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Creatine Monohydrate in Non-Athletic Adults: Are Health Benefits Independent of Exercise? A Critical Review

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Abstract

Background. Health claims for creatine extend beyond sport, but many benefits occur with exercise.

Aim. To distinguish health effects in non-athletic adults supported independently of exercise from exercise-adjunctive effects.

Material and methods. A structured critical narrative review evaluated 30 author-supplied full-text PMC articles and supplementary targeted searches of PubMed/MEDLINE and the Quality in Sport archive. Human trials and quantitative syntheses were prioritized; pediatric, athletic and preclinical evidence was treated as indirect.

Results. Muscle and functional benefits were most consistent in older adults when creatine accompanied resistance training; stand-alone effects on lean mass and strength were small or inconsistent. Cognitive effects did not require exercise but were modest and heterogeneous. Evidence for glycemic control, vascular function, inflammation, rehabilitation and chronic disease remained preliminary or confounded by co-interventions. Recommended doses were generally well tolerated in healthy adults, although serum creatinine could rise without impaired filtration.

Conclusions. Creatine is not a substitute for physical activity. Its best-supported health role is as an adjunct to exercise and adequate nutrition; universal stand-alone use for chronic-disease prevention is not justified.

Key words: creatine monohydrate, non-athletic adults, resistance exercise, healthy aging, cognition, metabolic health, safety.

1. Introduction

Creatine is synthesized from arginine, glycine and methionine and is also obtained from foods of animal origin. After tissue uptake, creatine and phosphocreatine form a reversible energy-buffering system that supports rapid adenosine triphosphate regeneration. Most body creatine is stored in skeletal muscle, but creatine metabolism is also relevant to the brain and other tissues with variable energy demand (Greenhaff, 1996; Kreider & Stout, 2021).

Creatine monohydrate is best known as an ergogenic aid, yet supplementation is increasingly promoted for healthy aging, cognition, metabolic health and chronic disease. This broader interest is biologically plausible, but biological plausibility is not equivalent to a clinically meaningful benefit. Non-athletic adults include healthy sedentary people, older adults, women across the lifespan, people consuming plant-based diets and patients with chronic illness. Their baseline creatine stores, capacity for exercise, medication use and clinical priorities differ substantially.

A central interpretative problem is that many positive health findings arise from trials in which creatine is combined with resistance or aerobic exercise. Such designs answer whether creatine can augment training, but not whether supplementation alone improves health. Exercise independently affects muscle protein synthesis, neural activation, insulin sensitivity, vascular function, balance and quality of life. Attributing the entire combined effect to creatine therefore exaggerates the evidence for stand-alone use.

Recent reviews in *Quality in Sport* have addressed creatine in adult health, clinical medicine and brain function (Miguel et al., 2025; Zimowski et al., 2026; Lewandowska et al., 2026). To avoid duplicating these broad summaries, the present review focuses on whether reported health effects are observed in creatine-only comparisons or primarily when supplementation is combined with structured physical activity.

The literature is methodologically uneven. Narrative reviews repeatedly cite the same small trials, and publication count can overstate the number of independent data sets. Samples are often small, intervention duration is short, and surrogate outcomes such as lean mass, inflammatory markers or serum creatinine are more common than disability, falls, hospitalization or disease progression. The contribution of creatine must therefore be judged according to study design, directness, co-interventions and clinical relevance.

Research Objective. The objective was to critically evaluate health-related effects of creatine monohydrate in non-athletic adults, with particular emphasis on whether benefits occur independently of exercise.

Research Problems. Which health outcomes are supported by direct human evidence? Which benefits are consistently observed only when creatine is combined with exercise? Which populations may plausibly respond to creatine alone, and what safety considerations limit routine use?

Research Hypothesis. The strongest evidence was expected for creatine as an adjunct to resistance exercise in older adults, whereas stand-alone effects on muscle, metabolic and disease-specific outcomes were expected to be smaller and less certain. Cognitive effects were expected to be partly independent of exercise but context-dependent.

2. Research materials and methods

2.1. Review question and design

This manuscript is a structured critical narrative review. The review question was framed around adults aged 18 years or older who were not recruited primarily because of competitive sport participation; oral creatine supplementation, preferentially creatine monohydrate; placebo, usual care or matched co-intervention comparators; and health-related outcomes involving muscle, cognition, metabolism, rehabilitation or safety.

The review was designed to separate three comparisons: creatine alone versus placebo or usual care; creatine plus exercise versus the same exercise program with placebo; and indirect mechanistic or preclinical evidence. This classification was chosen because the clinical meaning of a supplement effect differs from the effect of a combined lifestyle intervention.

2.2. Source identification and eligibility

The base corpus consisted of 30 open-access full-text publications supplied by the authors as PubMed Central links. The available full texts were examined for study design, participant or model characteristics, intervention details, outcomes and stated limitations. Funding and conflict-of-interest disclosures were considered when relevant to interpretation, but no duplicate extraction or formal source-level risk-of-bias scoring was performed. The corpus included systematic reviews and meta-analyses, randomized trials, narrative and mechanistic reviews, a position statement, a Mendelian-randomization study and selected animal investigations.

Supplementary, non-systematic searches of PubMed/MEDLINE and the Quality in Sport archive were used to identify recent quantitative syntheses and contextual publications. Search

combinations included 'creatine monohydrate' with 'older adults', 'sedentary', 'resistance training', 'without exercise', 'lean mass', 'cognition', 'kidney function', 'women' and 'clinical'. Because a complete search log and screening record were not maintained, this update is reported as contextual rather than reproducible. Publications retained from the update included Desai et al. (2025), Migiel et al. (2025), Naeini et al. (2025), Sharifian et al. (2025), Xu et al. (2024), Naddafha et al. (2026), Zimowski et al. (2026) and Lewandowska et al. (2026).

Human adult randomized trials and quantitative syntheses were prioritized. Evidence from athletes was retained only when it informed dosing, pharmacology or safety. Pediatric and animal studies were used only for age-specific uncertainty or mechanistic context and were not treated as proof of clinical efficacy in adults. Studies of alternative creatine salts were not considered equivalent to creatine monohydrate unless the reviewed publication justified that inference.

This was not a systematic review and no claim of exhaustive retrieval is made. A PRISMA flow diagram, formal meta-analysis and study-level risk-of-bias calculation were therefore not performed. Explicit eligibility rules and an evidence hierarchy were used to improve transparency without overstating methodological certainty.

2.3. Evidence classification and synthesis

Evidence was classified according to study design, directness to non-athletic adults, presence of a matched exercise co-intervention, consistency, precision and clinical relevance. Quantitative estimates were reproduced only from original trials or meta-analyses; no participant-level re-analysis or new statistical testing was conducted.

Confidence was described as moderate, low or very low. Moderate confidence required reasonably consistent human evidence from randomized trials or quantitative syntheses with directly relevant comparators. Low confidence reflected few trials, heterogeneous protocols, small samples or reliance on surrogate outcomes. Very-low confidence denoted predominantly mechanistic, animal or hypothesis-generating evidence. A change in a biomarker was not treated as proof of disease prevention, and multiple reviews summarizing the same trials were not counted as independent confirmation.

3. Research results

3.1. Evidence map and the role of exercise

The reviewed evidence divides into two patterns. The first is exercise-adjunctive: creatine is added to resistance or aerobic training and may improve training capacity or adaptation. This pattern dominates the evidence for muscle strength, lean mass, functional performance and

glycemic control. The second is exercise-independent: creatine is compared with placebo without a structured training program. This pattern is more common in cognition and safety research but is supported by fewer clinically decisive outcomes.

Table 1 summarizes the evidence according to the presence or absence of a structured exercise co-intervention. The most consistent findings indicate that creatine may modestly augment selected adaptations when an adequate physiological stimulus is present, rather than reproduce the effects of exercise independently. This pattern is particularly evident in older and postmenopausal adults. Sharifian et al. (2025) reported modest strength benefits when creatine was added to exercise, while Naddafha et al. (2026) found that benefits in postmenopausal women were concentrated in protocols using at least 5 g/day with resistance training; low-dose protocols without training showed little measurable effect.

Table 1. Exercise dependence of health-related evidence for creatine monohydrate in non-athletic adults.

Domain	Main population	Creatine without structured exercise	Creatine plus matched exercise	Confidence	Key limitation
Lean mass and strength	Older and postmenopausal adults	Small or inconsistent changes; early water-related mass gain can complicate interpretation	Most consistent improvement in strength and modest lean-mass gain with resistance training	Moderate for adjunctive use; low for stand-alone use	Few trials isolate supplementation; protocols and doses vary
Physical function	Older or rehabilitation populations	Insufficient evidence for falls, disability or independent living	Possible improvement in repeated-chair-rise or training tolerance	Low	Functional outcomes are secondary and samples are small
Cognition	Healthy adults, older adults, low dietary creatine or acute stress	Possible modest memory or processing-speed effects in selected contexts	Exercise is not required for the proposed cognitive effect	Low	Heterogeneous tests, small trials and inconsistent replication

Domain	Main population	Creatine without structured exercise	Creatine plus matched exercise	Confidence	Key limitation
Women and plant-based diets	Postmenopausal women, vegetarians and vegans	Muscle creatine may increase more when dietary intake is low; brain and clinical responses are inconsistent	Muscle benefits are clearest when adequate-dose creatine accompanies resistance training	Low to moderate in postmenopausal RT; low otherwise	Few female-only and non-athlete trials; vegetarian evidence largely involves athletes
Glycemic control	Sedentary adults and type 2 diabetes	Insufficient evidence for a reproducible stand-alone effect	Potential adjunct to exercise through training capacity and GLUT-4-related mechanisms	Low	Most positive trials combine exercise and creatine
Vascular and inflammatory outcomes	Healthy or selected clinical adults	Biological signals are inconsistent and based on surrogate markers	Exercise may explain part of the observed change	Very low to low	Small studies, many biomarkers and uncertain clinical relevance
Rehabilitation and chronic disease	Immobilization, liver disease, inflammatory bowel disease, post-viral fatigue	Preliminary, mixed or mechanistic evidence	May support rehabilitation when active is possible	Very low to low	Disease heterogeneity and scarcity of controlled trials
Renal safety	Healthy adults	No convincing reduction in measured filtration at recommended doses	Exercise does not appear necessary for safety	Moderate	Evidence is weaker in established kidney disease and complex patients

Source: authors' critical synthesis of the reviewed full-text publications and supplementary targeted searches.

3.2. Muscle mass, strength and physical function

Ageing reduces muscle mass, strength and power, but these outcomes do not decline in parallel. Creatine can increase intramuscular total creatine and may support repeated high-energy turnover, cellular hydration and training volume. These mechanisms make an interaction with resistance exercise more plausible than a large stand-alone anabolic effect.

Meta-analytic evidence in older adults generally favors creatine combined with exercise. The 2025 meta-analysis by Sharifian et al. included 20 studies and 1,093 participants and found a statistically significant but modest advantage for one-repetition maximum strength when creatine was added to exercise. Bone mineral density did not improve consistently. Earlier reviews similarly concluded that creatine can augment selected resistance-training adaptations, while evidence for functional outcomes remains uncertain (Candow & Chilibeck, 2010).

The distinction between early body-water changes and new contractile tissue is important. Desai et al. (2025) reported that creatine taken before a resistance-training program increased measured lean body mass during the initial supplementation period, but did not produce a clear additional gain during the subsequent training phase. A 2024 GRADE-assessed meta-analysis likewise reported small body-composition effects that were generally more evident when supplementation was combined with training (Pashayee-Khamene et al., 2024). These findings caution against interpreting every short-term increase in fat-free mass as muscle hypertrophy.

Evidence in postmenopausal women is particularly informative. A 2026 systematic review of seven randomized trials found small improvements in lean mass and leg-press strength overall, but subgroup interpretation indicated that benefits were concentrated in protocols using at least 5 g/day with resistance training; trials using 3 g/day or less without training showed no measurable effect. Bone density remained unchanged (Naddafha et al., 2026).

In a randomized study of 45 non-athletic older adults, both resistance-training groups improved oxidative-stress markers and quality of life, whereas strength gains were greater when creatine accompanied training. Because no creatine-only group was included and the authors found no definite independent effect of creatine on antioxidant outcomes or quality of life, the study primarily supports an adjunctive effect on strength (Amiri & Sheikholeslami-Vatani, 2023). Overall, the evidence supports creatine as an adjunct to progressive loading rather than a replacement for it.

3.3. Cognition and mental fatigue

The brain has high and continuous energy requirements, and oral creatine can increase cerebral creatine in some individuals, although the response is smaller and less predictable than in skeletal muscle. Cognitive studies are therefore relevant to the question of exercise-independent benefit, because most do not include structured training (Roschel et al., 2021; Forbes et al., 2022).

A meta-analysis of randomized trials reported a small pooled improvement in memory, with a larger signal in older adults. However, only a limited number of studies contributed,

several cognitive outcomes were correlated, and risk-of-bias concerns reduced certainty (Prokopidis et al., 2023). A broader 2024 meta-analysis reported significant pooled benefits for memory, attention time and processing-speed time. Certainty was moderate for memory and low for the remaining domains. Heterogeneity was low for memory and attention time but substantial for processing-speed time, while sensitivity analyses did not materially change the overall conclusions (Xu et al., 2024).

The largest directly relevant randomized trial included 123 healthy adults in a double-blind crossover design using 5 g/day for six weeks. The trial did not measure cerebral creatine concentrations. Bayesian analyses suggested a possible small cognitive benefit, whereas the effect only approached statistical significance for backward digit span and was non-significant for Raven's matrices. No improvement was found in the exploratory cognitive tests, and vegetarians did not benefit more than omnivores (Sandkühler et al., 2023).

Reviews report more favorable cognitive findings during sleep deprivation, acute mental fatigue, ageing or low dietary creatine intake, conditions in which cerebral energy availability may be more limiting (Candow et al., 2023). Because cognition, mood and neurodegeneration have already been reviewed broadly in Quality in Sport (Lewandowska et al., 2026), the present analysis focuses on the role of exercise as a co-intervention. The available evidence suggests that cognitive effects can occur without exercise, but the observed benefits are generally modest and do not support the use of creatine as a treatment for dementia or other neurodegenerative disorders.

3.4. Women and adults consuming plant-based diets

Women remain underrepresented in creatine research. Reviews describe possible relevance during menstruation, pregnancy, postpartum recovery and menopause, but direct human intervention evidence is uneven and often extrapolated from exercise studies or mechanistic physiology (Smith-Ryan et al., 2021; Smith-Ryan et al., 2025).

Postmenopausal women are the best-studied female subgroup because muscle and bone loss become clinically important. The recent meta-analysis discussed above reinforces that exercise and adequate dose are major effect modifiers. Creatine alone at low doses has not demonstrated a reliable effect on bone density or physical function (Naddafha et al., 2026).

Vegetarians and vegans obtain little or no preformed dietary creatine and may show larger increases in muscle creatine stores after supplementation. However, baseline brain creatine is not consistently lower, and supplementation has not uniformly increased cerebral phosphocreatine. A systematic review reported favorable changes in creatine stores and some

performance or cognitive outcomes, but much of the literature involved athletes and did not establish long-term clinical benefits in sedentary adults (Kaviani et al., 2020). Lower baseline dietary intake increases biological plausibility, not certainty that universal supplementation improves health.

Pregnancy and lactation require particular caution. Animal and fetal studies support mechanistic hypotheses concerning hypoxic protection, but they cannot establish routine human dosing or safety (Tran et al., 2022). The absence of adequate clinical trials precludes general recommendations during pregnancy or breastfeeding.

3.5. Glycemic, vascular and inflammatory outcomes

Skeletal muscle is a major site of glucose disposal, providing a rationale for creatine in metabolic health. Proposed mechanisms include greater training capacity, glycogen storage and GLUT-4 translocation. Reviews identify encouraging findings in insulin-resistant adults or people with type 2 diabetes, but positive trials commonly combine creatine with exercise (Solis et al., 2021). The independent supplement effect therefore remains uncertain.

In trials that combine creatine with a structured exercise program, improvements in glycemic control may reflect enhanced training capacity, better adherence, a supplement-exercise interaction or a combination of these factors. Factorial trials comparing creatine alone, exercise alone, their combination and a control condition are needed before creatine can be recommended as an independent strategy for diabetes management.

Vascular and inflammatory hypotheses are similarly preliminary. Small studies and reviews describe possible effects on endothelial function, oxidative stress, cytokines and tissue injury, but findings are inconsistent and often based on surrogate markers (Clarke et al., 2020; Arazi et al., 2021; Cordingley et al., 2022). Exercise is a major confounder because it independently changes the same endpoints.

Creatine should not be described as a broad antioxidant or anti-inflammatory treatment. The evidence is more accurately summarized as mechanistically plausible, occasionally favorable in small studies and not yet linked to fewer cardiovascular events, disability or disease progression.

3.6. Rehabilitation and chronic disease

Medical-rehabilitation literature includes disuse atrophy, orthopedic recovery, neuromuscular disease and post-injury reconditioning. Creatine may be most useful when a patient can perform active loading but has limited training capacity. Evidence is less consistent

during immobilization, and creatine alone has not reliably prevented atrophy or accelerated functional recovery (Harmon et al., 2021).

Potential applications in chronic liver disease, inflammatory bowel disease and post-viral fatigue are supported mainly by physiological rationale and a limited, heterogeneous clinical evidence base (Wallimann et al., 2021; Casciola et al., 2023; Ostojic et al., 2025). Well-controlled clinical trials are required before these uses can be recommended in routine care.

Cancer-related immune and macrophage findings are predominantly mechanistic. A supplied study reported enhanced macrophage ATP production and anti-tumor activity, but this does not establish benefit, dose or safety in human cancer care (Peng & Saito, 2023). Likewise, diabetic-rat histopathology and fetal-sheep hypoxia experiments cannot be used as direct evidence for adult clinical efficacy (Gonçalves et al., 2022; Tran et al., 2022).

These disease areas were also discussed in a recent broad clinical review in *Quality in Sport* (Zimowski et al., 2026). In the studies considered here, creatine has not been shown to replace active rehabilitation or disease-specific treatment when illness limits physical activity.

3.7. Safety and practical use

Creatine monohydrate at recommended doses is generally well tolerated in healthy adults. Common practical effects are a small increase in body mass, particularly during loading, and occasional gastrointestinal discomfort when large doses are consumed at once. Dividing larger daily amounts into smaller doses may improve gastrointestinal tolerance (Kreider et al., 2017; Antonio et al., 2021).

Renal interpretation is nuanced because creatine is partly converted to creatinine. Supplementation can raise serum creatinine and lower creatinine-based estimated glomerular filtration rate without reducing true filtration. A 2025 systematic review and meta-analysis found a small increase in serum creatinine but no significant adverse effect on glomerular filtration rate, supporting the view that isolated creatinine changes can be pharmacokinetic rather than nephrotoxic (Naeini et al., 2025).

Controlled human evidence is reassuring regarding kidney function in healthy adults, although data remain limited in people with established chronic kidney disease (Longobardi et al., 2023). Evidence is also insufficient for severe liver disease, pregnancy and breastfeeding; these populations require condition-specific assessment rather than extrapolation from renal-safety reviews (Wallimann et al., 2021; Tran et al., 2022). Mendelian-randomization findings are indirectly reassuring but cannot replace prospective safety studies of defined oral doses (Zhou et al., 2024).

For a healthy adult who chooses supplementation, plain creatine monohydrate is the best-supported formulation. A maintenance dose of 3-5 g/day is commonly used; loading is optional and primarily accelerates tissue saturation. Product purity, appropriate dosing, total clinical context and realistic expectations are more important than proprietary forms. Persistent symptoms or unexplained laboratory changes require medical review.

Table 2. Practical interpretation of creatine use outside competitive sport.

Question	Evidence-based interpretation
Can creatine replace exercise?	No. It does not reproduce the mechanical, neural, balance, cardiovascular or psychosocial effects of physical activity.
Where is benefit most likely?	As an adjunct to progressive resistance exercise in older or functionally limited adults, and possibly for selected cognitive tasks under increased metabolic demand.
Is loading required?	No. Approximately 3-5 g/day gradually saturates tissues; loading only accelerates the process and can increase gastrointestinal symptoms or early body mass.
Does higher serum creatinine prove kidney injury?	No. Creatinine may rise because of creatine turnover. Interpretation should consider supplementation, muscle mass and, when indicated, cystatin C or measured filtration.
Who needs medical advice?	People with known kidney disease, severe liver disease, pregnancy or breastfeeding, unexplained laboratory abnormalities, or serious chronic illness should seek individual medical advice because direct safety data are limited.
Can creatine treat chronic disease alone?	Current evidence does not support using it instead of established medical, nutritional or rehabilitation care.

Source: authors' practical synthesis of the reviewed evidence. This table does not replace individualized medical advice.

4. Discussion

4.1. Which benefits appear independent of exercise?

The review question produces a different hierarchy from a general review of creatine. Skeletal-muscle and functional evidence is the strongest overall, but it is also the most dependent on a training co-intervention. Cognitive research provides the clearest possibility of an exercise-independent effect, yet its average benefit is small, inconsistent and concentrated in selected contexts. Renal safety is also independent of exercise, but safety is not itself a therapeutic benefit.

The evidence is strongest for defined uses rather than broad health claims. Creatine reliably increases tissue creatine stores and may modestly enhance selected adaptations to resistance

training. However, these findings should not be extrapolated to sedentary adults as evidence of independent protection against muscle loss, chronic disease or cognitive decline.

Expected benefits therefore depend on the clinical and behavioral context. Older adults who participate in progressive resistance training may obtain a modest additional benefit from creatine, whereas supplementation without changes in physical activity, dietary protein intake or clinical management is less likely to produce meaningful effects. Possible differences in people with low dietary creatine intake or during acute cognitive stress require confirmation in prospective studies.

4.2. Clinical relevance, limitations and research priorities

The clinical importance of small changes in lean mass or laboratory markers should not be assumed. Future trials should prioritize strength, gait, chair-rise performance, falls, disability, patient-reported function and sustained independence. Factorial designs are needed to separate creatine, exercise and interaction effects. Trials should also report baseline diet, sex, menopausal status, habitual activity, tissue-response markers, product verification and adherence.

The evidence base has several limitations. Many publications are narrative reviews with overlapping authorship and repeated citation of the same trials. Primary studies are commonly small and short, and healthy male participants remain overrepresented. Animal studies and mechanistic biomarkers are useful for hypothesis generation but cannot define routine clinical practice. Supplement-industry relationships occur in parts of the literature; transparent funding, preregistration and independent replication are essential.

This review has several limitations. The initial corpus was supplied by the authors rather than generated by a fully systematic search, and the supplementary update was contextual rather than supported by a complete reproducible search and screening log. No formal risk-of-bias tool or meta-analysis was applied. Consequently, the confidence categories are interpretative and should not be treated as GRADE ratings. The analysis nevertheless distinguishes creatine-only comparisons from exercise-adjunctive studies and assigns lower weight to indirect evidence.

Further research should focus on adults who cannot initially tolerate standard exercise volumes, because this population is often cited in clinical discussions but has rarely been studied directly. Dose-response trials should determine whether creatine improves readiness or capacity for rehabilitation rather than only altering body mass. Cognitive studies require preregistered primary outcomes, adequate statistical power and stratification by age, diet, sleep

loss and baseline brain creatine. Safety studies should also include well-characterized clinical populations and distinguish absence of evidence from evidence of harm.

5. Conclusions

1. Creatine monohydrate has health relevance beyond sport because the creatine-phosphocreatine system supports cellular energy homeostasis, but this mechanism does not guarantee a clinically meaningful effect.

2. The strongest evidence in non-athletic adults concerns muscle strength and lean mass in older and postmenopausal adults when creatine is combined with progressive resistance exercise.

3. Stand-alone supplementation has not consistently improved muscle mass, physical function, glycemic control, vascular outcomes or chronic-disease endpoints.

4. Cognitive benefits can occur without exercise, but average effects are modest, heterogeneous and most plausible during ageing, low dietary creatine intake or increased metabolic demand.

5. Recommended doses are generally well tolerated in healthy adults. A rise in serum creatinine may reflect creatine turnover rather than reduced filtration, although medically complex patients require individualized assessment.

6. Creatine should be presented as a potential adjunct to exercise, adequate nutrition and evidence-based care, not as a replacement for physical activity or a universal stand-alone health intervention.

Disclosure

Supplementary Materials

No supplementary materials are included with this manuscript. The full-text source set is identified in the References section.

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Conflicts of Interest

The authors declare no conflict of interest.

Declaration of the use of generative AI and AI-assisted technologies in the writing process

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