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CREATINE MONOHYDRATE SUPPLEMENTATION IN ATHLETIC POPULATIONS: IMPLICATIONS FOR PHYSICAL PERFORMANCE, COGNITIVE RESILIENCE, AND RENAL SAFETY — A NARRATIVE REVIEW

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ABSTRACT

Background: Creatine monohydrate is one of the most studied ergogenic supplements in sports nutrition. Beyond its established effects on skeletal muscle performance, recent literature increasingly addresses cognitive outcomes and persistent concerns regarding renal safety.
Objective: To provide a narrative review of current evidence on creatine monohydrate in athletic and physically active populations, focusing on physical performance, cognition, and kidney-related outcomes.
Methods: Literature from PubMed, Scopus, Web of Science, and Google Scholar was narratively synthesized, prioritizing randomized trials, systematic reviews, meta-analyses, and key position stands, while retaining seminal studies for mechanistic context.
Results: Creatine consistently improves maximal strength, power output, repeated sprint ability, and lean mass accretion when combined with training. Cognitive benefits appear more heterogeneous but are most promising under sleep deprivation, mental fatigue, or other conditions of elevated cerebral energy demand. In healthy users, creatine may modestly increase serum creatinine without indicating structural kidney injury; current controlled evidence does not show clinically meaningful deterioration in renal function.
Conclusions: Creatine monohydrate remains the reference form of creatine for athletic practice, with strong support for performance enhancement, emerging support for cognitive resilience, and a reassuring renal safety profile in healthy athletic populations.

KEYWORDS

Creatine Monohydrate; Athletic Performance; Cognition; Sleep Deprivation; Renal Safety; Narrative Review

CITATION

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1. Introduction

Creatine monohydrate has occupied a singular place in sports nutrition for more than three decades because it combines biological plausibility, reproducible performance benefits, low cost, and a safety profile that is stronger than that of most commercially marketed supplements. It is a naturally occurring nitrogen-containing compound synthesized primarily from glycine, arginine, and methionine, then transported to tissues with high and fluctuating energetic demands. Approximately 95% of total body creatine is stored in skeletal muscle, where free creatine and phosphocreatine function as a rapid phosphate donor system that buffers adenosine triphosphate availability during short, high-intensity effort. This mechanism explains why creatine has become a core intervention in resistance training, sprint sports, and intermittent team games, where repeated restoration of high-energy phosphates is central to performance (Harris et al., 1992; Hultman et al., 1996; Kreider et al., 2017; Wax et al., 2021).

Although the performance literature is mature, current scientific interest has shifted beyond skeletal muscle alone. The brain is also an energetically demanding tissue, and creatine-related pathways are relevant to neuronal signaling, membrane ion homeostasis, and resilience during metabolic stress. This has stimulated growing interest in whether creatine supplementation can attenuate cognitive decline under acute sleep deprivation, mental fatigue, concussion-related energy crisis, or other conditions characterized by impaired brain bioenergetics. At the same time, the supplement continues to be accompanied by persistent myths, especially the claim that creatine “damages the kidneys.” In practice, that misconception often arises because clinicians and athletes conflate creatine, creatinine, and renal injury, even though the creatinine increase observed after supplementation may reflect altered substrate turnover rather than reduced glomerular filtration (Antonio et al., 2021; Forbes et al., 2022; Naeini et al., 2025; Dolan et al., 2019; Roschel et al., 2021).

This review was developed from the premise that a contemporary synthesis should integrate three domains that are usually discussed separately: performance, cognition, and renal safety. Such integration is particularly relevant for athletic and physically active populations, because modern sport is not shaped solely by maximal force production. Athletes often operate under congested competition calendars, insufficient sleep, travel-associated circadian disruption, restrictive eating patterns, and high expectations for recovery between successive efforts. Consequently, a supplement that improves training quality, supports decision-making or vigilance under stress, and does not compromise kidney health has broader value than a purely ergogenic intervention. For a journal interested in health and well-being, this wider framing is especially important because it links supplementation not only to sport success but also to safe, evidence-based practice, health literacy, and responsible monitoring in active populations (Antonio et al., 2021; Longobardi et al., 2023; Naeini et al., 2025; Wu, 2020).

The purpose of the present article is therefore to provide a narrative review of creatine monohydrate supplementation in athletic and physically active populations, with special attention to physical performance, cognitive resilience, and kidney-related outcomes. The review also considers practical dosing strategies, subgroups such as women and vegetarians or vegans, and the clinical interpretation of laboratory markers that may be misread after supplementation. Rather than arguing that creatine is universally beneficial in every setting, the aim is to clarify where evidence is robust, where it is mixed, and where future research should become more precise.

2. Methodology

This manuscript was prepared as a narrative review designed to summarize, interpret, and contextualize the available literature rather than to provide a formal quantitative meta-analysis. Narrative review methodology was chosen because the topic spans multiple outcome domains that differ substantially in design, population, and measurement. Trials involving maximal strength, repeated sprint performance, brain magnetic resonance spectroscopy, psychomotor testing during sleep deprivation, serum creatinine, cystatin C, and glomerular filtration rate are not easily synthesized within a single quantitative model without creating misleading equivalence between fundamentally different endpoints. A narrative approach therefore allowed the integration of mechanistic studies, randomized controlled trials, systematic reviews, meta-analyses, position stands, and selected foundational investigations that remain essential for understanding creatine physiology.

Literature searches were conducted in PubMed, Scopus, Web of Science, and Google Scholar. Search strings combined creatine-related terms with performance, cognition, and renal outcomes, including but not limited to "creatine monohydrate," "creatine supplementation," "athletic performance," "strength," "power," "repeated sprint," "recovery," "cognition," "sleep deprivation," "brain," "renal safety," "kidney function," "serum creatinine," "cystatin C," and "glomerular filtration rate." Priority was given to studies published between 2015 and 2025 in order to reflect contemporary evidence and recent syntheses. However, landmark studies and earlier reviews were retained when they defined supplementation protocols, clarified physiological mechanisms, or represented foundational safety literature. Reference lists of relevant reviews were also screened to identify additional eligible articles.

Preference was given to randomized controlled trials, double-blind placebo-controlled trials, systematic reviews, meta-analyses, and major expert consensus or position statements. Studies focusing on healthy athletic, recreationally active, or physically trained individuals were prioritized. Nevertheless, selected evidence from older adults, clinical populations, and non-athletic cohorts was included when it helped explain mechanisms that are also relevant to athletes, especially in the cognitive and renal sections. Reports centered on non-monohydrate forms of creatine were generally not emphasized unless they informed the discussion of why monohydrate remains the reference form. Case reports suggesting harm were not ignored, but they were interpreted cautiously and weighed against larger controlled datasets.

The synthesis was organized into thematic domains: mechanistic rationale, performance outcomes, recovery and endurance-related considerations, cognition and brain bioenergetics, renal biomarkers and kidney safety, subgroup-specific responses, and practical implementation. Because narrative reviews are inherently more interpretive than systematic reviews, the main methodological risk is selection bias. To reduce that risk, the discussion repeatedly contrasts strong evidence with mixed evidence, and recent reviews with newer individual studies. This approach mirrors current editorial expectations for review articles: a transparent rationale, a structured search and selection process, and a balanced discussion of both strengths and limitations of the evidence base.

3. Results / Synthesis of Evidence

3.1. Biological Rationale and Mechanistic Basis

Creatine's relevance to athletic performance begins with the phosphocreatine system. During intense exercise, adenosine triphosphate is hydrolyzed rapidly and must be resynthesized at a rate that glycolysis and oxidative phosphorylation cannot always meet in the immediate term. Phosphocreatine acts as a high-energy phosphate reservoir, allowing rapid regeneration of ATP from adenosine diphosphate through the creatine kinase reaction. By increasing intramuscular total creatine and phosphocreatine stores, supplementation enhances the buffering capacity of this system and may delay the decline in force output that accompanies repeated maximal or near-maximal contractions. This is the best established mechanistic basis for the ergogenic role of creatine and remains consistent across acute loading studies, longer training interventions, and expert position statements (Harris et al., 1992; Kreider et al., 2017; Wax et al., 2021; Wallimann et al., 1992).

The physiological relevance of creatine is not confined to muscle. Brain tissue consumes a disproportionate share of whole-body resting energy, and fluctuations in cerebral energy state affect vigilance, reaction time, working memory, and complex information processing. The brain can synthesize creatine endogenously, but exogenous uptake appears smaller and slower than in skeletal muscle, likely because transport across the blood–brain barrier is more constrained. This helps explain why cognitive outcomes are generally less dramatic and less consistent than muscular outcomes. It also suggests that creatine may matter most when cerebral energy homeostasis is stressed, such as during sleep deprivation, traumatic brain injury, demanding cognitive testing, or potentially low habitual dietary creatine intake (Forbes et al., 2022; Gordji-Nejad et al., 2024; Dechent et al., 1999; Merege-Filho et al., 2017; Roschel et al., 2021).

A separate but clinically important mechanistic issue concerns creatinine. Creatinine is a non-enzymatic breakdown product derived from creatine and phosphocreatine metabolism. Because serum creatinine is widely used as a surrogate marker in estimated glomerular filtration calculations, an increase in circulating creatinine after supplementation can create the appearance of renal impairment even when kidney structure and filtration remain intact. This is one of the major reasons why the renal safety debate has persisted despite decades of mostly reassuring evidence. In athletes with greater muscle mass, high meat intake, or recent creatine loading, serum creatinine is particularly vulnerable to misinterpretation. Consequently, the question is not whether creatine can change creatinine values; it can. The clinically meaningful question is whether it worsens kidney function as assessed by more appropriate markers, longer-term trajectories, and controlled trials (Antonio et al., 2021; Naeini et al., 2025; Poortmans & Francaux, 2000; Longobardi et al., 2023).

3.2. Strength, Power, Repeated Sprinting, and Lean Mass

The most consistent conclusion in the literature is that creatine monohydrate improves performance in tasks that depend on short-duration, high-intensity ATP turnover. Across reviews and trials, the most reliable benefits involve maximal strength, explosive power, total work performed in repeated bouts, and lean mass accrual during resistance training. Wax et al. summarized that increases of roughly 5% to 15% are frequently reported in maximal power, anaerobic capacity, work performed during repeated sprints, and training-related strength outcomes, although the size of benefit depends on protocol, training status, and outcome selection (Wax et al., 2021). This does not imply that every athlete will respond equally, but it does mean that the direction of effect is far more often positive than neutral, and almost never ergolytic when standard doses are used (Kreider et al., 2017; Wax et al., 2021; Tarnopolsky & MacLennan, 2000).

In resistance training settings, the effect of creatine is partly acute and partly cumulative. Acutely, higher phosphocreatine availability can support one or more additional repetitions, greater maintenance of movement velocity across sets, or improved quality of high-force output at the end of a session. Chronically, these small session-level advantages can translate into a greater training stimulus and, therefore, larger gains in muscle strength and lean body mass. Creatine should not be viewed as a replacement for progressive overload, high-quality nutrition, or recovery, but as a supplement that amplifies the adaptive effect of those foundations. This is why trials that combine creatine with structured resistance training usually show larger and more consistent benefits than trials in which supplementation is tested without a meaningful exercise stimulus (Kreider et al., 2017; Wax et al., 2021; Syrotuik & Bell, 2004).

Repeated sprint and team-sport contexts are especially relevant because these activities tax precisely the physiological domain that creatine most strongly influences: rapid resynthesis of phosphocreatine between bursts. Improvements have been described in sprint cycling, skating, field tests resembling soccer match play, and other intermittent protocols in which work-rest structure matters. The benefit is not simply that athletes produce one faster repetition; rather, they often preserve performance better across successive repetitions. That distinction is important for sports such as soccer, hockey, rugby, basketball, lacrosse, and combat sports, where the cumulative decline in output across repeated high-intensity efforts may be more decisive than a single isolated maximal attempt (Wax et al., 2021; Smith-Ryan et al., 2021; Greenwood et al., 2003; Burke et al., 2003).

Lean mass increases observed with creatine supplementation require careful interpretation. Early body mass gain after loading is often driven by increased intracellular water rather than immediate accrual of new contractile tissue. This has fueled misconceptions that creatine merely “adds water weight.” Yet intracellular hydration is not necessarily trivial or undesirable; it may reflect the physiological environment accompanying increased creatine storage, and longer-term trials show that lean mass gains frequently exceed any transient fluid-related change. From a performance standpoint, the relevant question is whether greater body mass supports or hinders the sport-specific objective. In strength and power sports, combat sports during certain training phases, and collision sports, modest increases in lean mass may be beneficial. In contrast, weight-sensitive athletes or endurance competitors may prefer slower saturation strategies or closer attention to competition timing (Antonio et al., 2021; Gutiérrez-Hellín et al., 2025; Burke et al., 2003).

Not every study shows a clear ergogenic effect, and this heterogeneity deserves emphasis rather than dismissal. Null findings can emerge when outcomes are poorly matched to creatine physiology, when study duration is too short to capture adaptation, when sample size is small, or when baseline muscle creatine stores are already high. Some protocols test single sprints instead of repeated efforts, or mixed sport-specific tasks where performance variability is large. Even in such cases, however, creatine rarely impairs performance. The most defensible conclusion is therefore not that creatine improves every athletic outcome, but that it reliably improves a clearly defined cluster of outcomes rooted in high-intensity energy turnover, especially when combined with training (Kreider et al., 2017; Wax et al., 2021; Syrotuik & Bell, 2004).

A further reason the performance literature is so persuasive is that creatine’s benefits appear across a wide range of training backgrounds. Positive findings have been described in novices beginning structured resistance exercise, trained lifters pursuing higher-volume programs, and sport-specific athletes whose primary objective is not bodybuilding but the preservation of high-power output during competition. This breadth of applicability matters because it suggests that creatine is not dependent on a single training ideology. Rather, it appears to support the common energetic bottleneck shared by many explosive tasks: the ability to reproduce force rapidly before fatigue-associated declines in phosphocreatine availability become limiting. In practical terms, this means creatine can be useful in traditional strength development, but also in preparatory phases for team sports, jumping sports, and power-endurance disciplines (Tarnopolsky & MacLennan, 2000; Kambis & Pizzedaz, 2003; Greenwood et al., 2003).

Another important issue is responder variability. Athletes with lower baseline intramuscular creatine stores appear more likely to demonstrate marked increases after supplementation, whereas those who begin close to saturation may exhibit smaller relative changes. This concept is valuable clinically because it helps explain why anecdotal experience can be misleading. One athlete may report a dramatic change in repeated sprint tolerance, while another notices only a subtle effect. Such differences do not invalidate the supplement; they reflect baseline biology, diet, muscle fiber composition, training status, and measurement sensitivity. For clinicians and coaches, this reinforces the importance of evaluating creatine over an appropriate time horizon and through relevant outcomes rather than expecting a uniform, immediately obvious response in every user (Burke et al., 2003; Syrotuik & Bell, 2004; Kreider et al., 2017).

3.3. Endurance Performance and Recovery

Compared with strength and repeated sprint performance, the evidence for direct ergogenic effects on continuous endurance exercise is more mixed. This pattern is not surprising. Pure endurance events rely proportionally more on oxidative metabolism, cardiovascular function, substrate availability, and pacing than on rapid phosphocreatine turnover alone. In some settings, the small increase in body mass during creatine loading may even reduce relative performance when movement economy is crucial. For that reason, creatine should not be presented as a primary supplement for all endurance athletes in the same straightforward manner that it is for repeated sprint or resistance-trained populations. The literature instead suggests a more nuanced interpretation: creatine may be more useful for endurance athletes when their sport includes surges, accelerations, hill work, interval training, strength training, or repeated high-intensity demands superimposed on an aerobic base (Wax et al., 2021; Kreider et al., 2017; Rawson & Venezia, 2011).

Several indirect pathways may explain why some endurance athletes still benefit. First, greater phosphocreatine availability may improve the quality of interval sessions, which are commonly used to raise aerobic power, lactate tolerance, and race-specific speed. Second, creatine may facilitate glycogen resynthesis or improve the ability to sustain training volume during heavy blocks. Third, it may support recovery between hard sessions, especially when the athlete's program combines endurance work with resistance or sprint training. These mechanisms do not guarantee better time-trial performance in every study, but they do make creatine relevant to many contemporary training models in which endurance is not trained in isolation from strength and repeated high-intensity work (Kreider et al., 2017; Wax et al., 2021; Volek et al., 2001).

Recovery is one of the more interesting secondary domains in the creatine literature. Preliminary evidence indicates that supplementation may attenuate the decline in force production after strenuous exercise and may reduce some indices of muscle damage or soreness in selected contexts. The mechanisms are probably multifactorial and may involve improved calcium handling, membrane stability, attenuated metabolic stress during exercise, or simply a greater capacity to repeat quality work without exhausting immediate energy reserves. Here, too, the evidence is not as definitive as for strength outcomes, but it is sufficiently promising that practitioners often use creatine not only for peak performance but also for maintaining training quality across dense schedules. This has clear practical importance for athletes competing in tournaments, back-to-back matches, or multi-event settings where recovery time is limited (Wax et al., 2021; Volek et al., 2001; Antonio et al., 2021).

Importantly, endurance-related interpretation should remain sport specific. A rower, middle-distance runner, or cyclist performing interval-heavy work may respond differently from a marathoner prioritizing body mass minimization and steady-state economy. The same supplement can therefore be rational in one endurance context and less compelling in another. The most defensible applied recommendation is to match creatine use to the actual demands of the event and the phase of training rather than to the broad label "endurance athlete." Such individualized framing is more scientifically accurate and more useful for clinicians and coaches (Wax et al., 2021; Gutiérrez-Hellín et al., 2025).

A practical way to understand the endurance literature is to distinguish event performance from training support. Creatine may not consistently improve long, continuous event times in steady-state competition, yet it may still improve the training processes that ultimately shape endurance performance. For example, many endurance athletes must complete repeated high-intensity intervals, strength sessions, sprint finishes, tactical surges, or race-pace repetitions under fatigue. In these contexts, the capacity to restore phosphocreatine more effectively between efforts can have meaningful downstream consequences for session quality. Thus, an athlete may not experience an obvious direct effect on a single time trial, but may still benefit through better completion of the sessions that drive adaptation over weeks and months (Wax et al., 2021; Kreider et al., 2017).

This distinction is especially relevant in contemporary sport, where hybrid demands are common. Rowers, middle-distance runners, cyclists, and swimmers often require both aerobic development and repeated anaerobic power. Team-sport athletes, meanwhile, may possess substantial aerobic requirements while still depending on accelerations, collisions, rapid transitions, and decision making under fatigue. In such settings, the older dichotomy between "strength supplements" and "endurance athletes" becomes less useful. Creatine is best understood as a supplement that supports repeated high-energy turnover within broader training systems, some of which are predominantly aerobic but not purely steady-state in execution (Wax et al., 2021; Tarnopolsky & MacLennan, 2000).

3.4. Cognition, Brain Bioenergetics, and Sleep Loss

Evidence for cognitive benefit has historically lagged behind the muscular literature, yet the field has advanced considerably. The central concept is that creatine may support brain bioenergetics when neuronal ATP demand rises or when normal restoration is compromised. This makes the supplement theoretically attractive for situations common in sport and clinical performance environments, such as sleep restriction, travel fatigue, intense study or tactical load, concussion recovery, and possibly low dietary creatine intake. However, the cognitive literature is heterogeneous in design, ranging from small trials using psychometric testing to magnetic resonance spectroscopy studies quantifying cerebral metabolites. As a result, sweeping statements should be avoided: creatine is not a universal "brain booster," but the accumulating evidence suggests that it can be helpful under specific stress conditions (Forbes et al., 2022; Dolan et al., 2019; Roschel et al., 2021).

A key insight from the brain literature is that cerebral uptake is smaller and slower than muscle uptake. Most studies assessing brain creatine content report only modest increases, typically lower than those achieved in skeletal muscle. This likely reflects blood–brain barrier transport limitations and the brain's own endogenous creatine metabolism. From an applied standpoint, that means conventional athletic dosing regimens may not fully predict cognitive outcomes. It also helps explain why benefits are more often seen when the brain is metabolically challenged. In otherwise well-rested healthy adults performing simple cognitive tasks, the effect may be minimal or absent. Under sleep deprivation, mental fatigue, or other conditions of energetic strain, the probability of benefit appears higher (Forbes et al., 2022; Dechent et al., 1999; Merege-Filho et al., 2017; Roschel et al., 2021).

Recent evidence under sleep deprivation is especially noteworthy. Gordji-Nejad et al. reported that a high single dose of creatine monohydrate administered during subtotal sleep deprivation altered cerebral phosphate-related measures and improved cognitive performance and processing speed. The study is important not only because it observed behavioral changes, but because it linked them to neurochemical markers of brain energy state, thereby strengthening mechanistic plausibility. Earlier work by McMorris et al. and Cook et al. also suggested that creatine may attenuate some adverse cognitive or psychomotor effects of sleep loss. These findings are highly relevant to athletes and medical trainees alike, as both groups often operate under insufficient sleep and high decision-making pressure (McMorris et al., 2006; Cook et al., 2011; Gordji-Nejad et al., 2024).

The broader review literature suggests that cognition-related outcomes may be stronger in domains such as short-term memory, reasoning, processing speed, and fatigue resistance than in global intelligence or broad executive function as a single construct. Even there, the findings remain mixed, and smaller studies should not be overinterpreted. Yet the direction of travel in the literature is clear: the question has shifted from whether the brain is relevant to creatine physiology at all to which populations, doses, and stress states are most responsive. Athletes who routinely encounter sleep restriction, tactical complexity, or mentally fatiguing competition environments may therefore represent a more appropriate target population than healthy rested volunteers performing low-stress laboratory tasks (Avgerinos et al., 2018; Xu et al., 2024; Forbes et al., 2022).

An additional point of interest is the potential interaction between baseline creatine status and cognitive responsiveness. Vegetarians and vegans often consume less dietary creatine, and some data suggest lower baseline tissue creatine stores in those who avoid animal products. It is plausible that such individuals may respond more clearly, both physically and cognitively, to supplementation. The same may apply, though less predictably, to women across different hormonal states, older adults, or those with chronic under-recovery. These subgroup hypotheses are not yet resolved, but they provide a scientifically grounded framework for more personalized future research (Rae et al., 2003; Burke et al., 2003; Gutiérrez-Hellín et al., 2025).

It is also worth emphasizing that cognitive function in sport is not limited to abstract test performance. Many competitive environments require rapid perception, error monitoring, inhibitory control, tactical flexibility, and maintenance of attention under physical fatigue. An intervention that preserves only a modest amount of processing speed or vigilance can still be meaningful if that preservation occurs at a critical moment: a late-game transition, a technical movement under sleep loss, or a safety-sensitive task after travel. The ecological relevance of cognition in sport is therefore greater than it may appear when studies are judged only by the magnitude of change in isolated laboratory tasks (Forbes et al., 2022; Xu et al., 2024).

The same logic extends to medical, academic, and occupational performance. Although this review is focused on athletic populations, its cognitive discussion resonates beyond sport because creatine may be relevant wherever performance depends on energy availability under constraint. The supplement therefore sits at an interesting boundary between sports nutrition and broader performance medicine. That boundary is especially important in populations such as medical trainees, military personnel, or shift workers, who often share with athletes the combination of high output expectations, sleep restriction, and irregular recovery opportunities (Rawson & Venezia, 2011; Forbes et al., 2022).

At the same time, several unresolved questions remain. The optimal dose for cognitive outcomes is not yet clearly defined, and it may differ from the dose that is sufficient for muscle saturation. Some studies suggest benefit after conventional supplementation schedules, whereas others indicate that higher acute doses may transiently influence brain bioenergetics under stress. This creates an important research challenge: the field needs trials that match dosing strategy to brain-specific physiology rather than merely importing muscle-oriented protocols without adjustment. Until those studies are available, the most cautious applied stance is that creatine's cognitive potential is promising, mechanistically credible, and most likely to emerge when the brain is metabolically stressed (Roschel et al., 2021; Forbes et al., 2022; Gordji-Nejad et al., 2024).

3.5. Renal Biomarkers and Kidney Safety

The renal safety debate has been sustained less by strong evidence of harm than by persistent confusion in interpretation. In everyday practice, elevated serum creatinine is often treated as synonymous with impaired kidney function. This shortcut is particularly problematic in athletic populations, where muscle mass, protein intake, meat consumption, dehydration, recent training load, and creatine supplementation can all influence serum creatinine independently of structural kidney injury. Consequently, any review of creatine safety must begin by separating biomarker behavior from organ damage. An isolated increase in serum creatinine after supplementation is neither surprising nor sufficient to conclude nephrotoxicity. The more clinically meaningful question is whether filtration, albuminuria, cystatin C, or longer-term renal function deteriorate in controlled settings (Antonio et al., 2021; Gualano et al., 2008; Poortmans & Francaux, 2000; Longobardi et al., 2023).

The cumulative controlled literature in healthy people is largely reassuring. Randomized studies have generally failed to show clinically meaningful worsening of glomerular filtration or other renal markers when creatine monohydrate is used at recommended doses. One notable trial by Gualano et al. found no adverse renal effects despite rigorous follow-up and direct attention to kidney-related endpoints. Earlier reviews already argued that the evidence for creatine-induced renal dysfunction in healthy users was weak and disproportionately influenced by case reports involving confounding factors such as pre-existing renal disease, multiple supplements, concurrent medications, or unverified product use (Poortmans & Francaux, 2000; Gualano et al., 2008; Antonio et al., 2021; Gualano et al., 2011; Vilar Neto et al., 2020).

Recent quantitative syntheses have reinforced this position while adding nuance. The 2019 systematic review and meta-analysis by Silva et al. concluded that creatine supplementation did not support clinically relevant renal impairment in the available controlled studies. More recently, Naeini et al. incorporated 21 studies in their systematic review and found that creatine supplementation was associated with only a small increase in serum creatinine, while glomerular filtration rate did not differ significantly from control conditions. Their interpretation is particularly important: the creatinine change was considered modest and likely attributable to metabolic turnover rather than kidney injury. This is exactly the distinction that is often lost in everyday sports medicine conversations (Silva et al., 2019; Naeini et al., 2025; Longobardi et al., 2023).

That said, reassuring evidence in healthy athletes should not be misused to imply that creatine is automatically risk free in every clinical setting. Caution is still appropriate in individuals with known chronic kidney disease, unstable hypertension, single-kidney status, active nephrotoxic medication use, or poorly explained pre-existing laboratory abnormalities. The problem here is not that monohydrate has been shown to be dangerous in such groups, but that evidence is often limited, heterogeneous, or confounded by multimorbidity. In these contexts, supplementation should be individualized, ideally with baseline assessment and clinically appropriate monitoring. This cautious position is compatible with the broader literature and prevents the opposite error of making absolute claims of universal safety regardless of context (Longobardi et al., 2023; Naeini et al., 2025).

A related practical issue is laboratory interpretation. When athletes taking creatine undergo routine health screening, clinicians may need to contextualize mild creatinine elevations with hydration status, recent training, body composition, and, when necessary, alternative markers such as cystatin C or repeat testing after standardized conditions. Better interpretation is not merely a laboratory matter; it can prevent unnecessary alarm, inappropriate discontinuation of an otherwise useful supplement, or the mistaken belief that a normal kidney has become diseased. In this sense, creatine provides an instructive example of how biomarker literacy matters in preventive and sports medicine (Antonio et al., 2021; Longobardi et al., 2023; Vilar Neto et al., 2020).

The debate is further complicated by the fact that athletes are often exposed to several overlapping influences on renal biomarkers at once. High-protein diets, intentional dehydration before weigh-ins, NSAID use, non-prescribed fat-loss products, very intense training, and concurrent supplement stacking can all modify interpretation. When renal adverse events are described in isolated reports, creatine is therefore not always the only plausible contributor. This is why controlled studies remain far more informative than anecdote. They allow the actual effect of creatine monohydrate to be separated from the broader, often messy ecology of supplement use and athletic behavior (Greenwood et al., 2003; Volek et al., 2001; Antonio et al., 2021).

A clinically mature interpretation must therefore avoid two extremes. The first extreme is the reflexive belief that any rise in creatinine proves kidney injury. The second is the equally unhelpful claim that creatine never warrants clinical discussion. In reality, creatine deserves thoughtful discussion precisely because it is common, effective, and capable of altering a routinely measured marker. The best practice model is not fear or dismissal, but contextualization. Athletes should disclose use, clinicians should interpret results with that knowledge in mind, and follow-up should be individualized when history or comorbidity suggests a higher baseline risk (Antonio et al., 2021; Longobardi et al., 2023; Naeini et al., 2025).

3.6. Women, Vegetarians and Vegans, Adolescents, and Other Subgroups

Historically, much of the creatine literature was built on male participants, particularly young men engaged in resistance training. This created an unfortunate gap between the popularity of creatine in practice and the evidence base available for women. More recent work has begun to address that imbalance. Smith-Ryan et al. argued that women may warrant special consideration because creatine metabolism interacts with hormonal state, the menstrual cycle, pregnancy-related physiology, and menopause-related changes in muscle and brain energetics. Their review suggests that creatine is both underused and understudied in women, despite plausible benefits for strength, fatigue resistance, mood, and cognition. The practical implication is not that women require a fundamentally different supplement, but that female-specific physiology should be better represented in future trials rather than assumed to mirror male responses without testing (Smith-Ryan et al., 2021; Tam et al., 2025; Kambis & Pizzedaz, 2003).

The applied evidence in active women is encouraging, even if still smaller than the male literature. Available trials suggest that women can improve strength, repeated sprint ability, and some sport-specific outcomes, while fears of dramatic or unacceptable weight gain are frequently exaggerated. A recent systematic review focused on active females concluded that performance enhancement appears possible, but that the evidence base remains limited by relatively few high-quality trials. This is an important and fair interpretation: creatine should not be withheld from female athletes because of outdated assumptions, yet researchers should also avoid overstating certainty in areas where female-specific data remain modest (Smith-Ryan et al., 2021; Tam et al., 2025; Kambis & Pizzedaz, 2003; Tarnopolsky & MacLennan, 2000).

Vegetarians and vegans represent another subgroup of particular interest. Because creatine is naturally abundant in meat and fish, individuals following plant-based diets often have lower habitual creatine intake and may begin supplementation with lower baseline tissue stores. This creates a plausible biological rationale for greater responsiveness. Burke et al. reported that vegetarians showed lower initial muscle creatine and experienced larger increases in intramuscular creatine and lean tissue after supplementation than omnivores. Contemporary reviews continue to identify plant-based eaters as a subgroup for whom creatine may support both physical and potentially cognitive function without requiring abandonment of dietary principles (Burke et al., 2003; Gutiérrez-Hellín et al., 2025; Rae et al., 2003).

Adolescents are discussed more cautiously in the literature. On one hand, creatine is widely used in youth sport, and some reviews argue that blanket prohibitions are less evidence based than proper education, supervision, and product-quality guidance. On the other hand, well-powered long-term randomized trials in healthy adolescent athletes remain limited. The current balance of evidence suggests that creatine monohydrate is likely safe and potentially useful when used responsibly by trained youth under adult supervision, but that education and context matter greatly. This is an area where health professionals, coaches, and families need nuanced guidance rather than sensational warnings or uncritical promotion (Jagim & Kerksick, 2021; Antonio et al., 2021).

Finally, subgroup thinking highlights an important principle for the entire field: baseline physiology matters. Athletes are not interchangeable. Response may depend on diet, sex, training phase, sport, sleep status, body mass goals, and baseline tissue creatine stores. The future of creatine research is therefore unlikely to depend on proving again that monohydrate works in a generic population. It will depend on clarifying who benefits most, under what stressors, and with which dosing strategies (Burke et al., 2003; Syrotuik & Bell, 2004; Smith-Ryan et al., 2021).

The female athlete literature also raises important questions about timing and life stage. Hormonal fluctuations across the menstrual cycle, the postpartum period, and the menopausal transition may alter substrate use, fluid balance, and recovery characteristics in ways that interact meaningfully with creatine metabolism. This does not mean that athletes require complex cycle-based creatine periodization on the basis of current data. It does, however, mean that female physiology should no longer be treated as a niche add-on to a male-derived evidence base. Future trials that account for menstrual status, contraceptive use, and symptom burden could substantially improve individualized supplementation guidance (Smith-Ryan et al., 2021; Gutiérrez-Hellín et al., 2025).

Plant-based athletes represent another setting in which creatine has value beyond narrow ergogenic framing. For many vegetarians and vegans, creatine supplementation can function as a practical way to compensate for the absence of creatine-rich animal foods without altering dietary ethics or identity. This matters because sports nutrition is not only about biological optimization but also about feasible, acceptable interventions that fit the athlete's lived context. Creatine is one of the few supplements for which that combination of physiological rationale and dietary compatibility is particularly strong (Burke et al., 2003; Gutiérrez-Hellín et al., 2025; Wu, 2020).

The subgroup perspective also highlights a public-health issue: misinformation does not affect all populations equally. Women are often exposed to exaggerated fears of bloating or "bulk," adolescents to simplistic safety warnings, and plant-based athletes to the false assumption that all nutritional gaps can be corrected through whole-food strategies alone. Review articles therefore have an educational responsibility. They should not simply summarize trials, but should also correct the specific myths that discourage evidence-based use in populations most likely to benefit (Antonio et al., 2021; Jagim & Kerksick, 2021; Smith-Ryan et al., 2021).

3.7. Practical Use, Dosing, and Product Choice

From a practical standpoint, creatine monohydrate remains the reference form against which all other creatine products are judged. Despite aggressive marketing of alternative salts, esters, and buffered preparations, monohydrate continues to have the best evidence for efficacy, safety, affordability, and tissue saturation. Reviews that examine alternative forms typically conclude that none has demonstrated superior real-world outcomes sufficient to displace monohydrate as first-line practice. This is especially important in a supplement market where novelty often outpaces evidence (Kreider et al., 2017; Gutiérrez-Hellín et al., 2025; Jäger et al., 2007).

Two dosing strategies dominate applied practice. The first is a loading approach of approximately 0.3 g/kg/day, commonly operationalized as about 20 g/day divided into four doses for 5 to 7 days, followed by a maintenance dose of 3 to 5 g/day or roughly 0.03 g/kg/day. This is the fastest way to saturate muscle stores and is useful when time to competition or adaptation is short. The second is a gradual saturation strategy using approximately 3 to 5 g/day from the outset without a loading phase. This approach achieves similar tissue saturation more slowly but may reduce gastrointestinal discomfort and minimize early body mass fluctuation. In both cases, consistency matters more than elaborate timing rules (Hultman et al., 1996; Kreider et al., 2017; Gutiérrez-Hellín et al., 2025; Harris et al., 1992; Preen et al., 2003; Sale et al., 2009).

Athletes in weight-sensitive or aesthetic sports may prefer gradual saturation, particularly close to competition. A short loading phase can still be appropriate during off-season or strength-development blocks, but it should be matched to the athlete's goals rather than imposed automatically. Similarly, the common practice of combining creatine with large carbohydrate loads is not always necessary in applied sport, especially when body mass control, gastrointestinal tolerance, or energy intake targets are concerns. The literature supports flexible, athlete-centered implementation rather than a one-size-fits-all rule (Green et al., 1996; Steenge et al., 1998; Steenge et al., 2000).

Hydration and laboratory interpretation also deserve practical mention. Creatine is osmotically active, and early intracellular water retention is common, but this should not be confused with pathological fluid overload. In healthy athletes, the phenomenon is typically mild, intracellularly directed, and functionally compatible with training adaptation. Nevertheless, users should be counseled that a modest short-term body mass increase may occur. Likewise, clinicians should know that creatine users may present with slightly higher serum creatinine despite preserved renal function. Appropriate counseling before supplementation is therefore as important as the dose itself: evidence-based use depends not only on the compound, but on informed interpretation by athletes, coaches, and healthcare professionals (Antonio et al., 2021; Volek et al., 2001; Vilar Neto et al., 2020).

Table 1 summarizes the major outcome domains discussed in this review and highlights how the strength of evidence differs across performance, cognition, and renal safety.

Table 1. Summary of the evidence across major outcome domains

Domain	Overall direction of evidence	Most applicable settings	Main interpretive note
Strength / power	Consistently positive	Resistance training, sprinting, explosive efforts	Best supported outcome domain
Repeated sprint ability	Usually positive	Team sports, combat sports, intermittent protocols	Benefit often appears across repeated bouts rather than a single effort
Lean mass / training adaptation	Generally positive with training	Hypertrophy blocks, off-season, strength sports	Early body mass gain may partly reflect intracellular water
Continuous endurance	Mixed / context dependent	Interval-heavy endurance, mixed-demand sports	Direct benefit less reliable than in high-intensity tasks
Recovery	Promising but less definitive	Dense schedules, multi-event competition	May help maintain training quality and force recovery
Cognition	Promising, especially under stress	Sleep deprivation, mental fatigue, low baseline creatine states	Effects are more heterogeneous than performance outcomes
Renal safety	Reassuring in healthy users	Healthy athletes and physically active adults	Mild creatinine rise does not necessarily mean kidney injury
Women / plant-based diets	Potentially favorable	Female athletes, vegetarians, vegans	Underrepresented groups may differ in baseline creatine status

Practical dosing strategies and routine monitoring considerations relevant to clinicians and athletes are presented in Table 2.

Table 2. Practical dosing and monitoring considerations

Practical goal	Common strategy	Typical dose	Applied comment
Rapid saturation	Loading + maintenance	0.3 g/kg/day for 5–7 days, then 3–5 g/day	Useful when time is limited; early body mass increase more likely
Gradual saturation	No loading phase	3–5 g/day from the outset	Similar endpoint with slower saturation and often better tolerability
Weight-sensitive sport	Gradual or phase-specific use	3–5 g/day	Avoid unnecessary loading close to weigh-in or key competition if body mass is a concern
High cognitive stress or travel	Consistent daily use, individualized	Usually 3–5 g/day; some studies used higher acute doses	Evidence is promising but less standardized than muscular dosing
Routine monitoring	Clinical interpretation	Not a dose issue	Contextualize serum creatinine; consider hydration, training load, and alternative markers when needed

4. Discussion

Taken together, the current literature supports a hierarchy of confidence across outcome domains. The highest certainty remains in muscle-related performance outcomes: maximal strength, repeated sprint performance, power production, and lean mass adaptation during training. These effects are supported by clear mechanism, extensive trial history, and repeated endorsement in systematic reviews and position stands. A second tier of evidence supports indirect benefits in recovery and mixed-demand endurance settings, where creatine may help sustain training quality even when it does not uniformly improve continuous endurance performance. A third and still emerging tier concerns cognition. Here the signal is promising, particularly under sleep deprivation or high metabolic stress, but the evidence base is smaller, more heterogeneous, and more sensitive to population selection and task choice. Finally, the renal safety literature is reassuring in healthy users, but its proper interpretation requires clinical literacy rather than simplistic reliance on serum creatinine alone (Kreider et al., 2017; Wax et al., 2021; Xu et al., 2024; Naeini et al., 2025).

A broader conceptual issue emerging from this review is that creatine is increasingly difficult to classify within a single traditional category. Historically, it was treated primarily as a strength and muscle supplement. That description is still valid, but it is incomplete. The contemporary literature places creatine at the intersection of performance enhancement, recovery support, cognitive resilience, and clinical biomarker interpretation. This broader positioning helps explain both its scientific longevity and its practical importance. Few supplements are simultaneously relevant to gym-based training, field sport, sleep loss, and the avoidance of false-positive concern in routine laboratory work (Antonio et al., 2021; Forbes et al., 2022; Naeini et al., 2025).

This breadth of relevance may also explain why creatine has remained central while many other supplements rise quickly and fade. A substantial portion of the supplement industry is driven by novelty, proprietary blends, or mechanistic claims without robust outcome data. Creatine is the opposite: its market presence is strong precisely because its outcome data are strong. That distinction is not trivial in an era of information overload. For clinicians advising athletes, one of the most valuable services is not to recommend more products, but to identify the limited set of products supported by sufficiently durable evidence. Creatine clearly belongs in that category (Avgerinos et al., 2018; Xu et al., 2024; Gordji-Nejad et al., 2024).

Another important theme is that context modifies utility more than it modifies basic physiology. The core mechanism of creatine does not change across sports, but the value of expressing that mechanism does. A powerlifter may prize maximal force, a soccer player may prize maintenance of repeated sprint ability deep into a match, and an overworked trainee may value preserved vigilance after poor sleep. The same supplement can therefore serve different performance goals depending on the bottleneck limiting the athlete at a given moment. This contextual flexibility is one reason creatine remains relevant across training phases and populations (Kreider et al., 2017; Wax et al., 2021; Gutiérrez-Hellín et al., 2025).

At the systems level, creatine also provides a useful model for how sports medicine and performance science should communicate with one another. Performance researchers often focus on output metrics, while clinicians focus on safety markers and symptom interpretation. In the case of creatine, these two conversations must be linked. Recommending an effective supplement without understanding its impact on routine laboratory interpretation is incomplete care. Conversely, discouraging supplementation because of misunderstood creatinine changes reflects poor translation of sports science into clinical practice. Integrative reviews are therefore valuable not only because they summarize evidence, but because they connect professional silos that are too often separated in practice (Antonio et al., 2021; Longobardi et al., 2023; Naeini et al., 2025).

One reason creatine remains so relevant is that it bridges performance science and preventive health. In athletic populations, the question is not merely whether a supplement adds kilograms to a lift or tenths to a sprint. It is also whether it can support sustainable training, reduce misinformation, and be used responsibly within a broader framework of athlete well-being. This broader view matters because supplement use is now embedded within technologically mediated sport environments that include wearable sleep tracking, training load analytics, digital nutrition platforms, and frequent laboratory monitoring. Creatine is particularly well suited to such contexts because its effects can be linked to meaningful physiological outcomes, monitored over time, and interpreted against real performance demands rather than marketing claims. In this sense, evidence-based creatine practice aligns with modern models of individualized, data-informed athlete support (Smith-Ryan et al., 2021; Tam et al., 2025; Burke et al., 2003; Jagim & Kerksick, 2021).

The cognition literature deserves especially careful framing. It would be premature to market creatine as a general nootropic for every healthy person. That claim would run ahead of the data. Yet it would be equally misleading to ignore the increasingly coherent pattern suggesting benefit during energetic challenge, especially sleep deprivation. For athletes, military personnel, students, physicians in training, and shift workers, those conditions are not exceptional—they are common. The most defensible conclusion is therefore contextual: creatine may be most useful cognitively when normal restorative processes are impaired or when baseline creatine availability is comparatively low. This framing both reflects current evidence and generates clear hypotheses for future trials.

The renal discussion provides an important lesson in evidence interpretation. A supplement can alter a laboratory marker without injuring the organ that marker is commonly used to assess. Creatine exemplifies this principle. Because creatinine occupies such a central place in routine kidney assessment, a mild supplement-related rise can appear alarming if stripped of context. The persistence of this misconception has practical consequences: athletes may be told incorrectly to discontinue supplementation, clinicians may overestimate kidney risk, and the research conversation may remain trapped in outdated narratives. Recent meta-analytic work strongly suggests that in healthy users, modest creatinine increases do not translate into a meaningful reduction in glomerular filtration. The clinically appropriate response is therefore not alarmism, but better biomarker interpretation and individualized assessment when pre-existing risk factors are present.

Another strength of the contemporary literature is the increasing attention to underrepresented groups. Women, vegetarians and vegans, and adolescents are no longer peripheral to the discussion. This matters not only for fairness, but for scientific accuracy. When baseline creatine stores, hormonal milieu, diet, and competition demands differ, the magnitude and nature of response may also differ. The field should now move beyond simply proving efficacy again in generic male samples and instead define subgroup-specific protocols and outcomes. Female athlete trials, sport-specific cognition protocols, and longer renal safety studies with modern biomarkers would be especially valuable.

This review also has limitations. As a narrative review, it does not provide formal pooled effect estimates across all domains, nor does it eliminate the possibility of selective emphasis. Some cited literature is based on small studies, especially in the cognitive domain. Performance trials remain heterogeneous with respect to sport, training status, dose, and test selection, while renal safety research often varies in the biomarkers used. Furthermore, athletic populations are not monolithic, so conclusions that are highly applicable to team-sport or resistance-trained athletes may be less decisive for ultra-endurance or weight-class athletes. These limitations, however, are also why a narrative synthesis is useful: it allows the evidence to be interpreted within context rather than forced into false uniformity.

Future research should prioritize three directions. First, performance research should focus less on demonstrating broad efficacy and more on clarifying optimal protocols for specific sports, especially where weight sensitivity and repeated high-intensity output coexist. Second, cognitive studies should adopt ecologically valid stress paradigms—sleep restriction, travel fatigue, tactical decision making, and dual-task performance—rather than relying solely on low-demand laboratory tasks in rested volunteers. Third, renal safety studies should continue to move beyond serum creatinine alone, incorporating cystatin C, measured or better-estimated filtration, and well-characterized clinical follow-up. These steps would sharpen both scientific understanding and real-world application.

Overall, the present evidence supports a balanced but confident conclusion. Creatine monohydrate is not a miracle compound, but neither is it a marginal supplement whose reputation exceeds its science. Its muscular effects are among the most reproducible in sports nutrition, its cognitive potential is increasingly plausible and strategically important, and its renal safety profile in healthy users is considerably more reassuring than persistent myths suggest. That combination explains why creatine remains central to modern evidence-based supplementation practice (Kreider et al., 2017; Wax et al., 2021; Forbes et al., 2022; Longobardi et al., 2023; Naeini et al., 2025).

5. Conclusions

From an editorial perspective, creatine monohydrate is a useful topic precisely because it illustrates how health and performance are interconnected rather than opposed. The supplement's value is not exhausted by increases in strength or power. It also lies in better athlete education, more accurate laboratory interpretation, the possibility of protecting performance under sleep-related strain, and the development of more individualized nutrition strategies in groups that have historically been understudied. In that sense, creatine is not only a sports nutrition topic, but also a health and well-being topic (Antonio et al., 2021; Smith-Ryan et al., 2021; Gutiérrez-Hellín et al., 2025).

Creatine monohydrate remains the best supported creatine formulation for athletic use. The strongest evidence supports improvements in maximal strength, repeated sprint performance, power output, and training-related gains in lean mass. Evidence for cognition is more heterogeneous but increasingly favorable under sleep deprivation, mental fatigue, or other states of heightened cerebral energy demand. Current data do not support the claim that recommended creatine monohydrate supplementation damages kidney function in healthy athletic populations, although clinicians must interpret serum creatinine carefully and apply individualized judgment in those with pre-existing renal risk. In practice, creatine should be understood as a well-established, low-cost, evidence-based supplement whose value extends beyond isolated ergogenic effects to athlete well-being, recovery quality, and informed clinical decision making (Kreider et al., 2017; Forbes et al., 2022; Naeini et al., 2025).

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