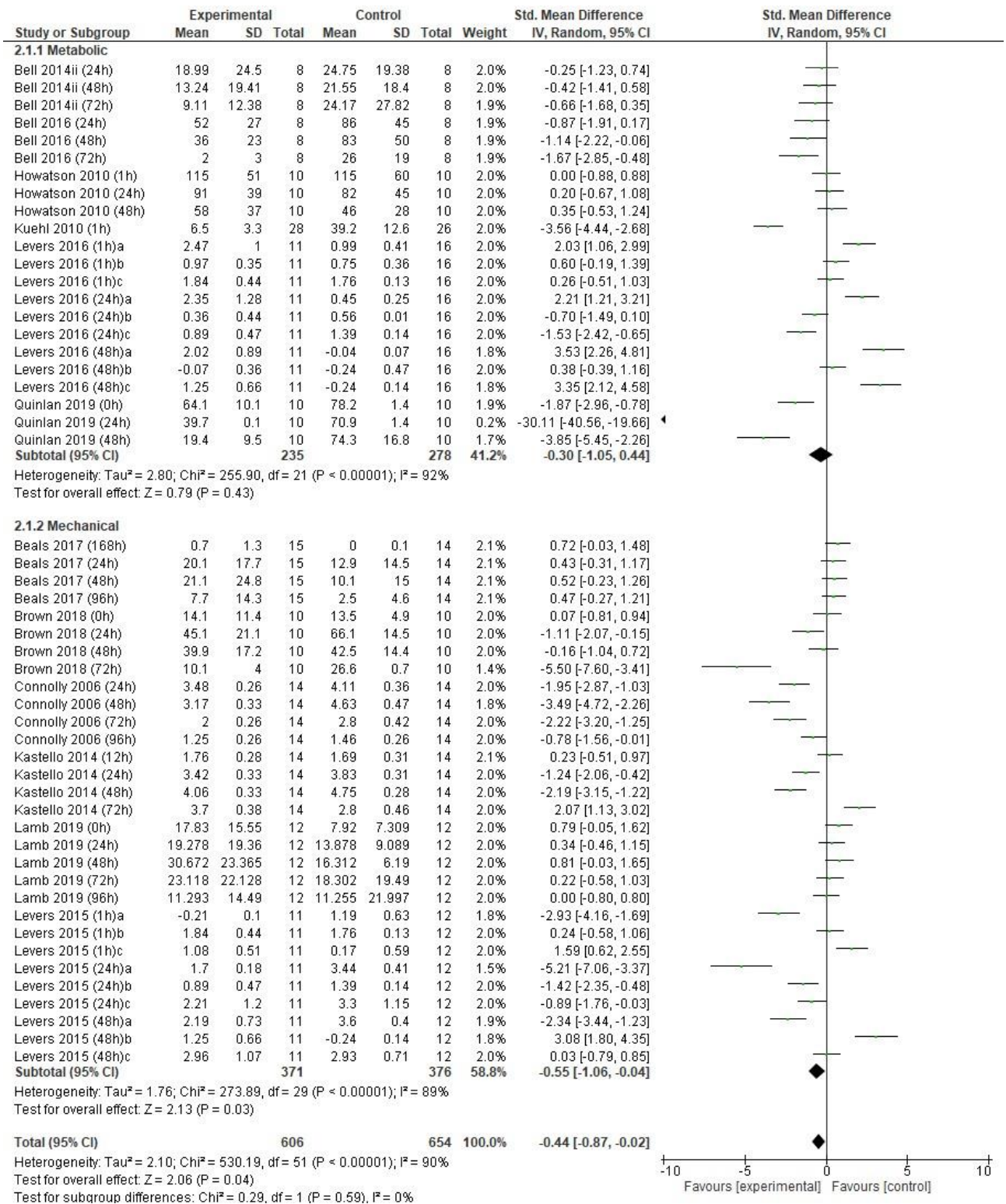
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555 **Figure 2.** Study selection from initial identification to inclusion.

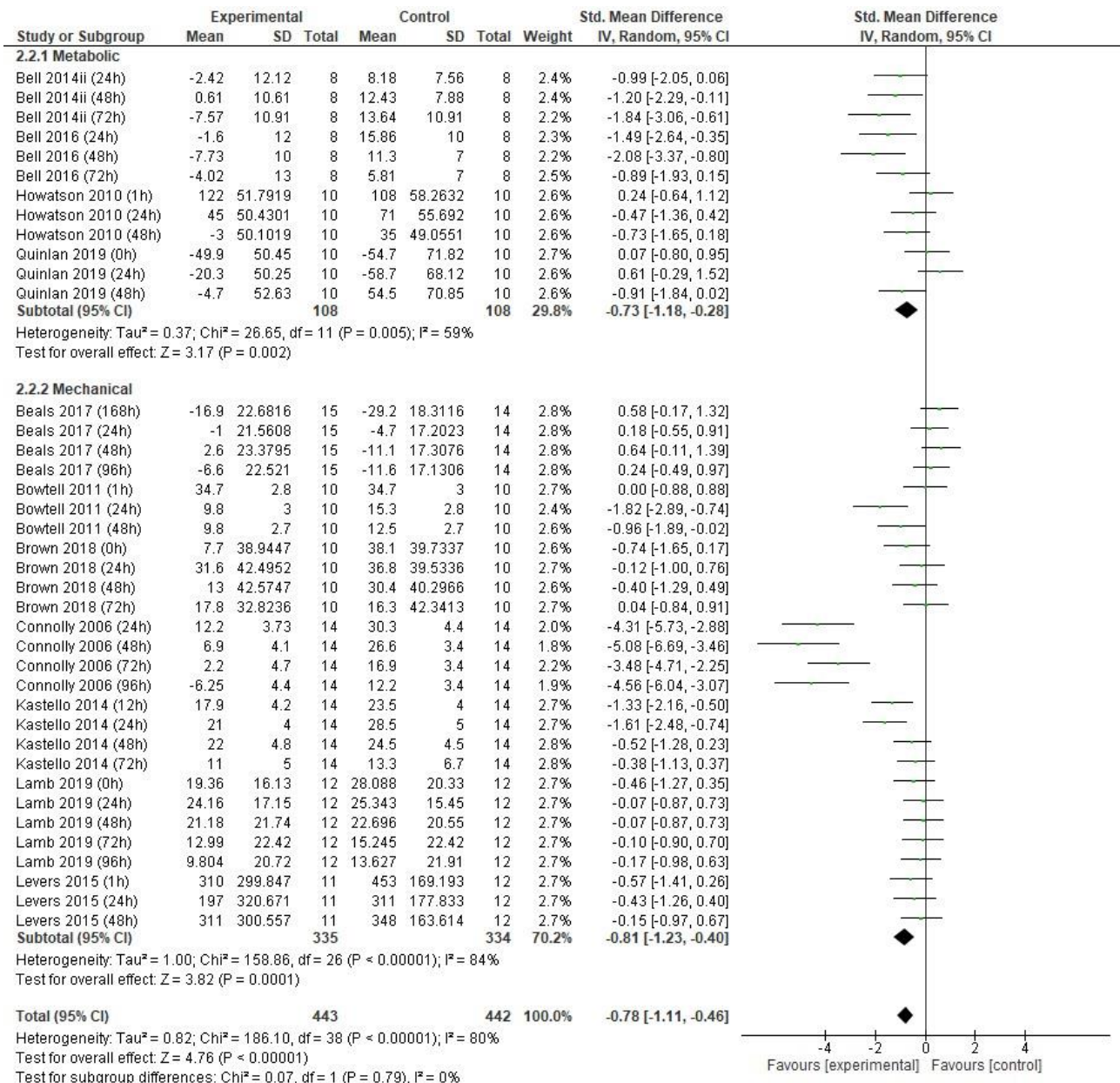
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558 **Figure 3.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 559 supplement or a placebo for measures of delayed-onset muscle soreness. The time point of
 560 measurement post exercise is displayed in brackets on the first column. a, b and c displayed in
 561 column 1 refer to soreness measured in different locations within the same study.

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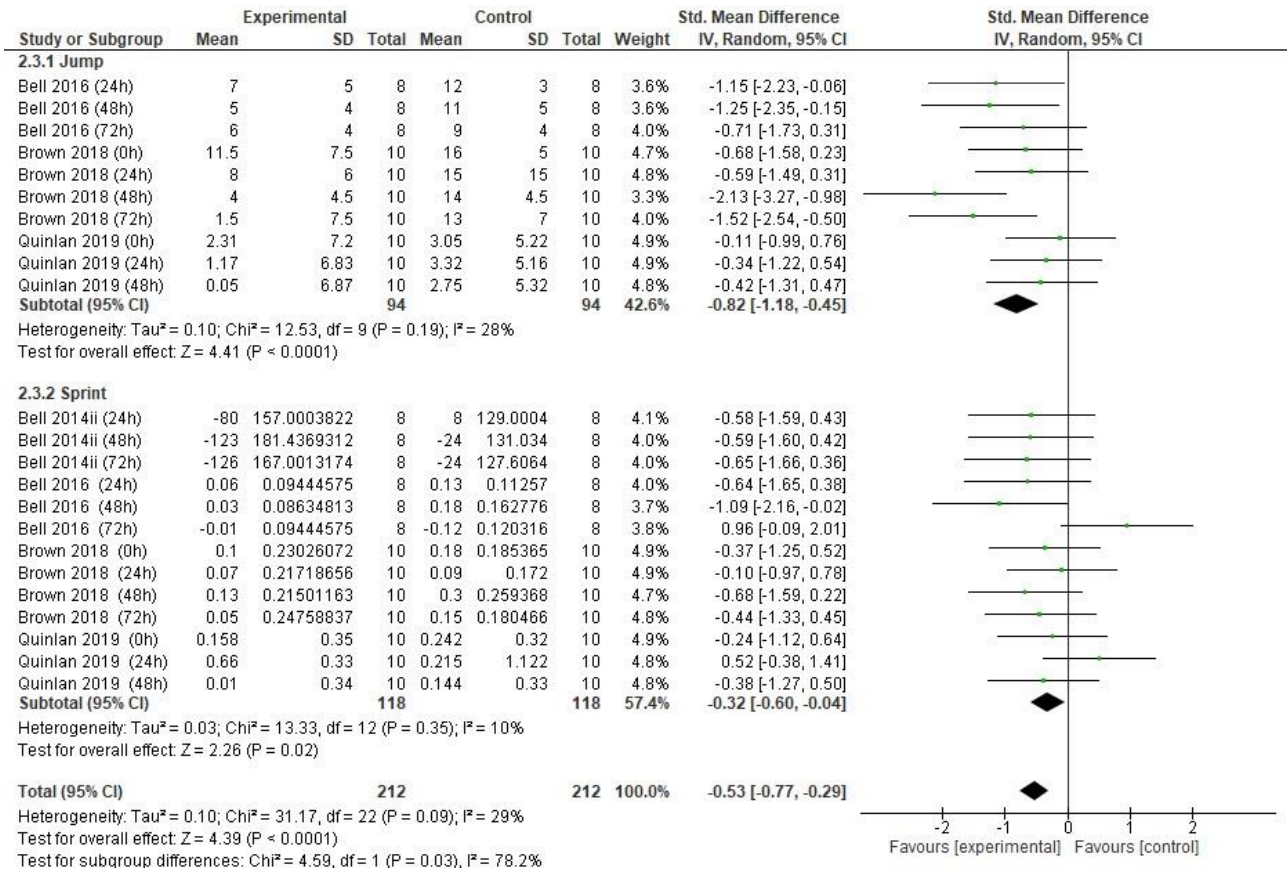


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564 **Figure 4.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 565 supplement or a placebo for measures of strength. The time point of assessment post exercise is
 566 displayed in brackets on the first column.

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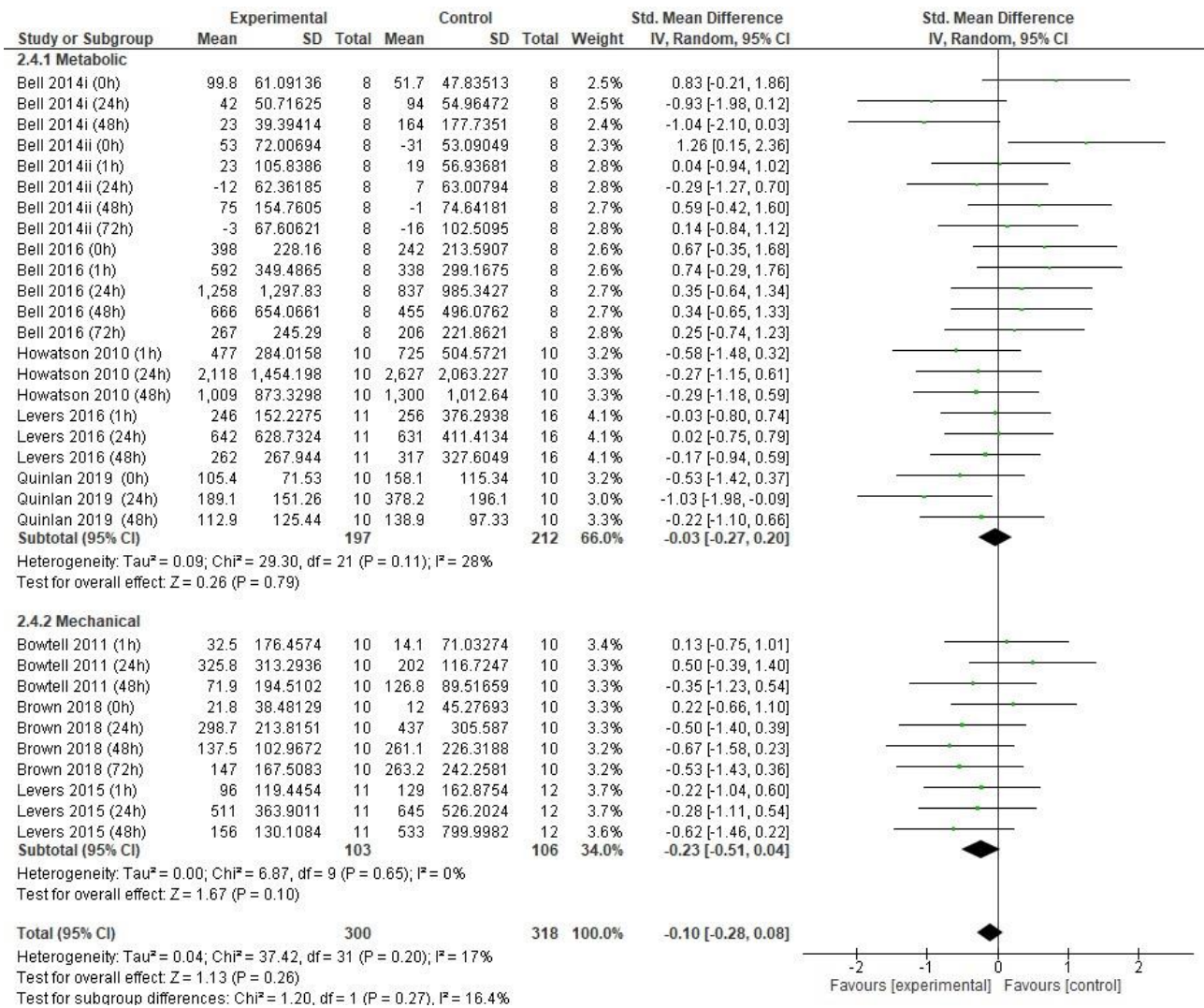


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570 **Figure 5.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 571 supplement or a placebo for measures of power. The time point of assessment post exercise is
 572 displayed in brackets on the first column.

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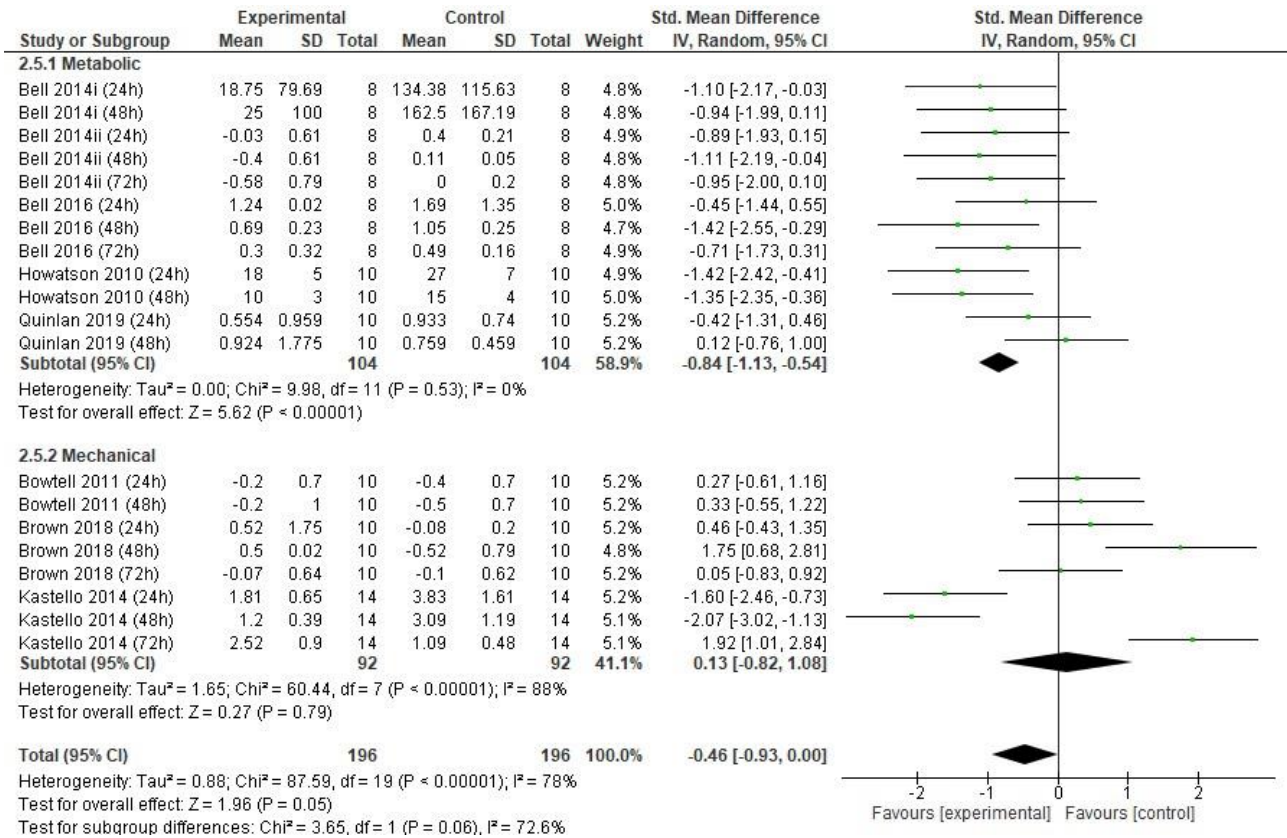


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576 **Figure 6.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 577 supplement or a placebo for creatine kinase. The time point of assessment post exercise is
 578 displayed in brackets on the first column.

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582 **Figure 7.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 583 supplement or a placebo for C reactive protein. The time point of assessment post exercise is
 584 displayed in brackets on the first column.

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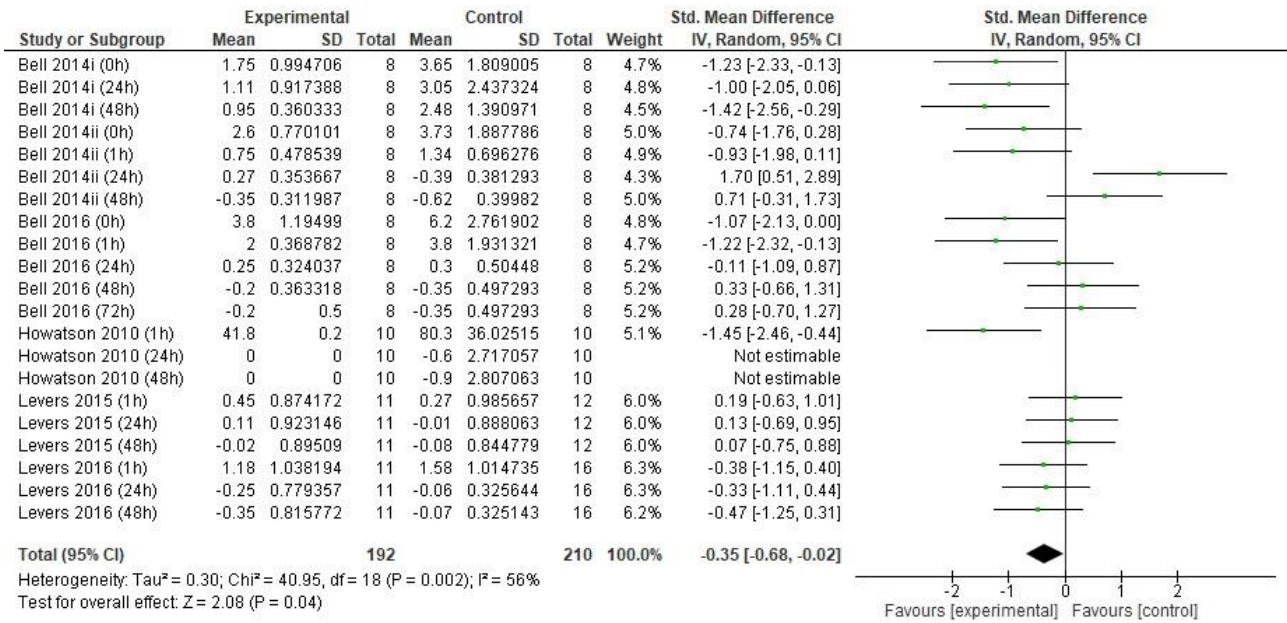
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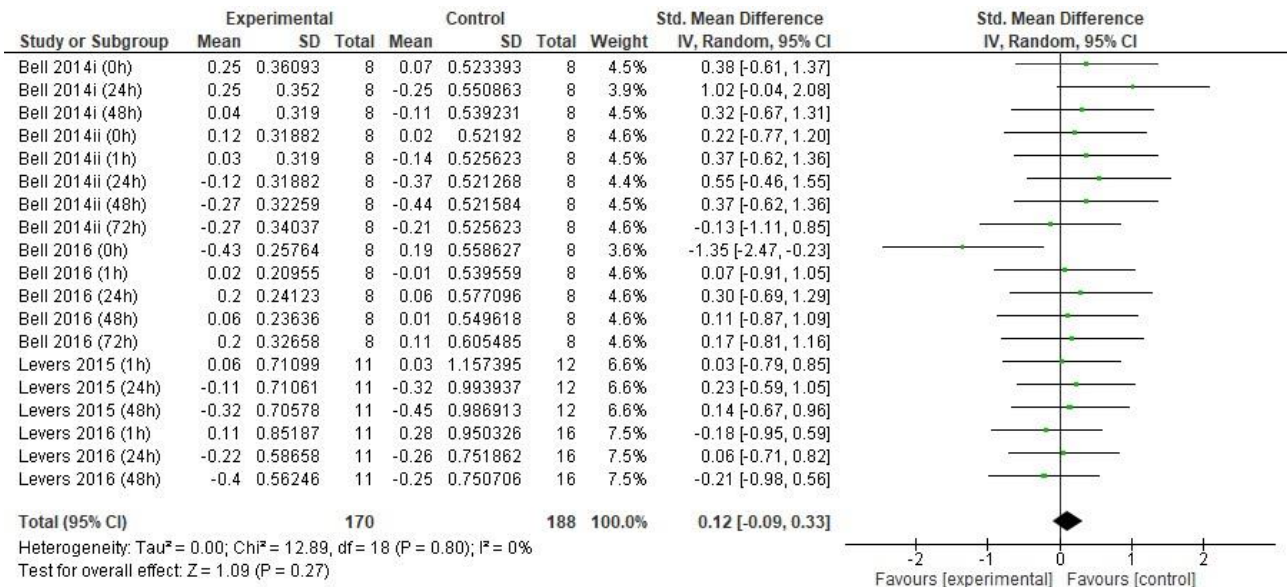
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592 **Figure 8.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 593 supplement or a placebo for IL-6. The time point of assessment post exercise is displayed in
 594 brackets on the first column.

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598 **Figure 9.** Forest plot demonstrating a comparison between the consumption of a tart cherry
 599 supplement or a placebo for TNFα. The time point of assessment post exercise is displayed in
 600 brackets on the first column.