

Alzchem Group AG
Human Nutrition Department

Selection of Scientific Studies of Prominent Creatine Topics

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1. Basics about Creatine

1.1. Metabolic Basis of Creatine in Health and Disease: A Bioinformatics-Assisted Review

Author: Bonilla, D.A.; Kreider, R.B.; Stout, J.R.; Forero, D.A.; Kerksick, C.M.; Roberts, M.D.; Rawson, E.S.

Publication: 2021, Nutrients, 13, 1238.

Link: <https://www.mdpi.com/2072-6643/13/4/1238>

Miniconclusion: this study explains the underlying roles and mechanism of creatine for the cellular energy metabolism.

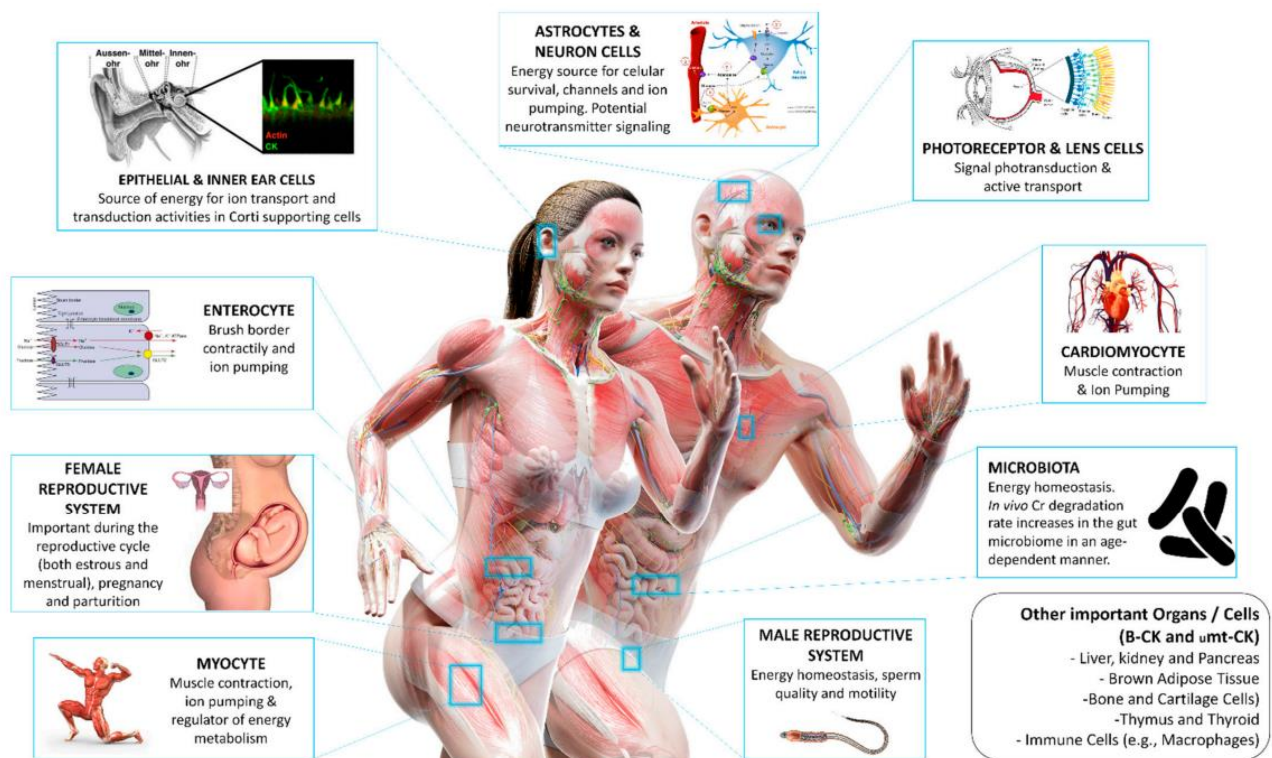


Figure 4. Importance of Cr metabolism in whole-body physiology. The CK/PCr system is essential for the chemo-mechanical energy transduction of cells/tissues with high, fluctuant, and constant energy demands. Source: designed by the authors (D.A.B.) using an anatomy template developed by 3dMediSphere (<https://www.turbosquid.com/>), licensed 3D standard Vray 3.60. accessed on 14 February 2020.

Figure 1: Bonilla et al. 2021

1.2. Creatine in Health and Disease

Author: Kreider, R.B.; Stout, J.R.

Publication: 2021, *Nutrients*, 13, 447

Miniconclusion: Assessment of peer-reviewed scientific and medical evidence related to creatine's role in promoting general health as we age and how creatine supplementation has been used as a nutritional strategy to help individuals recover from injury and/or manage chronic disease.

Link: <https://www.mdpi.com/2072-6643/13/2/447>

1.3. Common questions and misconceptions about creatine supplementation: what does the scientific evidence really show?

Author: Antonio, J., Candow, D.G., Forbes, S.C. et al.

Publication: 2021, *J Int Soc Sports Nutr* 18, 13

Miniconclusion: Most misunderstandings about creatine are either wrong (anabolic steroid, kidney damage, hair loss, dehydration, cramping, risk for adolescents, increase of fat mass, loading requirement, risk for elderly, works only in men, superior forms of creatine compared to monohydrate) or only true for very specific situations (water retention, lower efficiency in resistance sports).

Link: <https://www.tandfonline.com/doi/full/10.1186/s12970-021-00412-w>

1.4. Bioavailability, Efficacy, Safety, and Regulatory Status of Creatine and Related Compounds: A Critical Review

Author: Kreider, R.B.; Jäger, R.; Purpura, M.

Publication: 2022 *Nutrients* , 14, 1035

Miniconclusion: CrM continues to be the only source of creatine that has substantial evidence to support bioavailability, efficacy, and safety. Additionally, CrM is the source of creatine recommended explicitly by professional societies and organizations and approved for use in global markets as a dietary ingredient or food additive.

Link: <https://www.mdpi.com/2072-6643/14/5/1035>

1.5. The creatine kinase system and pleiotropic effects of creatine

Author: Wallimann, T., Tokarska-Schlattner, M. & Schlattner, U.

Publication: 2011, Amino Acids 40, 1271–1296

Miniconclusion: Creatine has three roles – temporal energy buffer, spatial energy buffer, metabolic regulator. Based on these roles, creatine has many positive roles on body functions.

Link: <https://link.springer.com/article/10.1007/s00726-011-0877-3>

1.6. The Application of Creatine Supplementation in Medical Rehabilitation

Author: Harmon, K.K.; Stout, J.R.; Fukuda, D.H.; Pabian, P.S.; Rawson, E.S.; Stock, M.S.

Publication: 2023, Nutrients, 13, 1825

Miniconclusion: Creatine’s potential efficacy as a supplemental agent via preservation of muscle mass, strength, and physical function. While rehab data is inconsistent, therapeutic aid potential is promising.

Link: [Nutrients | Free Full-Text | The Application of Creatine Supplementation in Medical Rehabilitation \(mdpi.com\)](#)

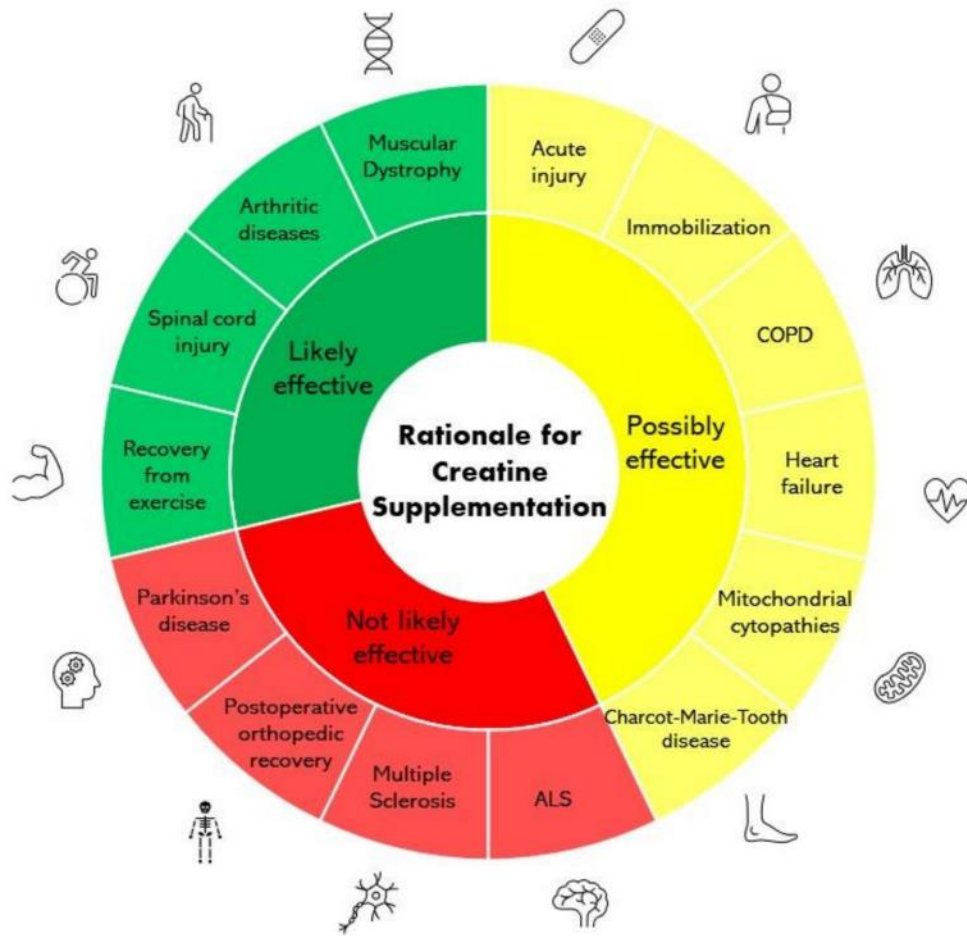


Figure 1. Rationale for examination of creatine supplementation as a rehabilitative aid. Abbreviations defined from clockwise: COPD = chronic obstructive pulmonary disease; ALS = amyotrophic lateral sclerosis.

Figure 2: Harmon et al. 2021

2. Food

2.1. Changing to a vegetarian diet reduces the body creatine pool in omnivorous women, but appears not to affect carnitine and carnosine homeostasis: A randomised trial

Author: Blancquaert, L., Baguet, A., Bex, T., Volkaert, A., Everaert, I., Delanghe, J., Derave, W.

Publication: 2018, British Journal of Nutrition, 119(7), 759-770

Miniconclusion: the body creatine pool declined over a 3-month vegetarian diet in omnivorous women, which was ameliorated when accompanied by low-dose dietary creatine supplementation. Carnitine and carnosine homeostasis was unaffected

Link: <https://doi.org/10.1017/S000711451800017X>

2.2. The influence of creatine supplementation on the cognitive functioning of vegetarians and omnivores

Author: Benton, D., & Donohoe, R.

Publication: 2011, British Journal of Nutrition, 105(7), 1100-1105.

Miniconclusion: This double blind placebo controlled study in young femals (n=128) creatine supplementation improved memory. Irrespective of dietary style, the supplementation of creatine decreased the variability in the responses to a choice reaction-time task.

Link: <https://doi.org/10.1017/S0007114510004733>

3. Post Viral Fatigue Syndrome (PVFS)/Long-COVID

3.1. Diagnostic and Pharmacological Potency of Creatine in Post-Viral Fatigue Syndrome

Author: Ostojic, S.M.

Publication: 2021, Nutrients, 13, 503

Miniconclusion: Findings from initial trials on the metabolic substrate of PVFS, along with promising results from interventional studies, show that creatine is rightfully on the list of the German Medical Doctors list of potentially helpful Dietary Supplements.

Link: [Nutrients | Free Full-Text | Diagnostic and Pharmacological Potency of Creatine in Post-Viral Fatigue Syndrome \(mdpi.com\)](#)

4. Energy

See 2. Basics about Creatine for additional information of Creatine and Energy.

More specifically:

Kreider & Stout 2021 Creatine in Health and Disease

Miniconclusion: Assessment of peer-reviewed scientific and medical evidence related to creatine's role in promoting general health as we age and how creatine supplementation has been used as a nutritional strategy to help individuals recover from injury and/or manage chronic disease.

Link: <https://www.mdpi.com/2072-6643/13/2/447>

Bonilla et al. 2021

Metabolic Basis of Creatine in Health and Disease: A Bioinformatics-Assisted Review

Miniconclusion: this study explains the underlying roles and mechanism of creatine for the cellular energy metabolism.

Link: <https://www.mdpi.com/2072-6643/13/4/1238>

4.1. Genetic Depletion of Adipocyte Creatine Metabolism Inhibits Diet-Induced Thermogenesis and Drives Obesity

Author: Lawrence Kazak, Edward T. Chouchani, Gina Z. Lu, Mark P. Jedrychowski, Curtis J. Bare, Amir I. Mina, Manju Kumari, Song Zhang, Ivan Vuckovic, Dina Laznik-

Bogoslavski, Petras Dzeja, Alexander S. Banks, Evan D. Rosen, Bruce M. Spiegelman

Publication: 2017, Cell Metabolism, Volume 26, Issue 4, Pages 660-671.e3

Miniconclusion: These results provide strong in vivo genetic support for a role of GATM and creatine metabolism in energy expenditure, diet-induced thermogenesis, and defense against diet-induced obesity.

Link: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5629120/>

5. Cardiovascular Health

5.1. Role of Creatine in the Heart: Health and Disease

Author: Balestrino, M.

Publication: 2021, Nutrients, 13, 1215.

Miniconclusion: Creatine effectiveness in this case may be because anthracyclines reduce expression of the creatine transporter, and because of the pleiotropic antioxidant properties of creatine. Moreover, creatine may also reduce concomitant muscle damage by anthracyclines.

Link: <https://www.mdpi.com/2072-6643/13/4/1215>

5.2. The Potential Role of Creatine in Vascular Health

Author: Clarke, H.; Hickner, R.C.; Ormsbee, M.J.

Publication: 2021, Nutrients, 13, 857.

Miniconclusion: There is evidence to suggest that creatine may possess unique properties that may impart novel benefits upon the vasculature, further clinical research is needed.

Link: <https://www.mdpi.com/2072-6643/13/3/857>

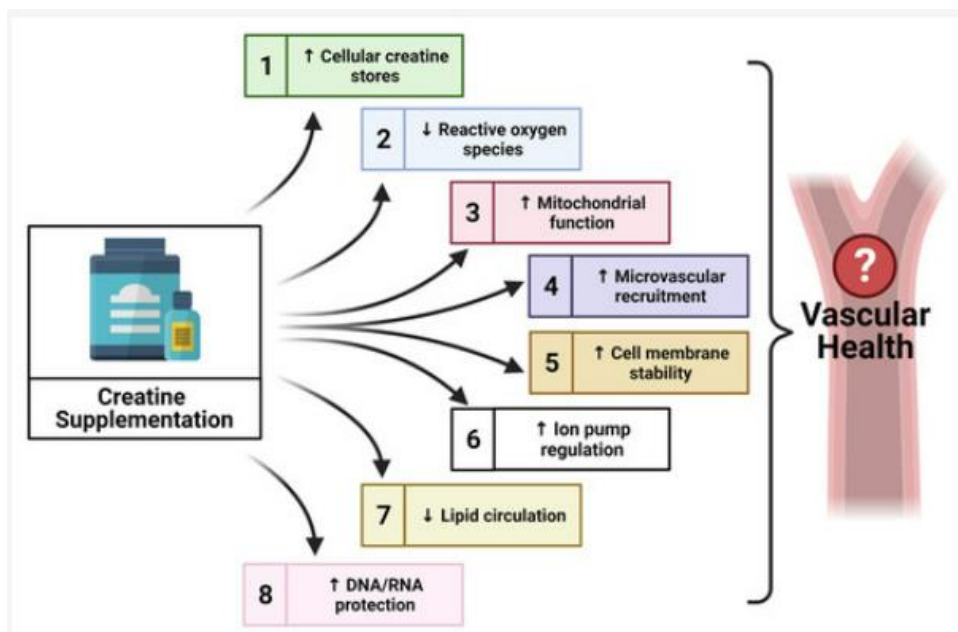


Figure 3: Clarke et al. 2021

6. Sarcopenia & older Adults

6.1. Meta-Analysis Examining the Importance of Creatine Ingestion Strategies on Lean Tissue Mass and Strength in Older Adults

Author: Forbes, S.C.; Candow, D.G.; Ostojic, S.M.; Roberts, M.D.; Chilibeck, P.D.

Publication: 2021, Nutrients, 13, 1912.

Miniconclusion: Overall, creatine (independent of dosing strategy) augments lean tissue mass and strength increase from RT vs. placebo. Previous loading phases improved the results.

Link: <https://www.mdpi.com/2072-6643/13/6/1912>

6.2. Current Evidence and Possible Future Applications of Creatine Supplementation for Older Adults

Author: Candow, D.G.; Forbes, S.C.; Kirk, B.; Duque, G.

Publication: 2021, Nutrients, 13, 745.

Miniconclusion: CR (especially when combined with RT) has some favourable effects on aging muscle, bone and fat mass, muscle and bone strength, and physical performance, primarily in healthy populations

Link: <https://www.mdpi.com/2072-6643/13/3/745>

7. Brain Health & Cognitive Function

7.1. Creatine Supplementation and Brain Health

Author: Roschel, H.; Gualano, B.; Ostojic, S.M.; Rawson, E.S.

Publication: 2021, *Nutrients*, 13, 586.

Miniconclusion: There is a potential for creatine supplementation to improve cognitive processing, especially in conditions characterized by brain creatine deficits, which could be induced by acute stressors (e.g., exercise, sleep deprivation) or chronic, pathologic conditions (e.g., creatine synthesis enzyme deficiencies, mTBI, aging, Alzheimer's disease, depression).

Link: <https://www.mdpi.com/2072-6643/13/2/586>

7.2. Creatine for the Treatment of Depression

Author: Kious, B.M.; Kondo, D.G.; Renshaw, P.F.

Publication: 2019, *Biomolecules*, 9, 406.

Miniconclusion: Clinical studies in neurological conditions such as PD have indicated that creatine might have an antidepressant effect, and early clinical studies in depressive disorders—especially MDD—indicate that creatine may have an important antidepressant effect.

Link: <https://www.mdpi.com/2218-273X/9/9/406>

8. Fertility (male & female)

8.1. Creatine Metabolism in Female Reproduction, Pregnancy and Newborn

Author: Muccini, A.M.; Tran, N.T.; de Guingand, D.L.; Philip, M.; Della Gatta, P.A.; Galinsky, R.; Sherman, L.S.; Kelleher, M.A.; Palmer, K.R.; Berry, M.J.; Walker, D.W.; Snow, R.J.; Ellery, S.J.

Publication: 2021, Nutrients, 13, 490.

Miniconclusion: Initial promising findings supporting creatine supplementation during reproductive cycle, pregnancy, parturition and gestation .No risks have been found when using high quality creatine.

Link: [Creatine Metabolism in Female Reproduction, Pregnancy and Newborn Health - PMC \(nih.gov\)](#)

8.2. Creatine as a Promising Component of Paternal Preconception Diet

Author: Ostojic, S.M.; Stea, T.H.; Engeset, D.

Publication: Nutrients 2022, 14, 586

Miniconclusion: Creatine, a conditionally essential nutrient, has caught attention as a male fertility-promoting candidate due to its role in sperm energy metabolism. As energy-demanding cells, spermatozoa can suffer from deficient creatine metabolism, with poor sperm count and motility are often associated with low creatine levels. A provision of supplemental creatine appears to positively affect sperm quality in pilot trials, suggesting a potential for using creatine to attenuate sub-fertility.

Link: [Nutrients | Free Full-Text | Creatine as a Promising Component of Paternal Preconception Diet \(mdpi.com\)](#)

9. Female Health

9.1. A 2-Year Randomized Controlled Trial on Creatine Supplementation during Exercise for Postmenopausal Bone Health

Author: Chilibeck, Philip D.; Candow, Darren G.; Gordon, Julianne J.; Duff, Whitney R.D.; Mason, Riley; Shaw, Keely; Taylor-Gjevre, Regina; Nair, Bindu; Zello, Gordon A.

Publication: May 5, 2023, Medicine & Science in Sports & Exercise,

Miniconclusions: Two years of creatine supplementation and exercise in postmenopausal women had no effect on bone mineral density, yet improved some bone geometric properties at the proximal femur.

Link: [https://journals.lww.com/acsm-
msse/Abstract/9900/A_2_Year_Randomized_Controlled_Trial_on_Creatine.273.aspx](https://journals.lww.com/acsm-msse/Abstract/9900/A_2_Year_Randomized_Controlled_Trial_on_Creatine.273.aspx)

If you have any questions, comments, or desire for further information, please do not hesitate to contact us at any time.

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