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From strength to cognition: The expanding role of creatine supplementation in health and disease

Abstract

Introduction and aim. Creatine monohydrate is one of the most extensively studied and widely used nutritional supplements, primarily recognized for its role in the improvement of skeletal muscle energetics and physical performance. However, mounting amount of evidence now supports its broader physiological impact beyond exercise, particularly in domains such as neuromuscular aging, cognitive function, and post-viral fatigue syndromes. The purpose of this narrative review is to comprehensively evaluate the effects of creatine supplementation across various domains of human health, including sports performance, cognitive function, aging-related outcomes, and post-viral fatigue syndromes such as long COVID. Particular attention is given to the impact of creatine on muscle strength, power output, recovery from exercise-induced muscle damage, neuroprotective mechanisms, and quality of life in different populations. By synthesis of findings from randomised controlled trials and recent clinical studies, this review seeks to clarify both the efficacy and safety profile of creatine, as well as its potential role as an adjunctive therapeutic strategy beyond traditional athletic contexts.

Description of the state of knowledge. Creatine augments intramuscular phosphocreatine stores, thereby optimising ATP resynthesis during high-intensity exercise and promoting anabolic adaptations. Neuroprotective mechanisms involve mitochondrial stabilisation, antioxidant activity, and modulation of neurotransmitter systems. These effects are mediated by systemic and cellular alterations in energy metabolism, hormone profiles, and inflammatory pathways.

Material and methods. This review was conducted following a narrative approach. Scientific publications were identified through a structured search of electronic databases including PubMed, Scopus, and Google Scholar, focusing on studies published between 2000 and 2025. Search terms included “creatine supplementation”, “exercise performance”, “cognition”, “aging”, “long COVID”, “muscle recovery”, and related keywords. Only peer-reviewed articles written in the English language were considered. The selection included randomised controlled trials, meta-analyses, and clinically relevant pilot studies. Additionally, to provide a comprehensive context for creatine use, related review articles, official regulatory documents, market reports, and position statements from authoritative organisations were also included.

Conclusions. Clinical trials demonstrate significant improvements in muscular performance parameters, cognitive processing speed, depressive symptomatology, and markers of muscle damage and regenerative capacity. The collective evidence supports creatine as a pleiotropic agent with potential applications extending beyond traditional sports nutrition into therapeutic domains addressing neurodegeneration, mood disorders, and post-viral fatigue syndromes. Given its broad applicability and favorable safety profile, creatine may hold value as a low-cost, scalable intervention in public health strategies aimed at promoting healthy aging, physical resilience, and cognitive well-being.

Keywords: creatine supplementation, muscle strength, cognitive function, aging, long COVID, depression, resistance training, neuroprotection.

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INTRODUCTION

Creatine (methylguanidinoacetic acid) is a naturally occurring nitrogenous organic acid synthesised endogenously from glycine, arginine, and methionine, primarily in the liver, kidneys, and pancreas. Approximately 95% of total body creatine is stored in skeletal muscle, where it functions as a phosphate donor through the creatine kinase (CK)/phosphocreatine (PCr)

system to facilitate rapid adenosine triphosphate (ATP) resynthesis during high-intensity, short-duration activities [1]. This phosphagen system serves as a critical energy buffer, especially under conditions of elevated metabolic demand such as resistance exercise, hypoxia, and neuronal excitation.

While creatine monohydrate has long been recognised for its ergogenic potential in enhancing muscular strength, power output, and lean body mass during training interventions [2-7],

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recent investigations have broadened its relevance to multiple physiological systems beyond skeletal muscle. In aging populations, creatine supplementation mitigates sarcopenia, improves muscle quality, and supports functional independence, likely via enhanced mitochondrial function, satellite cell activation, and anabolic signaling [8-12]. Randomised controlled trials have demonstrated its efficacy in improving lower-limb strength, chair-stand performance, and overall physical capacity in older adults, particularly when combined with resistance training [8,12].

The latest data also support creatine's neuroprotective and psychotropic potential. Creatine crosses the blood-brain barrier via the SLC6A8 transporter and accumulates in neural tissue, where it contributes to energy buffering and neurotransmitter regulation. Clinical trials on healthy individuals and patients with major depressive disorder or cognitive impairment have revealed improvements in working memory, processing speed, and mood following supplementation [13-18]. These effects are thought to be mediated through enhanced brain bioenergetics, stabilization of synaptic transmission, and possible modulation of serotonergic and dopaminergic signaling pathways.

More recently, the long-term follow-up of COVID-19 (post-acute follow-up of SARS-CoV-2 infection, PASC) have brought attention to creatine's potential role in alleviating persistent fatigue, cognitive dysfunction, and exercise intolerance. Preliminary clinical studies indicate that creatine may attenuate PASC symptoms via restoration of mitochondrial integrity, attenuation of oxidative stress, and promotion of cellular energy homeostasis [19,20].

This review synthesises current evidence from randomized controlled trials and mechanistic studies across four major domains: 1. sports performance and recovery, 2. neurocognitive health, 3. aging and sarcopenia, and 4. post-viral fatigue syndromes. By integrating these findings, the review aims to contextualize creatine's pleiotropic biological actions and assess its promise as a multi-system therapeutic adjunct.

The role of creatine supplementation in enhancing sports performance

Creatine monohydrate is one of the most extensively studied ergogenic aids, with consistent evidence supporting its efficacy in enhancing muscular strength, endurance, recovery, and training adaptations across various athletic populations. Its primary mechanism involves the replenishment of phosphocreatine stores in skeletal muscle, which enables rapid ATP resynthesis during high-intensity efforts. Studies have evaluated creatine's performance-enhancing effects both alone and in combination with other compounds.

Several investigations report significant improvements in maximal strength with creatine supplementation. In recreationally trained males, supplementation at 0.1 g/kg/day for 8 weeks produced greater 1RM gains in bench press and leg press versus placebo, along with increased lean body mass and training volume, indicative of enhanced neuromuscular adaptations and work capacity [1]. Similarly, a 6-week of supplementation with a multi-ingredient performance supplement (MIPS) containing 4 g/day creatine yielded significant increases in back squat strength (from 93.58 ± 12.48 kg to 106.27 ± 11.45 kg) and bench press (from 60.91 ± 11.42 kg to 66.94 ± 12.15 kg), alongside improved muscular endurance at 80% 1RM [3]. These outcomes support earlier findings where 0.07 g/kg/day creatine over 8 weeks enhanced strength in bench press, leg press, shoulder press, and triceps extension

exercises after only 2 weeks, though no effect was observed in isolated movements like biceps curl or lat pulldown [5].

In college football athletes, creatine combined with beta-alanine supplementation (Cr+BA) during a 10-week resistance training program resulted in greater lean mass accretion and fat mass reduction compared to creatine alone or placebo, while both creatine-containing groups demonstrated superior strength gains relative to placebo. Notably, resting testosterone levels increased in the creatine-only group, whereas other endocrine markers remained unchanged, suggesting potential hormonal modulation that could contribute to anabolic effects [4].

Creatine also enhances muscular endurance and fatigue resistance, allowing athletes to maintain higher training volumes during resistance programs, both of which are key drivers of hypertrophy and strength gains [1,3,5]. However, its relationship with exercise-induced muscle damage (EIMD) is complex. One study reported elevated muscle damage markers (creatine kinase and lactate dehydrogenase) in creatine users, possibly due to increased training intensity facilitated by supplementation [5]. Conversely, a 28-day supplementation (3 g/day) in healthy men demonstrated reduced muscle swelling, preserved range of motion, improved maximal voluntary contraction, and decreased muscle stiffness following eccentric elbow flexion exercises, suggesting accelerated recovery despite no significant changes in muscle soreness or urinary titin fragments [6].

In female cohorts, creatine's efficacy appears to be influenced by hormonal fluctuations. A randomised controlled trial involving recreationally active women using hormonal contraception or naturally menstruating showed that five days of high-dose creatine (20 g/day) improved fatigue resistance during the luteal phase, although peak and average power improvements were not statistically significant. Heart rate variability metrics revealed minor, non-significant improvements in autonomic recovery, emphasising the importance of considering menstrual cycle phase in supplementation research [7].

Overall, creatine supplementation consistently enhances high-intensity exercise performance by improving strength, endurance, and recovery across sexes and training levels. When combined with agents like beta-alanine, creatine may further optimize body composition and performance outcomes. Its effects on muscle damage markers and hormonal responses are multifactorial and may depend on dosage, training variables, and individual hormonal milieu. The compiled evidence from randomized controlled trials [1-7] affirms creatine's role as a foundational ergogenic aid in sports nutrition.

Creatine supplementation and its potential role in mental health and cognitive function

Creatine monohydrate is a critical modulator of cellular energy metabolism, facilitating the recycling of adenosine triphosphate (ATP) through the phosphocreatine system in not only muscle, but also brain tissue [13]. Supplementation with creatine has been shown to increase brain creatine levels, potentially enhancing neuronal energy availability in key regions associated with cognitive processing and mood regulation [13,18]. Despite this mechanistic rationale, findings on creatine's cognitive effects in healthy individuals remain inconclusive, with some studies reporting modest improvements in working memory and executive function, while others show no significant benefits. This variability may stem from differences in participant characteristics, supplementation regimens, and cognitive assessment methodologies [13].

In the context of depressive disorders, creatine supplementation has demonstrated promising clinical efficacy when combined with standard treatments. At a randomized controlled trial (RCT) involving 5 g/day creatine supplementation alongside cognitive behavioral therapy (CBT) yielded significantly greater reductions in depression severity, as measured by the PHQ-9, compared to placebo, with an adjusted mean difference of -5.12 [14]. Similarly, in major depressive disorder (MDD) patients receiving selective serotonin reuptake inhibitors (SSRIs), creatine augmentation produced faster and more substantial symptom improvement, observable as early as two weeks into treatment [15,18]. Neuroimaging studies further elucidate these clinical effects: proton magnetic resonance spectroscopy demonstrated increased prefrontal N-acetylaspartate concentrations, a marker of neuronal integrity, and diffusion tensor imaging revealed enhanced structural connectivity within rich club brain networks following creatine supplementation [18].

Research on treatment-resistant depression and bipolar depression suggests a potential therapeutic role for creatine as a mitochondrial modulator, although the risk of hypomanic or manic episodes in bipolar patients necessitates caution [16,17]. A six-week adjunctive trial of creatine in bipolar depression did not show significant changes in mean Montgomery–Åsberg Depression Rating Scale (MADRS) scores compared to placebo, yet remission rates ($MADRS \leq 12$) were significantly higher in the creatine group, indicating a possible benefit in achieving clinical remission [17].

Safety data across multiple RCTs indicate that creatine supplementation is well tolerated, with adverse events mostly limited to mild gastrointestinal symptoms and no serious psychiatric side effects reported [14–16]. However, isolated reports of hypomanic switches in bipolar patients warrant careful monitoring [16,17].

Regarding cognitive enhancement, studies combining creatine with other compounds such as caffeine and nootropic blends in resistance-trained individuals have shown limited additive effects of creatine alone on cognitive performance, suggesting that creatine's influence may be context-dependent or synergistic with other agents [15].

In conclusion, current evidence supports creatine monohydrate as a bioenergetic enhancer with potential as an adjunctive treatment of depressive disorders, contributing to both symptom amelioration and neurobiological restoration. While cognitive benefits are less consistently demonstrated, ongoing research should focus on identifying optimal dosing strategies, treatment durations, and specific patient populations to maximise therapeutic outcomes.

Targeting muscle function and aging: efficacy of creatine supplementation in elderly populations

Multiple randomised controlled trials and intervention studies have examined the role of creatine supplementation, often combined with resistance training or multi-ingredient formulations, in mitigating sarcopenia and improving muscle health in older adults.

In a 12-week RCT involving older males engaged in a home-based resistance exercise program combined with a multi-ingredient supplement containing creatine (M5), participants reported significant gains in total lean mass ($+1.09$ kg) and appendicular skeletal muscle mass ($+0.69$ kg) compared to placebo control group, along with reductions in fat mass and improvements in muscle-to-fat ratio [8]. These hypertrophic

effects were predominantly localised to type II muscle fibers, with type IIa and IIx fibers increasing by 30.9% and 28.5%, respectively, indicating enhanced fast-twitch muscle adaptations crucial for functional performance. Functional strength improvements were also reported, with leg press strength increasing by 16.6% and handgrip strength by 8.4%, effects that were more pronounced in sarcopenic subpopulations [8].

The anabolic response was linked to the high-quality protein sources in the M5 supplement (whey/casein), which have superior leucine content and bioavailability compared to collagen-based proteins used in the placebo, supporting optimal muscle protein synthesis in aging muscle [8]. Importantly, safety profiles were favorable, with no adverse renal effects despite a moderate rise in serum creatinine attributable to increased muscle mass and creatine intake [8].

Complementary studies support the efficacy of creatine supplementation in elderly cohorts. For instance, creatine combined with resistance training consistently enhances muscle mass and strength beyond exercise alone [9,10]. Meta-analyses reveal moderate to large effect sizes for improvements in lower-body strength and functional mobility tests in older adults supplemented with creatine [11,12]. The mechanisms are multifactorial and involve improved phosphocreatine stores, enhanced ATP resynthesis capacity, and improved muscle energy metabolism, which may blunt the catabolic milieu of aging [9,11].

Moreover, creatine supplementation may positively affect muscle quality, a composite measure of muscle strength relative to mass, thereby translating morphological gains into meaningful functional outcomes [8,10]. Some studies noted limited or variable effects on physical performance metrics such as gait speed or stair climb times, highlighting heterogeneity in protocol duration, dosing, and participant baseline status [8,12].

In terms of tolerability, creatine is well accepted in older populations, with no serious adverse events reported across multiple trials. Mild side effects, such as gastrointestinal discomfort, were infrequent and transient [8,11]. The safety of creatine supplementation, even in older adults with sarcopenia, is supported by stable renal function biomarkers, alleviating concerns about creatine's impact on kidney health in this demographic [8,10].

Collectively, these findings suggest that creatine, particularly when combined with resistance training and adequate high-quality protein intake, represents a viable, evidence-based strategy to enhance muscle mass, strength, and functional capacity in older adults, with the potential to attenuate or partially reverse sarcopenia-related declines.

Creatine supplementation as an adjunctive therapy in long COVID: Effects on brain metabolism and symptomatology

Post-acute sequelae of SARS-CoV-2 infection (PASC), commonly referred to as long COVID, is a multisystem condition characterised by persistent symptoms lasting for at least 12 weeks following the resolution of acute COVID-19, in the absence of alternative diagnoses. The clinical manifestations include chronic fatigue, cognitive dysfunction ("brain fog"), myalgia, post-exertional malaise, and reduced exercise tolerance. These symptoms are thought to be underpinned by mitochondrial dysfunction, impaired oxidative phosphorylation, neuroinflammation, endothelial damage, and disruptions in skeletal muscle energetics.

Recent evidence indicates that creatine supplementation may serve as a beneficial adjunct in the management of Long COVID syndrome, particularly in alleviating persistent fatigue and neurocognitive symptoms. In a double-blind parallel-group study involving eight Long COVID patients with moderate fatigue, daily administration of 4 g creatine combined with breathing exercises over three months resulted in a statistically significant elevation of total creatine levels across multiple brain regions ($p < 0.05$). In contrast with reductions observed in control subjects receiving breathing exercises alone. Importantly, the intervention group demonstrated a mean improvement in time to exhaustion by 54 seconds post-treatment ($p = 0.05$), suggesting enhanced exercise tolerance linked to creatine-induced metabolic support [19]. Complementing these findings, an 8-week randomised controlled trial with fifteen Long COVID patients compared the effects of creatine monohydrate alone (8 g/day), creatine combined with glucose (8 g creatine + 3 g glucose/day), and placebo. Both creatine-supplemented groups showed significant increases in brain creatine content, particularly in the right precentral white matter ($F = 34.740$, $p = 0.008$) and left paracentral grey matter ($F = 19.243$, $p = 0.019$). Notably, the creatine-glucose combination yielded marked symptom improvements, including reductions in body aches, breathing difficulties, concentration problems, and headaches, with large effect sizes (e.g., Cohen's $d > 0.8$) indicating clinically meaningful benefits. These preliminary data support the hypothesis that exogenous creatine, especially when co-administered with glucose, can effectively replenish cerebral creatine pools and mitigate Long COVID sequelae through enhanced bioenergetic mechanisms, such as improved ATP recycling, restoration of brain creatine levels and increasing energy availability [20]. Further large-scale, controlled studies are warranted to confirm these findings and elucidate the mechanistic underpinnings of creatine's therapeutic potential in post-viral fatigue syndromes.

DISCUSSION

Prevalence of Creatine Use Globally and in Different Populations

Global Data

Globally, creatine usage in the general adult population ranges from approximately 3% to 6%, especially in developed countries such as the US and EU member states [21,22]. There are no nationwide population studies in Poland specifically addressing creatine use, however data from the Chief Sanitary Inspectorate (GIS) show that creatine is one of the most frequently declared active ingredients in notified dietary supplements [23].

According to market reports, the rapid expansion of the global creatine supplement market underscores the increasing societal relevance of this compound beyond traditional sports nutrition. Recent forecasts estimate that global revenues from creatine products reached approximately USD 901 million in 2023, with projected growth to between USD 2.8 and 8 billion by 2030–2033, representing a compound annual growth rate (CAGR) of 17.8% to over 23% [24–26]. While North America currently dominates the market, accounting for nearly 39% of global sales, Europe contributes 30%, and the Asia-Pacific region is projected to grow at the fastest rate (CAGR ~27.5%) due to rising health awareness and urbanization [24,26].

Powdered formulations remain the most widely consumed, comprising 58–80% of sales, but alternative delivery forms such as capsules and ready-to-mix tablets are rapidly gaining traction –particularly through online channels, which now account for more than 37% of product distribution [24,27]. Importantly, market data also reflect shifting demographics, including a notable 320% year-over-year increase in creatine purchases among women and a growing interest in supplementation among older adults [28]. These trends suggest a broadening consumer base and emphasise the need for targeted public health strategies. Without standardised dosing recommendations, regulatory harmonisation, and widespread education on the safety and efficacy of creatine, the compound's growing popularity may outpace evidence-based guidance, potentially undermining its utility as a public health intervention.

Athletes

Creatine supplementation is highly prevalent among athletes, especially those engaged in strength, power, and high-intensity sports. Studies estimate that between 30% to 70% of competitive athletes use creatine at some point during their training cycles [21,29]. Usage rates are typically higher in male athletes and in sports such as bodybuilding, football, rugby, and sprinting disciplines. The popularity of creatine in these groups is largely driven by well-documented performance-enhancing effects on muscle strength, power output, and recovery.

Older adults

Data on creatine use among older adults is limited but suggests considerably lower prevalence compared to athletes. Surveys indicate that less than 5% of community-dwelling elderly individuals report creatine supplementation [30]. However, interest in creatine as a therapeutic agent for sarcopenia, frailty, and cognitive decline is increasing in clinical and research settings. Despite emerging evidence supporting safety and efficacy, creatine remains underutilised in this demographic due to limited awareness and lack of routine recommendation by healthcare providers.

Post-COVID-19 Patients

Research on creatine use specifically in individuals who recovered from COVID-19 or experienced long COVID is still in early stages. Preliminary clinical trials and observational reports suggest that creatine may improve muscle function, reduce fatigue, and support neurocognitive recovery in post-viral fatigue syndromes [31,32]. However, there is currently no large-scale epidemiological data quantifying the prevalence of creatine supplementation in this population, likely reflecting its novel application and ongoing research efforts.

Public health implications of creatine use across the lifespan

The potential public health impact of creatine supplementation in aging societies is increasingly recognised, particularly in light of its emerging benefits beyond athletic performance. As global populations continue to age, sarcopenia, cognitive decline, and loss of functional independence represent critical challenges to healthcare systems. Creatine has demonstrated efficacy in improving muscle strength, lean mass, and physical performance in older adults, which may help prevent frailty, reduce fall risk, and delay institutionalisation [33,34]. In addition,

tion, accumulating evidence suggests that creatine may exert neuroprotective effects by supporting mitochondrial function, buffering cerebral energy deficits, and modulating oxidative stress and inflammation – mechanisms implicated in age-related neurodegenerative disorders such as Alzheimer's and Parkinson's disease [35,36]. These findings raise the prospect of creatine as a low-cost, accessible intervention with the potential to enhance quality of life and reduce the burden of age-associated disability. Importantly, creatine supplementation is well-tolerated, with a strong safety profile in elderly populations when administered in clinically relevant doses (typically 3–5 g/day). Despite this, creatine remains underutilised in geriatric care, partly due to insufficient awareness among clinicians and the absence of formal public health guidelines. Integrating creatine into broader aging strategies, especially in the context of physical activity promotion, may offer a scalable, evidence-based tool to support healthy aging and reduce long-term healthcare costs.

Risks and safety concerns related to self-supplementation

Significant challenges exist regarding public understanding of creatine's safety, dosage, and application outside of athletic contexts. Many individuals rely on non-expert sources for supplement guidance, which may propagate misinformation or exaggerated claims. This underscores the importance of educational programs tailored to both consumers and healthcare professionals, to promote informed decision-making grounded in current scientific evidence. Clear communication regarding dosing, contraindications, and product quality is particularly crucial for non-athletic users, such as the elderly or those with chronic health conditions.

While creatine is generally considered safe when used within established limits, the regulatory environment poses additional risks. In the European Union and Poland, dietary supplements are not subject to the same rigorous pre-market approval as pharmaceuticals, which creates potential for product variability, contamination, and misleading labeling. Self-prescription, especially among vulnerable populations, may lead to inappropriate use or overlooked contraindications. International bodies such as the EFSA and WHO recognize creatine as a substance of interest but have not issued formal guidelines on its supplementation. The European Food Safety Authority (EFSA) of the European Union (EU) considers daily intakes up to 3 g safe for the general population, with higher doses tolerated in athletes [37]. However, EFSA has rejected health claims regarding cognitive benefits due to insufficient evidence. In Poland, the Chief Sanitary Inspectorate advises consumers to consult healthcare providers prior to use. These regulatory and educational gaps highlight the need for strengthened oversight, labeling standards, and risk communication to ensure safe use across demographics.

From a broader perspective, strategic implementation of creatine supplementation in aging societies could bring public health benefits. By mitigating sarcopenia, enhancing physical independence, and potentially alleviating depressive symptoms, creatine may serve as a cost-effective adjunct to current preventive health strategies. However, translating the scientific evidence into practice will require multidisciplinary coordination among researchers, clinicians, policymakers, and regulatory agencies.

Regulatory and Legal Frameworks in the EU and Poland

In the European Union (EU), dietary supplements are regulated as a category of food under Directive 2002/46/EC, which defines them as concentrated sources of nutrients or other substances with nutritional or physiological effects intended to supplement the normal diet, presented in dose form such as capsules or powders [38]. Additional regulatory instruments include Regulation (EC) No 1924/2006 on nutrition and health claims [39] and Regulation (EU) No 1169/2011 concerning consumer information [40]. The EU maintains positive lists of permitted vitamins and minerals, but regulation of other substances, such as creatine, amino acids, or botanical extracts, is decentralized and governed by individual Member States.

In Poland, dietary supplements are regulated in alignment with EU law but also fall under the national Act on Food and Nutrition Safety of 2006 [41]. Prior to market placement, manufacturers or distributors are required to notify the Chief Sanitary Inspectorate (Główny Inspektorat Sanitarny, GIS). This notification process is declarative in nature and does not entail pre-market approval. However, the Chief Sanitary Inspectorate retains the authority to issue administrative decisions, including product withdrawal, in the event of non-compliance, risk to health, or misleading claims [42].

Labeling requirements in Poland follow the EU framework and mandate disclosure of the term “dietary supplement,” a list of active ingredients with quantified amounts, recommended daily dosage, usage warnings (e.g., “should not be used as a substitute for a varied diet”), and a statement keeping the product out of reach of children [40,42]. Claims of therapeutic efficacy are prohibited, and only approved health claims under EU Regulation 1924/2006 may be used [39].

Unlike pharmaceuticals, dietary supplements are not subject to mandatory clinical trials prior to market entry. However, they remain under post-market surveillance conducted by public health authorities, primarily through the Sanitary and Epidemiological Station (Sanepid) in Poland. This framework allows for flexible and rapid market access but places significant responsibility on manufacturers to ensure product safety and regulatory compliance [41,42].

The Necessity of Educational Programs for Dietary Supplement Users

Given the widespread use of dietary supplements, including creatine, there is a clear and pressing need for structured educational programs aimed at consumers. Current evidence indicates that many users rely on informal sources such as social media, peer recommendations, or unregulated online content, which often provide incomplete or inaccurate information regarding appropriate dosing, potential side effects, and interactions with medications [43,44]. This knowledge gap can lead to misuse, suboptimal dosing strategies, and, in rare cases, adverse health outcomes. Educational initiatives should therefore focus on improvement of the knowledge related to the safety, efficacy, and regulatory standards of supplements, with particular emphasis on vulnerable populations such as adolescents, older adults, and individuals with chronic conditions. Moreover, integrating such programs into community health services, gyms, and healthcare settings would facilitate access to evidence-based guidance. Empowering users with scientifically sound information not only promotes safe supplementation practices but may also enhance adherence and

optimise health benefits. Finally, collaboration between regulatory agencies, healthcare professionals, and supplement industry stakeholders is essential to ensure that educational content is accurate, accessible, and updated in line with emerging scientific data.

A key challenge in translating the scientific evidence on creatine supplementation into public health practice lies in the persistent misinformation and limited awareness regarding its safety and dosing. Despite its well-established efficacy and safety profile in both athletic and clinical populations, creatine is still frequently mischaracterised as a steroid or illicit performance enhancer, contributing to public skepticism and underutilisation – particularly in non-athletic populations such as older adults [45,46]. The proliferation of non-evidence-based information on social media platforms further amplifies confusion, as users are often exposed to conflicting messages regarding optimal dosing strategies, loading protocols, and potential adverse effects. Compounding this issue is the lack of standardized labeling practices in the supplement industry, which may obscure the actual creatine content in multi-ingredient products or proprietary blends, thereby hindering informed consumer decision-making [47]. Moreover, healthcare professionals, including physicians, dietitians, and pharmacists, are rarely trained to advise on creatine use, resulting in missed opportunities for personalised guidance, especially in populations that may benefit from its therapeutic effects. Public health education frameworks also largely overlook creatine, despite its increasing popularity among adolescents and recreational athletes. Addressing these challenges will require targeted educational interventions, clearer regulatory oversight of labeling practices, and greater involvement of health professionals in the dissemination of accurate, evidence-based recommendations on creatine supplementation.

Creatine supplementation has emerged as a multifaceted and promising ergogenic and therapeutic agent with broad range of applications across sports performance, aging, cognitive health, and post-viral recovery. In resistance-trained individuals, creatine consistently enhances muscle strength, power output and endurance capacities, supporting accelerated adaptations during training programs. These effects are potentiated when combined with adjunct compounds such as beta-alanine, leading to increased lean mass and reduced adiposity [2-7]. In elderly populations, creatine shows promise in mitigating age-related declines in muscle mass and function by improving muscle protein synthesis and bioenergetic efficiency, thereby preserving functional independence and reducing sarcopenic risk [8-12]. Neuroprotective and neurocognitive benefits are substantiated by improved executive function, mood stabilization, and resistance to metabolic stress, with creatine demonstrating promising efficacy in depressive disorders and neurodegenerative disease models via modulation of cerebral energy metabolism and neurotransmitter systems [13-18]. Furthermore, creatine supplementation is a promising intervention for alleviating persistent fatigue and cognitive impairment associated with long COVID syndrome, potentially through restoration of mitochondrial function and attenuation of inflammatory cascades [19,20]. Collectively, creatine's mechanisms encompass enhancement of phosphocreatine availability, upregulation of anabolic signaling, modulation of endocrine responses, and anti-inflammatory effects, positioning it as a versatile and promising intervention for the optimisation of human performance and health across diverse physiological

and pathological conditions. Given its affordability, safety, and ease of administration, creatine holds substantial potential as a scalable public health strategy for supporting musculoskeletal and cognitive resilience in aging populations. Its broader implementation could contribute to reduced healthcare costs and improved quality of life, particularly in societies facing demographic shifts toward older age. Despite these encouraging findings, further rigorous clinical and mechanistic research is warranted to elucidate creatine's full therapeutic potential, explore its efficacy in additional clinical populations, and optimise dosing strategies for diverse health applications.

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