*Systematic Review and Meta-Analysis*

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# The effect of curcumin supplementation on functional strength outcomes and markers of exercise-induced muscle damage: A systematic review and meta-analysis

**Robert A Oxley and Daniel J. Peart**

## Abstract

**Background:** Curcumin is a polyphenol derived from the *Curcuma longa* L (turmeric) plant and has gained attention through its perceived anti-inflammatory characteristics. The potential interaction with exercise-induced muscle damage (EIMD) and delayed onset muscle soreness (DOMS) has led to investigation of curcumin as a post-exercise strategy that may have the potential to lessen acute reductions in functional strength (FS) following physical activity. **Aim:** The purpose of this review is to assess the evidence examining curcumin in relation to four outcome measures: FS, EIMD, DOMS and inflammation. **Methods:** A Medline, SPORTDiscus and CINAHL database search was undertaken with no publication date limit. Sixteen papers met the inclusion criteria and were included in this review. Three meta-analyses were completed for EIMD, DOMS and inflammation, respectively, with FS being excluded due to limited research. **Results:** Effect sizes were as follows: EIMD (0.15, −0.12, −0.04, −0.2 and −0.61 corresponding to 0, 24, 48, 72 and 96 h post-exercise, respectively), DOMS (−0.64, −0.33, 0.06, −0.53 and −1.16 corresponding to 0, 24, 48, 72 and 96 h post-exercise, respectively) and inflammation (−0.10, 0.26, 0.15 and 0.26 corresponding to 0, 24, 48 and 72 h post-exercise, respectively). A 96 h post-exercise inflammation meta-analysis was not conducted due to limited data. **Conclusion:** No effect sizes were statistically significant for EIMD ($p = 0.644$, 0.739, 0.893, 0.601 and 0.134), DOMS ($p = 0.054$, 0.092, 0.908, 0.119 and 0.074) and inflammation ($p = 0.729$, 0.603, 0.611 and 0.396). Further research is needed to thoroughly examine whether an effect exists.

## Keywords

Turmeric, supplements, recovery, physical activity, nutrition, ergogenic aid

## Introduction

Physical activity and exercise can improve both health (Warburton, 2006; Warburton and Bredin, 2017), physical fitness and athletic performance (Helgerud et al., 2001; Kraemer et al., 2002; Mendonca et al., 2016). Despite the potential benefits of exercise, Twist and Eston (2009) suggest that intense exercise may cause acute physical capacity decreases. These reductions have been observed for some years, acknowledged by both Selye's general adaptation syndrome (Selye, 1950) and Banister's fitness-fatigue theory (Banister et al., 1975). Such a transient reduction in physical ability following intense exercise may be a concern for both professional athletes and casual participants alike.

Hyldahl and Hubal (2014) propose several underlying factors responsible for reduced assessment performance, including exercise-induced muscle damage (EIMD), delayed onset muscle soreness (DOMS) and inflammation. EIMD is common following strenuous exercise, with Davis et al. (2007) suggesting that muscle damage may occur through concentric and eccentric muscle contractions. However, Clarkson and Hubal (2002) hypothesise that high-intensity eccentric contractions induce a much greater degree of damage, with research by Byrne and Eston (2002) observing reduced functional strength (FS) markers as a result of EIMD. Hyldahl and Hubal (2014) and Mackey and Kjaer (2017) propose several morphological and physiological mechanisms that may impact FS, including disruptions to the extracellular matrix,

Sport, Exercise and Rehabilitation, Northumbria University, Newcastle upon Tyne, UK

**Corresponding author:**
Robert A Oxley, Northumbria University, Room 242, Northumberland Building, Newcastle upon Tyne, NE1 8STUK.
Email: rob_oxley@outlook.com

degradation of structural or contractile proteins, and myofibre damage resulting from the repeated lengthening of sarcomeres.

Cleak and Eston (1992) propose that DOMS is another consequence of eccentric exercise, with more extended activity further increasing severity. Furthermore, Vila-Chã et al. (2012) suggest that DOMS can also impact FS outcomes, including reduced force production when measured using a maximum voluntary contraction (MVC). Cheung et al. (2003) and Gulick and Kimura (1996) propose a range of mechanisms responsible for DOMS, including connective tissue damage, muscle spasm, muscle damage, inflammation, enzyme efflux and variations in tissue fluid pressure.

Another potential consequence, acute inflammation, may also occur post-exercise, further reducing FS (Tuttle et al., 2020). Research by Bernecker et al. (2011), Fischer (2006) and Nieman et al. (2011) reported increases in plasma concentrations of proinflammatory biomarkers, including C-reactive protein (CRP), interleukin 6 (IL-6) and tumour necrosis factor alpha. The extent to which these markers circulate appears to be determined by exercise intensity (Nieman et al., 2011). Fatouros and Jamurtas (2016) propose a range of physiological mechanisms responsible for inflammation, including neutrophil and macrophage mobilisation to the site of tissue damage, synthesis of proinflammatory cytokines and increased leukocyte concentration within circulation.

Reductions in FS caused by EIMD, DOMS and inflammation present issues for athletes and casual exercise participants training over consecutive days. Due to the potentially reduced performance post-exercise, individuals may turn to natural solutions that can be taken safely and allow them to recover more rapidly. Common examples include various sources of protein, creatine or assorted multivitamins (Knapik et al., 2015).

Curcumin is a polyphenol derived from the *Curcuma longa* L plant, which has gained attention recently through its perceived anti-inflammatory characteristics (Porro et al., 2019). Research by Panahi et al. (2016) proposes that the substance may inhibit nuclear factor-kappa B (NF-κB), subsequently suppressing proinflammatory cytokines. Additionally, Mazidi et al. (2016) suggest that cytokine suppression may occur through downregulation of janus kinase-signal transducer and activator of transcription (JAK-STAT) signalling.

Another potential use of curcumin is to reduce EIMD; however, research is varied. While Tanabe et al. (2019a) report inconsistent findings in muscle soreness and creatine kinase (CK) activity, other research has observed reductions in EIMD (Fernández-Lázaro et al., 2020; McFarlin et al., 2016; Nakhostin-Roohi et al., 2016). Improvements in DOMS following intense exercise is another outcome that may be influenced by curcumin supplementation, with Nicol et al. (2015) and Amalraj et al. (2020) reporting improvements and visual analogue scale (VAS) scores.

Generally, curcumin has been found to be safe in humans, even at relatively high doses of up to 8 g/day (Chainani-Wu, 2003) and has been declared 'generally recognised as safe' by the Food and Drug Administration (Sharifi-Rad et al., 2020). In terms of side effects, a small amount of research has found curcumin to have contraceptive effects, though more research is needed to corroborate these findings (Naz, 2011; Rithaporn et al., 2003). Similarly, episodes of nausea and diarrhoea have been observed in patients receiving the supplement for extended periods (0.45 to 3.6 g per day for 1–4 months) (Sharma et al., 2004). These findings are similar to observations by Lao et al. (2006), reporting diarrhoea, headaches, rashes and yellow stools in patients receiving escalating doses.

Alongside potential use as an ergogenic aid, curcumin may also have clinical uses, and has been investigated as an antioxidant and for pain management, though primarily research has focused on inflammatory conditions (Hewlings and Kalman, 2017; Panahi et al., 2016).

Though proposed mechanisms of action vary, curcumin has been associated with downregulation of the NF-κB signalling pathway (Panahi et al., 2016) and by extension may be associated with reductions in inflammation. Consequently, the use of curcumin has broadly been associated with a range of inflammatory diseases including Parkinson's disease, Alzheimer's disease, cardiovascular disease, arthritis, cancer and metabolic syndrome among others.

While curcumin may be associated with a range of clinical uses, it displays poor small intestine absorption, limiting bioavailability (Liu et al., 2022). In light of this, research has investigated the use of various compounds to improve bioavailability. Historically research has primarily focused on the use of piperine to increase curcumin bioavailability, observing measurable increases in bioavailability (Hewlings and Kalman, 2017). More recently however, nanoparticle encapsulation has shown nine-fold improvements in bioavailability compared to the adjuvant use of piperine to improve bioavailability (Shaikh et al., 2009).

The conflicting evidence in the literature has led to some authors conducting systematic reviews on this topic. Fernández-Lázaro et al. (2020) recently examined the effect of curcumin on muscle damage, DOMS, inflammation and oxidative stress, but did not include any functional performance tests or a meta-analysis. Additionally, research by Suhett et al. (2020) examined curcumin and inflammation, muscle pain and damage, along with exercise performance and oxidative stress. However, like Fernández-Lázaro et al. (2020), this research also did not include a meta-analysis. A final example from Fang and Nasir (2020) examining curcumin interactions with muscle damage and soreness did include a meta-analysis, but the results displayed significant statistical heterogeneity ($I^2 = 94.5\%$).

As the body of literature around curcumin is growing, the objective of this review is to build on existing reviews by offering a comprehensive overview of all outcomes, with a meta-analysis where appropriate to support the development of objective conclusions. The aim is to

investigate the effect of curcumin supplementation on FS outcomes and markers of exercise-induced muscle damage.

## Methods

This systematic review was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Liberati et al., 2009).

### *Defining the research question*

To define the research question, the PICOS framework (Liberati et al., 2009) was used: P (population) 'participants over the age of 16', I (intervention) 'curcumin supplementation', C (comparator) 'the same conditions with placebo or control group', O (outcomes) 'changes in FS (e.g. MVC or jump height), exercise-induced muscle damage, delayed onset muscle soreness or inflammatory markers', and S (study design) 'all types of study design'.

### *Search strategy*

A structured search of the Medline (Ovid), SPORTDiscus and CINAHL (EBSCOhost) databases was conducted to include relevant literature and did not include any date or language filters at this stage.

Boolean operators 'OR' and 'AND' were used to include appropriate literature. The search terms that were included are as follows: ("curcumin" OR "curcuminoids" OR "curcuma longa" OR "turmeric") AND ("maximum voluntary contraction" OR "MVC" OR "counter movement jump" OR "CMJ" OR "squat jump" OR "SJ" OR "muscle damage" OR "MD" OR "exercise induced muscle damage" OR "EIMD" OR "delayed onset muscle soreness" OR "delay onset muscle soreness" OR "DOMS" OR "inflam*") NOT ("mice" OR "rat" OR "mouse" OR "murine" OR "pig" OR "horse").

All original articles selected from databases were transferred to the EndNote X9 (EndNote, 2013) software to check the presence of duplicates. The remaining article title and abstracts were screened against the inclusion and exclusion criteria described in the Study selection section. Any articles that did/did not meet the inclusion/exclusion criteria were deleted as appropriate.

### *Study selection*

Literature was screened in a three-step process: (i) selection based on titles; (ii) selection based on the abstract and (iii) selection based on the full article text.

The following inclusion criteria were applied: research/literature that (i) contained the ingestion of curcumin, a supplement containing curcumin or a supplement containing curcumin paired with an adjuvant to aid absorption (i.e. piperine) either before, during or after exercise; (ii) conducted on humans aged 16 and above; (iii) published in English or has an English language abstract available; (iv) with an identical experimental situation with a placebo or control group; (v) with clear information on the administration of curcumin or the curcumin supplement (dosage, time of intake and duration of consumption); (vi) in which the consumption of curcumin was administered orally in the form of a pill/capsule, powder, beverage or gum; (vii) where the measured outcome was a change in an FS outcome (maximum voluntary contraction, jump height) or changes in indices of inflammation or muscle damage (EIMD and DOMS).

The following exclusion criteria were applied (i) non-human animal studies; (ii) studies performed on participants with prior musculoskeletal pain or injury, including those with pain or injury caused by disease; (iii) unpublished and grey literature; (iv) studies with <5 participants; (v) non-peer-reviewed articles; (vi) research conducted in vitro; (vii) studies involving inflammation, EIMD or DOMS that was not the result of exercise or physical activity (i.e. injury or inflammatory disease) and (viii) systematic, narrative or literature reviews.

No inclusion or exclusion filters were applied for the participants training status, country of origin, body mass or gender.

### *Data extraction*

Studies meeting eligibility criteria were reviewed, and the following data was extracted: author's name(s), year of publication, study design, number of participants in each group, type of curcumin, curcumin dosage, ingestion day(s) and time(s), mean, standard deviation (SD) or standard error (SE) of the intervention and placebo group.

For studies that did not report numerical data relevant to this review, Web Plot Digitizer (Rohatgi, 2020) was used to extract the mean, SD or SE data used in the meta-analyses.

### *Risk of bias (individual studies)*

Papers were screened against the Cochrane RoB 2 (Sterne et al., 2019) signalling questions. This tool was used due to its ability to assess bias over several domains, increasing validity.

Questions fell under one of five domains: the randomisation process, deviations from intended interventions, missing outcome data, outcome measurement and selection of the reported result. Answers to the questions within these domains algorithmically (in conjunction with the assessor's decision) provided a judgement on the risk of bias for each study. The level of risk of bias was classified according to three levels: 'high risk', 'some concerns' or 'low risk'. This review considered selection, performance, detection, attrition, measurement and reporting bias.

### Risk of bias across studies

Across study risk of bias was assessed using the Cochrane RoB 2 tool (Sterne et al., 2019) and is reported as an overall risk of bias for each of the five domains discussed in the Synthesis of results section. All of the studies included in this systematic review were included in both the individual and across-study risk of bias assessment.

### Synthesis of results

Mean, and SD of MVC torque, creatine kinase concentrations, VAS measurements and IL-6 concentrations were extracted from relevant papers for the outcomes of FS, EIMD, DOMS and inflammation, respectively. For papers that did not report as SD, SE was used to calculate SD data using the following equation, taken from the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al., 2021): $SD = SE^* \sqrt{n}$.

Extracted data was then transposed into one of the four Microsoft Excel (2021) documents corresponding to the four outcome variables. The effect size (ES) was calculated using the Hedges *g* equation (Hedges and Olkin, 1985) and data was exported as a comma-separated value file to be used in the open-source JASP software (JASP Team, 2022). ES thresholds were interpreted as follows (Cohen, 2013): $< 0.2$ = negligible effect, 0.21 to 0.49 = small effect, 0.50 to 0.79 = moderate effect, $> 0.8$ = large effect.

Meta-analyses were conducted with studies using a parallel study design only to minimise the risk of the repeated bout effect impacting recovery. Crossover designs were still included in the qualitative synthesis. Table 1 shows ES for all study designs, including crossover studies. An FS meta-analysis was not conducted due to a lack of parallel design studies, though ES for all study designs were calculated and displayed in Table 1. For the EIMD and DOMS meta-analyses, all time points were included (0, 24, 48, 72 and 96 h post-exercise), however the 96 h post-exercise inflammation meta-analysis was not conducted due to a lack of literature. For each meta-analysis, a random-effects model was used due to variations in study characteristics.

Forest plots were constructed for the EIMD, DOMS and inflammation meta-analyses using JASP (http://www.jasp-stats.org).

Due to the relatively low number of studies included in each meta-analysis, $I^2$ was used to assess statistical heterogeneity. Heterogeneity was interpreted as per the Cochrane review handbook guidelines (Higgins et al., 2021), with thresholds of 0–40%, 30–60%, 50–90% and 75–100%, indicating minimal, moderate, substantial and considerable heterogeneity, respectively. Heterogeneity was classified using the above thresholds, with values of 50% or below being acceptable. In addition, *p*-values were used to assess statistical significance, being accepted at $<0.05$.

Meta-analysis data is reported as ES and 95% confidence intervals (CIs) unless otherwise stated.

### Additional analyses

No additional analyses were conducted.

**Table 1.** Comparison data between meta-analyses (all papers and parallel only).

| | | *All* | | *Parallel only* | |
|---|---|---|---|---|---|
| Outcome/time | | ES | CI | ES | CI |
| *FS* | 0 h | 0.47 | −0.19, 1.13 | - | - |
| | 24 h | 0.41 | −0.25, 1.07 | | |
| | 48 h | 0.59 | −0.07, 1.25 | | |
| | 72 h | 0.4 | −0.26, 1.06 | | |
| | 96 h | 0.6 | −0.06, 1.27 | | |
| *EIMD* | 0 h | 0.02 | −0.48, 0.51 | 0.15 | −0.48, 0.78 |
| | 24 h | −0.16 | −0.69, 0.38 | −0.12 | −0.82, 0.59 |
| | 48 h | −0.11 | −0.53, 0.32 | −0.04 | −0.70, 0.61 |
| | 72 h | −0.31 | −0.83, 0.20 | −0.2 | −0.95, 0.55 |
| | 96 h | −0.64 | −1.06, −0.22 | −0.61 | −1.41, 0.19 |
| *DOMS* | 0 h | −0.35 | −0.78, 0.08 | −0.64 | −1.30, 0.01 |
| | 24 h | −0.24 | −0.55, 0.07 | −0.33 | −0.72, 0.05 |
| | 48 h | 0.1 | −0.56, 0.77 | 0.06 | −0.93, 1.05 |
| | 72 h | −0.35 | −0.80, 0.11 | −0.53 | −1.19, 0.14 |
| | 96 h | −0.75 | −1.58, 0.09 | −1.16 | −2.43, 0.11 |
| *Inflammation* | 0 h | 0.19 | −0.26, 0.63 | −0.1 | −0.67, 0.47 |
| | 24 h | −0.18 | −0.84, 0.48 | 0.26 | −0.71, 1.23 |
| | 48 h | 0.3 | −0.19, 0.79 | 0.15 | −0.42, 0.72 |
| | 72 h | −0.07 | −0.81, 0.67 | 0.26 | −0.34, 0.86 |
| | 96 h | −0.18 | −0.70, 0.35 | - | |

Notes: –: Too few papers for meta-analysis; CI: confidence intervals; DOMS: delayed onset muscle soreness; EIMD: exercise-induced muscle damage; ES: effect size; FS: functional strength.

## Results

This systematic review and meta-analyses aim to investigate the effect of curcumin supplementation on FS outcomes and markers of EIMD.

### Study selection

For study selection see Figure 1 below.

### Study characteristics and outcome measures

Table 2 includes information about the 14 studies included in this systematic review and meta-analyses. Data are presented as per the PICOS framework (Liberati et al., 2009). Data includes author(s), population (fully completing the study, excluding those who withdrew), intervention, comparator, outcomes (relevant to this review), study design and the main conclusions observed.

### Risk of bias

*Risk of bias within studies.* Sixteen studies were assessed for bias, with six displaying some overall risk (Figure 2). Delecroix et al. (2017) displayed the highest overall risk of bias (80%). Tanabe et al. (2015), Tanabe et al. (2019a), Tanabe et al. (2019b), Drobnic et al. (2014) and McFarlin et al. (2016) also displayed risk of bias. These studies were classified as 'some concerns', particularly regarding their randomisation/allocation sequence (single-blinded), along with the description of these methods. While no papers displayed an overall high risk, Basham et al. (2019) exhibited a high risk of bias in selection of the reported result.

Ten papers displayed an overall low risk of bias (Amalraj et al., 2020; Basham et al., 2019; Cardaci et al., 2020; Faria et al., 2020; Hillman et al., 2021; Kisiolek et al., 2021; Mallard et al., 2020; Nicol et al., 2015; Salehi et al., 2021; Sciberras et al., 2015).

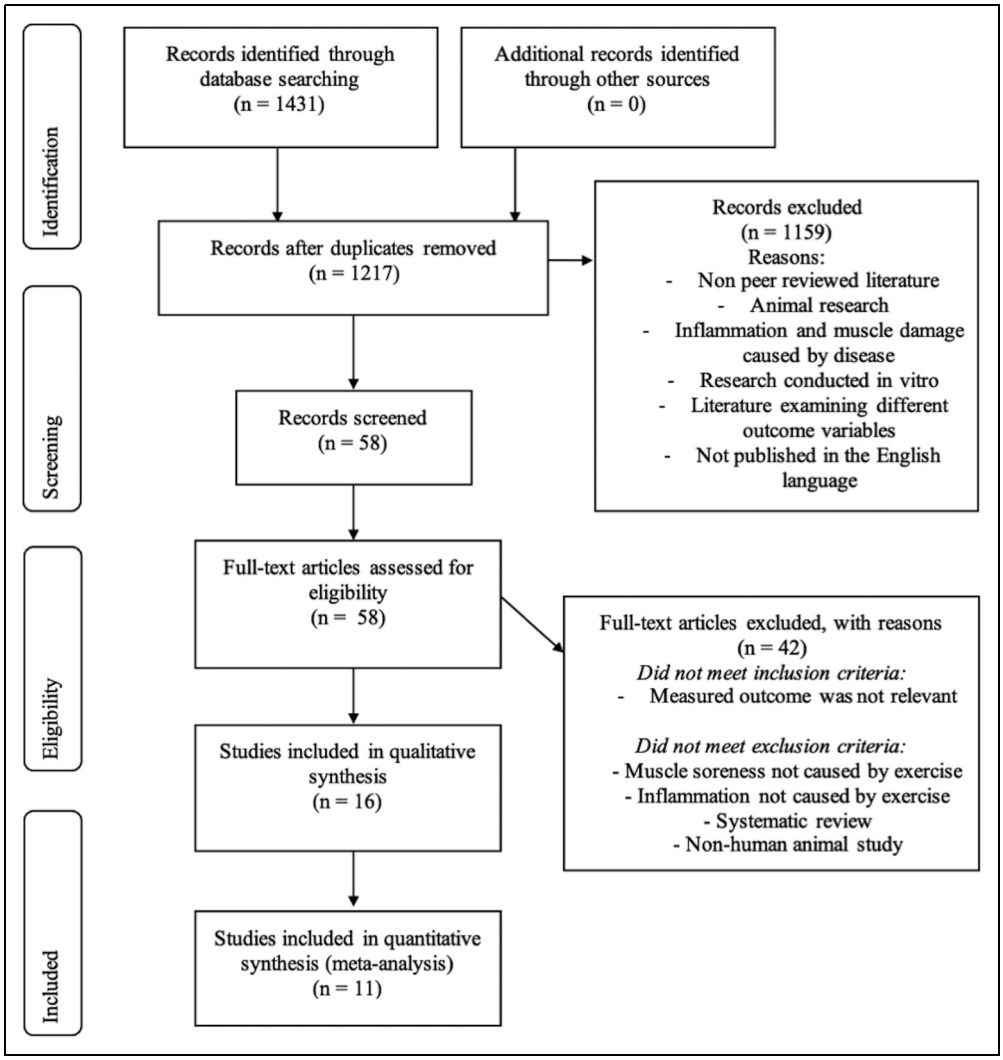


**Figure 1.** PRISMA flow chart detailing the selection process.

**Table 2.** Summary of studies included in this systematic review and meta-analysis.

| Author(s) and year published | Population | Intervention | Comparator | Outcomes | Study design | Main conclusion(s) (24 h post-exercise, compared to placebo) |
|---|---|---|---|---|---|---|
| Drobnic et al., 2014 | 20 Moderately active men (38.1 ± 11.1 and 32.7 ± 12.3 years) | 200 mg (Phytosome Meriva®) curcumin twice daily 48 h before exercise, continuing 24 h after | Placebo | CK, hsCRP, IL-8 and pain intensity | Single-blind randomised controlled trial | ↓ IL-8 (s) ↓ CK (ns) ↓ hsCRP (ns) ↓ pain intensity (ns) |
| Nicol et al., 2015 | 17 Moderately active men (33.8 ± 5.4 years) | 2.5 g Curcumin ingested daily, 48 h before and 72 h after exercise | Placebo | CK, IL-6, TNF-α, muscle pain, jump height | Double-blind crossover randomised controlled trial | ↓ Muscle pain (s) ↓ CK (ns) ↑ IL-6 (ns) ↑ jump height (ns) - TNF-α (ns) |
| Sciberras et al., 2015 | 11 Male recreational athletes (35.5 ± 5.7 years) | 500 mg (Meriva®) curcumin 72 h before and immediately after exercise | Placebo | CRP, IL-6, IL-10, IL-1RA | Double-blind crossover randomised controlled trial | ↓ IL-6 (ns) - CRP (ns) - IL1-RA (ns) - IL-10 (ns) |
| Tanabe et al., 2015 | 14 Healthy, untrained men (23.5 ± 2.3 years) | 150 mg of curcumin (Theracurmin) administered 1 h before and 12 h after exercise | Placebo | CK, IL-6, TNF-α, muscle pain, MVC torque | Single-blind randomised crossover trial | ↓ MVC torque (s) ↓ peak CK (s) - IL-6 (ns) |
| McFarlin et al., 2016 | 28 Non-resistance trained participants (20 ± 1 and 19 ± 2 years) | 400 mg Curcumin (Longvida®), 48 h before and 72 h after exercise | Placebo | CK, IL-6, IL-8, IL-10, TNF-α | Double-blind randomised controlled trial | ↓ CK (s) ↓ IL-8 (s) ↓ TNF-α (s) |
| Delecroix et al., 2017 | 16 Elite rugby players (20.7 ± 1.4 years) | 2 g Curcumin and 20 mg piperine taken three times a day 48 h before and after exercise | Placebo | CMJ, CK concentrations | Randomised controlled trial | ↓ CMJ height (ns) ↓ CK 72 h post-exercise |
| Tanabe et al., 2019a | 10 Healthy men (Exp 1 – 28.5 ± 3.4 years. Exp 2 – 29.0 ± 3.9 years) | 90 mg Curcumin (Theracurmin) twice daily (total 180 mg). Exp 1: 7 days pre-exercise. Exp 2: 7 days post-exercise | Placebo | CK, IL-8, TNF-α, MVC torque, muscle pain | Double-blind crossover trial | *Exp 1:* ↓ IL-8 (s) - MVC torque, TNF-α, CK (ns) *Exp 2:* ↓ CK (s) - MVC torque, IL-8, TNF-α (ns) |
| Tanabe et al., 2019b | 24 Healthy men (pre 28.8 ± 3.6 years, post 29.8 ± 3.4 years, control 28.0 ± 3.2) | 90 mg Curcumin (Theracurmin) twice a day (total 180 mg): Pre – 7 days before Post – 4 days after Control – 4 days after | Placebo | CK concentrations, muscle pain, MVC torque | Parallel randomised trial (single-blind) | ↓ Muscle pain (s) - MVC torque (ns) - CK (ns) |
| Amalraj et al., 2020 | 30 Participants (36 ± 11 years. Male [*n* = 12] and female [*n* = 18]) | 500 mg Curcumin (Cureit®) consumed daily during day 1, 2 and 3 of the trial | Placebo | CK concentrations, muscle soreness | Randomised double-blind placebo-controlled trial | ↓ Muscle soreness (s) - CK (ns) |
| Basham et al., 2019 | 20 Healthy men (21.7 ± 2.9 years) | Three 500 mg capsules of curcumin (CurcuFresh) daily for 28 days | Placebo | CK, TNF-α concentrations, muscle soreness | Randomised double-blind placebo-controlled between-subjects design | ↓ CK (s) ↓ Muscle soreness (s) - TNF-α (ns) |
| Cardaci et al., 2020 | 23 Active men and women (21.13 ± 1.06 years) | 2 g Curcumin and 20 mg piperine, 11 days total starting seven days prior to exercise | Placebo | Muscle soreness | Double-blind, randomised placebo-controlled trial | - Muscle soreness (ns) |

*(continued)*

**Table 2.** (continued)

| Author(s) and year published | Population | Intervention | Comparator | Outcomes | Study design | Main conclusion(s) (24 h post-exercise, compared to placebo) |
|---|---|---|---|---|---|---|
| Faria et al., 2020 | 28 Participants (36 ± 2 and 34 ± 2 years) | Three 500 mg capsules per day for 29 days before, then immediately before and after the half-marathon | Placebo | CK, IL-6, IL-10 | Double-blind, randomised placebo-controlled trial | ↑ IL-10 (s) - IL-6 (ns) - CK (ns) |
| Mallard et al., 2020 | 27 Strength-trained male participants (26 ± 5 and 26 ± 4 years) | 1 g Curcumin (500 mg HydroCurc mixed with 500 mg maltodextrin) or placebo, mixed with water, taken pre-exercise and post-exercise | Placebo | CK, hsCRP, IL-6, IL-10 and TNF-α, muscle pain | Double-blind, randomised placebo-controlled trial | ↑ IL-10 (s) ↑ IL-6 (s) ↓ Muscle pain (s) - CK, hsCRP, TNF-α |
| Salehi et al., 2021 | 65 Healthy females (21 ± 2) | 500 mg/day encapsulated curcumin or 500 mg/day encapsulated corn starch for 8 weeks | Placebo | CRP, LDH, TAC, MDA, VO2max | Double-blind, randomised placebo-controlled trial | ↓ CRP (s) |
| Hillman et al., (2021) | 22 Healthy recreationally trained individuals (22 ± 1 and 21 ± 2 years) | 500 mg Curcumin with 475 mg total curcuminoids or placebo (500 mg of maltodextrin) twice daily (1 g/day), repeated over 10 days | Placebo | CK, ESR, muscle soreness (VAS) | Double-blind placebo-controlled parallel group trial | - CK (ns) - ESR (ns) ↓ Muscle soreness (s) |
| Kisiolek et al., (2021) | 36 Healthy and physically active individuals (23.1 ± 3.7, 25.0 ± 3.6 and 25.6 ± 5.1 for control, curcumin fast and curcumin slow groups, respectively) | Longvida® Optimized Curcumin 1000 mg/day or rice flour placebo 1000 mg/day for 14 days | Placebo | CRP, IL-6, IL-1RA | Double-blind randomised placebo-controlled trial | - CRP - IL-6 - IL-1RA |

Notes: ↑: Increase compared to placebo; ↓: decrease compared to placebo; -: no observable difference to placebo; s: significant; ns: not significant; CK: creatine kinase; CMJ: countermovement jump; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; hsCRP: high sensitivity CRP; IL-1RA: interleukin 1 receptor antagonist: IL-6: interleukin 6; IL-8: interleukin 8; IL-10: interleukin 10; LDH: lactate dehydrogenase; MDA: malondialdehyde; MVC: maximum voluntary contraction; TAC: total antioxidant capacity; TNF-α: tumour necrosis factor alpha; VAS: visual analogue scale; VO2max: maximum oxygen uptake.

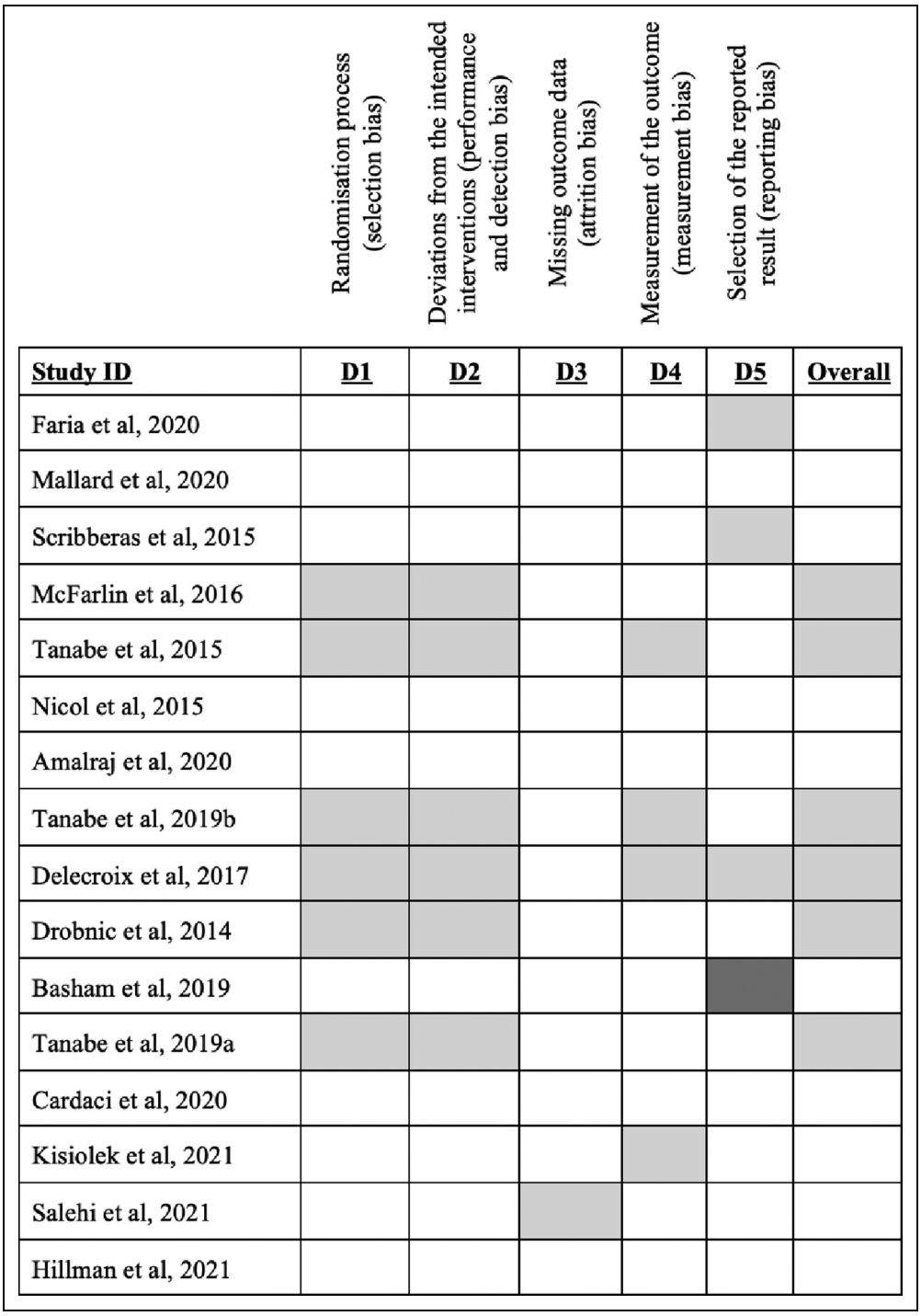


**Figure 2.** Individual risk of bias summary. White indicates low risk of bias, light grey indicates some concerns, dark grey indicates high risk of bias.

*Risk of bias across studies.* Primarily risk of bias across studies arose through selection, performance and detection bias with 37.5% of papers showing some concerns (Delecroix et al., 2017; Drobnic et al., 2014; McFarlin et al., 2016; Tanabe et al., 2015, 2019a, 2019b) (Figure 3). Twenty-five percent of the included papers showed some concerns for measurement bias, and 18.8% displayed some concerns for reporting bias. One paper (6.3%) displayed a high risk of reporting bias (Basham et al., 2019). Overall 62.5% of papers included in this systematic review displayed a low risk of bias.

## *Meta-analyses*

Primary meta-analyses were conducted using parallel study designs only to prevent results from being influenced

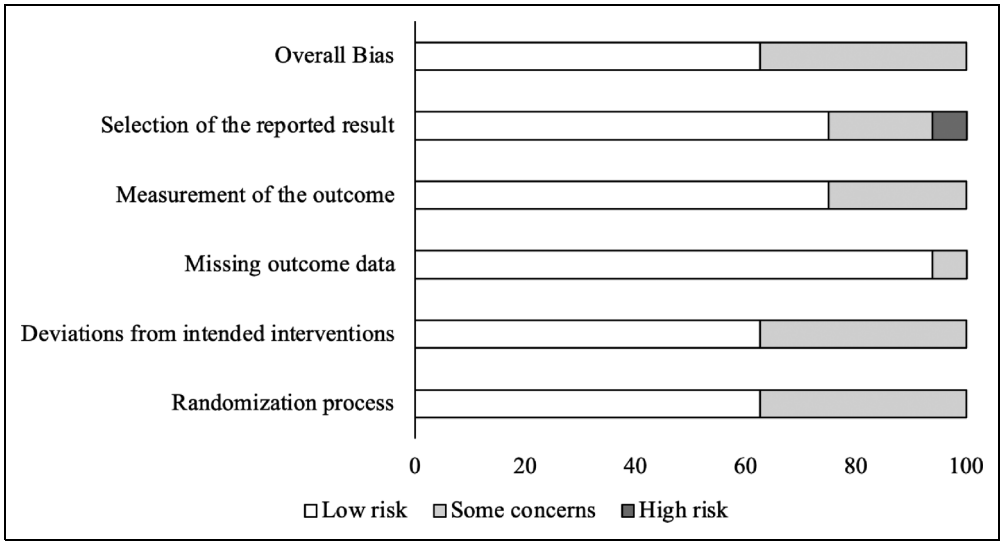


**Figure 3.** Across study risk of bias summary.

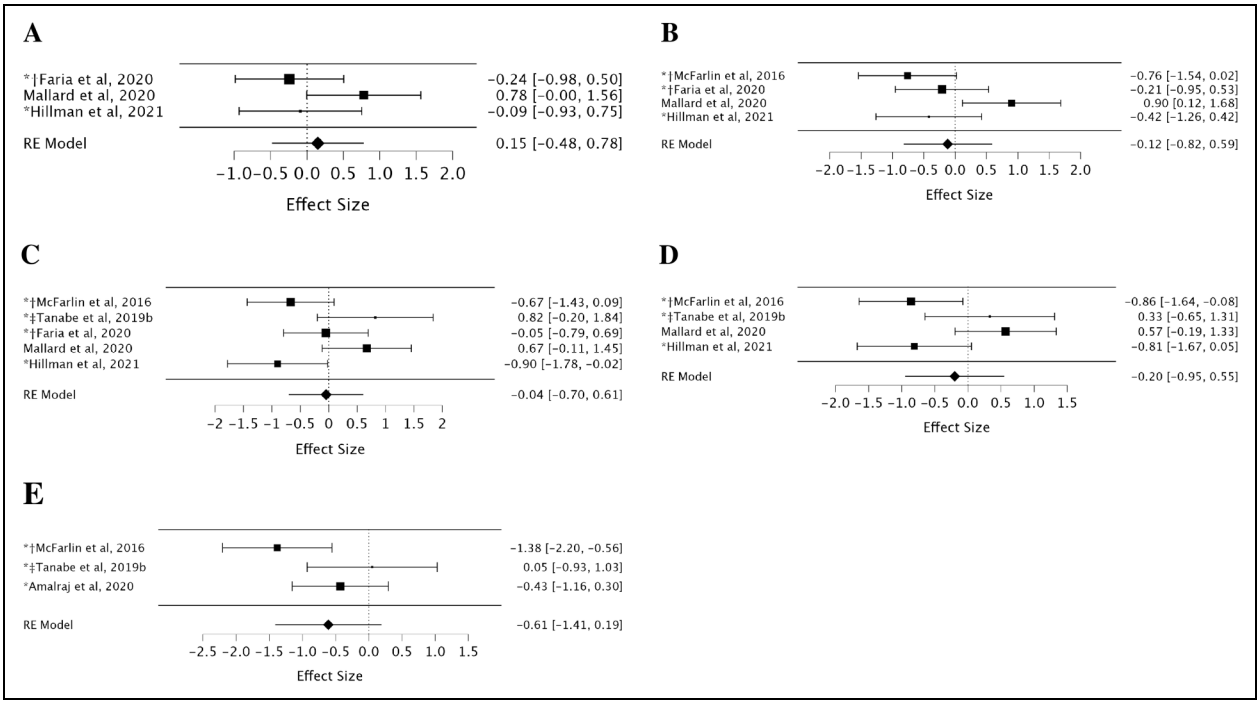


**Figure 4.** Changes in exercise-induced muscle damage at 0 h (a), 24 h (b), 48 (c), 72 h (d) and 96 h (e) post-exercise with supplementation (parallel only). *Indicates data was extracted using WebPlotDigitizer (Rohatgi, 2020). † Indicates standard deviation was calculated from standard error (Higgins et al., 2021). ‡ Indicates that data was extracted from the 'post' group within the study which was most relevant to other studies within this analysis.

by the repeated bout effect. ES differences are displayed in Table 1.

*Functional strength.* Due to the lack of literature using a parallel study design, a forest plot was not generated for FS. All paper ES and CIs were calculated using two papers with different study designs (Tanabe et al., 2019a, 2019b) and are displayed in Table 1. One paper was removed (Tanabe et al., 2015) as MVC torque was not measured in newton-metres and comparison with other literature was therefore inappropriate.

*EIMD.* Three, four, five, four and five papers were included in the EIMD meta-analyses, corresponding to 0, 24, 48, 72 and 96 h post-exercise, respectively (Figure 4). The largest negative ES of −0.61 (95% CI: −1.41, 0.19) was observed 96 h post-exercise, though this was not statistically significant ($p = 0.134$). Conversely the largest positive ES of 0.15

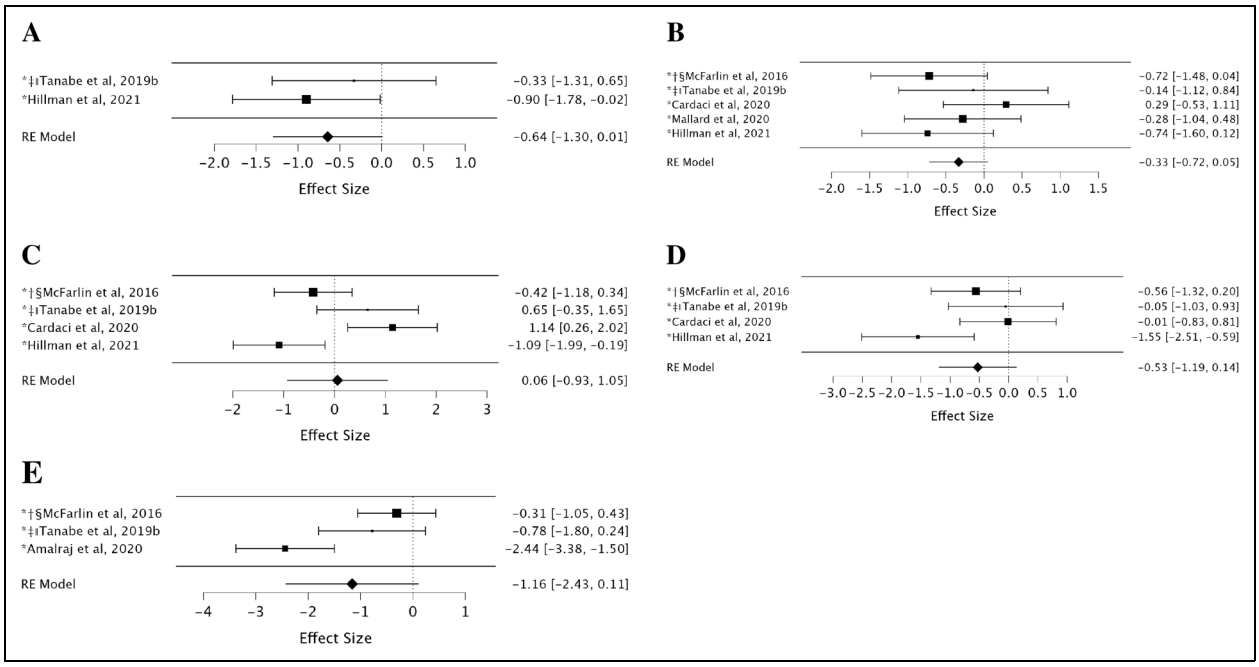


**Figure 5.** Changes in delayed onset muscle soreness at 0 h (a), 24 h (b), 48 h (c), 72 h (d) and 96 h (e) post-exercise with supplementation (parallel only). * Indicates data was extracted using WebPlotDigitizer (Rohatgi, 2020). † Indicates standard deviation was calculated from standard error (Higgins et al., 2021). ‡ Indicates that data was extracted from the 'pre' group within the study which was most relevant to other studies within this analysis. § Indicates that mean and standard deviation data was an average of left and right quadricep soreness. || Indicates that data was extracted from the 'palpation' group.

(95% CI: −0.48, 0.78) was observed 0 h post-exercise, this was also not significant ($p = 0.644$).

Statistical heterogeneity was revealed as moderate to substantial, indicating some variation between studies. $I^2$ statistics were as follows: 48.05% (0 h), 68.77% (24 h), 67.86% (48 h), 68.18% (72 h) and 63.23% (96 h).

One study by Basham et al. (2019) was removed due to high risk of bias in reported results (no reporting of CK concentrations at multiple time points post-exercise, despite reporting other outcomes this way). One paper by Drobnic et al. (2014) was removed for not reporting SD data or including this in the CK figure.

Data indicated an overall favour towards reduced CK concentrations; however, no time points were significant ($p = 0.644$, 0.739, 0.893, 0.601 and 0.134 for 0, 24, 48, 72 and 96 h, respectively), resulting in acceptance of the null hypothesis.

*DOMS.* Two, five, four, four and three papers were included in the DOMS meta-analyses, corresponding to 0, 24, 48, 72 and 96 h post-exercise, respectively (Figure 5). The largest beneficial ES of −1.16 (95% CI: −2.43, 0.11) was observed 96 h post-exercise, though this was not statistically significant ($p = 0.074$).

Statistical heterogeneity was revealed as minimal to considerable, indicating large variation between studies. $I^2$ statistics were as follows: < 0.001% (0 h), 7.37% (24 h), 80.08% (48 h), 56.49% (72 h) and 83.49% (96 h).

One study by Basham et al. (2019) was removed due to high risk of bias in reported results (no reporting of VAS scores at multiple time points post-exercise, despite reporting other outcomes this way).

Data indicated an overall trend towards reduced muscle soreness; however, no time points were statistically significant ($p = 0.054$, 0.092, 0.908, 0.119 and 0.074 for 0, 24, 48, 72 and 96 h, respectively), resulting in acceptance of the null hypothesis.

*Inflammation.* Four papers were included in the inflammation meta-analyses, with several papers reporting multiple post-exercise time points (Figure 6). The largest negative ES of −0.10 (95% CI: −0.67, 0.47) was observed at 0 h post-exercise, though this was not statistically significant ($p = 0.729$). The largest positive ES were observed at both 24 and 72 h post-exercise with 0.26 (95% CI: −0.71, 1.23) and 0.26 (95% CI: −0.34, 0.86), respectively, though neither of these were statistically significant ($p = 0.603$ [24 h] and 0.396 [72 h]).

Statistical heterogeneity was revealed as minimal to substantial, indicating some variation between studies. $I^2$ statistics were as follows: 37.15% (0 h), 68.94% (24 h), 41.93% (48 h) and 20.32% (72 h). One study by Kisiolek et al. (2021) was removed from this analysis due to reporting data in relation to supplement ingestion and time trial performance, and post-exercise intervals. One paper was removed (Salehi et al., 2021) as inflammation was assessed using CRP, along with a lack of specific time points post-exercise being reported.

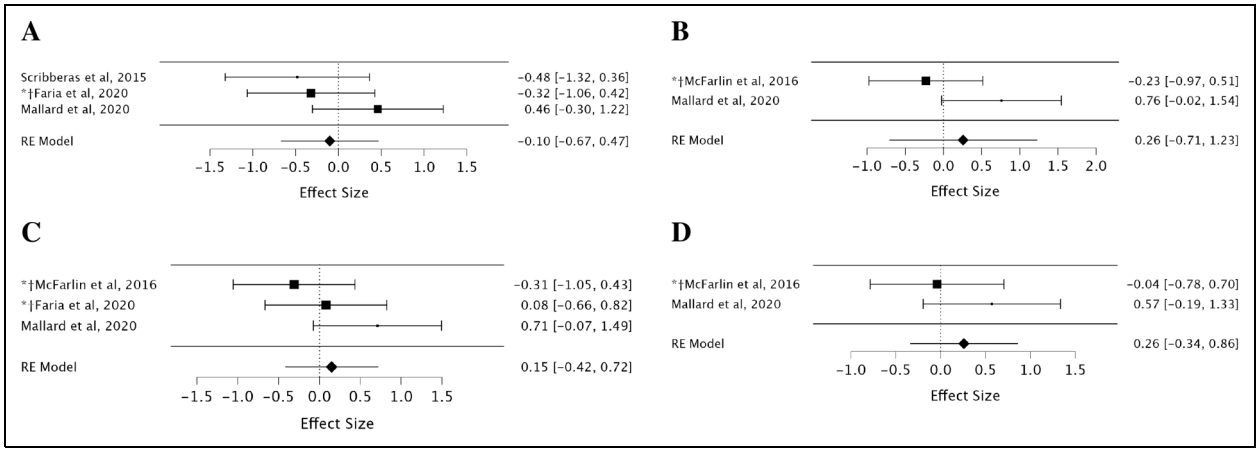


**Figure 6.** Changes in interleukin 6 at 0 h (a), 24 h (b), 48 h (c) and 72 h (d) post-exercise with supplementation (parallel only). * Indicates data was extracted using WebPlotDigitizer (Rohatgi, 2020). † Indicates standard deviation was calculated from standard error (Higgins et al., 2021).

Overall results indicated a slight trend towards increased IL-6 concentrations overall, however, no time points were statistically significant ($p = 0.729$, 0.603, 0.611 and 0.396 for 0, 24, 48 and 72 h, respectively), resulting in acceptance of the null hypothesis.

### *Synthesis of results*

Table 1 details findings from the four meta-analyses. ES indicated a small to medium effect for FS and DOMS and a small effect for EIMD and inflammation. The inclusion of crossover designs changed some of the mean ES, but the overall finding remained unchanged (i.e. all CIs included zero). All four meta-analyses were not statistically significant. Heterogeneity ranged from moderate to substantial.

## Discussion

This review aimed to assess the effect of curcumin supplementation on FS outcomes and markers of exercise-induced muscle damage. As such, the following sections are divided into specific outcomes (FS, EIMD, DOMS and inflammation), followed by a summary of strengths and limitations applicable to all outcomes (i.e. bioavailability). While the meta-analyses included parallel trials only, this discussion will refer to all papers alongside parallel research designs only.

Due to the search strategy utilised and studies included in this research, findings are broadly applicable to all outcome variables excluding FS and are not specific to one particular exercise type. As the two papers included in the FS outcome utilised similar exercise methodologies (Tanabe et al., 2019a, 2019b), our findings in relation to FS apply only to the methodologies adopted in this research.

### *Functional strength*

Previous research examining FS changes have observed varying results, with Tanabe et al. (2015) reporting statistically significant improvements 0, 48, 72 and 96 h post-exercise. Similar research by Tanabe et al. (2019a) observed significant improvements 3 to 7 days post-exercise, while further research Tanabe et al. (2019b) observed no statistically significant improvements over all time points. To our knowledge there are currently no systematic reviews investigating the relationship between curcumin and FS.

In this review we compared research with differing methodologies, owing to the lack of available literature examining FS. Despite potential trends towards smaller reductions in FS following supplementation, when using all papers, ES were as follows: 0.47 ($p = 0.162$), 0.41 ($p = 0.225$), 0.59 ($p = 0.080$), 0.4 ($p = 0.239$) and 0.6 ($p = 0.076$) for 0, 24, 48, 72 and 96 h post-exercise, respectively – indicating non-significant medium to large ES. ES for parallel papers only were as follows: 0.50, 0.27, 0.67, 0.51 and 0.74 for 0, 24, 48, 72 and 96 h post-exercise, respectively. Differences between studies utilising different methodologies were small, across all time points. There was little evidence of statistical heterogeneity ($I^2 \leq 0.001\%$), however, due to the small number of papers included this statistic may be open to bias (von Hippel, 2015) and should therefore be interpreted with caution.

Moreover, both papers included were conducted by the same researchers (Tanabe et al., 2019a, 2019b), and thus comparisons with previous research may be redundant. Additionally, as both papers included similar researchers, any concerns regarding bias may apply to the overall outcome and influence the results of this research. Bias assessment of papers included for this outcome revealed some risk of bias. One study in particular (Tanabe et al., 2019b) revealed risk in 60% of the assessed domains, relating to the single-blind design, randomisation method and potentially unblinded outcome assessors – consequently lessening the quality of the findings.

Despite previous research observing significant improvements individually, combined results were non-significant.

Furthermore, owing to potential bias concerns, current literature examining this outcome may not be appropriate for recommending curcumin supplementation to improve FS.

As many of the limitations across analyses are similar, these will be discussed at the end. However, one limitation that may be more applicable to this outcome is bias, as all papers displayed some concerns – potentially undermining findings.

## EIMD

Previous EIMD research has observed varying results, though the majority of these trended towards reduced EIMD with supplementation. Research by McFarlin et al. (2016) displayed a consistent trend towards reduced EIMD over all time points examined. These findings are somewhat similar to research by Nicol et al. (2015), who observed a non-significant 'small lowering impact'. Conversely, Tanabe et al. (2019b) displayed a trend towards an increase in CK concentrations at 48, 72 and 96 h post-exercise. Further research by Delecroix et al. (2017) observed no significant CK reductions.

One systematic review conducted by Suhett et al. (2020) reported beneficial effects of curcumin supplementation on muscle damage through decreased CK concentrations. However, their research also reported inconclusive findings, with muscle damage improvements occurring at inconsistent time points across studies.

Regarding EIMD in this review we observed an overall trend towards reduced CK concentrations, in analyses using all papers and parallel only (*all:* 0.02 [0 h], −0.16 [24 h], −0.11 [48 h], −0.31 [72 h] and −0.64 [96 h]; *parallel only:* 0.15 [0 h], −0.12 [24 h], −0.04 [48 h], −0.2 [72 h] and −0.61 [96 h]). Differences in ES between studies utilising different methodologies were small.

The majority of time points were not statistically significant ($p =$ all: 0.947 [0 h], 0.567 [24 h], 0.622 [48 h] and 0.237 [72 h]; *parallel only*: 0.644 [0 h], 0.739 [24 h], 0.893 [48 h], 0.601 [72 h] and 0.134 [96 h]). Only the 96 h post-exercise CK reductions were statistically significant, in analyses with all papers included ($p = 0.003$). Variation in ES between analyses with all papers and parallel only was observable, though the trend of effect was similar. Consequently, differences in research design may have a minimal impact on findings for this outcome measure.

Heterogeneity was revealed as minimal to substantial when all papers were included and moderate to substantial with parallel trials only, indicating some variation between studies – regardless of the methodology used.

Several papers included in this analysis revealed concerns regarding bias – with three papers displaying some concerns in at least one domain (Faria et al., 2020; McFarlin et al., 2016; Tanabe et al., 2019b) and two papers displaying 'some concerns' overall (McFarlin et al., 2016; Tanabe et al., 2019b). Concerns generally related to selection, performance and detection bias. One paper (Basham et al. 2019) was removed due to not reporting CK concentrations in relation to specific time points. Additionally, bias assessment for this paper indicated a high risk of reporting bias. One paper by Drobnic et al. (2014) was removed for not reporting standard deviation data or including this in the CK figure.

Additionally, research by Delecroix et al. (2017) was removed due to not reporting results in relation to baseline, rendering them unusable. Furthermore, this paper was found to have some risk of bias across multiple domains. Therefore, due to concerns regarding bias, these papers were removed.

This research contradicts previous individual studies, as the majority of ES were not significant, despite individual papers reporting significant results. When compared with a previous systematic review (Suhett et al., 2020), this research observed similarly inconsistent findings, potentially due to differences in study design, intervention methodology and/or participant training status.

Despite small observable trends towards reduced muscle damage, these are not conclusive, and the pooled ES is uncertain. As such, a beneficial effect of curcumin ingestion on EIMD cannot be claimed. The low number of studies included in this analysis is likely not enough to recommend curcumin to improve EIMD at an individual level. In the broader context, considerably more research is needed before recommending the use of curcumin in wider populations (e.g. clinical settings). Heterogeneity may be considered the primary limitation of this outcome, with all analyses displaying moderate variation at best, and should be considered when interpreting results – particularly at 24, 48 and 72 h post-exercise.

## DOMS

Previous research investigating curcumin and DOMS has reported varied results, with Tanabe et al. (2019b), observing increased soreness at 48 h post-exercise and reduced soreness at 72 and 96 h post-exercise. Varying pain status and severity were also reported by Nicol et al. (2015), who observed differences in relation to time. Generally, research examining this outcome fluctuates, potentially based on ingestion time, dosage and bioavailability.

Previous systematic reviews have also described varying results, with research by Fernández-Lázaro et al. (2020) reporting both significant and non-significant improvements in VAS scores at some time points but not others. This review highlights the potential impact of varied curcumin dosages and the effect this can have on VAS measurements. Furthermore, as subjective pain perception may vary considerably depending on the individual, DOMS may be the outcome most susceptible to variation, irrespective of ingestion time, dosage or bioavailability.

In this review ES indicated an overall trend towards reductions in muscle soreness using parallel trials only,

despite the 48 h post-exercise ES revealing a small increase (*parallel only*: −0.64, −0.33, 0.06, −0.53 and −1.16 for 0, 24, 48, 72 and 96 h post-exercise, respectively). When all papers were included, ES trended towards the same direction (*all*: −0.35, −0.24, 0.1, −0.35 and −0.75 for 0, 24, 48, 72 and 96 h post-exercise, respectively), despite differences in ES magnitude. Variation was small to medium between studies utilising different methodologies, depending on outcome measurement time. No time points in this analysis were statistically significant ($p =$ all: 0.109 [0 h], 0.125 [24 h], 0.760 [48 h], 0.134 [72 h] and 0.079 [96 h]; parallel only: 0.054 [0 h], 0.092 [24 h], 0.908 [48 h], 0.119 [72 h] and 0.074 [96 h]).

The overall findings of this paper differ to individual studies reporting significant results. However, when compared with a previous systematic review (Fernández-Lázaro et al., 2020), findings were somewhat comparable, due to similar papers being included in the analysis. Both papers observed considerable variation in results and magnitude of effect.

Statistical heterogeneity for DOMS papers varied substantially, from minimal at 0 and 24 h post-exercise to considerable at 48 and 96 h post-exercise, further supporting the hypothesis that ES variation relates to a multitude of factors and not simply ingestion of curcumin.

Risk of bias assessment revealed some concerns for two papers included in the parallel-only DOMS analyses (McFarlin et al., 2016; Tanabe et al., 2019b). No papers were deemed to have a high risk of bias. In terms of bias for other study designs, research by Tanabe et al. (2015, 2019a) presented some concerns and should be considered when reviewing all-paper ES.

Although ES indicated a trend towards reduced DOMS, all time points were not statistically significant. Additionally, the body of literature examining this outcome may be lacking, with current literature displaying considerable variation in heterogeneity alongside some concerns regarding bias. As such the supplemental use of curcumin to reduce muscle soreness may not be warranted based on current literature.

## Inflammation

Lastly this review investigated curcumin and inflammation. Previous research in this area has observed mixed results, with some authors reporting non-significant IL-6 reductions (McFarlin et al., 2016; Sciberras et al., 2015), no change (Faria et al., 2020; Kisiolek et al., 2021) or significant IL-6 increases (Mallard et al., 2020). One previous systematic review reported mostly non-significant effects (Suhett et al., 2020). Although a small number of researchers have observed significant IL-6 reductions, these improvements are rarely consistent. Furthermore, several papers, perhaps unexpectedly, report IL-6 increases, despite curcumin ingestion. This may potentially indicate that curcumin supplementation has a lesser impact on inflammation compared to other outcomes.

In this research, parallel trial ES indicated a trend towards increased IL-6 concentrations at all time points except immediately (0 h) post-exercise (*parallel only*: −0.10, 0.26, 0.15 and 0.26 for 0, 24, 48 and 72 h post-exercise, respectively). ES with all study designs were noticeably different, in both direction and magnitude, as such, interpreting results is difficult (*all*: 0.19, −0.18, 0.3, −0.07 and −0.18 for 0, 24, 48, 72 and 96 h post-exercise, respectively). While analyses with all papers (including crossover trials) could be influenced by the repeated bout effect, both Tanabe et al. (2015) and Nicol et al. (2015) implemented washout periods to minimise the probability of this. Small to medium variation between study designs was observed depending on measurement time.

Similarly to other outcomes, no results were statistically significant for analyses with parallel trials ($p = 0.729$, 0.603, 0.611 and 0.396 for 0, 24, 48 and 72 h, respectively). Furthermore, when all papers were included, results were also non-significant ($p = 0.413$, 0.600, 0.232, 0.853 and 0.515 for 0, 24, 48, 72 and 96 h post-exercise, respectively). This lack of statistical significance, irrespective of study design, therefore, results in acceptance of the null hypothesis.

In terms of heterogeneity, research examining inflammation ranged from minimal to substantial. Bias was less notable for this outcome, with only one of the four parallel studies displaying some concerns overall, however, this should still be considered when interpreting results. Ultimately, between the lack of statistical significance, notable heterogeneity, and the limited data available, reaching a consensus for inflammation may not be possible at this time. The primary limitation of this outcome may be the lack of research investigating exercise-induced inflammation specifically, rather than general inflammation.

## Summary

In this review, some strengths may be highlighted, for example, the systematic approach based on the PRISMA guidelines (Liberati et al., 2009), along with the risk of bias assessments using the Cochrane RoB 2 tool (Sterne et al., 2019).

In terms of findings, the main finding of this research is the uncertainty observed when individual studies are combined, despite individual studies reporting beneficial effects. These findings highlight ambiguity across all variables, irrespective of the number of studies included in each analysis. As this research observed no overall effects, it is therefore not possible to speculate on potential mechanisms of action.

To our knowledge, this research may be the first to include meta-analyses and investigate changes in FS. While these outcomes were not significant, other research has observed significant differences and suggests a potentially beneficial effect, highlighting the need for further research. Differences in inflammation ES were notable, though similar to other outcomes, it is currently not possible

to reach a consensus on whether supplementation is beneficial.

The remainder of this section will briefly discuss the limitations of the general body of curcumin literature followed by limitations of research included in this review before discussing limitations with this review in particular.

### *Limitations*

In terms of research discussed in this review, a notable limitation is the varying degrees of bias within and across studies which, when compounded with the small number of studies included, result in analyses that may be heavily influenced by one paper or particular authors, in the case of Tanabe et al. (2015, 2019a, 2019b). Concerns with bias primarily arose through single-blind study designs, and future research may benefit from using a double-blind design. Similarly, future investigations may benefit from utilising a similar methodology to previous research, as a further limitation of this study may be the considerable methodological variation (i.e. dosages and use of adjuncts) of the research included.

The primary limitation of this review was the limited number of papers included, arising largely because of the wider body of research, alongside the potentially rigorous inclusion and exclusion criteria employed.

To summarise, while curcumin may have potential, particularly regarding EIMD and DOMS, current research is not sufficient to provide recommendations. Limited research, bias concerns, substantial heterogeneity and many confounding variables all increase the difficulty when reaching a consensus; however, many of these factors can be addressed by conducting further research – allowing a potential consensus to be reached. This research recommends the following: a direct examination of curcumin and FS, in an adequately powered study, an increased number of participants, a focus on replicable supplementation procedures/methodologies (i.e. dosages, type of curcumin and use of adjuncts), more robust monitoring of confounding variables and improved study design to minimise the risk of bias (preferably double-blinded with third party statistician involvement for analysis).

Based on the findings of this research and uncertainty within the current evidence base, supplementation is not recommended at this time. Moreover, previous research based on animal models have observed reductions in iron absorption with curcumin supplementation (Chin et al., 2014), with similar associations being observed in humans (Tuntipopipat et al., 2009), though research in this area may be lacking. Due to the role of iron in various metabolic processes, including oxygen transport, and the potential negative relationship between curcumin and iron absorption, athletes are advised to consider the risks and benefits of curcumin usage prior to supplementation.

Despite this, previous research has observed dosages of up to 8g/day to be safe (Chainani-Wu, 2003), and supplemental use of curcumin has been declared as 'generally recognised as safe' by the Food and Drug Administration (Sharifi-Rad et al., 2020). Beyond this consumers may experience side effects.

## Conclusion

The aim of this systematic review and meta-analysis was to investigate the potential use of curcumin ingestion to improve FS, EIMD, DOMS and/or inflammation. In this regard, while individual research may have observed a beneficial effect, this research found no evidence of statistically significant changes upon analysis. Furthermore, this study highlights the need for methodological standardisation, as varying research methods may describe across study heterogeneity, rather than the variable potential impact of curcumin supplementation. Lastly, this study highlights the need for more research into markers of FS. As the evidence base for FS may be limited, research investigating this outcome may be disproportionately open to bias. Consequently, to thoroughly examine if an effect exists, substantially more research is needed for all outcome variables.

### Author contributions

RAO and DJP conceived the study. RAO ran the initial search and screened the retrieved records with support from DJP. RAO performed the statistical analysis. RAO and DJP contributed to drafts of the manuscript, and both authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on request.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Ethical approval

Ethical approval granted by the institutional ethics committee as a low-risk secondary data project.

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### ORCID iDs

Robert A Oxley https://orcid.org/0009-0008-3414-8106
Daniel J. Peart https://orcid.org/0000-0003-0849-3738

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