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SYSTEMATIC REVIEW

Creatine Supplementation and Upper Limb Strength Performance: A Systematic Review and Meta-Analysis

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Abstract
Background Creatine is the most widely used supplementation to increase performance in strength; however, the most recent meta-analysis focused specifically on supplementation responses in muscles of the lower limbs without regard to upper limbs.
Objective We aimed to systematically review the effect of creatine supplementation on upper limb strength performance.
Methods We conducted a systematic review and meta-analyses of all randomized controlled trials comparing creatine supplementation with a placebo, with strength performance measured in exercises shorter than 3 min in duration. The search strategy used the keywords 'creatine', 'supplementation', and 'performance'. Independent variables were age, sex and level of physical activity at baseline, while dependent variables were creatine loading, total dose, duration, time interval between baseline (T0) and the end of the supplementation (T1), and any training during supplementation. We conducted three meta-analyses: at T0 and T1, and on changes between T0 and T1. Each meta-analysis was stratified within upper limb muscle groups.
Results We included 53 studies (563 individuals in the creatine supplementation group and 575 controls). Results did not differ at T0, while, at T1, the effect size (ES) for bench press and chest press were 0.265 (95 % CI 0.132–0.398; $p < 0.001$) and 0.677 (95 % CI 0.149–1.206; $p = 0.012$), respectively. Overall, pectoral ES was 0.289 (95 % CI 0.160–0.419; $p = 0.000$), and global upper limb ES was 0.317 (95 % CI 0.185–0.449; $p < 0.001$). Meta-analysis of changes between T0 and T1 gave similar results. The meta-regression showed no link with characteristics of population or supplementation, demonstrating the efficacy of creatine independently of all listed conditions.
Conclusion Creatine supplementation is effective in upper limb strength performance for exercise with a duration of less than 3 min, independent of population characteristics, training protocols, and supplementary doses or duration.

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Key Points

Creatine supplementation is effective in upper limb strength performance.

Its effectiveness is independent of population characteristics, training protocols, and supplementary doses and duration.

1 Introduction

Despite creatine being a natural component of the diet found in low levels in red meat and seafood [1], creatine is the most widely used supplementation to increase strength performance [2]. Strength improvements following creatine supplementation are most commonly reported in the lower limb strength performance because lower limbs are germane to so many sporting pursuits. A recent meta-analysis on creatine supplementation and strength performance evaluated specific muscles or group of muscles of the lower limb [3]; however, upper limb responses to creatine supplementation could generate similar interest. To date, no meta-analysis has specifically focused on upper limb performances in response to creatine supplementation. Explosive upper limb performances are attributed to anaerobic metabolism. The predominant source of immediate energy is stored phosphocreatine levels in skeletal muscle, a high-energy phosphate. At the onset of anaerobic metabolism, phosphocreatine levels decrease via dephosphorylation to resynthesize adenosine triphosphate (ATP) from adenosine diphosphate (ADP). Increasing intramuscular creatine from exogenous creatine ingestion is postulated to enhance high-energy phosphate metabolism and increase strength performance. Anaerobic metabolism decreases until an equal contribution from the aerobic and anaerobic energy systems occurs after approximately 2–4 min [4]. In order to obtain the highest level of proof, only randomized controlled trials (RCTs) reporting potential placebo effects [5] and investigating the effects of creatine supplementation on short-term performance (3 min or less) [4] of the upper limb are the focus of this review. Similar to our previous review of lower limb strength performance [3], we examined the effects of creatine supplementation on the specific muscles or group of muscles of the upper limb.

Thus, we aimed to conduct a systematic review and meta-analyses of RCTs comparing the effects of creatine supplementation and placebo on upper limb strength performance measured after exercises of less than 3 min in duration. The meta-analyses were stratified by muscles or groups of muscles.

2 Methods

2.1 Literature Search

We reviewed all RCTs comparing a creatine supplementation group with a placebo group. Using the keywords ‘creatine supplementation’ and ‘performance’, we conducted a search of the PubMed, Cochrane Library, ScienceDirect and EMBASE databases on 7 October 2015. The search was not limited to specific years and no language restrictions were applied. To be included, the control group needed to receive a placebo during the supplementation period. The search strategy was inclusive of studies of healthy males or females, independent of age, imposing any supplementation dose, extending over various periods of supplementation, with or without training (previously or during supplementation), and without a history of weight loss induced by a restrictive diet. The major inclusion criterion was a description of strength performance at baseline and following supplementation or placebo with a double-blind randomization, and the duration of exercise when performance was measured had to be less than 3 min. We also included articles that only reported changes in performance. In the case of repeated and consecutive performances, for our meta-analysis we used restricted data of interest to the first performance as it described the most anaerobic response. Included articles also had to report a statistical dispersion of results, such as standard deviations or quartiles. In addition, reference lists of all publications meeting the inclusion criteria were manually searched to identify any further studies not found through electronic searching. The search strategy is described in Fig. 1. One author (CL) conducted all literature searches and collated the abstracts; two authors (CL and FD) separately reviewed

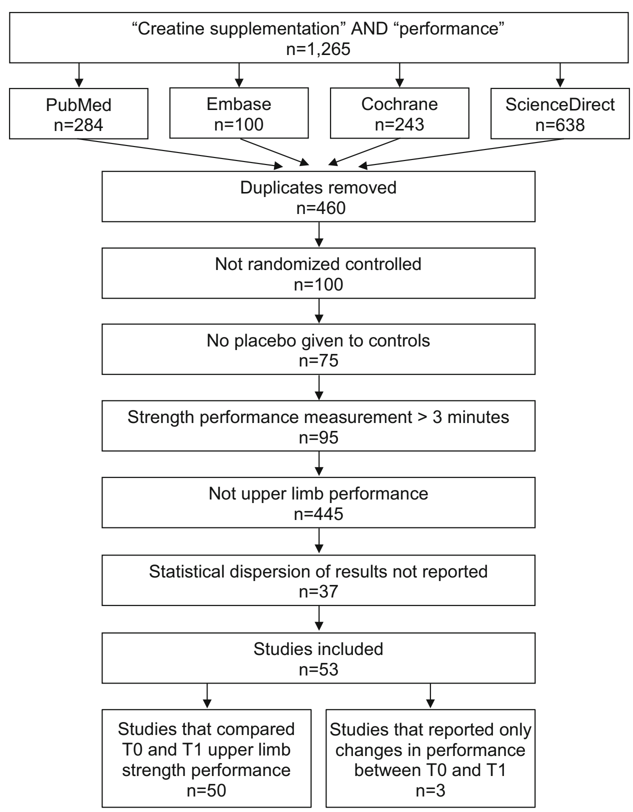

Fig. 1 Search strategy. *T0* baseline, *T1* following supplementation

the abstracts and, based on the selection criteria, decided the suitability of the articles for inclusion; and a third author (GN) was asked to review the article when consensus on suitability was not met. All authors then reviewed the eligible articles.

2.2 Quality of Assessment

The Consolidated Standards of Reporting Trials (CONSORT) statement was used for checking the quality of reporting [6], and the 25 items identified in the CONSORT criteria could achieve a maximal score of 37.

2.3 Statistical Considerations

Data were analysed using Stata version 13, 2013 (StataCorp LP, College Station, TX, USA). Heterogeneity in the study results was evaluated by examining forest plots, confidence intervals (CIs) and using formal tests for homogeneity based on the I^2 statistic. For example, a significant heterogeneity may be due to variability within characteristics of studies, such as for participants (age, sex, training status), supplementation (loading dose, total dose), or modality of training (type, number of repetitions, speed). Random effects meta-analyses (DerSimonian and Laird approach) were conducted when data could be pooled [7], and p values <0.05 were considered statistically significant.

We conducted three meta-analyses based on the time of supplementation. First, the meta-analysis was conducted at baseline (T0), in order to verify baseline homogeneity of the creatine supplementation group and the control group. We then conducted meta-analyses on absolute scores reported in the data following creatine supplementation (T1). Finally, we conducted a third group of meta-analyses with the relative percent changes (T1–T0)/T0 for both groups, adding some studies reporting only these changes.

Within each meta-analysis on upper limb strength performance, there was stratification for the upper limb muscle groups (pectoral, back, shoulders, biceps, triceps and forearm). In addition, for the meta-analysis with the relative percentage change, we added stratification on triceps, and also completed additional meta-analyses based on site-specific strength testing. Pectoral performances were stratified by bench press and chest press. In addition, bench press performances were stratified by maximal weight lifted and number of repetitions.

We described our results calculating the effect size (ES; standardized mean differences as SMD) of creatine supplementation for each dependent variable [7], with a positive ES denoting improved performance. A scale for ES has been suggested, with 0.8 reflecting a large effect, 0.5 a moderate effect, and 0.2 a small effect [8].

Meta-regression analyses were conducted to explore the influence of study characteristics on standardized mean differences. The following characteristics were considered: sex of the participants (male vs. both sexes), age, physical status at baseline (sedentary, recreation, competitive), characteristics of creatine supplementation (loading dose, total dose, duration of supplementation), characteristics of training during supplementation (strength, aerobic, mixed, none), time between T0 and T1, and muscle groups (pectoral, back, shoulders, biceps, triceps and forearm). Results were expressed as regression coefficients and 95 % CI.

3 Results

3.1 Overview of Studies Included

The initial search identified a possible 1265 articles (Fig. 1); however, consideration of selection criteria and removal of duplicates reduced these articles to 50 RCTs that compared T0 and T1 upper limb strength performances during exercise lasting less than 3 min in creatine supplementation and placebo groups. Three additional studies that reported only changes in performance between T0 and T1 were added [9–11]. All articles were written in English.

3.2 Quality of Articles

Quality assessment of the 53 included studies reporting T0 and T1 data, as outlined by the CONSORT criteria, varied from 22 to 65 %, where a higher percentage implies a higher quality of scientific reporting [12]. Of the included studies, 70 % had a quality reporting score exceeding 50 %, and all studies described double blinding to the supplementation. Overall, the studies performed best in the Sect. 4 and worst in the Sect. 2, with all studies describing ethical approval. Sixty-five percent of studies did not report any conflict of interest, 25 % were funded by creatine manufacturers, and 10 % did not provide any information regarding funding.

3.3 Characteristics of Individuals

3.3.1 Sample Size

In the 53 included studies, 563 individuals in the creatine supplementation group were compared with 575 individuals in the placebo group.

3.3.2 Sex

The proportion of females remained low (25 %), with nine studies restricted to only women [9, 13–19]. A further two studies failed to report participants' sex [20, 21]. In total, 432 males and 131 females were included in the creatine supplementation group, and 457 males and 118 females in the placebo group.

3.3.3 Age

Regardless of whether age was expressed as a median or a mean value, the studies reported an age range of between 18 [14] and 75 years [22] for all participants.

3.3.4 Training Status

Overall, 40 % of the studies recruited recreationally trained participants, 28 % recruited competitive athletes, and 21 % were conducted on sedentary individuals. The remaining studies did not report the training status of the population.

3.4 Characteristics of Intervention

3.4.1 Type of Supplementation

Several types and forms of creatine are available, with creatine monohydrate being the most common type examined in 49 of 53 studies. However, three other types of supplementation were cited in four studies: polyethylene glycosylated creatine [23], di-creatine citrate [22], and creatine phosphate [24].

3.4.2 Loading Dose

For all studies, the mean loading dose for creatine supplementation was 20.9 ± 4.5 g/day, and more than 80 % of studies described a loading dose for the supplementation. The most common loading duration was between 5 and 7 days. The frequency of daily loading varied between 1 and 5 times [25, 26]; however, the loading dose was most regularly divided into three to four times per day with a 5 g/dose.

3.4.3 Maintenance Dose

Only 38 studies had a maintenance dose, which varied between 1.25 and 27.0 g/day [23, 27]. The quantity of the maintenance dose varied more between studies compared with the loading dose. Participants consumed the maintenance dose once daily.

3.4.4 Total Dose of Supplementation

The mean total dose of supplementation was 152.2 ± 131.6 g across the duration of the studies. Participants were supplemented between 5 [28–30] and 98 days [16].

3.4.5 Time Between T0 and T1

The duration between baseline and T1 ranged from 5 to 166 days [16, 31].

3.4.6 Training

More than 80 % of studies declared that the supplementation (creatine or placebo) was associated with sports training independent of the specificity of the targeted population. Participants trained for endurance, strength, or both. Among the 49 studies for which the training status was reported, 53.1 % of participants performed strength training during the trial, 6.1 % experienced aerobic training, and 28.6 % participated in mixed training (endurance and strength). Only seven studies reported no training [16, 32–37]. The frequency of training was predominantly three times per week.

3.5 Outcome and Aim of the Studies

All studies shared similar outcomes with varying degrees of clarity. The key dependent variables of the studies were muscle strength and body composition (body weight, lean body mass, percentage of fat free mass, total body water). Additional outcomes were heterogeneous but included estimates of perceived fatigue and recovery capacity during exercises, functional capacity, cardiovascular function, systemic inflammation, muscle fibre area and adverse events.

3.6 Study Designs

All studies were double-blind, randomized, placebo-controlled trials. No study supported a crossover design.

3.7 Stratification

With our inclusion criteria, 36 studies reported total weight lifted in kilograms (kg) and ten studies reported the number of repetitions for the bench press, allowing us to complete two meta-analyses. First, we conducted a meta-analysis on pectoral performances stratified on global tasks for bench press ($n = 43$ studies) and chest press ($n = 4$). The next level of our meta-analysis targeted upper limb muscle groups: pectoral ($n = 44$), back ($n = 1$), shoulders ($n = 2$), biceps ($n = 6$), and forearm ($n = 4$) (Fig. 2). We also included three articles reporting changes in performance [9–11]. These studies were included in the pectoral and biceps stratifications.

3.8 Meta-Analysis at Baseline (T0)

The effects of creatine supplementation and placebo at baseline are available online in the electronic

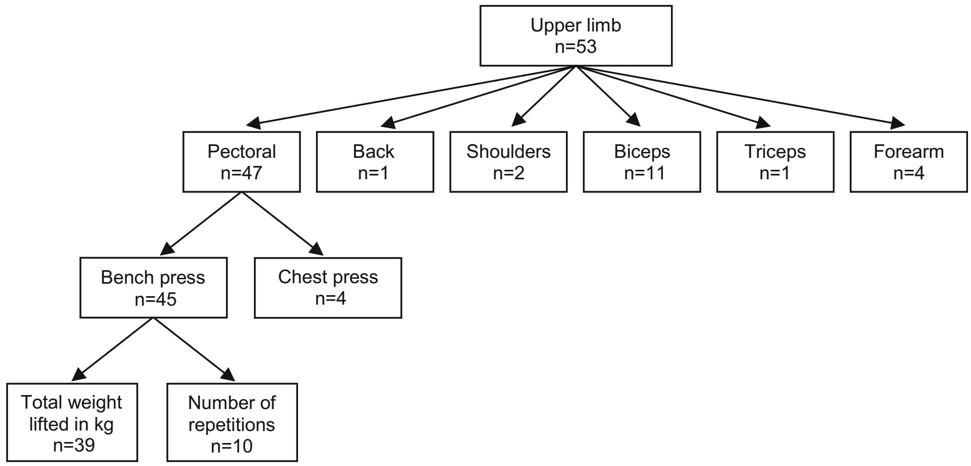

Fig. 2 Creatine supplementation and upper limb-type exercises: general analysis design

supplementary material (ESM). The meta-analyses conducted on stratification for bench press (ESM Fig. S1), pectoral (ESM Fig. S2), and upper limb (ESM Fig. S3) did not show any between-group differences.

3.9 Meta-Analysis After Supplementation (T1)

Results from the first level of stratification showed that ES of creatine supplementation on maximal weight lifted (kg) and number of repetitions at bench press were 0.238 (95 % CI 0.098–0.377; $p < 0.001$) and 0.244 (95 % CI −0.125 to 0.613; $p = 0.196$), respectively (Fig. 3 and ESM Fig. S4). The effects of creatine supplementation for stratified analysis on pectoral performances are presented in Fig. 4 and ESM Fig. S5. ES was also significant for bench press (ES = 0.265, 95 % CI 0.132–0.398; $p < 0.001$) and chest press (ES = 0.677, 95 % CI 0.149–1.206; $p = 0.012$). The overall ES remained significant at 0.289 (95 % CI 0.160–0.419; $p < 0.0001$). As shown in ESM Fig. S6, the overall ES for upper limb was significant at 0.317 (95 % CI 0.185–0.449; $p < 0.0001$). The two isolated muscle performances with an ES greater than zero were pectoral (0.287; 95 % CI 0.154–0.421; $p < 0.0001$) and biceps (0.387; 95 % CI 0.032–0.741; $p = 0.033$). Funnel plots from these meta-analyses verified the absence of publications bias (ESM Fig. S7).

3.10 Meta-Analysis of Changes between T1 and T0

Results from the first level of stratification showed that ES in strength performance changes following creatine supplementation, compared with controls, for maximal weight lifted (kg) and number of bench press repetitions were 0.243 (95 % CI 0.099–0.388; $p < 0.001$) and 2.789 (95 % CI 1.033–4.546; $p = 0.002$), respectively (ESM Fig. S8). Results from the second level of stratification showed that ES in strength performance changes following creatine supplementation, compared with controls, for pectoral was 0.447 (95 % CI 0.222–0.672; $p < 0.0001$) (ESM Fig. S9). Stratified analysis for pectoral muscle showed that performances following creatine supplementation, compared with controls, increased for bench press (ES = 0.386; 95 % CI 0.177–0.594; $p < 0.0001$) and chest press (ES = 2.227; 95 % CI 0.035–4.418; $p = 0.046$) (ESM Fig. S9). The overall ES for non-specified upper limb performances was 0.659 (95 % CI 0.421–0.898; $p < 0.0001$) (ESM Fig. S10). The muscle gain in performance was reported, with an ES of 0.466 (95 % CI 0.233–0.699; $p < 0.0001$) for pectoral, 7.052 (95 % CI 4.262–9.842; $p < 0.0001$) for back, 0.470 (95 % CI −0.157 to 1.097; $p = 0.307$) for shoulders, 1.230 (95 % CI 0.445–2.015; $p = 0.002$) for biceps, and 1.297 (95 % CI 0.113–2.480; $p = 0.032$) for triceps (ESM Fig. S10). Meta-analyses on absolute changes also gave similar results. Funnel plots for these meta-analyses appeared to display minor asymmetry for performances at T1 (ESM Fig. S7); however, asymmetry was more important in changes in performance between T0 and T1 (ESM Fig. S11) as variations were more heterogeneous than performances at T1.

3.11 Meta-Regression After Supplementation

The meta-regressions summarized in ESM Tables S1, S2 and S3 demonstrated that results after supplementation depended on results at baseline for meta-analyses that were stratified for bench press, pectoral performances, and for the whole upper limb.

4 Discussion

Fifty-three studies met our inclusion criteria to assess creatine supplementation for upper limb strength performance. The main finding was that creatine

Study	Population: Sex (%M)	Population: Age mean ±SD (y)	Population: Physical activity	Supplementation: Loading dose (g/d)	Supplementation: Total dose (g)	Supplementation: Duration (days)	Supplementation: Training	Time T0-T1 (days)	Effect size (95%CI)	Weight (%)
Maximal weight lifted										
Azizi [13]	0	21±2	Recreation	20	120	6	Strength	7	0.21 (-0.67, 1.09)	1.89
Bemben et al. [10]	100	19±0	Competition	20	390	63	Strength	63	0.22 (-0.74, 1.18)	1.61
Brenner et al. [14]	0	18±5	Competition	20	188	31	Strength	31	0.07 (-0.92, 1.06)	1.50
Brose et al. [43]	50	69±6	-	0	490	98	Strength	98	-0.8 (-1.17, 1.02)	1.23
Brose et al. [43]	50	68±4	-	0	490	98	Strength	98	0.39 (-0.63, 1.42)	1.40
Burke et al. [21]	-	33±9	Recreation	16.8	323	56	Mixed	32	0.47 (-0.34, 1.28)	2.22
Burke et al. [21]	-	33±9	Recreation	16.8	323	56	Mixed	32	0.47 (-0.47, 1.41)	1.65
Camic et al. [23]	100	22±3	Sedentary	0	70	28	-	28	0.19 (-0.35, 0.72)	5.06
Camic et al. [23]	100	22±3	Sedentary	0	35	28	-	28	0.19 (-0.34, 0.73)	5.06
Chrusch et al. [51]	100	70±6	Sedentary	26	578	72	Strength	70	0.85 (0.10, 1.60)	2.59
Earnest et al. [34]	100	30±4	Recreation	20	560	28	None		1.08 (-0.44, 2.59)	0.64
Ferguson and Syrotuik [15]	0	25±3	Recreation	0	266	70	Strength	70	-0.08 (-0.85, 0.69)	2.47
Gotshalk et al. [35]	100	65±5	-	25	178	7	None	7	0.28 (-0.65, 1.22)	1.68
Gualano et al. [16]	0	66±6	Sedentary	20	905	166	Mixed	166	0.50 (-0.23, 1.22)	2.76
Gualano et al. [16]	0	66±5	Sedentary	20	905	166	None	166	0.57 (-0.16, 1.31)	2.73
Herda et al. [54]	100	21±2	Recreation	0	150	30	Mixed	30	-0.29 (-1.04, 0.46)	2.62
Izquierdo et al. [28]	100	21±5	Competition	20	100	5	Aerobic	7	-0.26 (-1.16, 0.65)	1.79
Kelly et al. [52]	100	27±6	Competition	20	205	20	Strength	27	0.50 (-0.44, 1.44)	1.66
Law et al. [29]	100	23±4	Recreation	20	100	5	Strength	6	0.19 (-0.76, 1.15)	1.61
Noonan et al. [27]	100	20±1	Competition	20	1477	56	Mixed	56	-0.02 (-0.79, 0.75)	2.47
Noonan et al. [27]	100	20±1	Competition	20	559	56	Mixed	56	1.07 (0.24, 1.89)	2.15
Painelli et al. [42]	100	28±5	Recreation	20	-	-	Mixed	-	0.59 (-0.13, 1.31)	2.81
Pearson et al. [48]	100	21±3	Recreation	0	350	70	Strength	16	1.43 (0.31, 2.54)	1.19
Peeters et al. [24]	100	21±3	Recreation	20	393	42	Strength	42	0.25 (-0.54, 1.04)	2.32
Peeters et al. [24]	100	21±3	Recreation	20	393	42	Strength	42	-0.21 (-1.05, 0.63)	2.08
Pluim et al. [25]	100	23±5	Competition	22	194	34	Mixed	34	0.01 (-0.80, 0.82)	2.22
Selsby et al. [53]	100	21±3	Recreation	2.5	25	10	Strength	11	0.00 (-0.72, 0.72)	2.85
Stone et al. [55]	100	18±3	Competition	0	700	35	Mixed	35	0.15 (-0.74, 1.03)	1.88
Stout et al. [36]	100	20±1	Competition	21	641	56	Strength	56	-0.52 (-1.52, 0.48)	1.47
Syrotuik et al. [30]	100	23±2	Recreation	23	115	5	Strength	39	0.27 (-0.78, 1.32)	1.32
Syrotuik et al. [30]	100	23±2	Recreation	23	191	37	Strength	39	-0.33 (-1.39, 0.73)	1.32
Vanderberghe et al. [19]	0	21±3	Sedentary	20	430	74	Strength	70	0.16 (-0.74, 1.06)	1.80
Villanueva et al. [40]	100	68±6	Recreation	24.8	570	82	Strength	82	0.03 (-1.02, 1.08)	1.34
Volek et al. [49]	100	26±5	Recreation	25	560	84	Strength	84	0.33 (-0.58, 1.23)	1.78
Volek et al. [26]	100	21±6	Recreation	26	275	28	Strength	28	0.42 (-0.54, 1.39)	1.58
Zuniga et al. [56]	100	22±2	Recreation	20	140	7	Aerobic	7	-0.02 (-0.86, 0.82)	2.08
Subtotal (I-squared = 0.0%, p=0.875)									0.24 (0.10, 0.38)	74.80
Number of repetitions										
Camic et al. [23]	100	22±3	Sedentary	0	70	28	-	28	0.66 (0.11, 1.21)	4.82
Camic et al. [23]	100	22±3	Sedentary	0	35	28	-	28	0.18 (-0.36, 0.71)	5.06
Chilibeck et al. [46]	100	27±9	Competition	0	532	56	Mixed	57	0.49 (-0.45, 1.43)	1.66
Chrusch et al. [51]	100	70±6	Sedentary	26	578	72	Strength	70	0.51 (-0.22, 1.24)	2.74
Da Silveira et al. [41]	100	23±3	Competition	25	385	91	Mixed	91	-0.87 (-1.75, 0.01)	1.90
Larson-Meyer et al. [18]	0	19±2	Competition	15	350	15	Mixed	60	0.56 (-0.62, 1.73)	1.07
Painelli et al. [42]	100	28±5	Recreation	20	-	-	Mixed	-	0.52 (-0.19, 1.24)	2.84
Volek et al. [50]	100	24±5	Recreation	25	150	6	Strength	14	0.00 (-1.05, 1.05)	1.34
Volek et al. [49]	100	26±5	Recreation	25	560	84	Strength	84	-0.98 (-1.93, -0.02)	1.60
Warber et al. [31]	100	32±5	Competition	24	120	5	Mixed	5	1.00 (0.18, 1.82)	2.18
Subtotal (I-squared = 54.0%, p=0.021)									0.24 (-0.13, 0.61)	25.20
Overall (I-squared = 0.9%, p=0.456)									0.25 (0.13, 0.37)	100.0

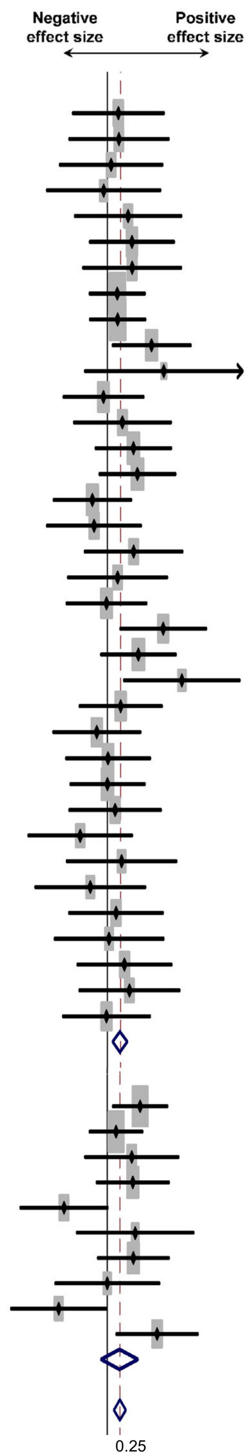

Fig. 3 Meta-analysis of maximal weight lifted ($n = 36$ studies) and number of repetitions ($n = 10$) at bench press. *M* male, *T0* baseline, *T1* following supplementation, *CI* confidence interval, *SD* standard deviation, – indicates not reported

supplementation improved upper limb strength performance, mainly at the site of the pectoral muscles (or pectoralis major and minor). Performances in bench pressing increased approximately 5.3 % with creatine supplementation.

4.1 Overview of Studies Included

This meta-analysis included a large number of studies that were heterogeneous in both study design and reported results. This is the first meta-analysis with rigorous

Study	Population: Sex (%M)	Population: Age mean ±SD (y)	Population: Physical activity	Supplementation: Loading dose (g/d)	Supplementation: Total dose (g)	Supplementation: Duration (days)	Supplementation: Training	Time T0-T1 (days)	Effect size (95%CI)	Weight (%)
Bench press										
Azizi [13]	0	21±2	Recreation	20	120	6	Strength	7	0.21 (-0.67, 1.09)	2.13
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Chilibeck et al. [46]	100	27±9	Competition	0	532	56	Mixed	57	0.49 (-0.45, -1.43)	1.87
Chrusch et al. [51]	100	70±6	Sedentary	26	578	72	Strength	70	0.76 (0.02, 1.51)	2.94
Da Silveira et al. [41]	100	23±3	Competition	25	385	91	Mixed	91	-0.87 (-1.75, 0.01)	2.14
Del Favero et al. [33]	100	24±3	Recreation	20	200	10	None	25	0.95 (-0.06, 1.96)	1.62
Earnest et al. [34]	100	30±4	Recreation	20	560	28	None		3.64 (1.16, 6.13)	0.27
Ferguson and Syrotuik [15]	0	25±3	Recreation	0	266	70	Strength	70	-0.08 (-0.85, 0.69)	2.76
Gotshalk et al. [35]	100	65±5	-	25	178	7	None	7	0.28 (-0.65, 1.22)	1.89
Gualano et al. [16]	0	66±6	Sedentary	20	905	166	Mixed	166	0.50 (-0.23, 1.22)	3.08
Gualano et al. [16]	0	66±5	Sedentary	20	905	166	None	166	0.57 (-0.16, 1.31)	3.05
Herda et al. [54]	100	21±2	Recreation	0	150	30	Mixed	30	-0.29 (-1.04, 0.46)	2.92
Izquierdo et al. [28]	100	21±5	Competition	20	100	5	Aerobic	7	0.34 (-0.57, 1.24)	2.00
Kelly et al. [52]	100	27±6	Competition	20	205	20	Strength	27	0.50 (-0.44, 1.44)	1.87
Larson-Meyer et al. [18]	0	19±2	Competition	15	350	15	Mixed	60	0.56 (-0.62, 1.73)	1.21
Law et al. [29]	100	23±4	Recreation	20	100	5	Strength	6	0.19 (-0.76, 1.15)	1.81
Noonan et al. [27]	100	20±1	Competition	20	1477	56	Mixed	56	-0.02 (-0.79, 0.75)	2.77
Noonan et al. [27]	100	20±1	Competition	20	559	56	Mixed	56	1.07 (0.24, 1.89)	2.41
Painelli et al.[42]	100	28±5	Recreation	20	-	-	Mixed	-	0.59 (-0.13, 1.31)	3.14
Pearson et al. [48]	100	21±3	Recreation	0	350	70	Strength	16	1.42 (0.31, 2.54)	1.34
Peeters et al. [24]	100	21±3	Recreation	20	393	42	Strength	42	0.25 (-0.54, 1.04)	2.60
Peeters et al. [24]	100	21±3	Recreation	20	393	42	Strength	42	-0.21 (-1.05, 0.63)	2.33
Pluim et al. [25]	100	23±5	Competition	22	194	34	Mixed	34	0.01 (-0.80, 0.82)	2.49
Selsby et al. [53]	100	21±3	Recreation	2.5	25	10	Strength	11	0.025 (-0.69, 0.74)	3.18
Stone et al. [55]	100	18±3	Competition	0	700	35	Mixed	35	0.14 (-0.74, 1.03)	2.12
Stout et al. [36]	100	20±1	Competition	21	641	56	Strength	56	-0.52 (-1.52, -0.48)	1.66
Syrotuik et al. [30]	100	23±2	Recreation	23	115	5	Strength	39	0.27 (-0.78, 1.32)	1.50
Syrotuik et al. [30]	100	23±2	Recreation	23	191	37	Strength	39	0.33 (-1.39, 0.72)	1.49
Vanderberghe et al. [19]	0	21±3	Sedentary	20	430	74	Strength	70	0.17 (-0.74, 1.07)	2.03
Villanueva et al. [40]	100	68±6	Recreation	24.8	570	82	Strength	82	0.03 (-1.02, 1.08)	1.51
Volek et al. [50]	100	24±5	Recreation	25	150	6	Strength	14	0.00 (-1.05, 1.05)	1.51
Volek et al. [49]	100	26±5	Recreation	25	560	84	Strength	84	0.22 (-0.68, -1.12)	2.02
Volek et al. [26]	100	21±6	Recreation	26	275	28	Strength	28	0.42 (-0.54, 1.39)	1.78
Warber et al. [31]	100	32±5	Competition	24	120	5	Mixed	5	1.00 (0.18, 1.82)	2.45
Zuniga et al. [56]	100	22±2	Recreation	20	140	7	Aerobic	7	-0.02 (-0.86, 0.82)	2.33
Subtotal (I-squared = 1.5%, p=0.443)									0.26 (0.13, 0.40)	94.07
Chest press										
Bermon et al. [32]	50	72±5	Sedentary	20	241	52	Strength	52	1.25 (0.17, 233)	1.41
Bermon et al. [32]	50	72±5	Sedentary	20	241	52	None	52	035 (-0.64, 1.34)	1.69
Brose et al. [43]	50	70±6	-	0	490	98	Strength	98	0.25 (-0.85, 1.34)	1.38
Brose et al. [43]	50	68±4	-	0	490	98	Strength	98	0.92 (-0.16, 1.99)	1.44
Subtotal (I-squared = 0.0%, p=0.518)									0.68 (0.15, 1.21)	5.93
Overall (I-squared = 2.4%, p=0.426)									0.29 (0.16, 0.42)	100.0

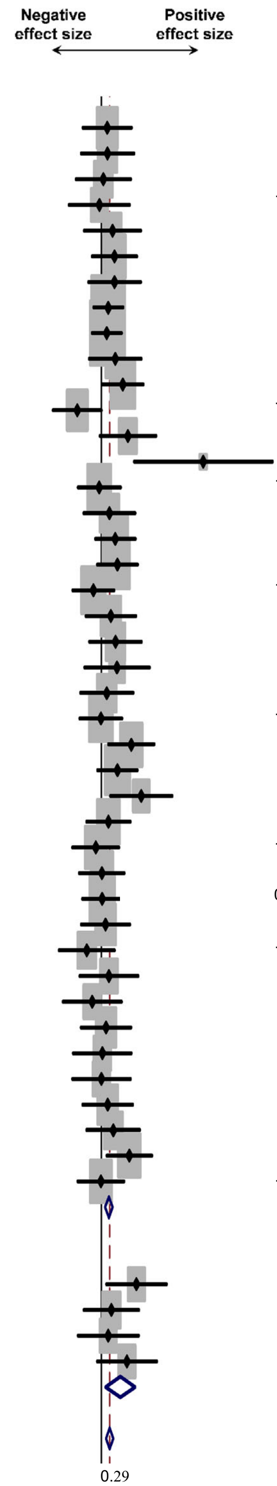

Fig. 4 Meta-analysis of pectoral performances stratified for bench press ($n = 42$ studies) and chest press ($n = 4$) tests. *M* male, *T0* baseline, *T1* following supplementation, *CI* confidence interval, *SD* standard deviation, – indicates not reported

inclusion criteria and a large number of studies focussing only on upper limb strength performance, without consideration of lower limb exercises.

4.2 Characteristics of Individuals

4.2.1 Age

Despite recent meta-analyses evaluating creatine supplementation during resistance training in older adults [38, 39], creatine supplementation has been studied most extensively in young trained males. Our study did not report an influence of age on the performances following creatine supplementation, in accordance with the literature [14, 32]. To our knowledge, no studies comparing responses between groups of different ages have been conducted.

4.2.2 Sex

Responses to creatine supplementation did not differ between males and females [16, 17, 37, 40–42]. More direct comparisons of the effect of creatine supplementation in males and females are needed to elucidate any sex differences in response to creatine. In our review, we included only two studies describing sex-based comparisons [32, 43].

4.2.3 Training Status

We did not observe an influence of training status on responses to creatine supplementation; however, participants without a history of training were reported to benefit more from creatine supplementation than those described as trained [44].

4.3 Characteristics of Intervention

Creatine supplementation regimens that included maintenance [9–11, 14, 18, 21, 23, 25, 32, 43, 45, 46] did not result in greater improvement from baseline in upper limb performance compared with short-term loading regimens [13, 35, 47]. Our meta-analysis was also unable to detect differences in performances based on the type of creatine used for supplementation, which could be attributed to most of the included studies (92 %) using the same form of creatine supplementation, i.e. creatine monohydrate. Although outside the scope of this review, comparisons of performances following creatine supplementation and other substances remain unknown. The effects of other substances added to creatine supplementation on performance also remain unknown.

To date, no study has compared different modalities of training. Interestingly, we did not report an influence of the training regimen on performance improvement, i.e. the increase of strength performance following creatine supplementation appeared similar between studies involving resistance training [48–53], mixed training [41, 42, 46, 54, 55] and also aerobic training alone [9, 28, 56].

4.4 External Validity

Results were strongest when data were stratified for bench press. Less precise information was obtained from pectoral and global upper limb meta-analyses because of the heterogeneity of tasks and units of measure.

4.5 Study Designs

These meta-analyses included only randomized, placebo-controlled trials, considered to be among the highest level of quality [57]. Most studies failed to report sufficient results to be included in this review. Typical limitations were incomplete results for all time points [58, 59] or lack of reporting of dispersion around results [19].

4.6 Stratification

Although numerous reviews and five meta-analyses have supported the efficacy of creatine supplementation in improving performance in various muscle groups, this is the first meta-analyses to conduct stratified analyses on upper limb muscles. One meta-analysis stratified arm flexor strength for specific measurements [60], another compared only upper and lower body performances [61], one did not report any exercises or body part [62], and the two meta-analyses that recruited only older individuals were restricted to few specific exercises [38, 39]. None explored all upper limb muscle groups. Therefore, we used the same methodology previously used for lower limb performances [3].

According to Cohen's classification, the creatine ES is small and is surrounded by considerable variance, explaining the fact that the efficacy of creatine is not consistent for all variables and populations studied. However, even if most ESs were relatively small, some were more important. Some studies with a higher ES dealt with older and sedentary people [22, 32, 40], while other studies were of lower quality and included a small number of subjects [34, 50]. Our current meta-analyses lend additional support to the effectiveness of creatine for performance tasks in a range that compares favorably with the five previous meta-analyses of other authors [38, 39, 60–62].

4.7 Meta-Regression

The literature provided several factors influencing performances following creatine supplementation. Some authors reported that strength performances were greater among sedentary individuals than in trained populations [60]. Adding resistance training to the creatine supplementation has been more successful than supplementation without training [60]. Despite the suggestion that creatine supplementation was more effective on strength performance in younger individuals [60], some studies demonstrated a significant effect of creatine among older individuals [16, 38, 39]. A sex effect has also been postulated [60]. However, in agreement with Branch [61], our meta-regressions failed to demonstrate any influence of sex, age, or training status before and during supplementation. We were also unable to demonstrate greater effects on specific muscles or groups of muscles. Therefore, creatine supplementation seemed to be effective on upper limb performances whatever the conditions.

4.8 Limitations

We inherited the limitations of all meta-analyses [57]; however, the use of rigorous inclusion criteria, i.e. double-blind RCTs, limited the publication bias according to funnel plots. Our general analysis design made it possible to combine results of different studies. The scarcity of publications with negative findings is common to all systematic review and meta-analyses, and may have also contributed to a bias of reporting. Safety in the use of creatine supplementation was not assessed, however it was not the purpose of the present study.

5 Conclusion

Creatine supplementation is effective in upper limb strength performance for exercise with a duration of less than 3 min, mainly at the site of the pectoral group of muscles. It was effective independent of population characteristics, training protocols, and supplementary doses or duration.

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Compliance with Ethical Standards

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Conflict of interest Charlotte Lanhers, Bruno Pereira, Geraldine Naughton, Marion Trousselard, François-Xavier Lesage, and Frédéric Dutheil declare that they have no conflicts of interest relevant to the content of this review.

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