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From Sports Performance to Healthy Aging, Creatine Finds New Momentum

From phosphocreatine and athletic performance to brain bioenergetics, cellular resilience and muscle preservation during pharmacological weight loss

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EDITORIAL POSITION

Creatine is not treated here as a "longevity molecule." The review distinguishes established muscular effects from promising but incomplete evidence in brain health, cellular resilience and GLP-1-associated lean-tissue preservation.

ABSTRACT

For several decades, creatine occupied a remarkably well-defined position in nutritional science: an ergogenic compound used primarily to support repeated high-intensity exercise, strength development and resistance-training adaptation. That description remains correct, but it is becoming incomplete. Contemporary research increasingly asks whether the creatine–phosphocreatine system may also be relevant in tissues and physiological states in which energetic reserve, functional capacity and resilience become limiting. This shift has brought creatine into research on sarcopenia and healthy aging, cerebral energy metabolism, cognitive performance under metabolic stress, neurodegenerative disease, and—most recently—the preservation of lean tissue and muscle function during the substantial weight loss produced by GLP-1 receptor agonists and related incretin-based therapies. The evidence, however, is uneven. Support for creatine monohydrate in muscular performance and resistance-training adaptation is extensive; evidence in older adults is increasingly persuasive, particularly when supplementation accompanies progressive resistance training. Brain bioenergetics is biologically plausible and supported by intriguing human experiments, but generalized cognitive claims remain unproven. Likewise, cellular-resilience and healthy-longevity narratives are mechanistically attractive but clinically immature. Finally, creatine as a strategy to protect muscle during GLP-1-associated weight loss has now entered dedicated prospective human testing, but efficacy data are not yet available. Creatine's renewed momentum therefore reflects not the discovery of a new compound, but a broader understanding of physiological reserve, tissue quality and bioenergetic resilience across the lifespan.

Keywords *creatine monohydrate; phosphocreatine; healthy aging; sarcopenia; skeletal muscle; brain bioenergetics; cognition; GLP-1 receptor agonists; semaglutide; tirzepatide; lean mass; resistance training.*

KEY CONCLUSIONS

- Creatine monohydrate remains the reference form: it has by far the largest evidence base for bioavailability, efficacy and safety.
- The strongest healthy-aging case is muscular: creatine can augment selected adaptations to resistance training in older adults; it does not replace training or adequate protein intake.
- Brain effects are scientifically credible but heterogeneous. Acute high-dose creatine has modified cerebral high-energy phosphate metabolism during sleep deprivation, whereas a generalized cognitive health claim has not been accepted by EFSA.
- GLP-1-associated "muscle loss" should not be reduced to a DXA lean-mass number. Functional outcomes, muscle quality, hydration and baseline vulnerability matter.
- A dedicated randomized pilot trial (NCT07625202) began in 2026 to test 10 g/day creatine during resistance training in adults initiating GLP-1 agonist therapy. No efficacy results are yet available.

EVIDENCE AT A GLANCE

DOMAIN	EVIDENCE	CURRENT INTERPRETATION	REFERENCE
High-intensity / resistance performance	**High**	Established use; extensive human evidence	Kreider et al., 2022
Older adults + resistance training	**Moderate–High**	Consistent support for selected strength and lean-tissue outcomes	Liu et al., 2025
Healthy cognition	**Low–Moderate / heterogeneous**	Interesting signals, but insufficient for a generalized EU health claim	EFSA, 2024
Brain bioenergetics under sleep deprivation	**Proof-of-concept**	Acute metabolic and cognitive effects demonstrated in a controlled trial	Gordji-Nejad et al., 2024
Alzheimer's disease	**Preliminary**	Pilot target-engagement and cognitive signals; no placebo-controlled efficacy proof	Smith et al., 2025
GLP-1-associated muscle preservation	**Investigational**	Plausible strategy; dedicated randomized trial now recruiting/underway	NCT07625202
Novel creatine forms	**Limited superiority evidence**	Delivery innovation may improve adherence; monohydrate remains benchmark	Kreider et al., 2022
Renal safety in studied populations	**Generally reassuring**	Serum creatinine may rise without equivalent fall in true GFR	Naeini et al., 2025

01 Introduction: an old molecule enters a new scientific conversation

Few nutritional compounds have undergone a reputational transformation comparable to creatine. For much of its modern history, the word creatine immediately evoked bodybuilding, strength sports, sprint performance and sports-nutrition powders. That association was not simply a marketing artefact. Creatine monohydrate became one of the most intensively studied nutritional ergogenic aids because its physiological rationale was unusually strong and its effects could be repeatedly measured in controlled settings.

The underlying chemistry is straightforward. Cells require adenosine triphosphate (ATP) to perform work. Because intracellular ATP reserves are small, tissues exposed to rapid changes in energy demand require systems capable of regenerating ATP rapidly. The creatine kinase/phosphocreatine system is one such system: phosphocreatine donates a high-energy phosphate to ADP, helping stabilize ATP availability when demand rises faster than oxidative phosphorylation can immediately respond.

That mechanism is particularly visible in skeletal muscle during high-intensity contraction, which explains why sport became the first major clinical and commercial application of creatine. Yet creatine kinase and phosphocreatine are not confined to a barbell or a sprint track. They also contribute to cerebral and cellular energetics in tissues that operate close to the limits of their energetic reserve.

The conceptual shift now taking place is therefore important. Researchers are increasingly asking whether increasing creatine availability may matter wherever energetic reserve becomes limiting: aging muscle, cognitively stressed brain, disease-associated bioenergetic dysfunction, prolonged caloric restriction or rapid pharmacological weight loss. This does not mean that every mechanistically plausible benefit has been clinically demonstrated. It means that creatine has moved from being studied primarily as a performance enhancer toward being studied as a potential modifier of physiological reserve.

02 Creatine is fundamentally a bioenergetic molecule

Approximately 95% of the body's creatine pool is located in skeletal muscle, although creatine and phosphocreatine metabolism also play important roles in the central nervous system. Creatine can be synthesized endogenously from amino-acid precursors and obtained through food, particularly meat and fish. Supplementation increases extracellular creatine availability and, over time, can increase tissue creatine stores.

The creatine kinase reaction—PCr + ADP + H+ ⇌ Cr + ATP—is better understood as an energy-buffering and energy-shuttling system than as a conventional stimulant. It helps stabilize ATP concentrations when energy demand changes quickly and participates in the spatial transfer of high-energy phosphate between sites of ATP production and ATP utilization.

The brain illustrates this distinction particularly well. Cerebral ATP turnover is high, yet the brain has limited energetic storage capacity. Neuronal activity therefore depends on tightly regulated coupling between energy demand and energy supply. Creatine transport into the brain is more constrained than uptake into skeletal muscle, but magnetic resonance spectroscopy and controlled supplementation studies show that cerebral creatine and high-energy phosphate metabolism can be modified under selected experimental conditions (Gordji-Nejad et al., 2024).

> ***PCr + ADP + H+ ⇌ Cr + ATP — a rapid, reversible energy-buffering reaction rather than a stimulant effect.***

03 The evidence base begins with performance—and it remains important

The renewed interest in creatine should not obscure the fact that its strongest evidence remains muscular. Creatine supplementation can increase the capacity of skeletal muscle to sustain repeated high-intensity effort and can enhance selected adaptations to resistance training. The effect is not magical: higher intramuscular creatine and phosphocreatine availability can improve repeated-work capacity and may permit a greater cumulative training stimulus over time (Kreider et al., 2022).

The evidence is sufficiently mature that creatine occupies an unusual regulatory position in Europe. EU legislation authorizes a health claim that creatine increases physical performance in successive bursts of short-term, high-intensity exercise under specified conditions. It also authorizes the claim that daily creatine consumption can enhance the effect of resistance training on muscle strength in adults over 55 years of age when the prescribed conditions of use are met (European Commission, 2017).

That second claim is conceptually important. Creatine is no longer relevant only to athletes seeking maximal output. It has a recognized interaction with resistance exercise in an aging population, which provides a regulatory and evidentiary bridge from sports nutrition toward healthy aging.

04 Healthy aging: muscle is not simply a cosmetic tissue

Contemporary gerontology increasingly treats skeletal muscle as an organ central to health rather than a marker of appearance. Muscle contributes to mobility, glucose disposal, resting and activity-related energy expenditure, skeletal loading, balance and resilience to illness. Age-related loss of muscle strength and mass therefore has consequences far beyond athletic capacity.

Sarcopenia is particularly important because aging affects muscle quantity, muscle quality, motor-unit function and anabolic responsiveness. Progressive resistance exercise remains the most powerful non-pharmacological intervention available to oppose these processes. Creatine is interesting precisely because it may amplify some of the adaptations produced by resistance training rather than attempting to replace the training stimulus.

Recent systematic-review evidence supports this interaction. A 2025 meta-analysis of eight randomized controlled trials involving 482 older participants found that creatine combined with resistance training improved lower-limb strength and lean tissue mass relative to placebo plus resistance training, although upper-body strength effects were less consistent and effect magnitude varied with intervention duration (Liu et al., 2025).

The most defensible model is therefore simple: resistance training provides the adaptive signal; adequate protein and energy provide substrate; creatine may increase the energetic and adaptive capacity with which muscle responds to that signal. This is scientifically stronger than representing creatine as an autonomous treatment for sarcopenia.

05 Lean mass is not the same thing as muscle

A methodological issue becomes increasingly important as creatine research moves into aging and obesity medicine: a change in “lean mass” measured by dual-energy X-ray absorptiometry (DXA) is not identical to a change in contractile skeletal muscle protein. Lean soft tissue includes water and multiple non-fat compartments. Creatine increases intracellular osmotic water retention in skeletal muscle, particularly during the early phase of supplementation, so some early increases in DXA-derived lean mass can reflect hydration rather than newly synthesized contractile tissue.

A 2025 randomized trial illustrates the point. After a seven-day creatine wash-in, the supplemented group gained approximately 0.5 kg more lean body mass than control, yet subsequent resistance-training-related lean-mass gains were not significantly different between groups. The authors explicitly identified hydration-related effects as a likely confounder in interpreting DXA-derived lean mass (Desai et al., 2025).

This does not invalidate lean-mass findings. It means they should be interpreted alongside strength, muscle thickness or volume, physical performance and, where feasible, direct measures of muscle composition. The same caution becomes crucial in GLP-1 research, where the central clinical question is not only how much non-fat tissue changes, but what type of tissue changes and whether function deteriorates.

06 Brain energy metabolism: perhaps the most interesting frontier

The brain is arguably where the modern creatine story becomes most intellectually interesting. Creatine kinase is expressed in the nervous system and phosphocreatine participates in cerebral energetic

homeostasis. The hypothesis is straightforward: under conditions in which neural energetic demand is elevated or energy metabolism is compromised, increasing creatine availability might provide additional buffering capacity.

A particularly informative randomized, double-blind crossover experiment published in Scientific Reports in 2024 exposed participants to approximately 21 hours of sleep deprivation and compared a high single dose of creatine monohydrate (0.35 g/kg) with placebo. Magnetic resonance spectroscopy showed creatine-associated changes in phosphocreatine-related ratios, ATP-related metabolites and pH regulation. Cognitive deterioration associated with sleep deprivation was also partially attenuated, including effects on memory and processing speed (Gordji-Nejad et al., 2024).

The context matters enormously. These participants were metabolically stressed through sleep deprivation. The findings therefore support the proposition that creatine may become more relevant when energetic demand challenges physiological reserve. They do not prove that routine high-dose creatine improves cognition in healthy, rested individuals. The distinction between stress-state rescue and generalized enhancement should remain explicit.

07 Alzheimer's disease: provocative data, but not yet therapeutic evidence

The brain-bioenergetics hypothesis became more interesting in 2025 with publication of a pilot study in Alzheimer's disease. Twenty participants received creatine monohydrate at 20 g/day for eight weeks. Brain total creatine increased by approximately 11%, and improvements were observed in several NIH Toolbox cognitive measures (Smith et al., 2025).

Those findings deserve attention—and restraint. The study was small and lacked a placebo group. Practice effects, expectation, regression toward the mean and other uncontrolled influences cannot be excluded. The study therefore demonstrates feasibility, biological target engagement and a potentially interesting clinical signal; it does not demonstrate treatment efficacy for Alzheimer's disease.

This evidentiary boundary is mirrored by European regulation. In 2024, EFSA concluded that a cause-and-effect relationship had not been established between creatine supplementation and improved cognitive function in the general healthy adult population. The European Commission subsequently refused authorization of that cognitive health claim in May 2026 (EFSA, 2024; European Commission, 2026). Emerging neuroscience and insufficient evidence for a population-level health claim can coexist without contradiction.

08 From energy buffering to "cellular resilience": where evidence becomes more experimental

Terms such as cellular resilience, mitochondrial support and healthy longevity are increasingly attached to creatine. They require careful definition. The creatine–phosphocreatine system interacts with mitochondrial energetics, cellular osmotic regulation and energy-dependent signaling. Experimental models have also associated creatine availability with cellular survival pathways and resistance to metabolic stress.

These mechanisms provide plausible explanations for why creatine could be useful during aging or disease. But a mechanistic pathway is not a clinical endpoint. There is no persuasive evidence that creatine

supplementation extends human lifespan, prevents neurodegenerative disease, or broadly slows biological aging.

A more defensible term is functional resilience. If an older adult retains greater strength, maintains training capacity, preserves mobility or better tolerates periods of physiological stress, that represents meaningful resilience without claiming an alteration in the fundamental rate of aging. Creatine does not need longevity hype to remain scientifically interesting; its established physiology is already substantial.

09 The GLP-1 revolution creates a new muscle problem—but it must be defined correctly

The most contemporary source of creatine's renewed interest comes from pharmacological obesity treatment. Semaglutide, tirzepatide and other incretin-based therapies can produce weight reductions that were previously uncommon outside bariatric surgery. Their cardiometabolic benefits are substantial, but their success has shifted attention from a simple question—how much weight is lost?—to a more sophisticated one: what tissue is lost, what tissue is preserved, and what happens to physical function?

Substantial weight loss almost inevitably includes some reduction in fat-free tissue. In the STEP 1 DXA exploratory analysis, semaglutide 2.4 mg was associated with a 9.7% decrease in total lean body mass while fat mass fell more substantially; the proportion of lean mass relative to total body weight consequently increased (Wilding et al., 2021).

In the SURMOUNT-1 DXA substudy, tirzepatide produced a mean body-weight reduction of 21.3%, fat-mass reduction of 33.9% and lean-mass reduction of 10.9%. Approximately 75% of the weight lost was fat mass and 25% lean mass, proportions that were broadly similar across clinically relevant subgroups (Look et al., 2025).

These data should prevent simplistic claims that GLP-1 therapies "destroy muscle." They demonstrate loss of lean tissue during major weight reduction. They do not establish that all lost lean tissue is skeletal muscle, that function necessarily deteriorates, or that incretin pharmacology produces a uniquely pathological catabolic state.

10 New evidence complicates the GLP-1 muscle narrative

The SEMALEAN prospective study illustrates why body composition and muscle function should not be conflated. Patients with obesity treated with semaglutide 2.4 mg experienced substantial reductions in body weight and fat mass. Lean mass declined initially and subsequently stabilized, while handgrip strength improved over twelve months and the prevalence of sarcopenic obesity decreased (Alissou et al., 2026).

In other words, less measured lean mass did not automatically translate into poorer muscle function. This distinction is likely to become increasingly important in obesity pharmacotherapy. Future studies should report appendicular muscle, muscle quality, intramuscular fat, strength, gait and functional capacity—not merely kilograms of DXA-derived lean tissue.

Clinical context also matters. A young adult with severe obesity and high baseline lean mass may tolerate an absolute lean-tissue reduction very differently from a 72-year-old adult with pre-existing sarcopenia. The clinically relevant endpoint is therefore not maximal preservation of every gram of fat-free mass. It is preservation of sufficient, functional and metabolically healthy skeletal muscle.

11 Why creatine becomes interesting in patients receiving GLP-1 therapies

Creatine enters this discussion through a convergence of several observations. Major pharmacological weight loss reduces energy intake; appetite suppression can make sufficient protein intake more difficult; the mechanical stimulus associated with carrying a larger body mass decreases; and rapid weight loss may expose pre-existing sarcopenia or limited muscular reserve. At the same time, resistance exercise is one of the most rational strategies available to defend muscle during weight loss, and creatine has substantial evidence for enhancing selected muscular adaptations to resistance training.

The resulting hypothesis is therefore persuasive but still testable: if creatine helps skeletal muscle respond to resistance exercise in other settings, could it improve preservation of muscle mass or function while a patient undergoes GLP-1-associated weight reduction?

In 2026, that question moved from speculation into formal clinical research. The University of Saskatchewan registered NCT07625202, a randomized pilot study in 40 adults beginning GLP-1 agonist therapy. Participants receive either 10 g/day creatine or placebo while completing a 12-week resistance-training program three days per week. The trial began in May 2026 and is scheduled to complete in 2027. At the time of writing, no efficacy results are available (ClinicalTrials.gov, 2026).

TRIAL SNAPSHOT • NCT07625202

SPONSOR	University of Saskatchewan
POPULATION	40 adults initiating GLP-1 agonist therapy
INTERVENTION	Creatine monohydrate 10 g/day vs placebo
CO-INTERVENTION	Resistance training 3 days/week for 12 weeks
KEY OUTCOMES	Functional performance, lean tissue mass, fat mass and bone outcomes
STATUS	Started 25 May 2026; estimated completion 31 December 2027; no efficacy results yet

12 Creatine should be one component of a muscle-preservation strategy, not the strategy itself

Even if ongoing trials ultimately demonstrate benefit, the clinical model will almost certainly remain multimodal. Muscle preservation during major weight loss depends on baseline muscle reserve, age, magnitude and speed of weight loss, protein intake, total energy intake, resistance exercise, habitual physical activity, endocrine status and comorbidity.

Creatine cannot compensate for severe protein insufficiency. It cannot reproduce mechanical loading. It cannot prevent disuse atrophy in the absence of muscular stimulus. Current multidisciplinary guidance for GLP-1 therapy emphasizes nutritional adequacy, preservation of muscle and bone, resistance exercise, dietary quality and ongoing monitoring rather than reliance on a single supplement (Mozaffarian et al., 2025).

For patients undergoing substantial pharmacological weight reduction, the most defensible conceptual model is therefore: effective obesity pharmacotherapy + adequate protein intake + progressive

resistance training + monitoring of body composition and function ± targeted nutritional adjuncts such as creatine. The plus/minus sign matters. Creatine is a plausible adjunct, not a replacement for nutrition and exercise management.

13 A methodological challenge: creatine itself can alter the endpoint we are trying to measure

The forthcoming GLP-1 studies will face an unusual experimental problem: creatine increases intracellular muscle water, and DXA records that water as part of lean soft tissue. Creatine could therefore appear to "preserve lean mass" without preserving an equivalent quantity of contractile protein.

That does not make the effect meaningless. Cell hydration can influence muscle physiology, and creatine may simultaneously enhance training capacity and adaptation. It does mean that future GLP-1 trials should avoid relying exclusively on DXA.

Meaningful studies should combine body-composition measurements with functional outcomes such as handgrip strength, lower-limb strength, chair-rise performance, gait speed and, where feasible, imaging capable of more directly characterizing skeletal muscle. The key scientific question is not whether creatine keeps a DXA number higher. It is whether creatine helps preserve biologically and functionally meaningful muscle during substantial pharmacological weight loss.

14 Formulation innovation: new delivery systems do not automatically mean better creatine

The commercial resurgence of creatine has produced micronized powders, capsules, tablets, effervescent preparations, gummies, ready-to-drink products and multiple creatine salts. Here another scientific distinction is essential: the enormous clinical evidence base belongs primarily to creatine monohydrate.

Alternative forms may improve solubility, palatability, serving size or manufacturing characteristics, but the literature has not demonstrated a consistent physiological superiority over creatine monohydrate. A critical review of alternative forms concluded that creatine monohydrate remains the form with substantial supporting evidence for bioavailability, efficacy and safety (Kreider et al., 2022).

Innovation in this category should therefore be described primarily as delivery innovation unless superiority of the active form itself is demonstrated. For older adults or people using GLP-1 medicines, convenience, gastrointestinal tolerance and adherence may genuinely matter. But formulation convenience cannot substitute for dose accuracy, chemical stability and shelf-life validation.

15 Dosing: muscle and brain research should not be conflated

One reason public discussion has become confusing is that different research questions involve very different doses. For skeletal-muscle saturation, a traditional loading protocol uses approximately 20 g/day divided into several doses for five to seven days, followed by 3–5 g/day; an alternative is simply 3–5 g/day without loading, allowing tissue saturation to develop more gradually. The authorized European claim regarding resistance-training-related strength in adults over 55 is based on 3 g/day under specified training conditions (European Commission, 2017).

Brain studies have sometimes used considerably larger amounts. The acute sleep-deprivation experiment used 0.35 g/kg as a single dose, while the Alzheimer's pilot used 20 g/day for eight weeks. The new GLP-1 pilot is testing 10 g/day (Gordji-Nejad et al., 2024; Smith et al., 2025; ClinicalTrials.gov, 2026).

These doses should not be casually interchanged. A dose used experimentally to overcome constrained cerebral creatine uptake cannot automatically become a consumer recommendation for "brain health." Likewise, 10 g/day being tested during GLP-1 therapy does not establish 10 g/day as an optimal dose for patients using semaglutide, tirzepatide or other incretin therapies. Dose must follow the biological question and the evidence.

16 Safety: unusually strong evidence, with an important diagnostic caveat

Creatine monohydrate has one of the largest safety datasets among widely consumed sports supplements. Large evidence reviews and analyses of clinical-trial adverse events have not identified a pattern consistent with the widespread perception that appropriate creatine supplementation is intrinsically dangerous in studied populations (Gonzalez et al., 2025; Kreider et al., 2022).

Renal safety deserves particular attention because creatine metabolism produces creatinine. A 2025 systematic review and meta-analysis found no significant deterioration in measured glomerular filtration rate associated with creatine supplementation, although serum creatinine can increase modestly (Naeini et al., 2025).

The distinction is clinically important. Serum creatinine is a surrogate used to estimate renal filtration. Increasing creatine intake can alter creatinine generation and therefore affect a creatinine-based estimated GFR without representing equivalent structural renal damage. In people receiving GLP-1 therapies, nausea, vomiting or reduced fluid intake can independently predispose susceptible individuals to dehydration. The correct conclusion is therefore neither "creatine damages the kidneys" nor "kidney function is irrelevant," but that biomarker interpretation requires clinical context, particularly in patients with renal disease, dehydration risk or significant comorbidity.

17 The regulatory reality is more conservative than the emerging science

The creatine story illustrates the difference between scientific exploration and legally substantiated health communication. Within the European Union, creatine has authorized claims relating to high-intensity physical performance and to enhancement of the effects of resistance training on muscle strength in adults over 55 under specified conditions (European Commission, 2017).

By contrast, a proposed claim concerning improved cognitive function was rejected after EFSA concluded that the available evidence did not establish a cause-and-effect relationship; the European Commission formalized that refusal in 2026 (EFSA, 2024; European Commission, 2026).

> There are currently no authorized EU health claims stating that creatine prevents cognitive decline, protects against Alzheimer's disease, increases lifespan, improves mitochondrial health, prevents sarcopenia, or prevents muscle loss caused by GLP-1 medicines. That does not make the research invalid. It means research hypotheses, clinical evidence and commercial claims occupy different

evidentiary levels. Manufacturers entering healthy-aging or GLP-1-adjacent nutrition should resist the temptation to market ahead of the evidence.

18 What "healthy aging" should mean in the creatine field

The phrase healthy aging can easily become scientifically vague. Applied rigorously to creatine, it should not mean that the compound has been demonstrated to slow aging itself. It should mean that creatine may influence physiological characteristics that strongly determine how people age functionally.

Muscle strength is one. Training capacity is another. Maintenance of physical independence is potentially another. Brain energetic resilience may eventually become one, although that evidence remains less mature. An older organism often operates with less reserve: anabolic responsiveness declines, neuromuscular function changes, recovery may become slower and cognitive systems can become more vulnerable to sleep deprivation, disease and metabolic stress.

A molecule whose principal biological function involves rapid buffering of cellular energy demand therefore has an obvious rationale for investigation. But the intellectually responsible sequence is equally obvious: plausibility should generate experiments, not conclusions.

19 A new generation of creatine research

The next phase of creatine science will probably look very different from the research that originally established the supplement. Instead of asking only whether creatine increases a one-repetition maximum or repeated sprint output, researchers are beginning to ask whether it can preserve muscular function during aggressive weight reduction, amplify resistance-training responses in vulnerable older adults, alter cerebral energetic reserve, improve cognition under metabolic stress, modify functional decline in neurodegenerative disease, or support recovery during illness and inactivity.

Some of these hypotheses will survive rigorous testing. Others probably will not. That is exactly how the field should develop. The durability of creatine as a scientific subject derives from the fact that it does not depend on a single fashionable receptor or pathway. Its physiological role is fundamental and measurable: maintaining rapid energy availability where cells need it.

20 Conclusion: creatine's new momentum comes from a broader definition of performance

Creatine is not abandoning sports performance. Science is broadening the definition of performance. For an athlete, performance may mean power output, training volume or repeated sprint capacity. For an older adult, it may mean standing from a chair, maintaining leg strength and remaining physically independent. For a sleep-deprived worker, it may mean maintaining processing capacity under energetic stress. For a patient undergoing substantial GLP-1-associated weight loss, it may mean losing adipose tissue while preserving sufficient functional muscle to protect long-term physical capacity.

These applications are not equally proven. The evidence supporting creatine monohydrate for skeletal-muscle energetics and resistance-training adaptation is strong. Its role in healthy aging is increasingly credible, particularly when paired with progressive resistance exercise. Its effects on brain bioenergetics are compelling enough to justify continued clinical investigation, but cognitive and neurodegenerative indications

remain investigational. Its proposed role in GLP-1-associated muscle preservation is now being tested directly in humans, but efficacy is not yet established.

The most interesting future for creatine therefore lies neither in bodybuilding nostalgia nor in longevity hype. It lies in a more mature concept: maintaining energetic and functional reserve across changing physiological demands. After decades of being considered a sports supplement, creatine may ultimately prove to be something broader—but also simpler: a nutritional tool for helping tissues regenerate energy, adapt to stress and preserve function.

21 Clinical and product-development implications

For clinicians and nutrition professionals, the practical implication is not that every patient using creatine or a GLP-1 medicine requires a new protocol. It is that muscle quality, functional reserve and nutritional adequacy deserve explicit monitoring when weight loss is large or the patient is older, frail, sedentary or already sarcopenic. In those settings, resistance exercise, adequate protein and individualized nutritional assessment are primary; creatine may be considered an evidence-based adjunct for muscular adaptation, while its GLP-1-specific benefit remains investigational.

For manufacturers, the central strategic opportunity is equally clear. The category is expanding from sports performance toward healthy aging, active longevity and medical-nutrition adjacency. That does not justify unsupported disease or cognition claims. It does justify investment in validated creatine monohydrate formats, dose fidelity, stability, adherence, older-adult usability and clinical research that measures function rather than marketing-friendly surrogate endpoints alone.

RESPONSIBLE COMMUNICATION FRAMEWORK

- Say what is established: creatine supports high-intensity performance and can enhance selected resistance-training adaptations.
- Say what is promising: brain bioenergetics, stress-state cognition and functional resilience are active research areas.
- Say what is not yet proven: prevention of dementia, extension of lifespan, generalized “mitochondrial rejuvenation,” or protection from GLP-1-associated muscle loss.
- Separate ingredient evidence from delivery-format evidence: a novel gummy, liquid, salt or proprietary format does not inherit superiority simply because creatine monohydrate works.
- Use functional endpoints—strength, gait, chair-rise, quality of life—alongside body composition when targeting healthy aging or pharmacological weight loss.

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23 Declarations and editorial notes

REVIEW TYPE	Narrative review and critical perspective based on published literature, regulatory sources and a registered clinical trial. It is not a systematic review and does not claim exhaustive retrieval of all available studies.
ETHICS APPROVAL	Not applicable; the article analyzes publicly available published and registered research.
FUNDING	Self-funding academic and scientific work.
COMPETING INTERESTS	N/A
CORRESPONDENCE / ORCID	jmlopez@consultant.com
REGULATORY NOTE	Health-claim language should be adapted to the jurisdiction and intended commercial use. Research findings discussed in this review should not be converted into unauthorized disease-risk, therapeutic or cognitive claims.

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