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

ABSTRACT

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

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

INTRODUCTION

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

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

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

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

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

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

MATERIALS AND METHODS

Literature Search

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

Insert table 1 here*

Outcome Variables

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

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

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

Inclusion and Exclusion Criteria

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

Extraction of Data

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

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

Statistical Analysis

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

RESULTS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

DISCUSSION

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

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

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

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

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

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

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

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

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

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

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

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

Conclusion

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

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

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

Authors confirm there are no conflicts of interest.

REFERENCES

Abbott, W., Brashill, C., Brett, A., and Clifford, T. 2019. Tart Cherry Juice: No Effect on Muscle Function Loss or Muscle Soreness in Professional Soccer Players After a Match. Int J Sport Physiol. 1-21.

Aoi, W., Naito, Y., Takanami, Y., Kawai, Y., Sakuma, K., Ichikawa, H., Yoshida, N., and Yoshikawa, T. 2004. Oxidative stress and delayed-onset muscle damage after exercise. Free Radical Bio Med. **37**: 480–487.

Batterham, A.M., and Hopking, W. 2006. Making meaningful inferences about magnitudes. Int J of Sport Physiol. **2**(1): 50-7.

Beals, K., Allison, K. F., Darnell, M., Lovalekar, M., Baker, R., Nieman, D. C., Vodovotz, Y., and Lephart, S. M. 2017. The effects of a tart cherry beverage on reducing exercise-induced muscle soreness. Isokinet and Exerc Sci. **25**(1): 53-63.

400 Bell, P. G., Walshe, I., Davison, G. W., Stevenson, E. J., and Howatson, G. 2014a. Montmorency
401 cherries reduce the oxidative stress and inflammatory responses to repeated days high-
402 intensity stochastic cycling. Nutrients. **6**(2): 829-843.
403
404 Bell, P. G., Walshe, I. H., Davison, G. W., Stevenson, E. J., and Howatson, G. 2014b. Recovery
405 facilitation with Montmorency cherries following high-intensity, metabolically challenging
406 exercise. Appl Physiol Nutr Metab. **40**(4): 414-423.
407
408 Bell, P.G., Stevenson, E. J, Davison, G., and Howatson, G. 2016. The effects of montmorency tart
409 cherry concentrate supplementation on recovery following prolonged, intermittent
410 exercise. Nutrients. **8**(7): 441.
411
412 Betteridge, D. J. 2000. What is oxidative stress? Metabolism. **49**(2): 3-8.
413
414 Bongiovanni, T., Genovesi, F., Nemmer, M., Carling, C., Alberti, G., and Howatson, G. 2020.
415 Nutritional interventions for reducing the signs and symptoms of exercise-induced muscle
416 damage and accelerate recovery in athletes: current knowledge, practical application and
417 future perspectives. Eur J Appl Physiol. 1-32.
418
419 Bowtell, J. L., Sumners, D. P., Dyer, A., Fox, P. and Mileva, K. N. 2011. Montmorency cherry juice
420 reduces muscle damage caused by intensive strength exercise. Med Sci Sports Exerc. **43**(8):
421 1544-1551.
422
423 Brancaccio, P., Maffulli, N., and Limongelli, F. M. 2007. Creatine kinase monitoring in sport
424 medicine. Br Med Bull. **81**(1): 209-230.
425
426 Brown, M. A., Stevenson, E. J., and Howatson, G. 2019. Montmorency tart cherry (Prunus cerasus
427 L.) supplementation accelerates recovery from exercise-induced muscle damage in
428 females. Eur J Sport Sci. **19**(1): 95-102.

Clarkson, P. M., and Sayers, S. P. 1999. Etiology of exercise-induced muscle damage. Can J Appl Physiol. ***24***(3): 234-248.

Clarkson, P. M., and Hubal, M. J. 2002. Exercise-induced muscle damage in humans. Am J Phys Med Rehabil. **81**(11): S52-S69.

Connolly, D. A., McHugh, M. P., Padilla-Zakour, O. I., Carlson, L., and Sayers, S. P. 2006. Efficacy of a tart cherry juice blend in preventing the symptoms of muscle damage. Brit J Sports Med. **40**: 679–683.

Dimitriou, L., Hill, J. A., Jehnali, A., Dunbar, J., Brouner, J., McHugh, M. P., and Howatson, G. 2015. Influence of a montmorency cherry juice blend on indices of exercise-induced stress and upper respiratory tract symptoms following marathon running—a pilot investigation. *J* Int Soc Sports Nutr*.* **12**(1): 22.

Halliwell, B., and Chirico, S. 1993. Lipid peroxidation: Its mechanism, measurement, and significance. Am J Clin Nutr. **57**: 715S-724S.

Higgins, J.P.T. and Altman, D.G. 2008. Assessing the risk of bias in included studies. In: Higgins, J.P.T. and Green, S. Cochrane Handbook for Systematic Reviews of Interventions. Chichester: Wiley Blackwell.

Higgins, J.P.T. and Green, S. 2011. Cochrane Handbook for Systematic Reviews of Interventions.. Chichester: Wiley Blackwell.

Howatson, G., Van Someren, K., & Hortobagyi, T. 2007. Repeated bout effect after maximal eccentric exercise. *Int J Sport Med.* ***28***(7):557-563.

Howatson, G., and Van Someren, K.A. 2008. The prevention and treatment of exercise-induced muscle damage. Sports Med, **38**(6):483-503.

Howatson, G., McHugh, M. P., Hill, J. A., Brouner, J., Jewell, A. P., Van Someren, K., Shave, R. E., and Howatson, S. A. 2010. Influence of tart cherry juice on indices of recovery following marathon running. Scand J Med Sci Sports. **20**:843–852.

Kastello, G. M., Bretl, M. C., Clark, E. R., Delvaux, C. L., Hoeppner, J. D., McNea, L. P., Mesmer, J. A., Meyer, C. G., Mitchener, C. L., Rivera, D. A., Ruhl, S. N., Schuller, K. M., Steffen. J. L. and Strauss, J. D. 2014. The effect of cherry supplementation on Exercise induced oxidative stress. Int J Food Nut Sci. **1**(1).

Keane, K. M., Bailey, S. J., Vanhatalo, A., Jones, A. M., and Howatson, G. 2018. Effects of Montmorency tart cherry (L. Prunus Cerasus) consumption on nitric oxide biomarkers and exercise performance. Scand J Med Sci Sports. 20(7):1746-1756.

Kuehl, K. S., Perrier, E. T., Elliot, D. L., and Chesnutt, J. C. 2010. Efficacy of tart cherry juice in reducing muscle pain during running: a randomized controlled trial. J Int Soc Sports Nutr. **7**(1): 17.

Kupusarevic, J., McShane, K., and Clifford, T. 2019. Cherry gel supplementation does not attenuate subjective muscle soreness or alter wellbeing following a match in a team of professional rugby union players: A pilot study. Sports. ***7***(4):84.

Lanier, A. B. 2003. Use of nonsteroidal anti-inflammatory drugs following exercise-induced muscle injury. Sports Med. **33**(3):177-186.

Lamb, K. L., Ranchordas, M. K., Johnson, E., Denning, J., Downing, F., and Lynn, A. 2019. No effect of tart cherry juice or pomegranate juice on recovery from exercise-induced muscle damage in non-resistance trained men. Nutrients. **11**(7): 1593.

Levers K, Dalton R, Galvan E, Goodenough C, O'Connor A, Simbo A, Barringer N, Mertens-Talcott S, Rasmussen C, Greenwood M, Riechman S, Crouse S, and Kreider R. (2015). Effects of powdered Montmorency tart cherry supplementation on an acute bout of intense lower body strength exercise in resistance trained males. J Int Soc of Sports Nutr. **12**(1): 41.

Levers, K., Dalton, R., Galvan, E., O'Connor, A., Goodenough, C., Simbo, S., Mertens-Talcott S. Rasmussen C, Greenwood M, Riechman S, Crouse S, and Kreider, R. B. 2016. Effects of powdered Montmorency tart cherry supplementation on acute endurance exercise performance in aerobically trained individuals. J Int Soc of Sports Nutr. **13**(1): 22.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A., Clarke, M., Devereaux, P. J., Kleijnen, J., and Moher, D. 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. Ann Intern Med. **151**:65-94.

Lowe, D. A., Warren, G. L., Ingalls, C. P., Boorstein, D. B., and Armstrong, R. B. 1995. Muscle function and protein metabolism after initiation of eccentric contraction-induced injury. J Appl Physiol. *79:*1260–1270.

Marzocchella, L., Fantini, M., Benvenuto, M., Masuelli, L., Tresoldi, I., Modesti, A., and Bei, R. 2011. Dietary flavonoids: molecular mechanisms of action as anti-inflammatory agents. Recent Pat Inflamm Allergy Drug Discov. **5**(3): 200-220.

McCormick, R., Peeling, P., Binnie, M., Dawson, B., and Sim, M. 2016. Effect of tart cherry juice on recovery and next day performance in well-trained Water Polo players. Med Sci Sports Exerc. **13**(1): 41.

Quinlan, R., and Hill, J. 2019. The efficacy of tart cherry juice in aiding recovery following intermittent exercise. Int J Sport Physiol. *1-7.*

Sonkodi, B., Berkes, I., and Koltai, E. 2020. Have We Looked in the Wrong Direction for More Than 100 Years? Delayed Onset Muscle Soreness Is, in Fact, Neural Microdamage Rather Than Muscle Damage. Antioxidants, **9**(3): 212.

Toumi, H., and Best, T. M. 2003. The inflammatory response: friend or enemy for muscle injury? Brit J Sports Med, **37**:284–286.

Vitale, K. C., Hueglin, S., and Broad, E. 2017. Tart cherry juice in athletes: A literature review and commentary. Curr Sports Med Rep. **16**:230-239.

530 **TABLES**

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532 **Table 1:** Review Inclusion Criteria

Population:	Healthy males and females with no restriction on age, activity level or training status.
Intervention:	Supplementation with a tart cherry product before, or before and after a single bout of exercise.
Comparator:	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.
Outcomes:	Measurements of muscular soreness, muscular strength, muscular power and blood biomarkers creatine kinase, C reactive protein, interleukin-6 and tumour necrosis factor alpha.
Study Design:	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 *et al.* (2017) †	Recreationally active *n*=19 male, *n*=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 *et al.* (2014a) ‡	Male trained cyclists *n*=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) ↔ TNFα (0, 24, 48)
Bell *et al.* (2014b) ‡	Male trained cyclists *n*=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) ↔ TNFα (0, 1, 24, 48, 72)
Bell *et al.* (2016) ‡	Male semi-professional soccer players *n*=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) ↔ TNFα (0, 1, 24, 48, 72)
Bowtell *et al.* (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 *et al.* (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 conentrate with negligible phytochemical content diluted with 100ml of water and fortified with maltodexterin 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 *et al.* (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 *et al.* (2008) ‡	Marathon runners *n*=13 male, *n*=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 *et al.* (2014) †	Untrained participants *n*=10 male, *n*=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 *et al.* (2010) ‡	Marathon runners *n*=36 male, *n*=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 *et al.* (2019) †	Non-resistance trained males n=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 *et al.* (2015) †	Resistance trained males *n*=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 *et al.* (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 *et al.* (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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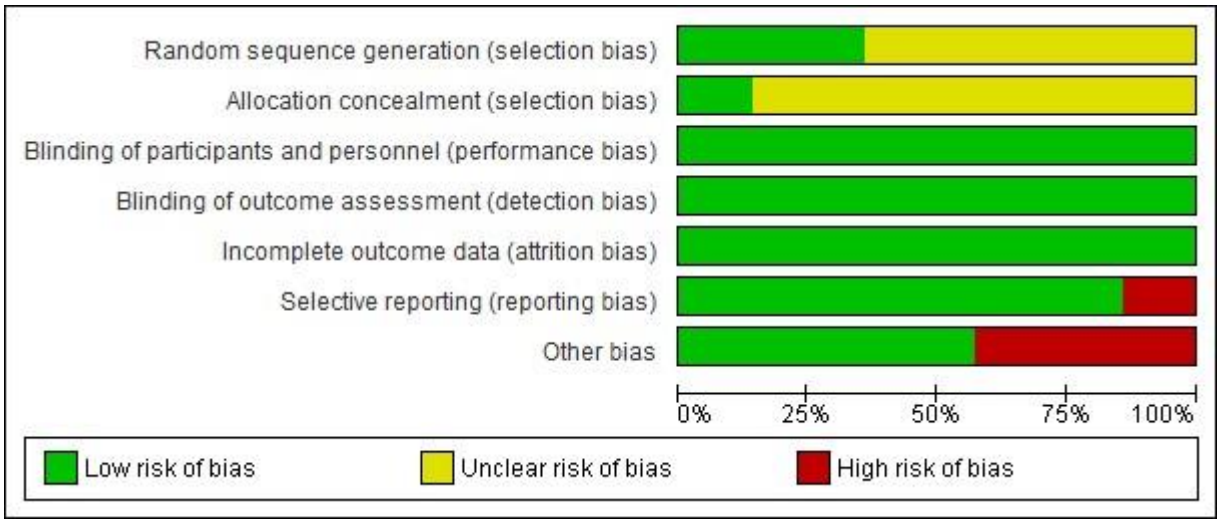

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548 **Figure 1a.** Risk of bias percentile chart, in accordance with the Cochrane Collaboration (Higgins

549 and Altman, 2008).

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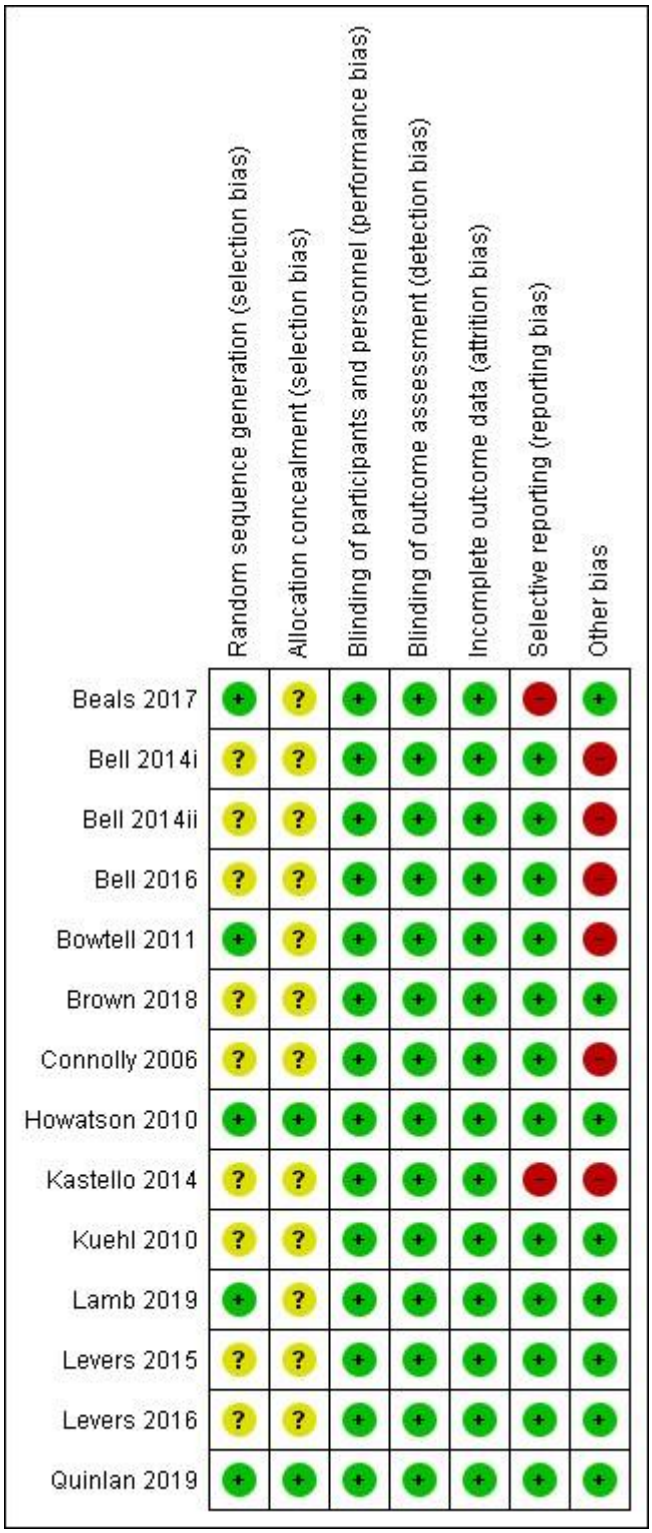
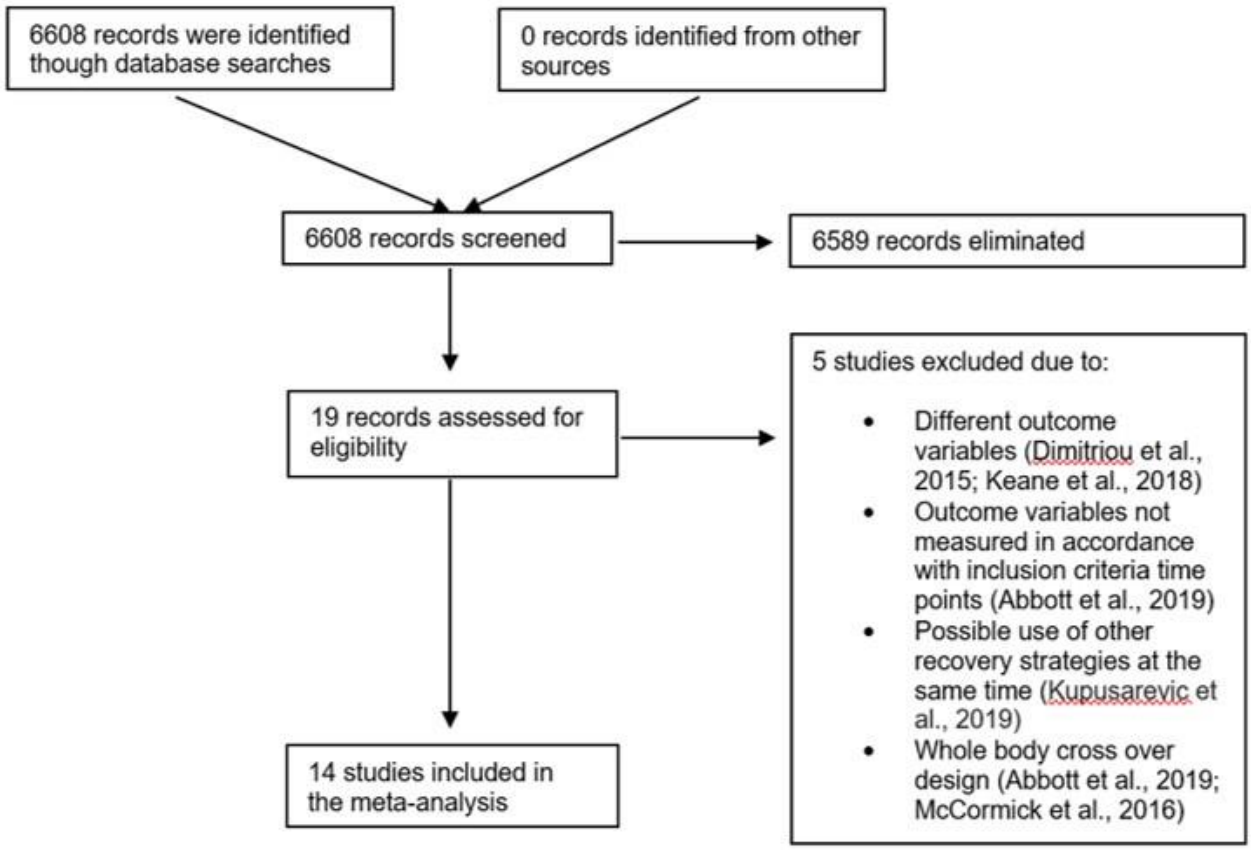


Figure 1b. Risk of bias summary for each included study.



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

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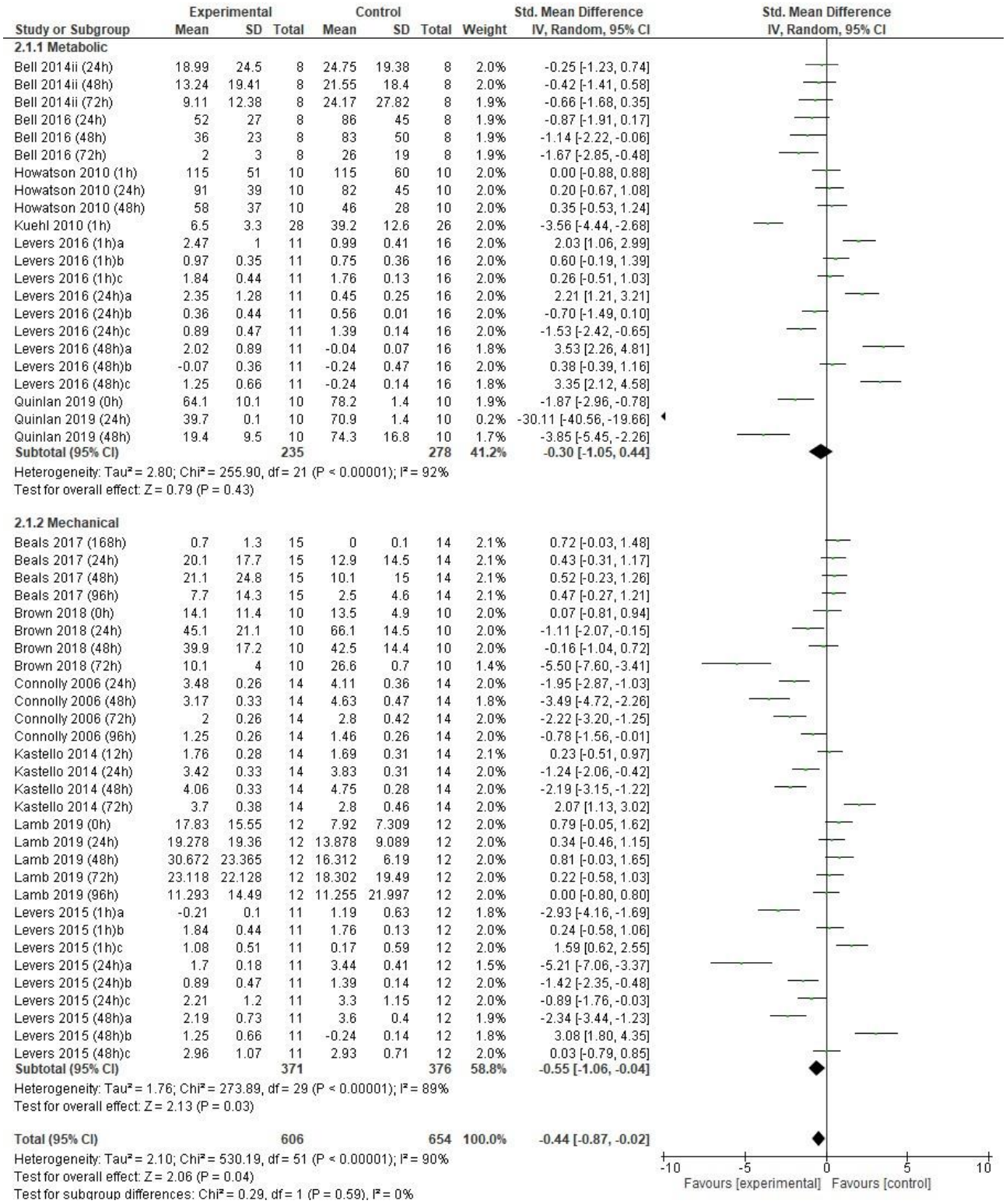


Figure 3. Forest plot demonstrating a comparison between the consumption of a tart cherry supplement or a placebo for measures of delayed-onset muscle soreness. The time point of measurement post exercise is displayed in brackets on the first column. a, b and c displayed in column 1 refer to soreness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

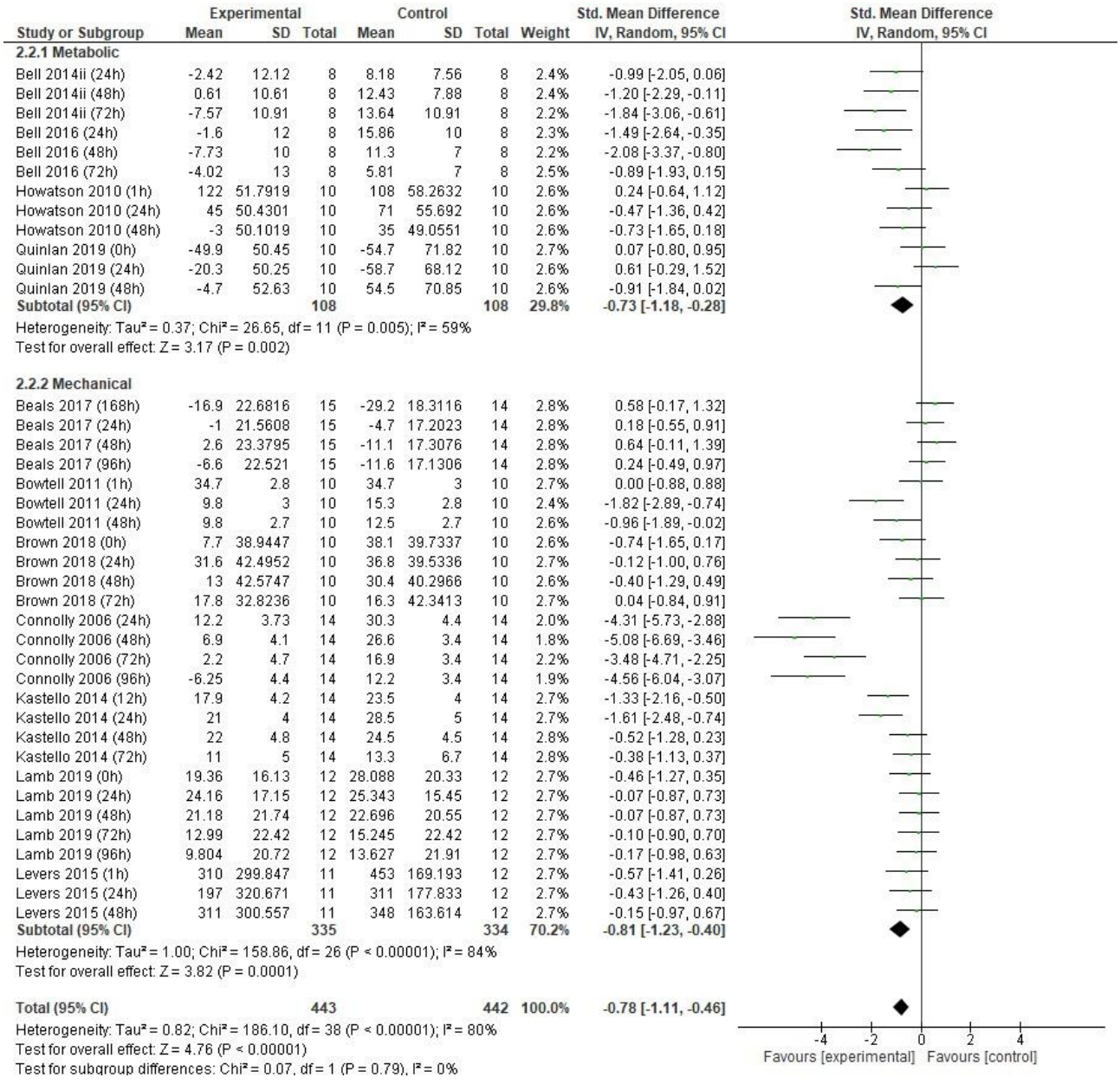


Figure 4. Forest plot demonstrating a comparison between the consumption of a tart cherry supplement or a placebo for measures of strength. The time point of assessment post exercise is displayed in brackets on the first column.

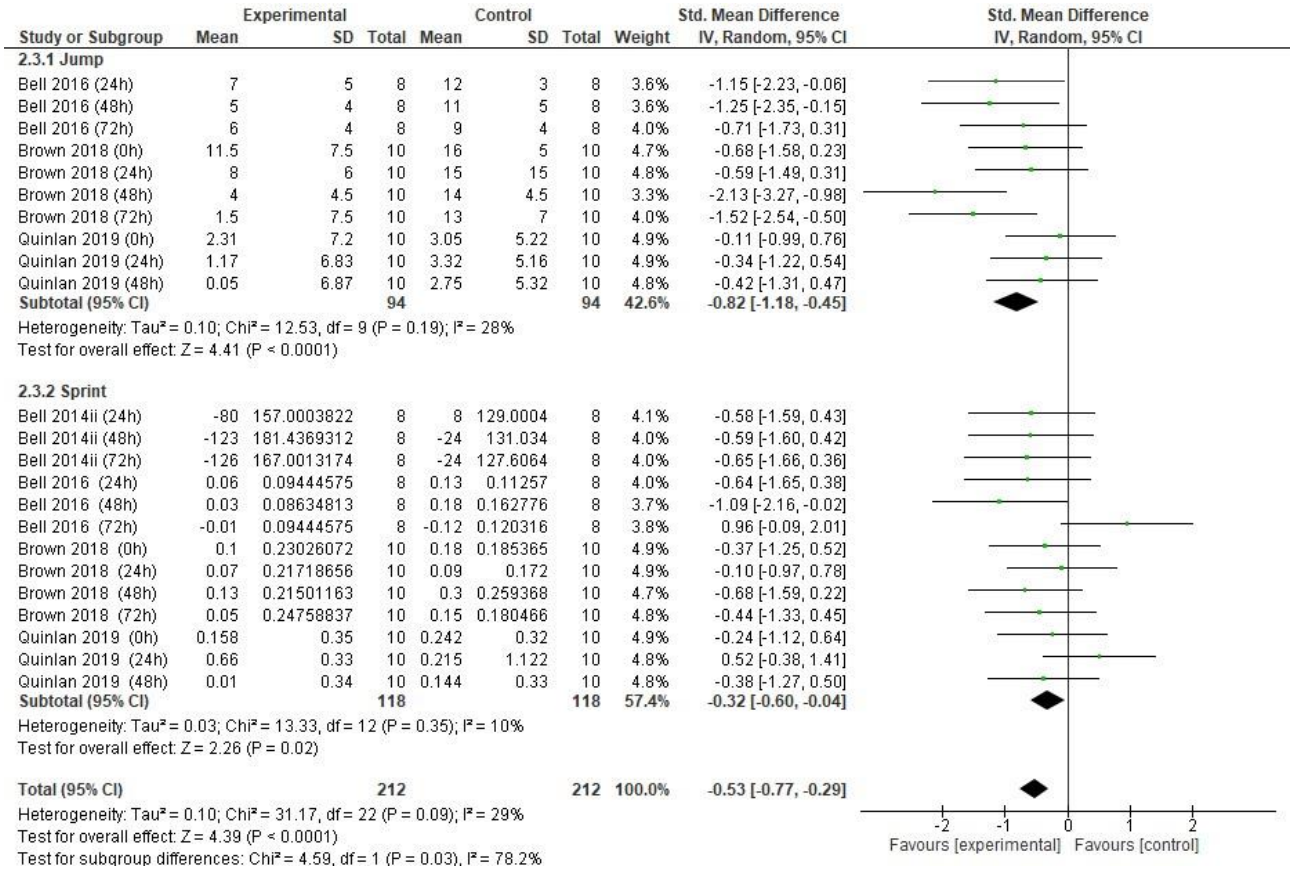


Figure 5. Forest plot demonstrating a comparison between the consumption of a tart cherry supplement or a placebo for measures of power. The time point of assessment post exercise is displayed in brackets on the first column.

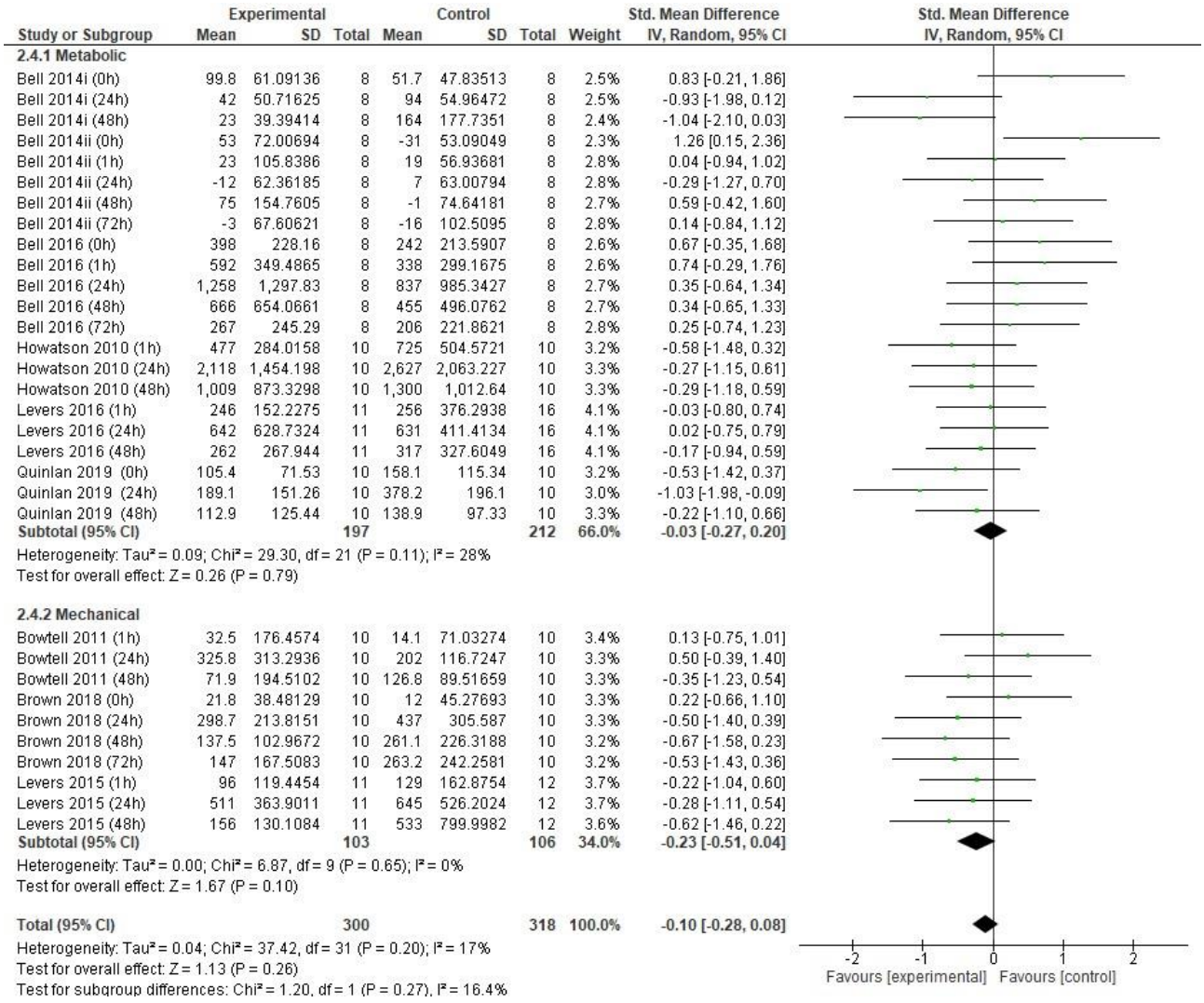
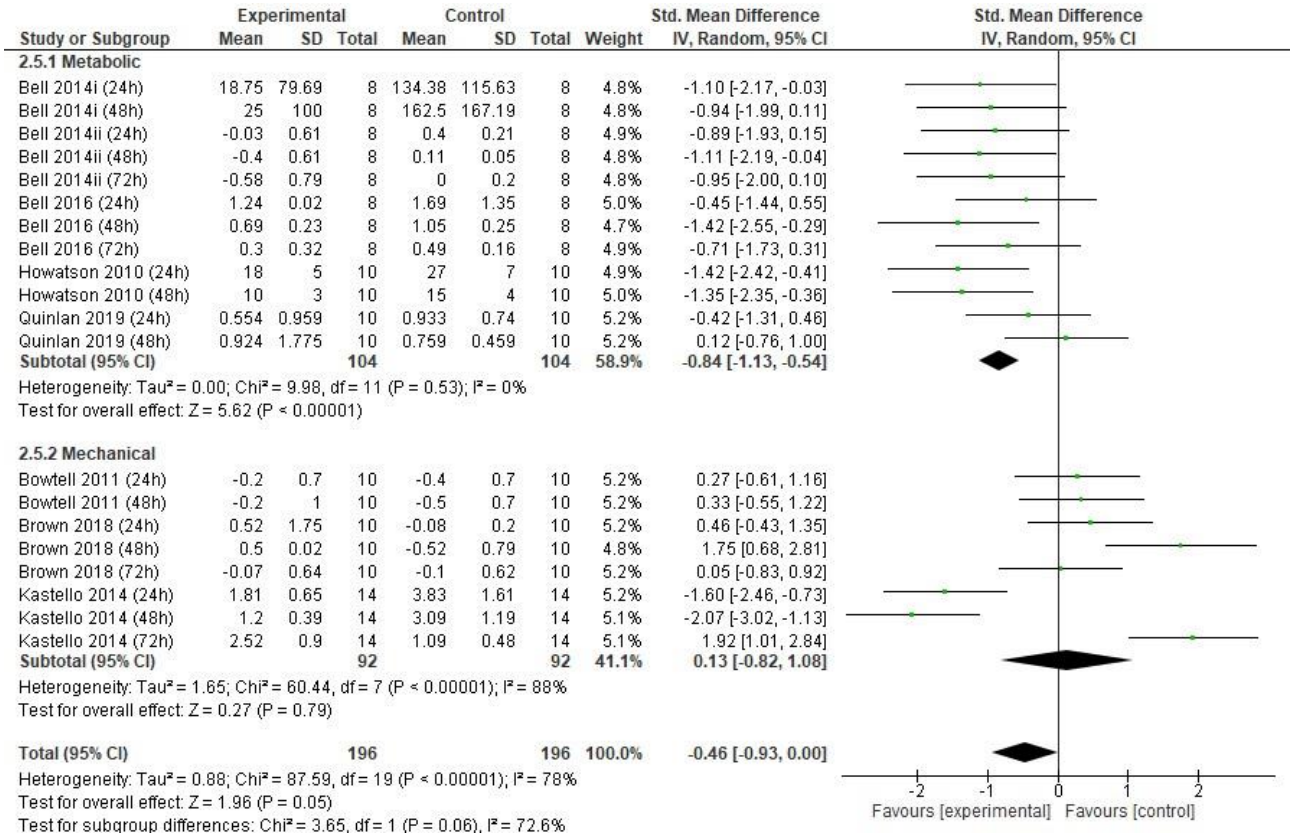


Figure 6. Forest plot demonstrating a comparison between the consumption of a tart cherry supplement or a placebo for creatine kinase. The time point of assessment post exercise is displayed in brackets on the first column.



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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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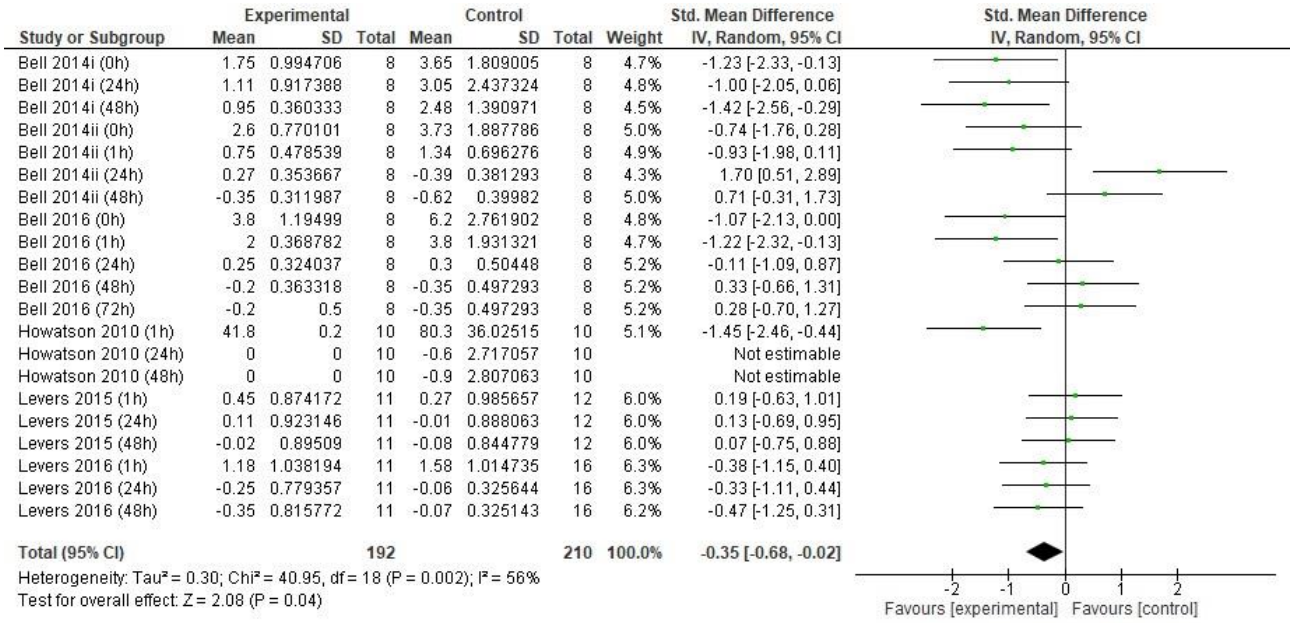

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592 **Figure 8.** Forest plot demonstrating a comparison between the consumption of a tart cherry
593 supplement or a placebo for IL-6. The time point of assessment post exercise is displayed in
594 brackets on the first column.

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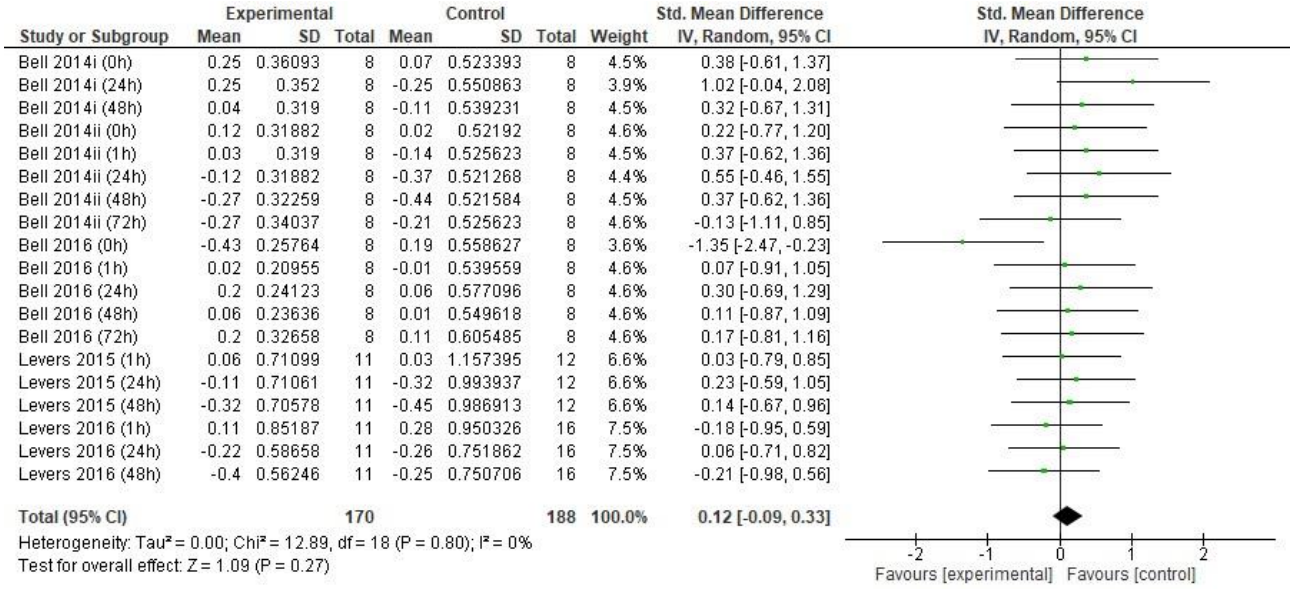

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598 **Figure 9.** Forest plot demonstrating a comparison between the consumption of a tart cherry
599 supplement or a placebo for TNFα. The time point of assessment post exercise is displayed in
600 brackets on the first column.