

# SCIENTIFICALLY DEBATABLE: IS CREATINE WORTH ITS WEIGHT?

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**KEY POINTS**

- Phosphocreatine is a critical fuel for sprinting and other brief activities requiring high power outputs. Creatine supplementation in the diet can increase creatine and phosphocreatine levels in the muscles, but there are large individual differences in this response.
- Creatine use is common. Surveys indicate that 17–74% of athletes of various ages in a variety of sports use creatine supplements.
- Creatine supplementation has been shown to improve performance of brief (<30 s) high-intensity exercise, but there is limited evidence that it can enhance performance during exercise lasting longer than about 90 s.
- Creatine supplementation during resistance training may allow athletes to complete more repetitions per set of a given exercise and may allow them to “recover” more rapidly between sets.
- There appears to be no association between creatine supplementation and adverse side-effects in apparently healthy individuals.

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**INTRODUCTION**

In an age when success in sports is often associated with increased future earnings and when many athletes have a “win at all costs” attitude, the use of dietary supplements has increased markedly. Creatine monohydrate is a commonly used supplement, accounting for about US \$400 million in annual sales in the United States alone (American Academy of Pediatrics, 2001). Athletes in the former Soviet Union may have been ingesting creatine to enhance performance as early as the 1970s (Kalinski, 2003), but the popularity of creatine with athletes increased substantially in the early 1990s by the revelation that Olympic gold medal winners Linford Christie and Sally Gunnell used creatine (Hawes, 1998). Moreover,

scientific publications reporting that dietary creatine supplementation could increase muscle creatine stores (Harris et al., 1992) and improve the performance of brief, high-power exercise (Greenhaff et al., 1993) lent credence to the anecdotal evidence of creatine benefits. Unlike many dietary supplements, much research has been conducted on creatine, but its efficacy as an ergogenic aid remains controversial. The purpose of this article is to summarize the available literature concerning the prevalence of, ergogenic effects of, and adverse events associated with creatine supplementation.

**RESEARCH REVIEW****The Role of Creatine in Energy Metabolism**

Creatine is a non-essential compound that can be obtained in the diet or synthesized by the liver, pancreas, and kidneys (Walker, 1979). Creatine exists in free and phosphorylated forms (i.e., phosphocreatine or PCr), and approximately 95% of the body’s creatine is stored in skeletal muscle, where its primary function is as an energy buffer. During times of increased energy demand, phosphocreatine (PCr) donates its phosphate to adenosine diphosphate (ADP) to produce adenosine triphosphate (ATP). Exercise tasks like sprinting and weightlifting that involve brief, intense efforts rely heavily on the ATP-PCr energy system. It is the only fuel system in the muscles that can produce energy at sufficiently high rates to accomplish these tasks. But the ATP-PCr energy system can provide ATP at maximal rates for only seconds before PCr stores are depleted. Consequently, it has been hypothesized that people who increase their muscle creatine levels by ingesting creatine supplements have a greater energy reserve available to support this type of activity. In addition to increasing muscle creatine stores, creatine supplementation may increase phosphocreatine resynthesis (Greenhaff et al., 1994), although this has not been shown in every case (Vandenberghe et al., 1999)

Following a creatine loading phase (typically 20 g/d for 5 d), muscle creatine levels increase approximately 25% to what appears to be a maximum of about 160 mmol/kg/dry muscle (Harris et al., 1992; Hultman et al., 1996). Thus, athletes can begin a high-intensity exercise task with greater levels of muscle creatine available for energy production. This is analogous to endurance athletes using carbohydrate loading to top off their glycogen stores prior to competition. There is considerable variability in the increase in muscle creatine following supplementation; some individuals are “non-responders” (little or no increase in muscle creatine), whereas others are “high responders” (>30% increase in muscle creatine) (Harris et al., 1992).

## Prevalence of Creatine Supplementation

Creatine supplementation is widespread in athletics (Greenwood et al., 2000; LaBotz & Smith, 1999; McGuine et al., 2001, 2002; Ronsen et al., 1999; Sheppard et al., 2000; Stanton & Abt, 2000), and reports indicate that many athletes ingest creatine over long periods of time (Juhn et al., 1999; Sheppard et al., 2000; Stanton & Abt, 2000). Surveys indicate that 17–74% of athletes of various ages and sport disciplines use creatine (Table 1) and that as many as 50% of the senior-class members of American high-school football teams use it (McGuine et al., 2001).

**TABLE 1.** Prevalence of creatine use in various populations of athletes.

Population	Creatine Users	Reference
High School Student-Athletes	17%	McGuine et al., 2002
High School Football Players (freshman through senior classes)	30%	McGuine et al., 2001
NCAA Athletes	28–41%	Greenwood et al., 2000; LaBotz & Smith, 1999
Military and Civilian Health Club Members	29–57%	Sheppard et al., 2000
Athletes in Power Sports	45–74%	Ronsen et al., 1999; Stanton & Abt, 2000

Despite the literature clearly showing that a brief (5 day) high-dose creatine-loading phase is sufficient to saturate muscles with creatine (Hultman et al., 1996), survey data indicate that athletes often ingest creatine supplements for weeks or months, rather than for several days before an athletic event (Table 2). Juhn et al. (1999) reported that baseball and football players most often ingest creatine in the off-season, which is the time of year when athletes undergo training to increase strength and/or body mass for the forthcoming competitive season. Thus, rather than ingesting creatine acutely to improve performance at a particular athletic event, many athletes use creatine chronically in an effort to increase muscle strength, muscle size, and body mass during training.

**TABLE 2.** Duration of creatine use in various populations of athletes.

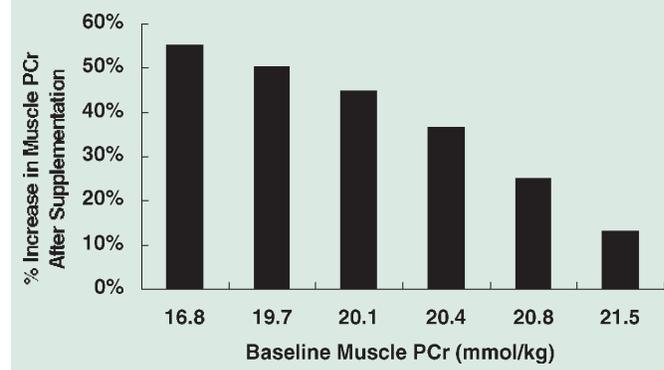
Population	Duration Creatine Supplementation	Reference
Powerlifters	4 to 56 d (loading phase) 14 to 91 d (maintenance phase)	(Stanton & Abt, 2000)
NCAA Football Players	3 months	(Juhn et al., 1999)
NCAA Baseball Players	5 months	(Juhn et al., 1999)
Health Club Members	40 weeks	(Sheppard et al., 2000)

## Factors Influencing Muscle Creatine Uptake Following Supplementation

The strongest determinant of how much creatine will be taken up into muscle following supplementation is the initial creatine content in that muscle (Harris et al., 1992; Hultman et al., 1996). Subjects with lower muscle creatine stores have the greatest increase in muscle creatine following supplementa-

tion, whereas subjects with higher creatine levels will experience little or no increase in muscle creatine (Figure 1). However, this cannot fully explain the large intersubject variability in the response.

**FIGURE 1.** Baseline levels of muscle phosphocreatine influence the magnitude of the increase in muscle phosphocreatine following creatine supplementation (adapted from Rawson et al., 2002).



Animal and *in vitro* research in the 1970s demonstrated that insulin enhanced the transport of creatine from the circulation into the skeletal muscle of rats (Koszalka et al., 1972; Haugland & Chang, 1975). Subsequently, several clinical studies reported increased muscle creatine uptake or decreased urinary creatine losses during creatine supplementation accompanied by insulin infusions, carbohydrate ingestion, and ingestion of a combination of carbohydrate and protein. For example, Green et al. (1996a, b) showed that ingesting a high dose of carbohydrate (~90 g, 4 times/day) concurrently with creatine can reduce urinary creatine losses and increase muscle creatine accumulation when compared to supplementation with creatine alone. Because, these high doses of carbohydrate may not be practical for all athletes, other investigators examined the effects of lesser amounts of carbohydrate or carbohydrate/protein combinations on muscle creatine uptake. For example, Preen et al. (2003) reported that the ingestion of creatine and 1 g glucose/kg body mass twice daily increased muscle total creatine by 9% more than ingestion of creatine alone, and Steenge et al. (2000) concluded that the ingestion of creatine with ~ 50 g of a carbohydrate-protein combination causes increases in muscle creatine similar to those observed after ingesting creatine with ~ 100 g of carbohydrate.

## Effects of Creatine Supplementation on Exercise Performance

Several hundred studies have examined the effects of creatine supplementation on exercise performance and have been summarized and reviewed elsewhere (Kreider, 2003; Lemon, 2002; Rawson & Volek, 2003). Initially, studies focused on the effects of creatine supplementation on exercise performance using laboratory tests and not on the performance of sport-specific or field tests. In controlled laboratory tests (e.g., cycling), creatine supplementation appears to improve performance of short-term (<30 s) high-intensity exercise, particularly when there are repeated bouts (Kreider, 2003). There is less convincing evidence that creatine supplementation can enhance exercise per-

formance during exercise of longer durations (>90 s) (Kreider, 2003). It makes intuitive sense that creatine may not prove ergogenic in longer exercise tasks given the relatively small contribution of phosphocreatine to energy production during tasks 1.5 to 3 minutes in length (Spriet, 1995). However, even when creatine supplementation did not improve the endurance component of prolonged cycle ergometry it did improve sprint performance within and after (Engelhardt et al., 1998) or after (Vandebuerie et al., 1998) the endurance phase. Therefore, it is possible that creatine supplementation may prove useful during sprinting episodes within and at the end of certain prolonged events such as cycling races.

Several studies have evaluated the ergogenic effects of creatine supplementation on sport-specific performance and on field tests. For instance, in track events, Skare et al. (2001) reported increased velocity in the 100-m sprint (11.68 vs. 11.59 s) and reduced total time of six intermittent 60-m sprints (45.63 vs. 45.12 s) in subjects ingesting creatine compared with no changes in the placebo-supplemented subjects. However, the finding of improved sports performance resulting from creatine supplementation is not consistent. As one of many examples, Op't Eijnde and colleagues (2001) found no effect of creatine supplementation on either power or precision of first and second services, baseline strokes, volleys, and shuttle run time in trained tennis players.

It should be emphasized that many studies have not reported an ergogenic effect of creatine supplementation (Lemon, 2002). In addition to the obvious implication that creatine supplementation is not a reliable ergogenic aid, these inconclusive findings have been attributed to various factors, including: 1) low sample size relative to the high variability of muscle creatine increases following supplementation, 2) consumption of meat (which contains creatine) by placebo-supplemented subjects, 3) type of exercise studied, and 4) duration of exercise test and rest period between bouts of exercise (Lemon, 2002). Kreider (2003) has stated that about 70% of studies conducted on creatine supplementation effects on brief, high-power exercise report some ergogenic benefit, and it is the position of the American College of Sports Medicine that “. . . exercise performance involving short periods of extremely powerful activity can be enhanced, especially during repeated bouts . . .” by creatine supplementation (Terjung et al., 2000).

To provide an unbiased review of the research on creatine supplementation and exercise performance, several investigators have performed meta-analyses, which compare and statistically analyze the results of selected published studies. In such meta-analyses, statistical “effect size” is calculated based on the magnitude of change (improvement), a weight is placed on the study results based on factors such as sample size, and studies are selected with strict criteria such as including only studies with randomized, placebo-controlled designs. For example, Misic and Kelley (2002) compared 29 studies that met their criteria and concluded that creatine supplementation did not enhance anaerobic performance. A different conclusion was reached by Branch (2003), who included 100 studies in his meta-analysis of the effects of short-term creatine supplementation on body composition

and performance. Branch (2003) found a significant increase in body mass and lean body mass and an improvement in repetitive bouts of laboratory-based isometric, isokinetic, and isotonic resistance exercise lasting 30 s or less, but not in running or swimming performance. The results of Branch are in agreement with many narrative review articles as well as the ACSM creatine roundtable, which suggests a benefit of creatine to exercise lasting 30 seconds or less.

### **Creatine supplementation and concurrent resistance training**

Given that many athletes appear to be ingesting creatine chronically (Table 2), it could be argued that they are not using creatine as a sports performance booster per se but instead are using creatine as a training aid during periods of intense resistance training (Greenwood et al., 2000; Juhn et al., 1999; LaBotz & Smith, 1999; Sheppard et al., 2000; Stanton & Abt, 2000). By ingesting creatine during weeks and months of resistance training, athletes hope to increase the quality of their workouts so that the potential benefits of creatine in the weight room will translate into improved performance on the playing field. This has not been confirmed with research, but the effects of creatine supplementation with concurrent resistance training on tests of strength and lean body mass have been documented.

Rawson and Volek (2003) reviewed 22 studies of the effects of creatine ingestion during resistance training. Sixteen of the studies reported a greater improvement in muscle strength and/or weight-lifting performance (maximal repetitions at a given percentage of maximal strength) in subjects ingesting creatine compared to placebo, one brief investigation (7 d) reported gains in the creatine group and no change in the placebo group, and five studies found no difference between creatine and placebo groups.

Meta-analyses have been conducted on studies of the effects of creatine on resistance training exercise. As described earlier, Branch (2003) found that body composition and performance of strength tests were improved with creatine supplementation. In concordance, Nissen and Sharp (2003) examined 18 studies that met their criteria for inclusion and concluded that creatine was one of only two supplements that increased lean body mass and muscular strength. The ACSM consensus statement on creatine supplementation reached a similar conclusion regarding the combined effects of creatine ingestion and resistance training and states that “creatine supplementation is associated with enhanced accrual of strength in strength-training programs (Terjung et al., 2000).”

The increase in muscle strength seen in subjects ingesting creatine during resistance training may result from creatine-supplemented subjects training at higher work loads than placebo-supplemented subjects. An athlete with increased muscle creatine and phosphocreatine stores would theoretically be able to perform more repetitions per set of a given exercise before the onset of fatigue. Additionally, increased stores of creatine in muscles may allow athletes to “recover” more rapidly between sets via accelerated phosphocreatine resynthesis (Greenhaff et al., 1994). Consistent with these hypotheses are the results of Volek et al. (1999), who reported that subjects ingesting creatine had increased bench-press lifting volume during a 12-week resistance training intervention

when compared with subjects ingesting placebo. Moreover, when Syroituik et al. (2000) held training volumes constant for creatine and placebo groups during an 8-week resistance training program, creatine-associated improvements in strength and weightlifting performance were not detected. Thus, subjects who ingest creatine during resistance training most likely do more work in the weight room than those who do not.

### **Are There Adverse Effects of Creatine Supplementation on Health?**

Researchers studying potential adverse events associated with creatine ingestion have focused on three areas: 1) the possibility that creatine supplementation might induce muscle dysfunction, 2) the association between creatine supplementation and heat illness, and 3) the effects of creatine supplementation on kidney health. Muscle dysfunction that presents itself as increased muscle injury or cramping has been theoretically associated with creatine supplementation based on the fact that creatine loading may increase intracellular water. Greenwood et al. (2003) examined the association between creatine supplementation and the incidence of injuries observed over three years of college football training and competition in NCAA Division IA athletes. The incidence of cramping, heat illness, muscle tightness, muscle pulls/strains, non-contact joint injuries, contact injuries, illness, number of missed practices due to injury, players lost for the season, and total injuries and missed practices were similar for creatine users and non-users, but no statistical analyses were performed. Rawson and colleagues (2001) reported no differences in markers of exercise-induced muscle damage following high-force eccentric exercise in subjects supplemented with creatine or placebo. Taken together, these data suggest that creatine supplementation has neither positive nor negative effects on muscle dysfunction in healthy adult populations.

Anecdotally, creatine has been associated with heat illness during exercise in the heat. Volek et al. (2001) examined this association by testing 20 healthy men who consumed either creatine (0.3 g/kg of body weight) or placebo for seven days. Subjects cycled for 30 min at 60–70%  $\text{VO}_2$  peak followed by three 10-s sprints in an environmental chamber at 37°C and 80% relative humidity. There were no differences between groups in heart rate, blood pressure, sweat rate, or rectal temperature, and there were no reports of adverse symptoms, including muscle cramping, despite increased peak power on the cycling test by subjects who ingested creatine.

Kreider and colleagues (2003) reported the effects of creatine ingestion over a 21-month period on various blood variables (metabolic markers, muscle and liver enzymes, electrolytes, lipid profiles, hematological markers, and lymphocytes) and on urinary measures of renal function in 98 college football players. Following the study, subjects were categorized into groups that did not take creatine, subjects who took creatine for 0–6 months, 7–12 months, and 12–21 months. There were no differences among groups in the blood and urine markers assessed with the exception of sodium, chloride, and hematocrit, all of which were within normal ranges and

deemed by the authors to be of no physiological or clinical significance. The results indicate that creatine supplementation for durations up to 21 months does not adversely affect markers of health status in intensely training athletes compared to athletes not ingesting creatine.

### **SUMMARY AND COMMENT**

Although roughly 300 studies have been carried out to test the effects of creatine on exercise performance, a definitive answer to the question “Does creatine work?” still eludes scientists. Although many reports have been inconclusive, on balance, the data suggest that creatine loading can improve performance in high-intensity exercise lasting less than 30 s. Studies reporting creatine benefits for resistance training exercise are more consistent in demonstrating positive effects. It appears likely that creatine allows some athletes to train with higher work loads. Still, motivation could be a confounding factor in these studies because it is difficult to blind studies when there is an obvious increase in body weight and “swelling” of muscles.

Although meta-analyses have been conducted in an attempt to compare results of many studies in an unbiased manner, there are several limitations with this statistical approach. The criteria for selection of studies are subjective and differ among investigators. Also, a problem of potentially biased sampling of studies exists because small sample sizes may have lead to erroneous positive results in many published studies and because many studies finding no effect are never published. Indeed, many abstracts of research on creatine supplementation have not been published. It is interesting to note that no studies reported negative effects of creatine supplementation on performance (unless it was secondary to an increase in body weight).

The fact that ingested creatine does increase muscle creatine concentration in some individuals indicates a potential for enhanced performance of brief high-intensity exercise. However, there is a large inter-subject variability in muscle creatine changes in response to supplementation. It is not clear why certain individuals are more likely than others to increase muscle creatine levels in response to creatine supplementation. Because there are exceptions to the rule that a high initial level of creatine in muscle dictates a poor response to creatine supplementation, differences in initial levels of creatine cannot fully explain the variability in response to creatine ingestion. Certain individuals may possess a gene variant that allows them to store more creatine in their muscles. If this is so, then small sample sizes, characteristic of most of the studies of creatine effects on exercise performance, could either over- or under-represent subjects who are predisposed to increase their muscle creatine levels in response to creatine supplementation.

Our overall conclusion is that the performance of some, but not all, individuals can benefit from creatine supplementation; there is no “magical” effect for everyone. If only some individuals experience a benefit, then do these individuals have an unfair advantage in sport performance? The ethical issues associated with creatine supplementation remain unclear.

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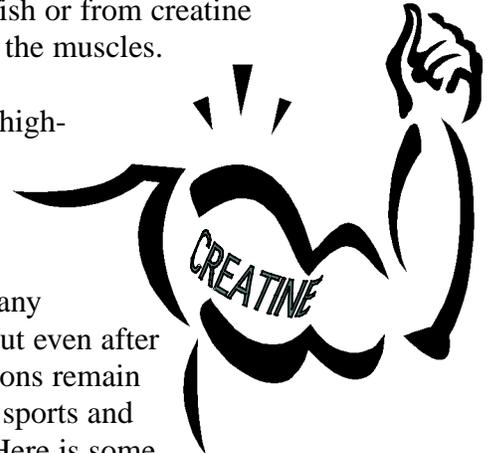
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## CREATINE: DOES IT WORK?

When athletes consume creatine in their diets, whether from meat and fish or from creatine supplements, some of the creatine will be absorbed from the blood into the muscles.

Once in the muscles, creatine can be combined with phosphate to form phosphocreatine, a vital—but very limited—source of energy for brief, high-power activities such as sprinting and resistance training. It follows that creatine users should have more phosphocreatine energy available to perform these kinds of activities, leading to improved performance.



This rationale for consuming creatine supplements sounds great, and many millions of dollars worth of creatine supplements are sold every year. But even after the completion of several hundred scientific investigations, many questions remain about the value of creatine supplementation for performance of various sports and about how much and when to use creatine—if it should be used at all. Here is some of what is known:

- Supplementing the diet with 20 grams of creatine daily (four 5-gram doses) for 4–5 days (i.e., “creatine loading”) will increase muscle levels of creatine in some, but not all, individuals. Doses of 5 grams raise blood creatine concentrations to the optimal amount that will maximize uptake of creatine into muscles. Creatine ingested in amounts greater than 20 grams per day will be wasted in the urine.
- Ingestion of 2 grams of creatine daily for 30 days takes longer but is just as effective as creatine loading for increasing the creatine concentration in muscle.
- Carbohydrates consumed with creatine supplements will increase creatine uptake by muscles compared to creatine supplements alone, but not by much.
- Creatine ingestion will likely increase body mass by a few pounds or kilograms, some of which will be extra muscle and the rest extra water. This weight gain could be detrimental in sports like running in which additional body weight may impair performance.
- Because creatine can make muscles appear larger by increasing the muscle uptake of water, it may enhance motivation to perform better and work harder in sports where increased muscle mass is desirable.
- Most laboratory studies of high-power tests lasting 30 seconds or less show slight, but potentially important improvements in performance in creatine users. A common example of such performance tests is repeated bouts of maximal cycling exercise, each bout lasting about 6–10 seconds.
- With laboratory performance tests that last between 30 and 90 seconds, the evidence for creatine effects on performance is predominantly positive, but is less persuasive than for activities lasting less than 30 seconds.

- As test durations exceed 90 seconds, it is progressively less likely that creatine users will perform better than non-users (Table 1S).

**TABLE 1S. Evidence that Supports or Refutes an Ergogenic Effect of Creatine for Various Performance Tests**

Performance Test	Evidence for Ergogenic Effect
Intense Brief Exercise (Laboratory Tests; <30 sec)	Convincing
Weight-lifting (when creatine is used concurrently with resistance training)	Convincing
Intense Exercise (Laboratory Tests; 30 sec to 3 min; intermittent effort)	Moderately Convincing
Convincing Intense Exercise (Laboratory Tests; >3 min)	Not Convincing
Intense Exercise (Field Tests such as Swimming and Sprinting)	Not Convincing

- When consumed in moderate doses, there seem to be no adverse effects of creatine supplementation in healthy adults.
- Scientists do not know the effects of creatine supplementation on children who are still growing. Individuals younger than 18 years of age should not take creatine supplements.
- Because the Food and Drug Administration does not tightly regulate supplements, there is no guarantee that all the ingredients in a product are stated on the label. There have been incidents where supplements are “spiked” with stimulants or prohormones that are banned by sport governing bodies.
- Don’t count on supplements to make you a champion. Using any supplement, including creatine, can never take the place of hard training and skill practice, good nutrition, sound sleep, and ample rest.

## SUGGESTED ADDITIONAL RESOURCES

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