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# Creatine supplementation: bioavailability and effects on physical and cognitive performance

**Authors:**

**Monika Gajda-Bathelt**
Beskid Oncology Center – Municipal Hospital of John Paul II in Bielsko-Biała
Wyzwolenia 18, 43-300 Bielsko-Biała, Poland
E-mail: monikagajda99@gmail.com
ORCiD: https://orcid.org/0009-0006-6231-607X

**Julia Adasiewicz**
Dr Anna Gostynska Wolski Hospital, Independent Public Health Care Institution
Marcina Kasprzaka 17, 01-211 Warsaw, Poland
E-mail: julia.adasiewicz@gmail.com
ORCiD: https://orcid.org/0009-0004-9704-8242

**Katarzyna Kwaterska**
Mazovian Bródnowski Hospital,
Kondratowicza 8, 03-242 Warsaw, Poland
E-mail: katarzyna.kwaterska90@gmail.com
ORCiD: https://orcid.org/0009-0000-3157-5438

**Agnieszka Benecka**
Pomeranian Medical University in Szczecin
Rybacka 1, 70-204 Szczecin, Poland
E-mail: abenecka@gmail.com
ORCiD: https://orcid.org/0009-0004-9295-7471

**Kamil Janawa**
Pomeranian Medical University in Szczecin
Rybacka 1, 70-204 Szczecin, Poland
E-mail: kjanawka@interia.pl
ORCiD: https://orcid.org/0009-0004-6779-7066

**Michał Tomaszek**
Beskid Oncology Center – Municipal Hospital of John Paul II in Bielsko-Biała
Wyzwolenia 18, 43-300 Bielsko-Biała, Poland
E-mail: michaltomaszek97@gmail.com
ORCiD: https://orcid.org/0009-0003-0135-7554

**Alicja Katarzyna Chojniak**
Beskid Oncology Center – Municipal Hospital of John Paul II in Bielsko-Biała
Wyzwolenia 18, 43-300 Bielsko-Biała, Poland
E-mail: alicja1998500@o2.pl
ORCiD: https://orcid.org/0009-0006-2641-3438

**Paweł Jan Kuna**
Beskid Oncology Center - Municipal Hospital of John Paul II in Bielsko-Biała
Wyzwolenia 18, 43-300 Bielsko-Biała, Poland
E-mail: pawelekuna1998@gmail.com
ORCiD: https://orcid.org/0009-0002-2684-7229

**Karol Kutyłowski**
Our Lady of Perpetual Help Hospital, Independent Health Care Institution
Gdyńska 1/3 05-200 Wołomin, Poland
E-mail: kutylowski.karol@gmail.com
ORCiD: https://orcid.org/0009-0000-8592-1711

**Agata Kutyłowska**
Dr Anna Gostynska Wolski Hospital, Independent Public Health Care Institution
Marcina Kasprzaka 17, 01-211 Warsaw, Poland
E-mail: agatakrol517@gmail.com
ORCiD: https://orcid.org/0009-0006-1967-9684

**Corresponding author:**
**Monika Gajda-Bathelt**
E-mail: monikagajda99@gmail.com

**Abstract**
Creatine supplementation is a well-established approach for improving outcomes in high-intensity exercise, yet the impact on cognitive function and the bioavailability of different creatine forms remain under active investigation. In this paper we summarize evidence on creatine bioavailability and its effects on physical and cognitive performance. Creatine monohydrate (CrM) is the gold-standard form, reliably increasing muscle phosphocreatine (PCr) stores and enhancing strength, power, sprint ability and fat-free mass. Creatine supplementation paired with resistance training enhances lean tissue mass and muscular strength in both younger and older individuals. Creatine also delays fatigue in high-intensity endurance sports and improves recovery during bouts of intermittent activity. Cognitive studies report modest benefits of creatine on memory and processing speed, particularly among older adults. Subgroup analyses show that vegetarians and elderly achieve greater creatine levels and cognitive benefits than omnivores and younger people. Side effects are minimal, except for minor gastrointestinal discomfort or weight gain from fluid retention. In summary, creatine monohydrate is highly bioavailable and consistently improves strength and power outcomes, with emerging evidence for cognitive enhancement. Evidence on alternative forms is limited, thus further research is needed to clarify their bioavailability and long-term safety.

**Keywords:** creatine, creatine monohydrate, supplementation, bioavailability, muscle strength, cognitive performance

## Introduction

Creatine is synthesized endogenously from the amino acids arginine and glycine in the liver, kidneys, pancreas and to some extent in the brain, as well as obtained from dietary sources – mainly red meat and fish (Kreider et al., 2022; Brosnan and Brosnan, 2016). Approximately 95% of total body creatine is stored in skeletal muscle, where it binds inorganic phosphate to form PCr, an essential buffer that rapidly regenerates adenosine triphosphate (ATP) during high-intensity physical activity (Kreider and Stout, 2021). Typical diet contains 1–2 g of creatine per day, but this can be insufficient to completely saturate muscle stores. Consequently, oral supplementation is used to raise muscle creatine and PCr by 20–40%, thereby increasing the ability for rapid energy production during exercise (Kreider et al., 2017).

CrM is the most extensively studied and effective form of creatine; numerous studies over the years have associated CrM supplementation to enhanced maximal strength, power output, and lean mass in athletes and active individuals (Wax et al., 2021). Systematic reviews and meta-analyses consistently report that adding CrM to resistance training produces greater gains in muscle mass and strength compared to training alone (Bonilla et al., 2024; Burke et al., 2023). Conversely, performance benefits in endurance sports are not as evident; creatine generally aids in activities involving short high-intensity bursts or sprint finishes, yet often fails to improve continuous endurance time-trials (Forbes et al., 2023; Wax et al., 2021).

Interest has grown in possible cognitive benefits of creatine, as brain cells also depend on the creatine-PCr system for energy (Avgerinos et al., 2018). Some studies suggest that supplementation raises brain creatine levels and may improve memory and executive functions in certain populations. However, findings have been mixed, potentially due to differences in subject characteristics, dosage levels, and cognitive tests used (Bonilla et al., 2024; Sandkühler et al., 2023). Notably, vegetarians (who have lower baseline muscle and brain creatine because of their diet) and older adults have been proposed as subgroups most likely to benefit cognitively from creatine (Prokopidis et al., 2023; Kaviani et al., 2020).

Simultaneously, numerous novel creatine forms, for example creatine ethyl ester (CEE), buffered forms, creatine hydrochloride (Cr-HCl), are marketed as having greater solubility or bioavailability than CrM. It is important to evaluate whether these forms actually increase systemic and muscle creatine more effectively than CrM. Claims of superior uptake have not been verified; for example, CEE is chemically unstable in solution and tends to convert to creatinine, resulting in lower bioavailability than CrM. Similarly, Cr-HCl is more soluble but has no proven advantage in raising muscle creatine levels in humans (Kreider et al., 2022).

This review analyzes evidence from recent studies to compare the bioavailability of creatine forms, and to evaluate the effects of creatine supplementation on physical and cognitive performance. We give particular attention to strength, power, and endurance outcomes, along with memory and executive function measures. We also emphasize findings in key subgroups, including athletes, older adults and vegetarians, to offer a perspective on the benefits, limitations, and future needs in creatine research.

**Bioavailability of Creatine Forms**

CrM remains the gold standard for supplementation because of its well-documented almost 100% absorption, stability and a large number of studies that have showed its effectiveness and safety (Kreider et al., 2022; Kreider et al., 2017; Jäger et al., 2011). CrM contains 87.9% creatine by molecular weight, while alternative forms have lower creatine content per gram: for example, creatine citrate – 40.6%, di-creatine citrate – 57.7%, creatine pyruvate – 59.8%, and Cr-HCl – 8.2%, indicating that higher doses are required to match the creatine provided by CrM (Kreider et al., 2022). CEE contains approximately 6.3% less creatine by weight compared to CrM, but it is chemically unstable. Several studies and reviews conclude that when ingested, a substantial amount of CEE is converted to creatinine rather than creatine, making it less bioavailable than CrM (Kreider et al., 2022, Giese and Lecher, 2009a; Giese and Lecher, 2009b). Similarly, claims that Cr-HCl is more bioavailable have not been supported; a trial using Cr-HCl demonstrated no higher increase in strength, hypertrophy, and hormonal responses than CrM (Eghbali et al., 2024). In summary, although alternative forms may improve solubility, existing evidence indicate that none of them reliably deliver more creatine into muscle than CrM (Kreider et al., 2022).

**Effects on Physical Performance**

**Strength and Power:** The use of creatine supplements, particularly when paired with resistance training, consistently improves muscular strength and power. There is a strong evidence supporting the claim that creatine combined with resistance training produces larger gains in muscle mass and strength in both young and older adults compared to training by itself (Bonilla et al., 2024; Wang et al., 2024). In adults aged over 48 years, CrM supplementation alone produces a modest but significant increase in lean body mass of approximately 0.6 kg. When the supplementation is paired with a structured resistance training regimen, lean mass gains are augmented by an additional 0.47 kg, resulting in n overall increase of approximately 1.1 kg (Bonilla et al., 2024; Delpino et al., 2022). A review focusing on muscle mass reports that supplementing with creatine alongside resistance training yields small but significant gains in direct measures of muscle hypertrophy across both upper and lower body muscle groups (Burke et al., 2023). These gains translate into measurable increases in both upper- and lower-body strength performance (Lanhers et al., 2017; Lanhers et al., 2015). Importantly, creatine benefits are seen in both men and women and across age groups (adolescents, young adults, elderly). Weight training and other power-focused sports (e.g. sprinting, jumping) consistently show enhanced performance with creatine (Kreider et al., 2022; Wax et al., 2021).

**Endurance and High-Intensity Intermittent Performance:** Creatine's effects on endurance performance are more nuanced. Creatine can prolong time to exhaustion in high-intensity aerobic exercise by increasing muscle PCr and assisting in ATP regeneration (Forbes et al., 2023). Creatine also enhances muscle glycogen resynthesis when co-ingested with carbohydrates, which may support repeated bouts in endurance sports (Roberts et al., 2016). In practice, studies report that creatine improves performance in activities demanding repeated bursts of effort or late-race sprints, for example final accelerations in running, cycling or rowing. It should be mentioned that for prolonged weight-bearing endurance activities like running, results are mixed; in many cases, increased body water weight from creatine may counteract aerobic gains (Forbes et al., 2023).

**Recovery:** Increasing evidence suggests that creatine supplementation might positively influence post-exercise recovery by attenuating markers of muscle damage and accelerating the restoration of muscular function. Several studies have noted reductions in serum creatine kinase levels following intense or damaging exercise in those given creatine versus a placebo, suggesting a protective effect on muscle integrity (Wax et al., 2021; Jiaming and Rahimi, 2021). For example, reduced concentrations of inflammatory markers and creatine kinase are reported in Ironman triathletes after competition when supplemented with creatine, indicating reduced muscle damage (Bassit et al., 2010). Although the primary research focus in creatine literature remains on performance enhancement, outcomes related to recover are particularly relevant in contexts involving repeated high-intensity efforts, such as tournaments or training camps with limited rest. Creatine supplementation results in a notably greater muscle strength recovery following muscle-damaging exercise (Cooke et al., 2009). Importantly, certain studies indicate that creatine supplementation may assist in minimizing muscle loss during immobilization and facilitate recovery during rehabilitation from exercise-induced injuries.

However, findings are inconsistent and further large-scale and well-controlled trials are necessary to determine whether it provides additional benefits when used alongside rehabilitation post-injury **(**Wax et al., 2021; Kreider et al., 2017).

**Effects on Cognitive Performance**

A growing body of studies has investigated creatine's impact on the brain. The mechanism is analogous to muscle: by increasing brain creatine and PCr levels, neuronal ATP turnover during cognitive tasks may be better supported (Gordji-Nejad et al., 2024; Sandkühler et al., 2023). Meta-analyses and randomized controlled trials indicate that creatine supplementation enhances cognitive abilities in adults, especially in memory, attention time, and information processing speed (Xu et al., 2024; Prokopidis et al., 2023).

**Memory:** Supplementing with creatine results in a slight yet statistically significant improvement in memory performance compared to placebo. Notably, the subgroup analysis based on age reveals a larger effect size in older adults (66–76 years) compared to younger individuals (11–31 years) (Prokopidis et al., 2023). Creatine supplementation particularly boosts performance in tasks requiring high levels of cognitive control (Avgerinos et al., 2018). These findings suggest that memory functions (short-term and working memory, reasoning) could be particularly sensitive to creatine, especially in populations with lower baseline stores, such as older adults or vegetarians, as will be described later in this paper (Prokopidis et al., 2023; Oliveira et al., 2023; Rae et al., 2003).

**Executive Function and Processing Speed:** The data regarding creatine's effect on executive function (such as planning, inhibition) is less consistent. The 2024 meta-analysis found no significant overall improvement in executive function tasks, information processing speed and attention scores (Xu et al., 2024). However, an acute dosing study showed that a single high oral dose (0.35 g/kg) of creatine given before sleep deprivation resulted in significant alterations in brain energetics and improved cognitive performance and processing speed under fatigue (Gordji-Nejad et al., 2024).

In the largest randomized controlled trial to date, creatine supplementation (5 g/day for 6 weeks) produced only a borderline improvement in cognitive performance. Side effects (most often mild gastrointestinal discomfort) were significantly more prevalent in the creatine group compared to the placebo group, and vegetarians did not exhibit greater cognitive gains than omnivores in that study. Nevertheless, the trial authors concluded that creatine's cognitive effects may be smaller than previously reported, yet deserve further investigation (Sandkühler et al., 2023; Rae et al., 2003). In general, pooled evidence shows modest cognitive benefits from creatine, particularly for memory-related outcomes. The uncertainty arises partly from the heterogeneity in study designs, subject populations, and cognitive measures. In a recent meta-analysis the evidence for memory improvements was assessed as moderate-certainty, while evidence for other cognitive domains remains low-certainty (Xu et al., 2024; Sandkühler et al., 2023). Given the current limitations in the literature, additional robust and large-scale studies incorporating heterogeneous cohorts are essential to determine the actual cognitive effectiveness of creatine supplementation.

**Subgroup Analyses: Athletes, Older Adults, and Vegetarians**

**Athletes:** Most creatine studies involve trained athletes or active individuals. In these populations, creatine's ergogenic effects on strength, power, sprint, and skill performance are well-documented (Wax et al., 2021 Kreider et al., 2017). For example, weightlifters, runners, swimmers, soccer and volleyball players exhibit a general increase by 10–20% in high-intensity exercise performance (Kreider et al., 2022). Physical performance enhancements may be more significant in males, but females can still derive benefits, especially when considering factors like hormonal status and baseline creatine levels. (Wang et al., 2024; Wax et al., 2021). Athletes typically tolerate creatine well, with the most common effect being small weight gain from muscle water retention (Antonio et al., 2021).

**Older Adults:** Creatine has been investigated as a countermeasure to age-related muscle loss and cognitive decline. Numerous studies have tested creatine plus resistance training in older adults (often ≥50 years). Reviews consistently conclude that creatine is safe for seniors and augments strength and lean mass gains when combined with exercise (Bonilla et al., 2024). Notably, a systematic review found that creatine improved measures of functional performance (e.g. sit-to-stand tests) in frail or chronically ill older adults (Davies et al., 2024). Cognitively, older adults may derive relatively greater benefit from creatine, with notable improvements in memory observed in the 66–76 age group. These findings align with the concept that older brains, with reduced baseline creatine, stand to gain more from supplementation (Prokopidis et al., 2023).

**Vegetarians:** Vegetarians have chronically lower dietary creatine intake, leading to lower serum and muscle creatine stores at baseline. Creatine supplementation in vegetarians dramatically raises muscle creatine and PCr concentrations—often to levels exceeding those of omnivores (Gutiérrez-Hellín et al., 2024). In vegetarian athletes, supplementation increases type-II muscle fiber area, lean mass, and strength, and also improves memory and intelligence. However, studies are mixed on whether vegetarians outperform omnivores in physical performance gains; most find similar strength and endurance benefits in both groups (Kaviani et al., 2020) Importantly, the magnitude of improvement in cognitive tasks is generally larger in vegetarians than in meat-eaters (Benton and Donohoe, 2011). In summary, vegetarians likely obtain equal or greater benefit from creatine, filling a dietary shortfall.

## Discussion

This review confirms that creatine monohydrate is a highly bioavailable supplement with robust benefits for muscle performance. By expanding muscle PCr stores, CrM consistently enhances high-intensity exercise outputs. Studies report significant additional gains in lean mass and strength when creatine is added to resistance training, with effect sizes that are clinically meaningful for athletes and aging adults. The performance benefits translate across a variety of sports (weightlifting, running, team sports) as well as functional tasks in older individuals (Bonilla et al., 2024; Kreider et al., 2022). Alternative creatine formulations have largely failed to show superior uptake or outcomes. For example, creatine ethyl ester is marketed for better absorption, but studies reveal rapid conversion to creatinine, negating the advantage. Cr-HCl dissolves more readily but has not been shown to increase muscle creatine content above that achieved by CrM. Thus, current evidence supports CrM as the reference standard; any claims of greater efficacy by other forms should be interpreted skeptically (Kreider et al., 2022). The cognitive effects of creatine are subtler and more variable than its physical effects. Nonetheless, accumulating data suggests creatine produces small but significant improvements in memory and information processing, especially in populations under metabolic stress (sleep deprivation, mental fatigue) or with lower baseline creatine, such as elderly and vegetarians (Gordji-Nejad et al., 2024); Prokopidis et al., 2023). The largest cognitive trials to date report at most modest gains, indicating that any brain benefits are likely smaller than those for muscle. The mechanisms may involve increased brain energy availability, but factors such as dose, duration, and individual variability need clarification. Notably, many cognitive studies used various tests, sample sizes, and health conditions, leading to heterogeneity. Future trials should standardize cognitive endpoints and explore optimal dosing for cognitive outcomes (Xu et al., 2024; Sandkühler et al., 2023) Subgroup comparisons reinforce that creatine's effects depend partly on baseline status. Older adults and vegetarians, who start with lower creatine stores, tend to gain more (Prokopidis et al., 2023 Kaviani et al., 2020). Athletes in high-intensity sports are the most studied group, and they reliably benefit in strength and power. In contrast, endurance athletes may benefit only in events with intermittent bursts or where fatigue resistance matters (Forbes et al., 2023; Wax et al., 2021). Physical performance enhancements may be more significant in males, but females may experience greater cognitive benefits from creatine supplementation in terms of processing speed (Wang et al., 2024; Xu et al., 2024).

**Safety and Limitations:** Across numerous trials, creatine monohydrate has shown an excellent safety profile, with side effects limited to weight gain (from intracellular water retention) and minor gastrointestinal discomfort (Sandkühler et al., 2023; Kreider et al., 2017). Concerns about kidney or liver damage have not been borne out in healthy individuals, including older subjects (Kreider et al., 2017). However, many cognitive trials are short-term and small, so long-term effects on body remain to be fully elucidated. Furthermore, most research has focused on healthy or athletic populations; data on clinical groups (e.g. neurological patients, injured individuals) are emerging but not comprehensive.

**Future Directions:** To strengthen conclusions, future research should prioritize well-powered randomized controlled trials in underrepresented subgroups such as post-stroke patients or vegans and standardize cognitive testing protocols. Direct comparisons of creatine formulations in humans would be valuable, as would dose–response studies for cognitive outcomes. Given the potential broad utility of creatine (affordable, safe, non-pharmacological), exploring its long-term effects on ageing, rehabilitation, and disease prevention is warranted.

## Conclusions

This paper underscores creatine monohydrate as a highly bioavailable supplement that reliably enhances physical performance in strength and power domains. Its ergogenic benefits are strongest in high-intensity, intermittent exercise and with progressive resistance training, yielding significant gains in strength, lean mass, and muscle function. Cognitive improvements from creatine appear modest but positive, particularly in memory and processing speed, and are most evident in older adults and vegetarians. Alternative creatine forms have not demonstrated advantages over monohydrate. Overall, creatine supplementation is supported by an extensive literature as safe and effective, with clear benefits and few downsides. Further well-designed studies are needed to optimize dosing strategies, understand effects in specialized populations, and fully elucidate creatine's impact on brain function.

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**Author's contribution:**

**Conceptualization:** Monika Gajda-Bathelt, Katarzyna Kwaterska, Julia Adasiewicz
**Methodology:** Monika Gajda-Bathelt, Michał Tomaszek
**Software:** Kamil Janawa
**Check:** Paweł Jan Kuna, Alicja Katarzyna Chojniak
**Formal analysis:** Kamil Janawa, Agnieszka Benecka
**Investigation:** Karol Kutyłowski, Agata Kutyłowska
**Resources:** Agnieszka Benecka
**Data curation:** Michał Tomaszek
**Writing – rough preparation:** Karol Kutyłowski, Agata Kutyłowska
**Writing – review and editing:** Monika Gajda-Bathelt, Katarzyna Kwaterska, Julia Adasiewicz
**Supervision**: Paweł Jan Kuna, Alicja Katarzyna Chojniak

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