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Effect of Creatine Supplementation on Body Composition and Performance: A Meta-analysis

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Background: Creatine supplementation (CS) has been reported to increase body mass and improve performance in high-intensity, short-duration exercise tasks. Research on CS, most of which has come into existence since 1994, has been the focus of several qualitative reviews, but only one meta-analysis, which was conducted with a limited number of studies. Purpose: This study compared the effects of CS on effect size (ES) for body composition (BC) variables (mass and lean body mass), duration and intensity (≤30 s, [ATP-PCr = A]; 30–150 s [glycolysis = G]; >150 s, [oxidative phosphorylation = O]) of the exercise task, type of exercise task (single, repetitive, laboratory, field, upper-body, lower-body), CS duration (loading, maintenance), and subject characteristics (gender, training status). Methods: A search of MEDLINE and SPORTDiscus using the phrase "creatine supplementation" revealed 96 English-language, peer-reviewed papers (100 studies), which included randomized group formation, a placebo control, and human subjects who were blinded to treatments. ES was calculated for each body composition and performance variable. Results: Small, but significant (ES > 0, $p \leq .05$) ES were reported for BC ($n = 163$, mean ± $SE = 0.17 \pm 0.03$), ATP-PCr ($n = 17$, 0.24 ± 0.02), G ($n = 135$, 0.19 ± 0.05), and O ($n = 69$, 0.20 ± 0.07). ES was greater for change in BC following a loading-only CS regimen (0.26 ± 0.03, $p = .0003$) compared to a maintenance regimen (0.04 ± 0.05), for repetitive-bout (0.25 ± 0.03, $p = .028$) compared to single-bout (0.18 ± 0.02) exercise, and for upper-body exercise (0.42 ± 0.07, $p < .0001$) compared to lower (0.21 ± 0.02) and total body (0.13 ± 0.04) exercise. ES for laboratory-based tasks (e.g., isometric/isotonic/isokinetic exercise, 0.25 ± 0.02) were greater ($p = .014$) than those observed for field-based tasks (e.g., running, swimming, 0.14 ± 0.04). There were no differences in BC or performance ES between males and females or between trained and untrained subjects. Conclusion: ES was greater for changes in lean body mass following short-term CS, repetitive-bout laboratory-based exercise tasks ≤ 30 s (e.g., isometric, isokinetic, and isotonic resistance exercise), and upper-body exercise. CS does not appear to be effective in improving running and swimming performance. There is no evidence in the literature of an effect of gender or training status on ES following CS.

Key Words: ergogenic aids, dietary supplements, nutrition, muscle strength

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Introduction

Creatine (methylguanidine acetic acid), a metabolite that is synthesized by the body and consumed as part of an omnivorous diet, plays an important role in energy metabolism. In the cell, creatine is phosphorylated to generate phosphocreatine (PCr), an energy substrate that undergoes dephosphorylation to resynthesize ATP from adenosine diphosphate (ADP) in the following reaction: $PCr + ADP + H^+ \leftrightarrows Cr + ATP$. Although creatine was first isolated in 1832 and proposed as an ergogenic supplement in the 1920s (17), the effects of creatine supplementation on performance and body composition were unknown until the early 1990s at which time it was shown that creatine supplementation could increase total muscle creatine and PCr (41). Since then, a considerable body of knowledge has come into existence that supports the efficacy of creatine in increasing body mass and performance in high-intensity, short-duration exercise tasks. As a result, creatine is currently one of the most popular dietary supplements in the world.

Several well-written reviews have summarized the body of knowledge surrounding creatine supplementation in a qualitative manner (5, 22, 48, 52, 66, 97, 115). One recently published meta-analysis of the efficacy of creatine supplementation includes a limited number of studies and does not address the areas of aerobic metabolism or body composition (63). Therefore, the purpose of this study was to employ meta-analytic techniques to evaluate the efficacy of creatine supplementation on effect size (ES) for various body composition variables and performance tasks across the intensity/duration spectrum. Specific questions of interest involved ES comparison for the following: (a) tasks relying on ATP-PCr versus anaerobic glycolysis versus oxidative phosphorylation for energy metabolism, (b) various body composition variables, (c) loading (≤14 days) versus maintenance creatine supplementation (>14 days) regimens, (d) trained versus untrained subjects, (e) male versus female subjects versus groups, including males and females, (f) laboratory-based versus field-based performance tasks, (g) single-bout versus repetitive-bout tasks, (h) upper-body versus lower-body versus total-body exercise tasks, and (i) sponsored versus non-sponsored research studies.

Methods

Literature Review and Study Selection

A search of MEDLINE and SPORTDiscus databases in December 2000 revealed, respectively, 336 and 129 citations containing the phrase "creatine supplementation". Abstracts and unpublished theses/dissertations were excluded from this analysis. The present study includes published English-language, peer-reviewed studies that presented original research data on human subjects. Minimum study criteria for inclusion were: (a) randomized group formation, (b) inclusion of a placebo control, (c) subjects who were blinded to treatments, and (d) dependent measures of body composition and/or physical performance with summary statistics (pre-supplementation and post-supplementation mean ± *SD*) for creatine and placebo treatments. Selected data were recorded from studies meeting inclusionary criteria and coded as described in the following sections.

Subject Populations and Study Designs

Sample sizes were recorded as the total number of subjects (n_{total}) as well as the number of subjects assigned to creatine ($n_{creatine}$) and placebo ($n_{placebo}$) treatments. Each study was classified according to design as randomized double-blind placebo-controlled (RDBPC), randomized double-blind placebo-controlled crossover (RDBPCX), randomized single-blind placebo-controlled (RSBPC), or single-group repeated-measures (SGRM). Demographic data included age (yrs) and subject gender (male, female, or combined [males and females]). The classification of trained state was based solely on the population description. Subjects described as "healthy, physically active" were considered to be trained.

Creatine Supplementation and Muscle Absorption

Creatine loading (≤14 d) and maintenance (>14 d) supplementation data included dosage (g/d), length (d), and creatine ingested (g) during both phases. Studies were also classified as to whether measurement of muscle [creatine] was included in the methodology (yes or no). If yes, the measurement method (i.e., biopsy, ^{31}P-magnetic resonance spectroscopy [^{31}P-MRS], or measurement of plasma and urine [creatine] and [creatinine]) was also recorded.

Performance Tasks

Performance modes were classified into one of the following 11 categories: arm ergometry (AE), bicycle ergometry (BE), isokinetic torque production (IK), isometric force production (IM), isotonic strength/endurance (IT), jumping performance (JP), kayaking performance (KY), running performance (RN), rowing performance (RW), ice-skating performance (SK), and swimming performance (SW).

Primary Energy System for Performance Tasks

The following classification was used to categorize the primary energy system for a given performance task. The ATP-PCr energy system was designated as the primary energy system for discrete high-intensity performance tasks of ≤ 30 s in duration. Anaerobic glycolysis was considered as the primary energy system for high-intensity tasks > 30 to ≤ 150 s in duration. Tasks > 150 s in duration were considered as relying primarily on oxidative phosphorylation. This classification system has been used in a previous review of creatine supplementation (115).

Description of Performance Task or Body Composition Variables

A description of the performance task included the type of task and the measured variable (e.g., power in W, energy in kJ, work in Nm, repetitions, mass lifted in kg). Running, jumping, swimming, and skating were classified as field-based performance tasks. Arm and leg ergometry, isokinetic, isometric, isotonic tasks, and simulated rowing and kayaking were classified as laboratory-based tasks. Performance tasks were also classified as single-bout or repetitive-bout exercise. The first bout of repetitive-bout exercise was classified as a single-bout exercise task. Reported body composition variables were primarily total body mass, lean body mass, fat mass, and estimated body fat percentage.

Pre-supplementation and Post-supplementation Values

Pre-supplementation and post-supplementation means and standard deviations (mean ± *SD*) for creatine and placebo groups or treatments were obtained from the original data for dependent variables. Standard errors (*SE*) were converted to standard deviations (*SD*) as follows: $SD = SE \cdot \sqrt{n}$, where n was the group sample size. Data originally reported in graphical form were converted to numeric values with the use of a millimeter ruler. Briefly, a conversion factor was determined from the y-axis scale (i.e., a units / b mm). The distance (d) from the top of the bar or middle of the data point to the smallest y-axis value was then measured. Finally, the mean value was calculated as $[(a/b) \cdot d]$. In cases where the graph origin did not have a y-axis coordinate of 0, the smallest y-axis value used to calculate a was added to the above calculation. The same factor was used to convert error bars (*SD* or *SE*) to a numeric *SD* value.

Percent Change From Baseline

The relative (%) change from baseline following supplementation was calculated for placebo and creatine treatments as $[(\text{mean}_{post} - \text{mean}_{pre}) / \text{mean}_{pre} \cdot 100]$.

Statistical Significance and Manufacturer Involvement

The statistical significance of creatine in improving the performance task or body composition variable was coded as yes (significant) or no (non-significant). Manufacturer sponsorship/involvement or any financial support of the study was coded as yes or no based on information in the acknowledgment sections of the reviewed studies.

Effect Size (ES) of Creatine Supplementation

The ES of creatine supplementation for each dependent variable was calculated using procedures described by Thomas and French (100). Briefly, ES was calculated as follows: $ES = [(\text{mean}_{Cr\text{-}post} - \text{mean}_{Pl\text{-}post}) / s_p]$, where $(\text{mean}_{Cr\text{-}post} - \text{mean}_{Pl\text{-}post})$ equaled the difference between the mean values for the creatine and placebo groups following supplementation, and s_p equaled the pooled standard deviation of the two groups. Each ES was then corrected (ES_{corr}) to adjust for any positive bias due to small samples. The variance of each individual ES was also calculated. The absolute value of ES was reported for tasks in which a smaller value is associated with improved performance (e.g., running, rowing, skating, swimming). Therefore, a positive ES denotes improved performance.

Statistical Analysis

The effect of various categorical independent variables on ES was analyzed by independent *t* test or ANOVA using *SAS* for Windows 8.0 (SAS Institute Inc., Cary, NC, USA). Associations between selected variables were examined by chi-square test of independence or Pearson correlation coefficient. The criterion for significance for all analyses was $\alpha = 0.05$. Unless otherwise indicated, all data are mean ± *SE*.

Results

General Study Characteristics

Ninety-six published investigations (100 studies) totaling 1,847 subjects met the study design criteria for inclusion in this analysis. These studies are listed in Table 1. The average sample size was 19 ± 1, with a range of 4 to 80 subjects. Study design characteristics are presented in Table 2. Briefly, most (93%) of the research on creatine supplementation has come into existence since 1994. Most (71%) studies are randomized, double-blind, placebo-control investigations of the effects of an acute (19.7 ± 0.5 g/d for 9 ± 1 d) creatine loading regimen on young (26 ± 1.1 years), trained (77%) males (68%). Twenty-four (24%) studies included males and females as subjects. The effect of creatine supplementation on females was the focus of only 9 (9%) studies. Only 22 (22%) studies investigated the effects of low-dose maintenance following acute creatine loading. Few studies measured muscle absorption of supplemented creatine. Methodologies used in studies that measured creatine absorption included needle biopsy ($n = 10$, 10%), ^{31}P-MRS ($n = 10$, 10%), or measurement of urinary/plasma [creatine] and [creatinine] ($n = 7$, 7%). There was no association between manufacturer involvement (acknowledgment of manufacturer = s support or other financial assistance) and reporting at least one significant finding following creatine supplementation ($\chi^2 = 2.23$, $p = .135$; Table 2). Furthermore, there was no ES difference between studies in which there was acknowledgment of manufacturer's support or other financial assistance and studies where no such support was indicated (0.224 ± 0.03 vs. 0.21 ± 0.02, $p = .68$).

Studies Excluded From the Meta-analysis

Several studies that are listed in Table 3 reported only change from baseline (Δ) or percent change (%Δ) following supplementation (34, 35, 53, 54, 76, 106–108, 110). Since pre-supplementation and post-supplementation means and standard deviations of dependent variables for placebo and creatine treatments are required to correctly calculate effect size as well as the percent change from baseline (%Δ), the following results exclude dependent variables ($n = 83$) from these studies for which only the change from baseline (Δ or %Δ) was reported.

Overall ES Following Creatine Supplementation

The ES frequency distribution for all body composition and performance variables was approximately normal (Figure 1), with positive skewness revealed in the normal probability and box-and-whiskers plots (not shown). The exclusion of ES values greater than 1.72 ($n = 10$) and less than –1.28 ($n = 2$) resulted in a distribution with a range of approximately six standard deviation units, but the statistical analysis for this subset was no different than the analysis for the entire distribution. Therefore, unless otherwise indicated, the following results include outliers ($n = 984$). A small but significant ES (0.22 ± 0.02, 95%CI = 0.19, 0.25, $p < .0001$) was observed across all body composition and performance variables following creatine supplementation. The mean change in these variables from baseline following creatine supplementation (5.7 ± 0.5%, 95%CI = 4.7, 6.6%) was significantly greater ($p < .0001$) than that observed following placebo supplementation (2.4 ± 0.4%, 95%CI = 1.6, 3.2%).

Table 1 Summary of Studies Used in the Meta-analysis of the Efficacy of Creatine Supplementation to Improve Body Composition and/or Performance

First author	Year	n	n_C	n_P	Sex	Age	TS[1]	Design[2]	Creatine supplementation[3]					ES areas of study[4]
									Loading		Maint		Total	
									g/d	d	g/d	d	g	
Aaserud	1998	14	8	6	M	21	T	RDBPC	15	5	2	9	93	RN
Andrews	1998	20	10	10	M	64	U	RDBPC	20	5	—	—	100	IM
Balsom	1993	18	9	9	M	26	T	RDBPC	20	6	—	—	120	BC,BE,RN
Balsom	1993	16	8	8	M	27	T	RDBPC	25	6	—	—	150	BC,BE
Balsom	1995	7	7	7	M	25	T	SGRM	20	6	—	—	120	BC,BE,JP
Barnett	1996	17	9	8	M	21	U	RDBPC	20	6	—	—	120	BC,BE
Becque	2000	23	10	13	M	22	T	RDBPC	20	5	2	37	174	BC,IT
Bermon	1998	32	8	8	M/F	74	U	RDBPC	20	5	3	47	241	BC,IM,IT
Birch	1994	14	7	7	M	20	U	RDBPC	20	5	—	—	100	BE
Bosco	1995	14	7	7	M	—	T	RDBPC	20	5	—	—	100	IT,JP
Bosco	1997	14	8	6	M	21	T	RDBPC	20	5	—	—	100	JP,RN
Brenner	2000	16	7	9	F	19	T	RDBPC	20	7	2	28	196	BC,IK,IT
Burke	1996	32	16	16	M/F	21	T	RDBPC	20	5	—	—	100	BE,SW
Burke	2000	41	20	21	M	21	T	RDBPC	7.7	21	—	—	162	BC,IK
Casey	1996	9	9	9	M	27	T	SGRM	20	5	—	—	100	BE
Cooke	1997	80	40	40	M	24	T	RDBPC	20	5	—	—	100	BC,BE
Cooke	1995	12	6	6	M	24	U	RDBPC	20	5	—	—	100	BE
Dawson	1995	18	9	9	M	22	T	RDBPC	20	5	—	—	100	BC,BE
Dawson	1995	22	11	11	M	22	T	RDBPC	20	5	—	—	100	BC,BE
Deutekom	2000	23	11	12	M	22	T	RDBPC	20	6	—	—	120	BC,BE,IK,IM
Earnest	1997	11	6	5	M	28	T	RDBPC	20	4	10	6	140	BC,RN

(*continued*)

(Table 1 *continued*)

First author	Year	n	n_C	n_P	Sex	Age	TS[1]	Design[2]	Creatine supplementation[3]					ES areas of study[4]
									Loading		Maint		Total	
									g/d	d	g/d	d	g	
Earnest	1995	8	4	4	M	31	T	RDBPC	20	14	—	—	280	BC,BE,IT
Earnest	1996	34	20	14	M/F	50	U	RDBPC	20	5	10	51	610	BC
Edwards	2000	21	11	10	M	22	T	RDBPC	20	6	—	—	120	BC,RN
Engelhardt	1998	12	12	12	M	25	T	SGRM	6	5	—	—	30	BE
Febbraio	1995	6	6	6	M	24	U	SGRM	20	5	—	—	100	BE
Francaux	2000	14	7	7	M	21	T	RDBPC	21	14	—	—	294	BC
Gilliam	2000	23	11	12	M	23	U	RDBPC	20	5	—	—	100	BC,IK
Gordon	1995	17	9	8	M	59	U	RDBPC	20	10	—	—	200	BE,IK
Green	1996	24	12	12	M	24	T	RDBPC	20	5	—	—	100	BC
Green	1996	22	6	4	M	23	T	RDBPC	20	3	—	—	60	BC
Greenhaff	1994	8	8	8	M	29	T	SGRM	20	5	—	—	100	BC
Greenhaff	1993	12	6	6	M/F	23	T	RDBPC	20	5	—	—	100	IK
Grindstaff	1997	18	9	9	M/F	15	T	RDBPC	21	9	—	—	189	AE,BC,SW
Haff	2000	36	15	21	M/F	20	T	RDBPC	22	42	—	—	941	BC,JP
Hamilton	2000	24	11	13	F	23	T	RDBPC	25	7	—	—	175	BC,IK,IT
Jacobs	1997	26	14	12	M/F	25	T	RDBPC	20	5	—	—	100	BC,BE
Jakobi	2000	14	7	7	M	22	U	RDBPC	20	5	—	—	100	BC,IM
Javierre	1997	12	6	6	M	21	T	RDBPC	25	3	—	—	75	RN
Jones	1999	16	8	8	M	27	T	RDBPC	20	5	5	70	450	BE,SK
Kamber	1999	10	10	10	M	28	T	RDBPCX	20	5	—	—	100	BC,BE
Kelly	1998	18	9	9	M	27	T	RDBPC	20	6	5	21	225	BC,IT
Kirksey	1999	36	15	21	M/F	20	T	RDBPC	22	42	—	—	924	BC,BE,JP
Kreider	1996	28	8	9	M	26	T	RDBPC	20	28	—	—	560	BC
Kreider	1998	25	11	14	M	20	T	RDBPC	16	28	—	—	441	BC,BE,IT
Larson-Meyers	2000	14	7	7	F	19	T	RDBPC	15	5	6	60	375	BC,IT,JP
Ledford	1999	9	9	9	F	27	T	RDBPCX	20	5	—	—	100	BC,BE
Leenders	1999	19	7	7	F	19	T	RDBPC	20	6	10	8	200	BC,SW
Maganaris	1998	10	10	10	M	28	T	RDBPCX	10	5	—	—	50	BC,IM
McKenna	1999	13	6	7	M/F	20	T	RDBPC	30	5	—	—	150	BC,BE
McNaughton	1998	16	16	16	M	21	T	RDBPCX	20	5	—	—	100	BC,KY
Mihic	2000	30	15	15	M/F	22	T	RDBPC	20	5	—	—	100	BC

Miura	1999	8	8	8	M	—	T	RDBPCX	20	5	—	—	100	BC,BE,IM
Mujika	1996	20	10	10	M/F	20	T	RDBPC	20	5	—	—	100	BC,SW
Mujika	2000	17	8	9	M	20	T	RDBPC	20	6	—	—	120	BC,JP,RN
Nelson	2000	36	19	17	M/F	25	T	RDBPC	20	7	—	—	140	BE
Noonan	1998	39	13	13	M	20	T	RDBPC	20	5	8	51	508	BC,IT,JP,RN
Noonan	1998	39	13	13	M	20	T	RDBPC	20	5	26	51	1426	BC,IT,JP,RN
Odland	1997	9	9	9	M	25	T	RDBPCX	20	3	—	—	60	BE
Ööpik	1998	6	6	6	M	23	T	RDBPCX	20	5	—	—	100	BC,IK
Pearson	1999	16	8	8	M	21	T	RDBPC	5	70	—	—	350	BC,IK,IT
Peeters	1999	34	11	14	M	21	T	RDBPC	20	3	5	39	255	BC,IT
Peeters	1999	34	9	14	M	21	T	RDBPC	20	3	5	39	255	BC,IT
Peyrebrune	1998	14	7	7	M	20	T	RDBPC	9	5	—	—	45	SW
Prevost	1997	18	9	9	M/F	24	T	RDBPC	19	5	2.3	6	107	BC,BE
Rawson	1999	20	10	10	M	67	U	RDBPC	20	10	4	20	280	BC,IK,IM
Rawson	1999	17	9	8	M	65	U	RDBPC	20	5	—	—	100	BC,IK,IM
Redondo	1996	18	9	9	M/F	21	T	RDBPC	21	7	—	—	145	RN
Rico-Sanz	2000	14	7	7	M	24	T	RDBPC	20	5	—	—	100	BC,BE
Rossiter	1996	38	19	19	M/F	23	T	RDBPC	20	5	—	—	97.5	RW
Schedel	2000	7	7	7	M	22	T	SGRM	20	7	—	—	140	RN
Schneider	1997	9	9	9	M	26	U	SGRM	25	7	—	—	175	BC,BE
Shomrat	2000	24	7	8	M	28	U	RSBPC	21	6	—	—	126	BC,BE
Smith	1999	9	9	9	M/F	30	T	SGRM	18	5	—	—	91.5	BC,IT
Smith	1998	5	5	5	M/F	31	U	SGRM	20	5	—	—	102	BC,IT
Smith	1998	4	4	4	M/F	58	U	SGRM	20	5	—	—	102	BC,IT
Smith	1998	15	8	7	M/F	23	U	RDBPC	20	5	—	—	100	BE
Snow	1998	8	8	8	M	23	U	RDBPCX	20	5	—	—	100	BC,BE
Stone	1999	42	9	11	M	18	T	RDBPC	20	35	—	—	700	BC,BE,IT,JP
Stone	1999	42	11	11	M	18	T	RDBPC	7.9	35	—	—	275	BC,BE,IT,JP
Stout	1999	26	9	8	M	20	T	RDBPC	21	6	—	—	126	BC
Stout	2000	15	7	8	F	19	T	RDBPC	20	5	—	—	100	BC,BE
Stout	1999	26	9	8	M	20	T	RDBPC	21	6	—	—	126	BE

(*continued*)

(Table 1 *continued*)

First author	Year	*n*	n_C	n_P	Sex	Age	TS[1]	Design[2]	Creatine supplementation[3]					ES areas of study[4]
									Loading		Maint		Total	
									g/d	d	g/d	d	g	
Stroud	1994	8	8	8	M	26	T	SGRM	20	5	—	—	100	BC,RN
Tarnopolsky	1997	7	7	7	M/F	42	U	RDBPCX	10	14	4	7	168	BE,IM
Tarnopolsky	2000	24	24	24	M/F	22	T	RDBPCX	20	4	—	—	80	BC,BE,IM
Terrillion	1997	12	6	6	M	21	T	RDBPC	20	5	—	—	100	BC,RN
Theodorou	1999	22	22	22	M/F	19	T	RDBPC	25	4	5	56	380	BC,SW
Thompson	1996	10	10	10	F	20	T	SGRM	2	42	—	—	84	IT,SW
Urbanski	1999	10	10	10	M	26	T	RDBPCX	20	5	—	—	100	BC,IM
VanLeemputte	1999	16	8	8	M	21	T	RDBPC	20	5	—	—	100	IM
Vanakoski	1998	7	7	7	M/F	24	T	RDBPCX	20	3	—	—	58.5	BE
Vandebuerie	1998	12	12	12	M	24	T	RDBPCX	25	4	15	1	115	BE
Vandenberghe	1997	19	10	9	F	20	U	RDBPC	20	4	5	70	430	BC,IK,IT
Vandenberghe	1997	13	7	6	F	20	U	RDBPC	20	4	5	70	430	BC,IK
Vandenberghe	1996	9	9	9	M	21	U	RDBPCX	40	6	—	—	240	IK,IM
Viru	1994	10	5	5	M	24	T	RDBPC	30	6	—	—	180	BC,RN
Vogel	2000	16	7	9	M	22	T	RDBPC	20	5	—	—	100	BC,BE
Volek	2000	19	9	10	M	26	T	RDBPC	25	6	5	78	540	BC
Volek	1997	14	7	7	M	24	T	RDBPC	25	6	—	—	150	BC,IT
Volek	1999	19	10	9	M	26	T	RDBPC	25	5	5	77	390	BC,IT
Vorgerd	2000	7	7	7	M/F	39	U	RDBPCX	11	7	4	28	194	BE,IM
n		100	100	100		99			100	100	22	22	100	
Mean		19	9	9		26.0			19.7	9	6.5	37	199	
SE		1	1	1		1.1			0.5	1	1.2	6	21	
Maximum		80	24	24		74			40	70	26	78	1426	
Minimum		4	4	4		15			2	3	2	1	30	

Note. [1]Trained state: T = trained; U = untrained. [2]Study design: RDBPC = randomized double-blind placebo control; RDBPCX = randomized double-blind placebo control crossover; RSBPC = randomized single-blind placebo control; SGRM = single group repeated measures. [3]Creatine supplementation: loading dose (g/d) and length (d); maintenance dose (g/d) and length (d); total creatine ingested (g). [4]Areas for which effect sizes exist (number of dependent variables): AE = arm ergometry 9 (6); BC = body composition (156); BE = bicycle ergometry (363); IK = isokinetic torque (55); IM = isometric force (80); IT = isotonic strength (107); JP = jumping (41); KY = kayaking (6); RN = sprint running (85); RW = rowing (2); SK = skating (4); SW = swimming (44).

Table 2 Characteristics of Studies Used in the Meta-analysis of the Efficacy of Creatine Supplementation

Variable	Frequency %
Publication year	
1993	3
1994	4
1995	8
1996	12
1997	13
1998	18
1999	20
2000	22
Study design	
RDBPC	71
RDBPCX	16
RSBPC	1
SGRM	12
Subject gender	
Male	68
Female	8
Both	24
Trained state	
Trained	77
Untrained	23
Maintenance supplementation	
No	78
Yes	22
Measurement of muscle [Cr]	
No	73
Yes: biopsy	10
Yes: ^{31}P-MRS	10
Yes: urine [Cr]/[Creat]	7
Manufacturer sponsorship / statistical significance*	
No/no	8
Yes/no	9
No/yes	55
Yes/yes	28

Note. *Association between manufacturer involvement in the study in any capacity (yes/no) based on acknowledgment, and statistical significance (yes/no) based on at least one significant finding. $\chi^2 = 2.23$, $p = .135$.

Table 3 Studies With Variables Not Used in the Meta-analysis

Investigator	Year	Mode	Variable	Placebo (meanΔ)	Creatine (meanΔ)	Sign
Green	1996	BC	Change in mass (kg)	—	1.25	Y
Green	1996	BC	Change in mass (kg)	—	1.35	Y
Kreider	1996	BC	Change in mass (kg)	0.90	1.90	Y
			Change in LBM (kg)	0.67	2.00	Y
			Change in fat mass (kg)	–0.05	–0.12	N
Kreider	1998	IT	Total lifting volume (kg)	1105	1558	Y
Rawson	1999	IK	Sum of peak torque (Nm)	–236	499	Y
Vandenberghe	1997	IK	Change in mean output (Nm)	0.02	1.0	Y
		BC	Change in LBM (kg)	1.4	2.3	Y
Vandenberghe	1996	IK	Change in torque (Nm)	–0.43	4.60	Y
Vandenberghe	1999	IK	Change in torque (Nm)	0.40	4.40	Y
Vogel	2000	BC	Change in body mass (kg)	–2.1	–0.90	Y

Baseline Muscle (Total Creatine), Creatine Uptake, and ES for Performance Variables

Seven of 10 studies that measured pre-supplementation and post-supplementation muscle [total creatine] by biopsy also included performance tasks (6, 16, 29, 33, 60, 90, 112). The association between baseline muscle [total creatine] (124.6 ± 2.5 mmol/kg) and percent change in muscle [total creatine] (18.1 ± 1.8%) was not significant ($n = 7$, $r = –0.62$, $p = .135$). Performance ES ($n = 75$) was not associated with pre-supplementation muscle [total creatine] ($r = 0.09$, $p = .44$) or percent change in muscle [total creatine] ($r = –0.01$, $p = .95$). A categorical "response to creatine supplementation" variable was created using the median increase in muscle [total creatine] (22.8 mmol/kg) in these seven studies. The percentage of significant effect sizes following a creatine uptake of > 22.8 mmol/kg was greater than that observed following creatine uptake of lower magnitude (36.4 vs. 7.6%, $\chi^2 = 9.6$, $p < .002$). However, there was no observed effect ($p = .56$) of this variable on performance ES ($n = 19$ "responder", 0.12 ± 0.09; 95%CI = –0.07, 0.30 vs. $n = 53$ "non-responder", 0.06 ± 0.04; 95%CI = –0.02, 0.15).

Body Composition Comparison of ES By Supplementation Regimen, Subject Training Status, and Gender

The influences of the duration of creatine supplementation, training status of subjects, and gender of subjects on body composition ($n = 163$) are presented in Table 4. A greater ($p = .0003$) ES for body composition change occurred following short-term loading regimens (0.26 ± 0.03) compared to regimens including both loading and low-dose maintenance supplementation, the ES of which (0.04 ± 0.05) was not significantly greater than zero. There was no difference between untrained (0.14 ±

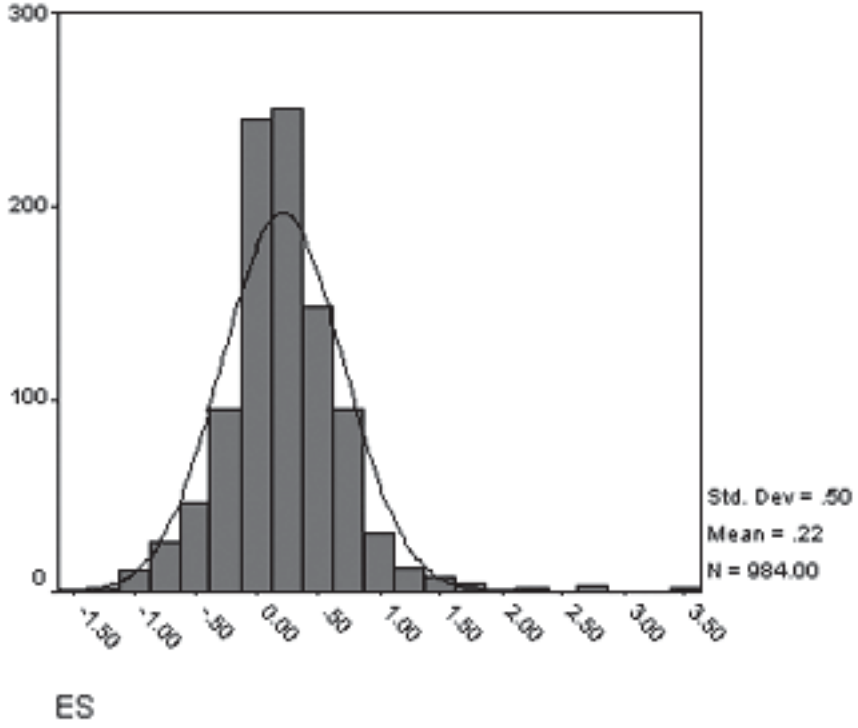

Figure 1 — Frequency distribution of corrected effect sizes for all performance and body composition variables. Normal distribution is superimposed over histogram.

0.09) and trained (0.18 ± 0.03) subjects in mean body composition ES, although the mean ES following supplementation in trained subjects was significantly greater than zero (95%CI = 0.12, 0.24). The mean body composition ES was greater than zero for males (0.22 ± 0.04, 95%CI = 0.15, 0.29) but not for females (0.04 ± 0.10, 95%CI = –0.18, 0.26) or groups including male and female subjects (0.09 ± 0.05, 95%CI = –0.03, 0.21). The effects of creatine supplementation on ES for specific body composition variables are presented in Table 5. The primary body composition variables reported in the literature are body mass (BM), lean body mass (LBM), and estimated %fat. Significant ES existed for LBM (0.33 ± 0.06, 95%CI = 0.20, 0.46, $p < .0001$) and BM (0.16 ± 0.04, 95%CI = 0.08, 0.25, $p < .0001$), with average increases of 2.2 ± 0.7% and 1.2 ± 0.3%, respectively. Across the literature, estimated %fat and fat mass were unaffected by creatine supplementation.

Performance Comparisons of ES By Supplementation Regimen, Exercise Type, Subject Training Status, and Gender

Influences of supplementation duration, type of exercise, and subject demographics on ES for performance variables are presented in Table 6. The mean ES following a

Table 4 Comparison of Body Composition ES for Different Durations of Creatine Supplementation, Trained Versus Untrained Subjects, and Male Versus Female Subjects

Study variable	*n*	ES	95%CI	% change following creatine
Supplementation regimen				
Loading only	98	0.26 ± 0.03*	0.19, 0.33	0.6 ± 0.3
Loading + maintenance	65	0.04 ± 0.05	–0.07, 0.14	0.1 ± 0.6
Trained state of subjects				
Trained	133	0.18 ± 0.03	0.12, 0.24	0.4 ± 0.4
Untrained	30	0.14 ± 0.09	–0.04, 0.31	0.2 ± 0.4
Gender of subjects				
Male	111	0.22 ± 0.04	0.15, 0.29	0.8 ± 0.4
Female	20	0.04 ± 0.10	–0.18, 0.26	–1.6 ± 1.2
Male/female	32	0.09 ± 0.06	–0.03, 0.21	0.1 ± 0.4

Note. ES and % change values expressed as mean ± *SE.* *$p < .0003$ vs. other mean.

Table 5 Effect of Creatine Supplementation on ES for Selected Measures of Body Composition

Variable	ES			% change from baseline	
	n	*M* ± *SE*	95%CI	Placebo	Creatine
All ES*	163	0.17 ± 0.03	0.11, 0.23	–0.1 ± 0.2	0.4 ± 0.3
LBM (kg)*	33	0.33 ± 0.06	0.20, 0.46	0.6 ± 0.2	2.2 ± 0.7
Body mass (kg)*	82	0.16 ± 0.04	0.08, 0.25	0.3 ± 0.1	1.2 ± 0.3
Fat mass (kg)	10	0.09 ± 0.07	–0.08, 0.26	0.4 ± 0.9	–2.5 ± 0.8
%fat	32	–0.02 ± 0.06	–0.14, 0.10	–2.0 ± 0.8	–3.2 ± 1.0
TBW (L)	2	0.60 ± 0.28	–2.95, 4.15	–0.2 ± 1.0	1.8 ± 0.3

Note. Placebo and creatine values expressed as mean ± *SE.* *ES > 0, $p < .0001$.

creatine supplementation regimen that included both loading and maintenance phases (0.26 ± 0.04) was similar to a regimen consisting of only short-term loading (0.22 ± 0.02). ES for repetitive bouts of exercise (0.26 ± 0.03) was greater than that for single-bout or first-bout exercise (0.18 ± 0.03, $p = .0395$). ES for upper-body exercise following creatine supplementation (0.42 ± 0.07) was greater ($p < .0001$) than lower-body (0.22 ± 0.02) or total body exercise (0.13 ± 0.05). ES for laboratory-based performance tasks (0.25 ± 0.02) was significantly greater ($p = .016$) than field-based (0.15 ± 0.04) performance tasks. There were no differences in ES between

Table 6 Comparison of Performance ES for Different Durations of Creatine Supplementation, Single-Bout Versus Repetitive-Bout Exercise, Laboratory-Based Versus Field-Based Exercise, Trained Versus Untrained Subjects, Male Versus Female Subjects, and Location of Muscle Groups Used in the Task

Variable	*n*	ES	95%CI	% change following creatine
Supplementation regimen				
Loading only	630	0.21 ± 0.02	0.17, 0.25	5.0 ± 0.5
Loading + maintenance	191	0.26 ± 0.04	0.18, 0.33	12.4 ± 1.7*
Number of exercise bouts				
Single bout	322	0.18 ± 0.02	0.13, 0.23	7.2 ± 0.8
Repetitive bout	499	0.25 ± 0.03*	0.21, 0.30	6.4 ± 0.8
Type of exercise				
Laboratory-based	635	0.25 ± 0.02*	0.21, 0.29	8.7 ± 0.7*
Field-based	186	0.14 ± 0.04	0.08, 0.21	0.0 ± 0.5
Trained state of subjects				
Trained	642	0.24 ± 0.02	0.20, 0.28	6.0 ± 0.6
Untrained	179	0.17 ± 0.03	0.11, 0.23	9.2 ± 1.3*
Gender of subjects				
Female	49	0.21 ± 0.06	0.09, 0.34	14.8 ± 3.8*
Male	548	0.22 ± 0.02	0.18, 0.27	5.5 ± 0.7
Male/female	224	0.23 ± 0.04	0.16, 0.30	7.9 ± 1.1
Muscle group location				
Lower body	583	0.21 ± 0.02	0.17, 0.25	6.6 ± 0.6
Upper body	102	0.42 ± 0.07†	0.27, 0.56	17.5 ± 2.4†
Total body	136	0.13 ± 0.04	0.04, 0.22	–0.9 ± 0.5

Note. Values are mean ± *SE*. *$p < .05$ vs. other mean(s). †$p < .05$ upper body > lower body > total body.

groups consisting of males (0.22 ± 0.02), females (0.20 ± 0.07), and both males and females (0.24 ± 0.04); or between trained (0.24 ± 0.02) and untrained (0.17 ± 0.03) subjects.

ES for Tasks Relying on the ATP-PCr Energy System

The effects of creatine supplementation on exercise tasks ≤ 30 s in duration are illustrated in Figure 2 and Table 7. Across all ES for activities ≤ 30 s in duration (n = 617), the mean ES (0.24 ± 0.02) was significantly greater than zero. The mean improvement from baseline following creatine supplementation (7.5 ± 0.7%) was greater than that observed following placebo supplementation (4.2 ± 0.6%). Modes for which creatine supplementation has improved performance include BE, IK, IM, and IT. With the exception of arm ergometry, the overall ES within each of the modes presented in Figure 2 was significantly greater than zero ($p \leq .05$). Specific

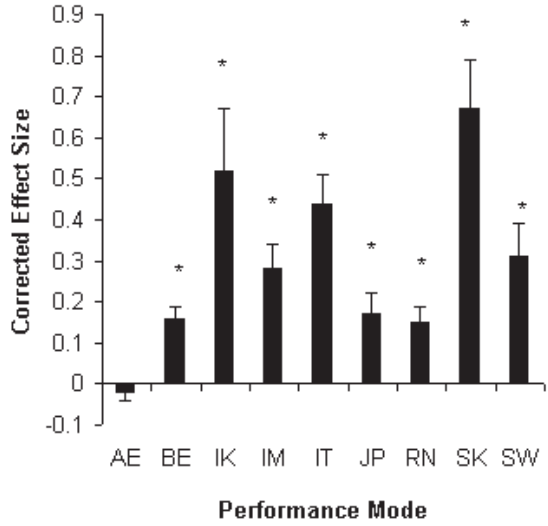

Figure 2 — Corrected effect sizes for performance tasks ≤ 30 s in duration. *ES > 0, $p \leq .05$. Performance modes: AE = arm ergometry, BE = bicycle ergometry, IK = isokinetic torque production, IM = isometric force production, IT = isotonic strength, JP = jumping, RN = sprint running, SK = speed skating, SW = swimming.

Table 7 Effect of Creatine Supplementation on ES for Selected Measures of Anaerobic Performance ≤ 30 s in Duration

Variable	ES			% change from baseline	
	n	*M* ± *SE*	95%CI	Placebo	Creatine
All ES*	617	0.24 ± 0.02	0.20, 0.28	4.2 ± 0.6	7.5 ± 0.7
Repetitions*	21	0.64 ± 0.18	0.27, 1.00	22.9 ± 7.3	45.4 ± 7.2
Work (Nm)*	38	0.29 ± 0.08	0.14, 0.45	–2.1 ± 1.2	3.2 ± 1.1
Mass (kg)*	30	0.51 ± 0.16	0.19, 0.83	13.4 ± 2.7	24.7 ± 3.9
Time (s)*	92	0.36 ± 0.06	0.25, 0.47	2.8 ± 1.0	7.4 ± 2.5
Force (N)*	38	0.29 ± 0.07	0.15, 0.43	4.1 ± 1.4	9.2 ± 1.5
Rate (rev/min)*	31	0.34 ± 0.11	0.11, 0.56	1.7 ± 0.4	3.4 ± 0.7
1-RM (kg)*	20	0.32 ± 0.10	0.12, 0.52	5.6 ± 1.2	11.2 ± 1.6
Rate (stride/s)*	5	0.26 ± 0.07	0.07, 0.46	0.0 ± 0.0	1.5 ± 0.4
Work (J)*	83	0.21 ± 0.05	0.11, 0.30	3.0 ± 0.6	6.5 ± 1.0
Power (W)*	163	0.20 ± 0.03	0.14, 0.25	4.2 ± 1.6	5.6 ± 0.6
VJ (cm)	18	0.04 ± 0.07	–0.12, 0.19	–0.2 ± 0.9	3.0 ± 1.1
Distance (m)	6	0.02 ± 0.02	–0.04, 0.08	0.2 ± 0.2	0.3 ± 0.2
Rate (m/s)	14	–0.01 ± 0.05	–0.22, 0.02	–2.4 ± 1.0	–0.7 ± 0.9
% decrement	51	–0.04 ± 0.06	–0.16, 0.09	6.3 ± 1.8	–0.6 ± 2.3

Note. Placebo and creatine values expressed as mean ± *SE*. *ES > 0, $p < .05$.

variables that have improved following creatine supplementation are repetitions lifted, work accomplished (Nm, J), mass lifted (1-repetition maximum [1-RM], kg), time (s), force production (N), cycle ergometer revolutions/min, and power (W). The mean ES for each of these performance variables was significantly greater than zero ($p \leq .05$).

ES for Tasks Relying on Anaerobic Glycolysis

The effects of creatine supplementation on exercise tasks of 30 to 150 s in duration are illustrated in Figure 3 and Table 8. Across all dependent variables of anaerobic endurance (n = 135), the mean ES (0.19 ± 0.05) was greater than zero. The mean improvement from baseline following creatine supplementation (4.9 ± 1.5%) was greater than that observed following placebo supplementation (–2.0 ± 0.6%). The mean ES for BE, IM, and IT exercise were significantly different from zero. However, ES for IK, JP, KY, RN, and SW modes were not different than zero. Specific anaerobic endurance variables that have improved following creatine supplementation are work accomplished (Nm, J) and power (W). The mean ES for each of these performance variables was significantly different from zero.

ES for Tasks Relying on Oxidative Phosphorylation

As shown in Table 9, the overall mean ES for activities of > 150 s in duration (n = 69) was 0.20 ± 0.07 (95%CI = 0.06, 0.34, p = .0032). The only performance mode with a mean ES greater than zero was bicycle ergometry (0.28 ± 0.1, 95%CI = 0.08, 0.48;

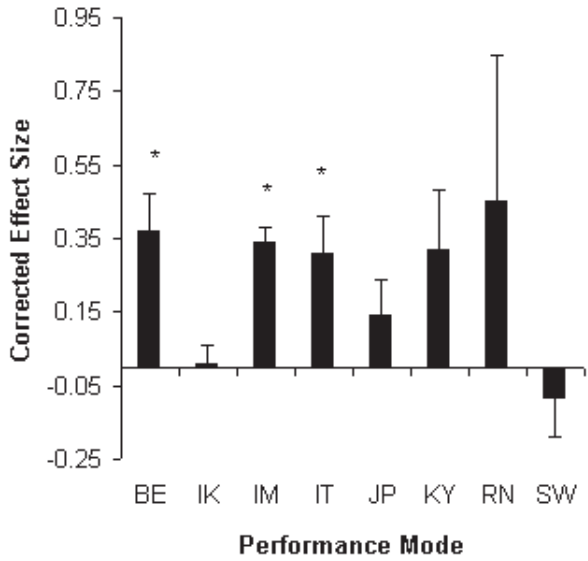

Figure 3 — Corrected effect sizes for performance tasks 30 to 150 s in duration. *ES > 0, $p \leq .05$. Performance modes: BE = bicycle ergometry, IK = isokinetic torque production, IM = isometric force production, IT = isotonic strength, JP = jumping, KY = kayaking, RN = sprint running, SW = swimming.

Table 8 Effect of Creatine Supplementation on ES for Selected Measures of Anaerobic Performance Tasks > 30 to ≤ 150 s in Duration

Variable	ES			% change from baseline	
	n	*M* ± *SE*	95%CI	Placebo	Creatine
All ES*	135	0.19 ± 0.05	0.10, 0.28	–2.0 ± 0.6	4.9 ± 1.5
Repetitions*	2	0.63 ± 0.02	0.40, 0.86	9.9 ± 9.9	32.3 ± 3.1
Work (Nm)*	18	0.31 ± 0.04	0.22, 0.40	0 ± 0	20.5 ± 7.2
VO_2 (L/min)*	6	0.30 ± 0.06	0.24, 0.36	1.1 ± 0.6	8.0 ± 0.4
Power (W)*	11	0.23 ± 0.09	0.03, 0.43	–1.0 ± 3.8	5.6 ± 2.9
Rate (m/s)*	8	0.12 ± 0.09	0.05, 0.20	0.3 ± 0.3	1.4 ± 0.2
Work (J)*	41	0.09 ± 0.04	0.01, 0.16	–6.8 ± 1.4	–4.1 ± 2.3
Time (s)	42	0.23 ± 0.13	–0.04, 0.50	–0.4 ± 0.5	6.3 ± 2.1
Distance (cm)	5	0.05 ± 0.11	–0.25, 0.34	0.8 ± 1.5	–0.2 ± 2.1

Note. Placebo and creatine values expressed as mean ± *SE*. *ES > 0, $p < .05$.

Figure 4). The mean ES for the other modes of aerobic activity (isokinetic and isotonic exercise, kayaking, running, rowing, and swimming) was 0.04 ± 0.07 (95%CI = –0.10, 0.18).

Discussion

Although numerous reviews support the efficacy of creatine supplementation in improving performance and increasing body mass (5, 22, 48, 52, 66, 97, 115), a previous meta-analysis, including a limited number of studies, reported no ergogenic effect of creatine on anaerobic performance (63). This meta-analysis includes a larger number of studies and also addresses the efficacy of creatine supplementation in the areas of body composition and aerobic performance. The mean effect size for all performance and body composition variables in this meta-analysis was significantly greater than zero (mean ± *SE* = 0.22 ± 0.02). This effect size is small according to Cohen's classification (18) and is surrounded by considerable variance (range = –1.4 to 3.52; *SD* = 0.50), highlighting the fact that the efficacy of creatine is not consistent for all variables and populations studied. It should also be pointed out that the meta-analysis has acknowledged limitations, as described by LeLorier et al. (58). For example, there may be a disproportionate number of studies in the literature that meet inclusionary criteria and also report statistically significant findings. Nevertheless, the mean improvement following creatine supplementation (5.7 ± 0.5%) was significantly greater than that observed following placebo supplementation (2.4 ± 0.4%). In addition to being statistically significant, this difference in improvement (3.3 ± 0.47%) is also of physiologic significance in many performance tasks. Therefore, this meta-analysis lends additional support to the effectiveness of creatine in increasing total and lean body mass, and performance in high-intensity, short-duration, repetitive tasks such as the number of weight-lifting repetitions and resistance.

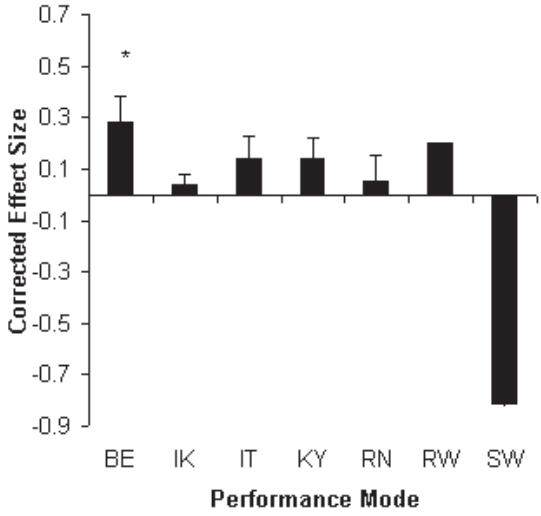

Figure 4 — Corrected effect sizes for performance tasks > 150 s in duration. *ES > 0, $p \leq .05$. Performance modes: BE = bicycle ergometry, IK = isokinetic torque production, IT = isotonic strength, KY = kayaking, RN = sprint running, RW = rowing, SW = swimming.

Table 9 Effect of Creatine Supplementation on ES for Selected Measures of Aerobic Performance Greater Than 150 s in Duration

Variable	ES			% change from baseline	
	n	*M* ± *SE*	95%CI	Placebo	Creatine
All ES*	69	0.20 ± 0.07	0.06, 0.34	0.3 ± 0.5	2.7 ± 1.2
HR (beats/min)*	5	0.65 ± 0.09	0.41, 0.90	–0.3 ± 0.6	–4.5 ± 0.8
Time (s)	14	0.19 ± 0.18	–0.20, 0.57	–1.2 ± 1.3	3.3 ± 3.0
Work (J)	4	0.42 ± 0.20	–0.13, 0.96	–3.5 ± 2.1	14.7 ± 4.1
Power (W)	9	0.28 ± 0.18	–0.14, 0.71	1.6 ± 1.0	5.7 ± 2.7
Work (Nm)	2	0.04 ± 0.04	–0.49, 0.57	1.4 ± 0.2	5.1 ± 0
VO_2 (L/min)	30	0.14 ± 0.11	–0.09, 0.38	0.6 ± 0.5	–0.8 ± 1.5
Time (min)	5	–0.19 ± 0.11	–0.49, 0.12	4.3 ± 1.9	12.4 ± 5.0

Note. Placebo and creatine values expressed as mean ± *SE*. *ES > 0, $p < .05$.

Effect of Creatine on Energy Metabolism and Performance

It is logical to hypothesize that any ergogenic effect of creatine supplementation would be best observed in high-intensity, short-duration tasks, since ATP for the performance of such tasks comes from the ATP-PCr energy system. Of the 96 published papers in this meta-analysis, 61 (64%) measured 617 performance vari-

ables of ≤ 30 s in duration, with 45 reporting an ergogenic effect (1–3, 6, 8, 10, 12, 13, 15, 16, 21, 24, 36, 38–40, 47, 49–51, 54, 55, 59, 64, 67, 69, 72–76, 81, 82, 85, 91, 96, 102, 103, 105–108, 111, 112, 114). Although 17 studies (7, 9, 19–21, 23, 27, 32, 45, 46, 56, 60, 70, 71, 77, 78, 90) reported no ergogenic effect, the significant overall effect size of 0.24 ± 0.02 supports the efficacy of creatine supplementation in tasks of ≤ 30 s in duration. As illustrated in Figure 2 and Table 7, creatine supplementation improves leg ergometer performance (revolutions/min, power [W] and work [Nm, J]), isotonic lifting mass (repetitions, 1-RM), isometric force production (N), and isokinetic torque production (Nm).

It has been suggested that creatine supplementation may improve prolonged anaerobic performance due to buffering action and less reliance on glycolysis resulting in decreased lactate formation (115). Twenty-five studies measured the effect of creatine on performance of 135 predominantly anaerobic variables of 30 to 150 s in duration, with 17 of these studies reporting improved performance following creatine supplementation (11, 12, 26, 28, 38, 44, 57, 59, 61, 75, 87, 88, 92, 95, 99, 102, 109) and 8 reporting no ergogenic effect (14, 29, 65, 71, 82, 98, 101, 104). Although smaller than the effect size for shorter-duration tasks, the overall effect size (0.19 ± 0.05) following creatine supplementation is significant and supports the hypothesis that creatine may also improve performance in tasks such as isotonic lifting mass (repetitions), isometric work (Nm), and leg ergometer power and work (W, J) that rely primarily on anaerobic glycolysis.

Although the effect of creatine supplementation on aerobic performance has received much less research attention, it has been suggested that creatine may modify substrate utilization during aerobic activity and possibly improve endurance performance (94). Eighteen studies measured the effect of creatine supplementation on 69 aerobic variables that were longer than 150 s in duration. Improved aerobic performance following creatine supplementation was reported in some (33, 61, 64, 68, 79, 80, 87, 93, 109) but not other studies (4, 7, 28, 89, 94, 95, 101, 105, 114). The overall effect size for these variables was significantly greater than zero (0.20 ± 0.06, 95%CI = 0.06, 0.34). Exclusion of large ES (n = 12) from one study (68) resulted in a mean ES of 0.09 ± 0.07 (95%CI = –0.04, 0.22). Bicycle ergometry was the only mode of aerobic exercise for which a significant ES was observed. As demonstrated in Figures 2–4, the ergogenic potential of creatine supplementation diminishes with increasing duration of activity.

It has been suggested that "responders" to creatine supplementation have a low baseline muscle total creatine and/or a greater increase in muscle total creatine following supplementation (16, 37, 41). Total muscle total creatine was measured by biopsy before and after supplementation in seven performance studies (6, 16, 29, 33, 60, 90, 112). Although the percentage of significant performance findings was greater for a higher compared to a lower uptake of creatine, the actual effect sizes between "responders" and "non-responders" were similar and negligible.

Effect of Creatine on BM and LBM

Changes in BM (ES = 0.17 ± 0.05) and LBM (ES = 0.36 ± 0.06) have been reported following creatine supplementation. Of 67 studies which measured body mass/composition, 43 reported increases in BM or LBM (3, 4, 6, 8, 13, 15, 20, 21, 23, 24, 32, 34, 35, 37, 39, 44, 45, 49–51, 53, 54, 59, 61, 62, 65, 67, 69, 71–73, 77, 85, 90, 91, 94, 99, 105, 109–113), and 24 reported no change in BM or LBM following creatine

supplementation (7, 9, 25–27, 31, 38, 40, 55–57, 60, 64, 75, 76, 79, 82, 87, 89, 92, 93, 96, 98, 102). Supplemented creatine may increase intramuscular water content due to osmotic action (42, 111). This mechanism would explain the often-reported increase in BM following short-term creatine supplementation. Another proposed mechanism is increased training volume following creatine supplementation, which may represent an indirect long-term mechanism leading to increases in BM and LBM. It has also been suggested that creatine may influence protein anabolism and/or catabolism. Creatine may function at the transcriptional or translational level to stimulate contractile protein biosynthesis (43, 116). It has been further suggested that increased cellular hydration may serve as a signal for increased protein synthesis and/or decreased protein degradation (54, 116). Regardless of the involved mechanism(s), ES following acute loading was greater than long-term maintenance supplementation (0.26 ± 0.04 vs. 0.04 ± 0.05; Table 4), suggesting a greater absolute gain in mass early in a supplementation regimen and a more modest, gradual gain with maintenance supplementation. It is important to point out, however, that maintenance supplementation was often combined with resistance training, during which increased BM and LBM also occurred in the placebo group. More research is needed to examine all of these potential mechanisms.

Effect of Supplementation Duration, Exercise Type, Training Status, and Gender on Performance ES

Creatine supplementation regimens which included maintenance dosages resulted in greater improvement from baseline in performance (12.3 ± 1.8%) compared to short-term loading regimens (5.3 ± 0.5%), but there was no difference in ES (0.26 ± 0.04 vs. 0.22 ± 0.02; Table 6). Since maintenance supplementation is usually accompanied by training, which also elicits improvement in the placebo group, this finding suggests the presence of an augmented ergogenic effect of creatine when combined with training. The explanatory mechanism (i.e., indirect effect of increased training volume or direct stimulation of protein synthesis) awaits further study.

It has been suggested that creatine supplementation may improve ATP resynthesis between repetitive bouts of exercise (37). The ES for repetitive-bout exercise (second and higher bouts, 0.25 ± 0.03) was greater than the ES for single-bout (and the first of multiple-bout) exercise (0.18 ± 0.02; Table 6). This finding would seem to support this ergogenic mechanism, although others have failed to find evidence of enhanced ATP resynthesis following repetitive exercise (29, 108). Several studies have reported the effects of creatine supplementation on the decline in performance over multiple bouts of high-intensity, short-duration (≤30 s) exercise (13, 19, 21, 23, 47, 60, 64, 67, 70, 85, 90, 105). The mean ES for percent decrement in performance in these studies was not significantly different from zero (–0.04 ± 0.06; 95%CI = –0.16, 0.09; Table 7), suggesting a resistance to fatigue associated with creatine supplementation. These findings support the possibility of improved performance in multiple bouts of high-intensity, short-duration exercise.

The majority of performance variables (77%, n = 635) were measured in a laboratory setting. Jumping, sprint running, skating, and swimming were considered as field-based performance tasks in this meta-analysis. These performance modes have received much less research attention than laboratory-based tasks such as bicycle ergometry, isokinetic, isometric, and isotonic performance. The fact that

a greater ES was observed in the laboratory setting is no doubt related to greater internal validity and control of extraneous factors, such as ambient conditions, that could potentially affect performance. However, the ultimate application of the ergogenic effect of creatine or any supplement will be on the playing field in actual competition (i.e., a field-based setting). Although more research is needed on the effect of creatine supplementation in field settings, the observed ES of 0.14 ± 0.04 indicates that creatine supplementation has minimal effectiveness in improving swimming, running, and jumping performance. It has been speculated that the increased body mass following creatine supplementation may be ergolytic for these activities (64).

There was no difference between trained and untrained subjects in ES for body composition or performance variables, but untrained subjects exhibited a greater percent change in performance from baseline, which may be explained by the presence of a training or learning effect. It should be pointed out, however, that the classification of training status was less than perfect. For example, "healthy, physically active" subjects were considered as trained in this meta-analysis. Since creatine supplementation has been reported to benefit deconditioned patients with congestive heart failure (2, 33), gyrate atrophy (86), mitochondrial cytopathies (95), and McArdle's disease (114), the effects of trained state on the ergogenic effect of creatine merit additional investigation.

Creatine supplementation has been studied most extensively in trained male subjects. The effects of creatine supplementation on female subjects has been the focus of only nine studies of 41 performance variables, with an ergogenic effect reported in three studies (55, 96, 107). It has been reported that females may have higher endogenous muscle creatine (30) and that those with high endogenous muscle creatine do not respond as favorably to supplemental creatine (37). It is unclear if the paucity of support for an ergogenic effect of creatine in females is due to a physiologic mechanism or simply the unavailability of data. This meta-analysis found the relative improvement from baseline following creatine supplementation to be greater in females (14.8 ± 3.8%) than males (5.5 ± 0.7%) and subject groups consisting of males and females (7.9 ± 1.1%). Furthermore, there was no difference between males and females in ES for performance variables. More direct comparisons of the effects of creatine supplementation in males and females are needed to elucidate any gender differences in response to creatine supplementation.

The effect of creatine supplementation is more pronounced in upper-body performance tasks (ES = 0.42 ± 0.07) than in lower-body (0.22 ± 0.02). Total body exercise is unaffected by creatine supplementation (0.13 ± 0.04). The reason for this observation is unclear. It is possible that preferential uptake of supplemented creatine by upper-body musculature could be related to a report of greater creatine uptake by fast-twitch fibers (16), but there has been no comparison of creatine uptake between upper-body and lower-body musculature. This issue merits further investigation.

Researchers often receive funding or support from dietary supplement manufacturers. Such relationships might present a potential conflict of interest. On the one hand, the supporting entity would presumably want objective research findings that are based on statistical probability. On the other hand, the supporting entity would also have a vested interest in the outcome of the study. The percentage of studies that reported at least one significant finding and also acknowledged

manufacturer involvement was similar to the percentage of non-sponsored studies with a significant finding. Furthermore, there was no difference in mean ES between studies receiving support and those receiving no support. It is important to point out, however, that no attempt was made to ascertain the degree of manufacturer support, which could range from simple donation of supplements to full financial sponsorship. Moreover, manufacturers are unlikely to publish a non-ergogenic study. Within the limits of these data, sponsorship of creatine research by supplement manufacturers does not appear to be a source of bias.

There are several limitations to this meta-analysis. First, the quality of each study, which is considered in some meta-analyses, was not considered in the present study. This is acknowledged as a potential weakness. Second, some studies employed methods for which there was insufficient or unknown reliability. The distinction that was made between "laboratory-based" and "field-based" tasks is debatable. It may be argued that this distinction is irrelevant so long as the methodology is valid, reliable, and objective. On the other hand, there is merit to examining skills that are actually employed in competition. Third, this meta-analysis did not address the potential health effects of long-term creatine supplementation, which is a source of concern among clinicians. Creatine supplementation has also been reported to excessively elevate lower leg muscle compartment pressure following endurance exercise (84). This side effect could result in impaired performance and medical intervention. It was also assumed that all supplemented creatine was free of impurities. Although a recent retrospective study reported no adverse effects of creatine supplementation (9.7 $g \cdot d^{-1}$ for up to 4 years) on blood chemistry, muscle injury, or other side effects (83), the long-term effects of creatine remain largely unknown. Therefore, it would behoove all potential and current users of creatine to continue to seek current information about the effects of creatine from authoritative sources.

In conclusion, ES was greater for lean body mass following short-term CS, repetitive-bout exercise tasks ≤ 30 s, and upper-body exercise. Creatine supplementation has improved repetitions accomplished, mass lifted (kg), force (N) and power (W) generated, and work accomplished during high-intensity, short-duration (≤30 s) isotonic, isometric, isokinetic, and leg ergometer exercise. ES for performance tasks diminishes with increasing duration of exercise, an observation that is consistent with energy system specificity for various exercise tasks along the intensity/duration continuum. Creatine supplementation does not appear to improve swimming and running performance. The literature does not support an effect of gender or training status on ES following creatine supplementation.

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