

# The Role of Creatine in Health and Disease



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*Disclosures:* Receive industry sponsored research grants and serve as a scientific and legal consultant.

# Background

Kreider et al. *JISSN*. 14, 18, 2017

- Creatine (primarily as CrM) is one of the ***most popular nutritional ergogenic aids*** for athletes.
- CrM supplementation ***increases intramuscular creatine concentrations, can improve exercise performance, and/or improve training adaptations.***
- CrM supplementation ***may enhance post-exercise recovery, injury prevention, thermoregulation, rehabilitation, and concussion and/or spinal cord neuroprotection.***
- ***A number of clinical applications*** of creatine supplementation have also been studied.



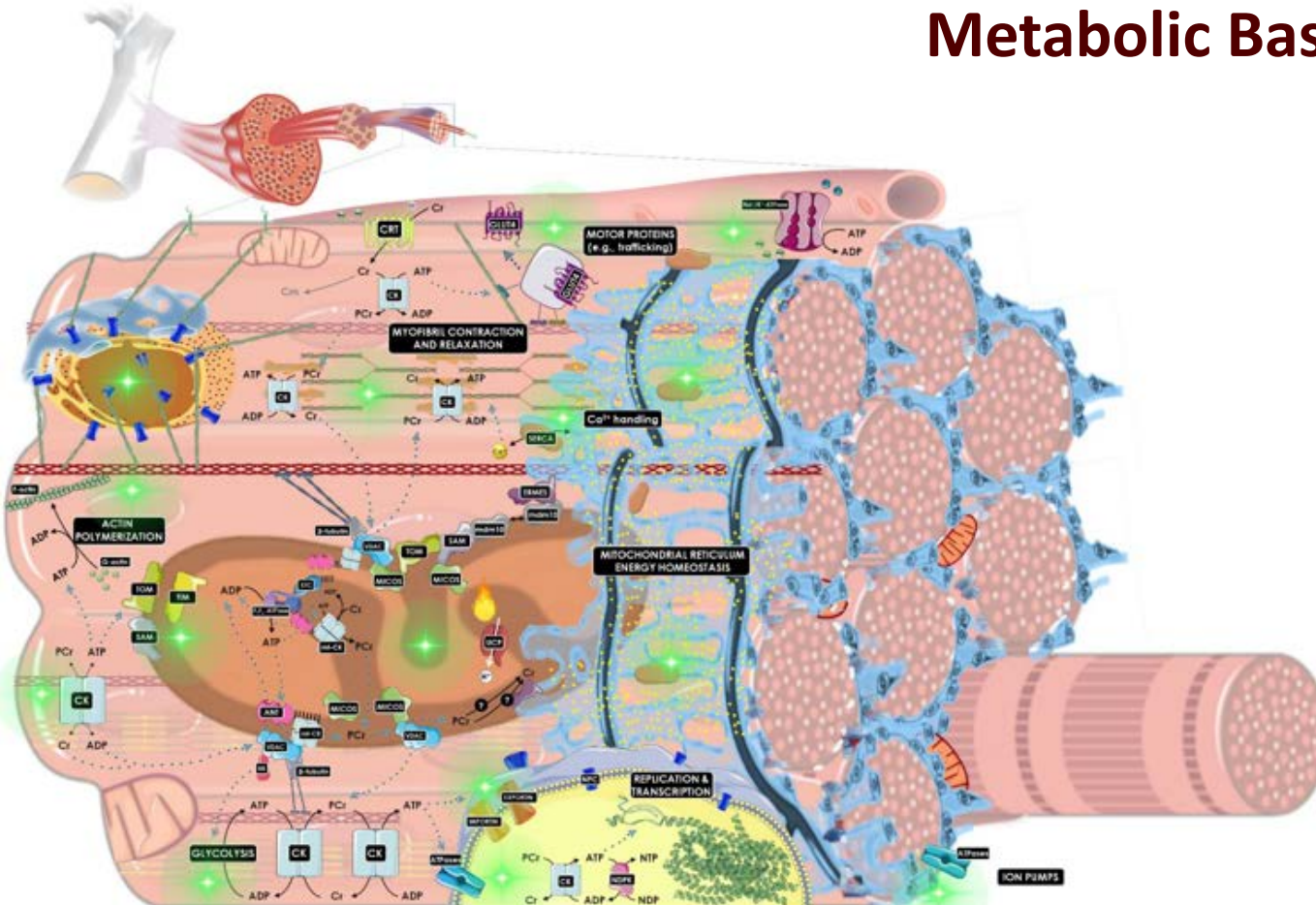
# Metabolic Basis for Creatine in Health

Bonilla et al. *Nutrients*: 13, 1238, 2021

General overview of the CK/PCr system. This chemo-mechanical energy transduction network involves structural and functional coupling of the:

- **Mitochondrial Reticulum** (mitochondrial interactosome and oxidative metabolism),
- **Phosphagen and Glycolytic System** (extramitochondrial ATP production),
- **Nucleoskeleton and Cytoskeleton Complex** (nesprins interaction with microtubules, actin polymerization,  $\beta$ -tubulins),
- **Motor Proteins** (e.g., myofibrillar ATPase machinery, vesicles transport)
- **Ion pumps** (e.g., SERCA,  $\text{Na}^+/\text{K}^+$ -ATPase).

\* **Green sparkled circles** (CK/PCr important functional processes)

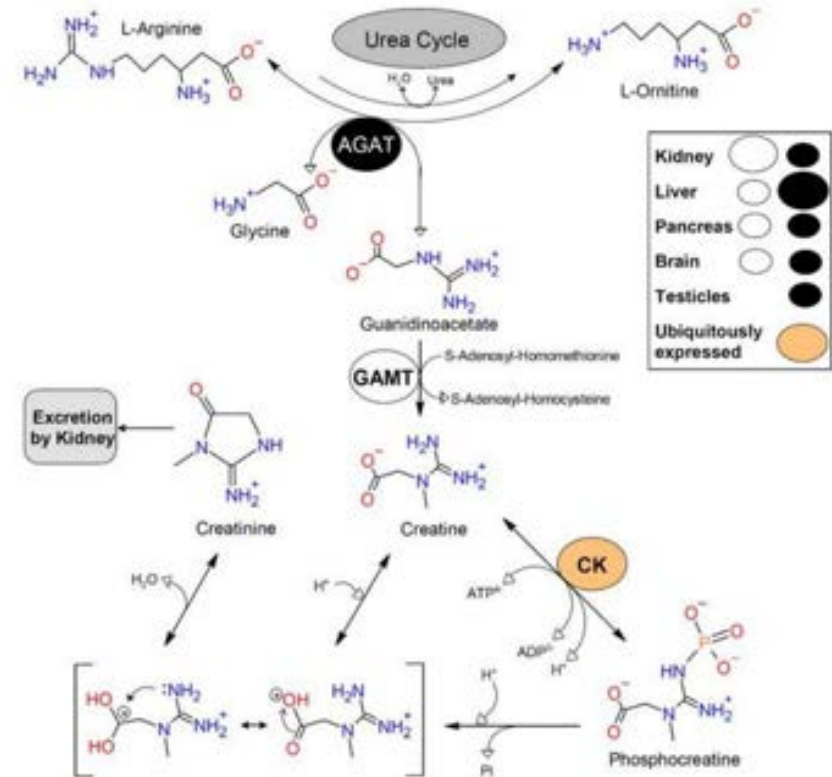


ANT: adenine nucleotide translocase; CK: creatine kinase; Cr: creatine; Crn: creatinine; CRT:  $\text{Na}^+/\text{Cl}^-$ -dependent creatine transporter; ERMES: endoplasmic reticulum-mitochondria encounter structure; ETC: electron transport chain; GLUT-4: glucose transporter type 4; HK: hexokinase; mdm10: mitochondrial distribution and morphology protein 10; MICOS: mitochondrial contact site and cristae organizing system; NDPK: nucleoside-diphosphate kinase; NPC: nuclear pore complex; SAM: sorting and assembly machinery; SERCA: Sarco/Endoplasmic Reticulum  $\text{Ca}^{2+}$  ATPase; TIM: translocase of the inner membrane complex; TOM: translocase of the outer membrane complex; UCP: uncoupling protein; VDAC: voltage-dependent anion channel. Green sparkled circles – CK/PCr important functional processes.

# Creatine Synthesis

Bonilla et al. *Nutrients*: 13, 1238, 2021

- Creatine (N-(aminoiminomethyl)-N-methyl glycine) is a naturally occurring **nitrogen-containing compound** that plays an **integral role in cellular metabolism**.
- Creatine is endogenously **synthesized** from the amino acids **arginine** and **glycine** by L-arginine:glycine amidinotransferase (**AGAT**) to guanidinoacetate (**GAA**).
- The GAA is then **methylated** (i.e., CH<sub>3</sub> added) by the enzyme guanidinoacetate N-methyltransferase (**GAMT**) with **S-adenosyl methionine** (SAME) to form **creatinine**.
- The **creatinine** is then **rehydrated** to **creatine** in the **liver**. Creatine is then **phosphorylated** to **phosphocreatine** by creatine kinase (**CK**) in muscle cells.
- The **kidney, liver, pancreas, and some areas within the brain** contain **AGAT**. Most **GAA** is formed in the kidney and converted by **GAMT** to **creatinine** in the **liver**.



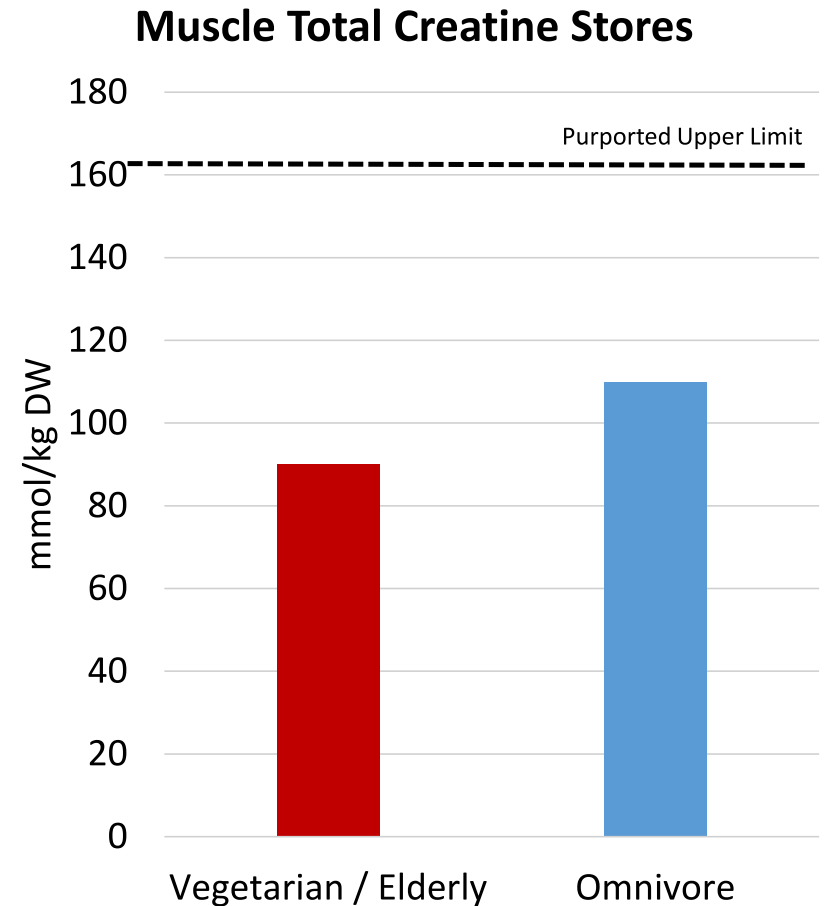
Bonilla et al. *Nutrients*: 13, 1238, 2021



# Creatine Availability

Bonilla et al. *Nutrients*: 13, 1238, 2021

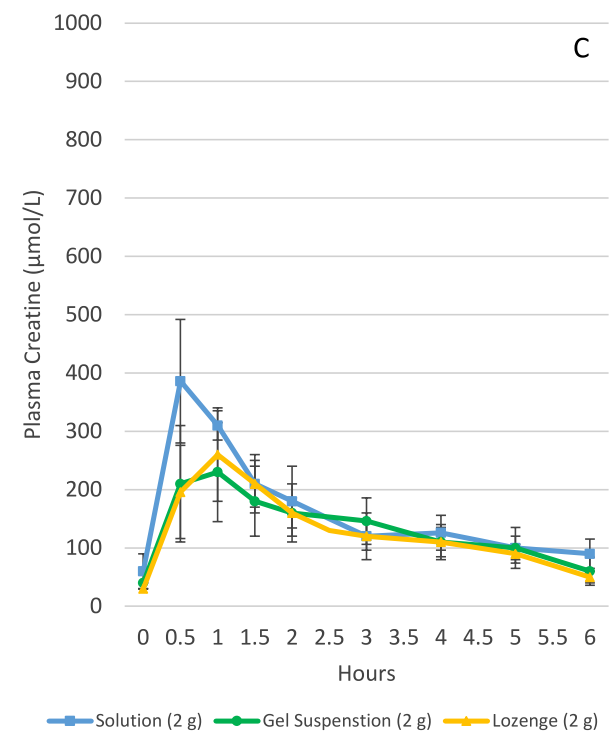
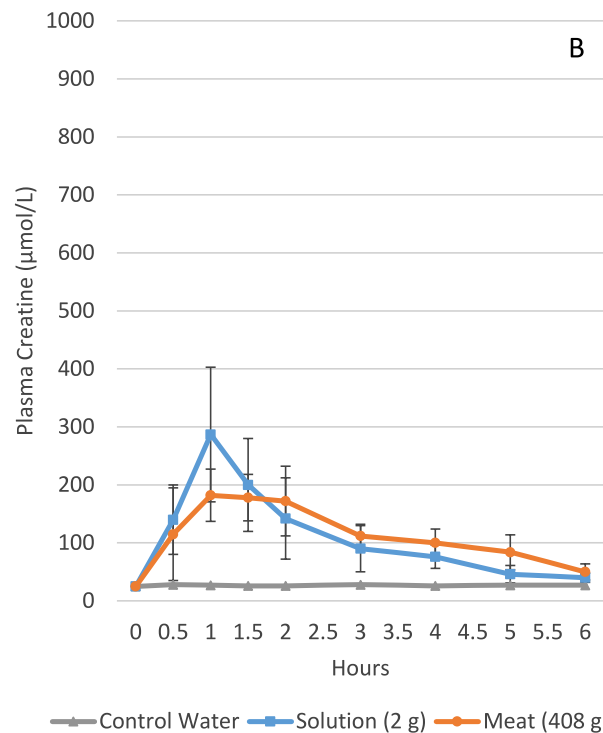
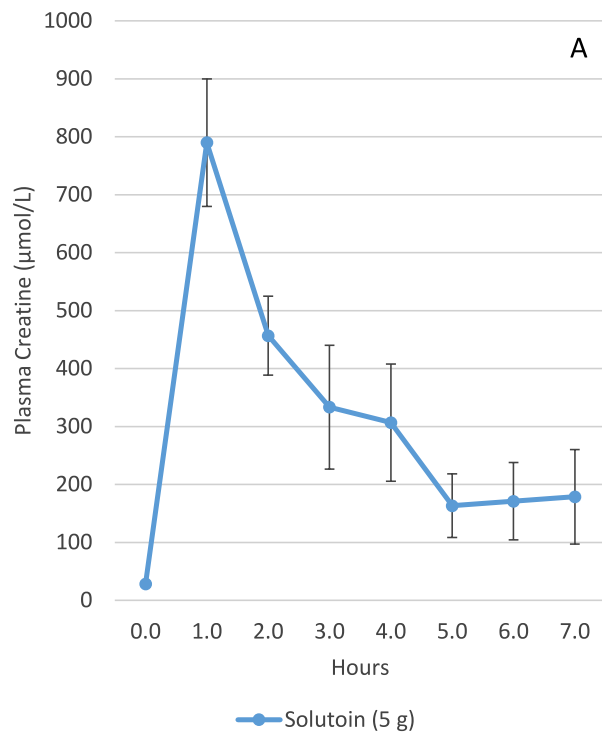
- Creatine is **stored in muscle (95%)** with the remaining found in the **heart, brain** and **testes**.
- About **2/3 is stored as PCr** and 1/3 free Cr
- **Vegans & elderly** typically have **less muscle Cr**.
- **About ½ of the daily need** for creatine is obtained from **endogenous synthesis** (1 – 2 grams/day)
- Active individuals need to consume **2 – 4 grams/day of creatine** in their diet to maintain creatine stores.
- **Meat & fish** contain about **1-2 grams/lbs.** of Cr



Kreider et al. *J Int Soc Sports Nutr.* 2017; 14: 18.

# Bioavailability of Creatine

Harris et al. *Clin Sci* 83: 367-74, 1992; Harris et al., *J Sports Sci.* 20:147-151, 2002

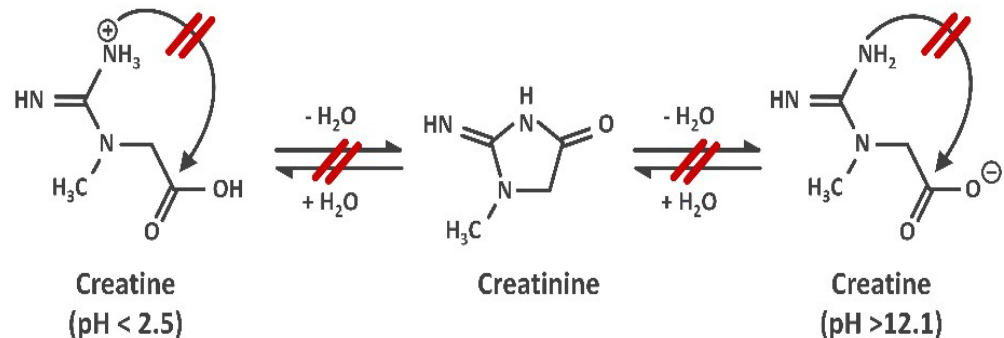
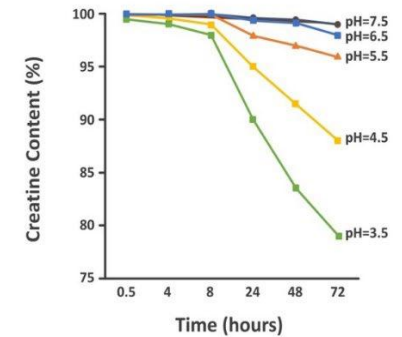
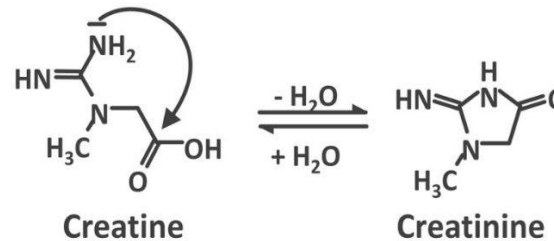


Changes in plasma creatine concentrations after administration of 5 grams of creatine monohydrate (CrM) in solution (Panel A); water, 2 grams of CrM administered in solution, or 408 grams of slightly cooked meat containing 5.4 grams of creatine (Panel b); or 2 grams of CrM provided in solution, gel suspension, or in a hard candy lozenge (Panel C). From Kreider et al. *Nutrients*, 2022.

# Stability of Creatine Monohydrate

Jäger et al. *Amino Acids*. 40:1369-83, 2011; Kreider, Jäger, Purpura. *Nutrients*, 14(5):1035, 2022

- CrM is very **stable in powder form**
- Conversion of creatine to creatinine increases in beverages with pH between 2.5 – 12.1
- Conversion is halted with pH < 2.5 which is why **CrM is not converted to creatinine during digestion and is 100% bioavailable.**



# Creatine Monohydrate

## *Supplementation Protocols*



Kreider et al. *J Int Soc Sports Nutr.* 14:18, 2017.  
Kreider & Stout. *Nutrients.* 13(2): 447, 2021

- ***Loading/Maintenance Protocol***
  - Ingest 0.3 g/kg/d (15-25 g/d) of CrM for 5-7 d
  - Ingest 0.03 g/kg/d (3-5 g/d) of CrM to maintain
  - Promotes a **20 – 40% increase in 7-days**
- ***Low Dose Protocol***
  - Ingest 0.03 g/kg/d (3-5 g/d) of CrM
  - Promotes about **15 – 20% increase in 30-days**
- ***General Health***
  - Ingest 0.03 g/kg/d (3-5 g/d) of CrM

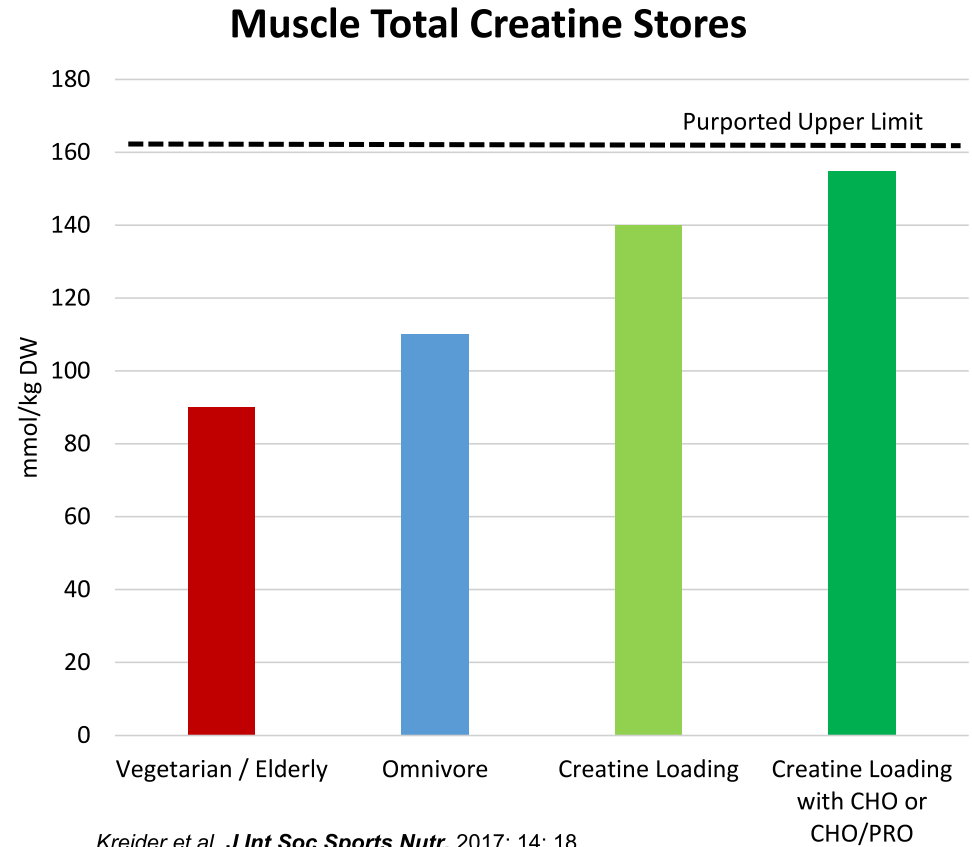
*\*Takes about 4-6 weeks for muscle creatine levels to return to baseline after loading.*



# Creatine Monohydrate Supplementation

*Bonilla et al. Nutrients: 13, 1238, 2021*

- Dietary supplementation with CrM can **increase muscle creatine stores by 20 – 40%** depending on initial levels.
- **“Non-responders”** are people who have higher creatine stores and only observe a **10 – 15% increase in muscle creatine with loading**. Better termed **“less responsive”**
- **Co-ingestion with CHO and CHO/PRO maximizes saturation and all become “responders”**



# ISSN Position Stand

## Creatine

1. **Creatine monohydrate** is the **most effective ergogenic nutritional supplement currently available to athletes in terms of increasing high-intensity exercise capacity and lean body mass during training.**
2. **Creatine monohydrate** supplementation is **not only safe, but has been reported to have a number of therapeutic benefits** in healthy and diseased populations ranging from infants to the elderly. There is **no compelling scientific evidence** that the short- or long-term use of creatine monohydrate (**up to 30 g/day for 5 years**) has **any detrimental effects** on otherwise healthy individuals or among clinical populations who may benefit from creatine supplementation.

issn

international society of sports nutrition  
The ISSN - Why Go Anywhere Else?

Reader or Journal of the International Society of Sports Nutrition (2017) 14:18  
DOI 10.1186/s12970-017-0173-z

Journal of the International  
Society of Sports Nutrition

REVIEW

Open Access

### International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine

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Daren G. Candow<sup>7</sup>, Susan M. Kleiner<sup>8</sup>, Anthony L. Almada<sup>9</sup> and Hector L. Lopez<sup>10\*</sup>

#### Abstract

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations which may help explain the observed improvements in high-intensity exercise performance leading to greater training adaptations. In addition to athletic and exercise improvement, research has shown that creatine supplementation may enhance post-exercise recovery, injury prevention, thermoregulation, rehabilitation, and concussion and/or spinal cord neuroprotection. Additionally, a number of clinical applications of creatine supplementation have been studied involving neurodegenerative diseases (e.g., muscular dystrophy, Parkinson's, Huntington's disease), diabetes, osteoarthritis, fibromyalgia, aging, brain and heart ischemia, adolescent depression, and pregnancy. These studies provide a large body of evidence that creatine can not only improve exercise performance, but can play a role in preventing and/or reducing the severity of injury, enhancing rehabilitation from injuries, and helping athletes tolerate heavy training loads. Additionally, researchers have identified a number of potentially beneficial clinical uses of creatine supplementation. These studies show that short and long-term supplementation (up to 30 g/day for 3 years) is safe and well-tolerated in healthy individuals and in a number of patient populations ranging from infants to the elderly. Moreover, significant health benefits may be provided by ensuring individual low dietary creatine ingestion (up to 3 g/day) throughout the lifespan. The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN).

**Keywords:** Ergogenic aids, Performance enhancement, Sport nutrition, Athletes, Muscular strength, Muscle power, Clinical applications, Safety, Children, Adolescents

#### Background

Creatine is one of the most popular nutritional ergogenic aids for athletes. Studies have consistently shown that creatine supplementation increases intramuscular creatine concentrations, can improve exercise performance, and/or improve training adaptations. Research has indicated that creatine supplementation may enhance post-exercise recovery, injury prevention, thermoregulation, rehabilitation, and

concussion and/or spinal cord neuroprotection. A number of clinical applications of creatine supplementation have also been studied involving neurodegenerative diseases (e.g., muscular dystrophy, Parkinson's, Huntington's disease), diabetes, osteoarthritis, fibromyalgia, aging, brain and heart ischemia, adolescent depression, and pregnancy. The purpose of this review is to provide an update to the current literature regarding the role and safety of creatine supplementation in exercise, sport, and medicine and to update the position stand of International Society of Sports Nutrition (ISSN) related to creatine supplementation.

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<https://jissn.biomedcentral.com/articles/10.1186/s12970-017-0173-z>

# Bioavailability, Efficacy, Safety

Kreider, Jäger, Purpura. *Nutrients*. 14, 1035, 2022

- ***CrM remains the only source of creatine that has substantial evidence of bioavailability, efficacy and safety and is considered GRAS by the U.S. FDA, is approved for use with accompanying health claims in the EU, has been extensively reviewed and approved by Health Canada, and is approved to be sold in major global markets.***
- The ***bioavailability, efficacy, safety, and regulatory status of other purported sources of creatine are less clear with only a few having some data some data supporting efficacy compared to placebo*** (see Table 3).
- There is ***no evidence*** that ***other “forms” of creatine are more bioavailable, effective, or safer forms of creatine compared to CrM.***

Table 3

Categorization of purported sources of creatine based on bioavailability, efficacy, and safety.

Strong Evidence	Some Evidence	No Evidence
Creatine Monohydrate	Creatine Citrate	5-Hydroxytryptamine Creatine
	Creatine Pyruvate	Creatine Benzyl Ester
	Magnesium Creatine Chelate	Creatine Beta-Alaninate
	Creatine Ethyl Ester	Creatine Carnitine
	Creatine HCl	Creatine Ethyl Ester Malate
	Creatine Nitrate	Creatine Ethyl Ester Pyruvate
	Buffered Creatine Monohydrate	Creatine Fumarate
		Creatine Gluconate
		Creatine Glutamate
		Creatine Hydroxycitrate
		Creatine Lactate
		Creatine Malate
		Creatine Maleate
		Creatine Methyl Ester HCL
		Creatine Monohydrate Dextrose
		Creatine Orotate
		Creatine Phosphate Lactate
		Creatine Pyroglutamate
		Creatine Pyruvate Monohydrate
		Creatine Serum
		Creatine Sulfate Monohydrate
		Creatine Taurinate
		Creatine Trinitrate
		Creatine $\alpha$ -ketoglutarate
		Creatine-CoA
		Creatinol-O-Phosphate
		Creatyl-L-Leucine
		Di-Acetyl Creatine Ethyl Ester
		Disodium Creatine Phosphate
		Methyl-Amino-Creatine
		Phospho-Creatine
		Polyethylene Glycosylated Creatine

*South Korea: CrM was approved by the MFDS for use as a dietary supplement in 2008 with an accompanying health claim.*

# Creatine in Health and Disease

*Kreider & Stout, Nutrients 2021, 13(2), 447*



- T Cell Anti-tumor Immunity & Cancer Therapy
- Heart Disease
- Vascular Health
- Inflammatory Bowel Disease
- Chronic Dialysis Patients
- Post-Viral Fatigue & Long-COVID
- Mitochondrial Dysfunction
- Safety, Efficacy & Regulatory Status
- Depression
- Fertility
- Skin Health
- Creatine Synthesis & Transporter Deficiencies
- Pregnancy & Newborn Health
- Children and Adolescents
- Exercise, Performance & Recovery
- Medical Rehabilitation
- Women's Health
- Aging & Older Adults
- Brain Health
- Glucose Management and Diabetes
- Immune Support

# Creatine for Health

*Kreider & Stout, Nutrients 2021, 13(2), 447*

*Creatine monohydrate  
supplementation promotes general  
health throughout the lifespan.*

*Recommended that all individuals  
consume 3 grams/day of CrM  
throughout the lifespan.*





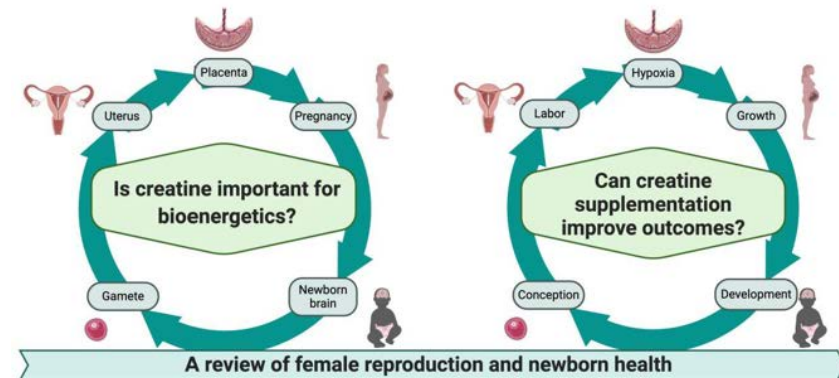
# Pregnancy & Newborn Health

*Muccini et al. Nutrients 2021, 13(2), 490*



Stacey Ellery, PhD

- Creatine Metabolism in Female Reproductive Health
  - Oocytes and Surrounding Cells
  - Follicular Fluid, the Oviduct and Oviductal Fluid
  - The Endometrium
  - The Myometrium
- Human Placenta
- Maternal Creatine Metabolism during Pregnancy
- Fetal Creatine Metabolism
- Use of Supplementary Creatine to Prevent Perinatal Brain Injury
- Creatine Metabolism in the Neonate, with a Focus on the Potential Consequences of Preterm Birth



# Children & Adolescents

Jagim et al. *Nutrients* 2021, 13(2), 664



Andrew Jagim, PhD

- There is strong rationale for creatine use in pediatric patients with **neuromuscular and metabolic disorders** such as **myopathies, muscular dystrophy, muscle-wasting conditions, cancer cachexia, clinical depression, traumatic brain injuries, spinal cord injuries, orthopedic injuries, and periods of bed rest or immobilization.**
- Although data are limited, therapeutic benefits have been reported in several of these conditions.
- Studies in **adolescent athletes generally report improvements exercise capacity with no adverse events.**



# Exercise, Performance, and Recovery

*Wax et al., Nutrients. 13(5), 1915, 2021*



Ben Wax, PhD

- **Strength & Power**

- < 2 Weeks
- > 2 Weeks
- Athletes & Sport Performance
- Untrained

- **Prolonged High Intensity Exercise**

- **Sport Specific Performance**

- Agility
- Sprint Performance
- Jump Performance

- **Competitive Athletes**

- American Football
- Track & Field
- Swimming
- Endurance Performance
- Soccer
- Hockey
- Squash/Handball
- Wrestling
- Tennis
- Volleyball

- **Recovery**

- Intermittent Exercise
- Loss of force, muscle damage, soreness, inflammation
- Immobilization

- **Other Considerations**

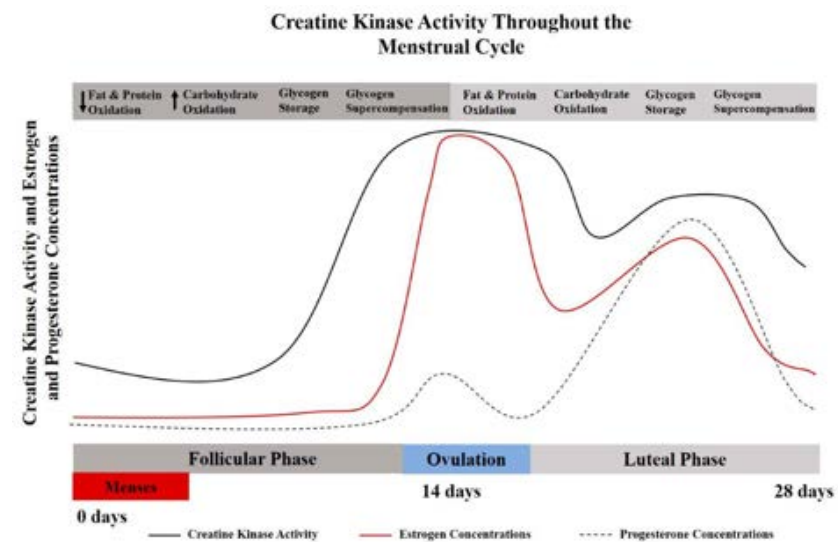
# Women's Health

Smith-Ryan et al. *Nutrients* 2021, 13(3), 877

- Females typically have **70–80% lower endogenously produced creatine stores compared to males**.
- Due to hormone-related changes to CK and PCr, CrM supplementation may be important during **menses, pregnancy, post-partum, during and post-menopause**.
- CrM supplementation among **pre-menopausal females** appears to be effective for improving strength and exercise performance.
- **Post-menopausal females** may also experience benefits in skeletal muscle size and function and favorable effects on bone when combined with resistance training.
- Pre-clinical and clinical evidence indicates positive effects from creatine supplementation on **mood and cognition**, possibly by restoring **brain energy levels** and homeostasis.



Abbie Smith-Ryan, PhD



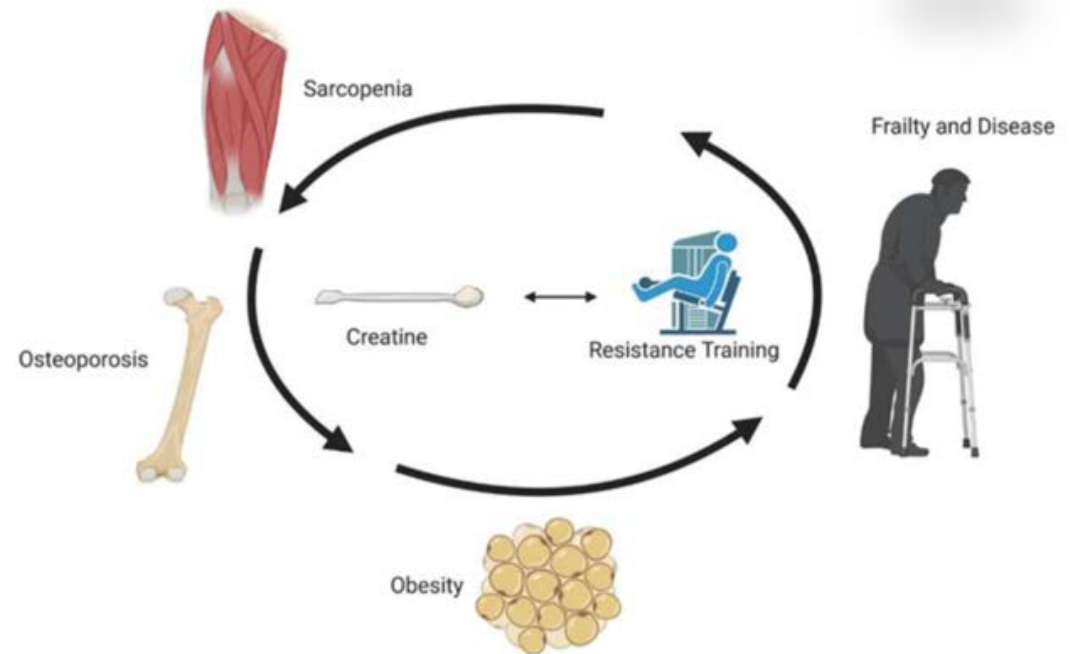
# Creatine for Older Adults

Candow et al. *Nutrients* 2021, 13(3), 745

- CrM supplementation, primarily when combined with resistance training (RT), has ***favorable effects on aging muscle, bone and fat mass, muscle and bone strength, and tasks of physical performance in healthy older adults.***
- More research is needed on the role of CrM supplementation older adults with ***osteosarcopenia, sarcopenic obesity, physical frailty, or cachexia.***



Darren Candow, PhD



Potential effect of creatine, with and without resistance training.



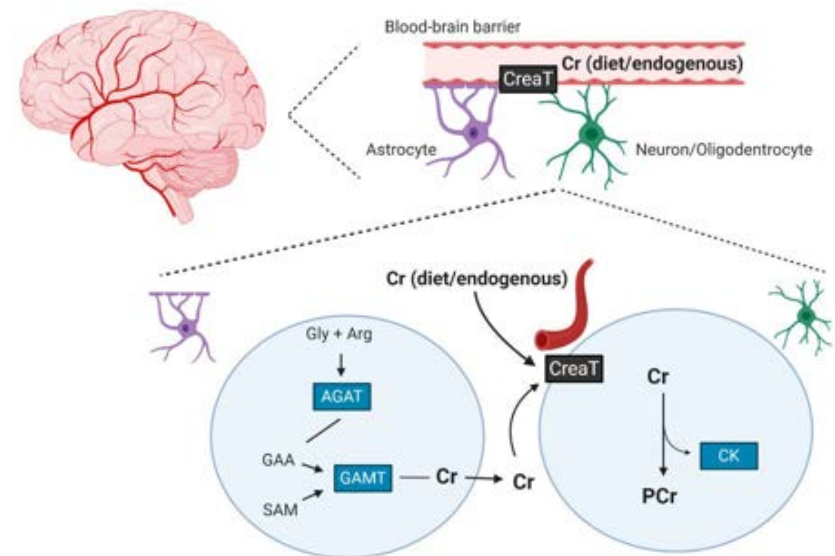
# Brain Health

Roschel et al. *Nutrients* 2021, 13(2), 586



Eric Rawson, PhD

- Creatine supplementation has been reported to **increase brain PCr content by 5–15%** and thereby **enhance brain bioenergetics**.
- 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, mild **traumatic brain injury, aging, Alzheimer's disease, depression**).
- Despite this, the **optimal creatine protocol** able to increase brain creatine levels **is still to be determined**.
- Supplementation **studies** concomitantly assessing **brain creatine and cognitive function are needed**.



# Heart Health and Disease

*Balestrino, Nutrients 2021, 13(4), 1215*



Maurizio Balestrino, MD

- ***In heart failure, myocardial creatine content decreases*** and is associated with the decreased force of contraction.
- ***Cr supplementation*** can increase PCr availability thereby providing an ***important energy-source during ischemic events, improve heart contraction, and decrease ischemia-induced arrhythmias.***
- CrM supplementation may also ***prevent cardiac toxicity of the chemotherapy compounds*** because anthracyclines reduce expression of the creatine transporter, and because of the pleiotropic antioxidant properties of creatine thereby reducing muscle damage.



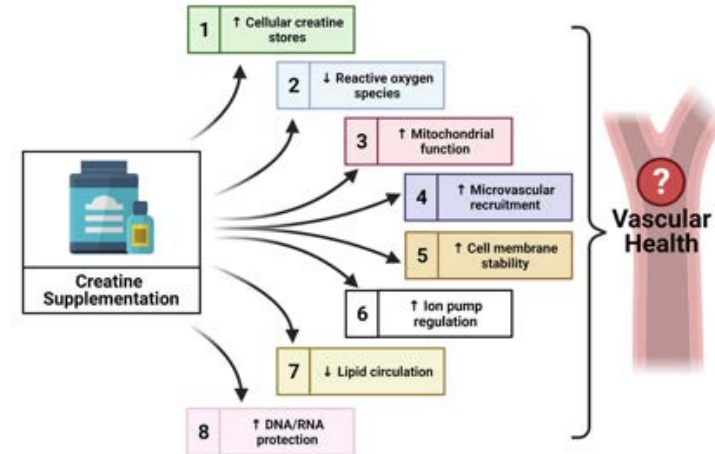
# Vascular Health

Clarke et al., *Nutrients* 2021, 13(3), 857



Holly Clarke, cPhD

- Increase natural **endothelial cell stores of high-energy metabolites**.
- Serve as a **direct- and indirect- antioxidant**, scavenging free radicals which could thereby improve eNOS efficiency, NO synthesis, and NO bioavailability.
- Improve the integrity and **efficiency of the mitochondria** resulting in **reduced mtROS production**.
- Increase microvascular density, recruitment, **and vasomotor function**.
- Improve **extracellular membrane stability** and decrease leakiness.
- Aid in the **function of endothelial cell and vascular smooth cell** energy-dependent ion pumps, benefiting the propagation of endothelium-derived hyperpolarization factors.
- **Reduce** circulating amounts of damaging **lipids such as LDL-C and total cholesterol**.
- **Protect DNA and RNA** from cytotoxic stimuli such as oxidative stress.



# Creatine in Disease

*Kreider & Stout, Nutrients 2021, 13(2), 447*

*Creatine monohydrate  
supplementation has potential  
therapeutic benefit for a number of  
populations!*



# Creatine Synthesis & Transporter Deficiencies

*Kreider & Stout, Nutrients 2021, 13(2), 447*

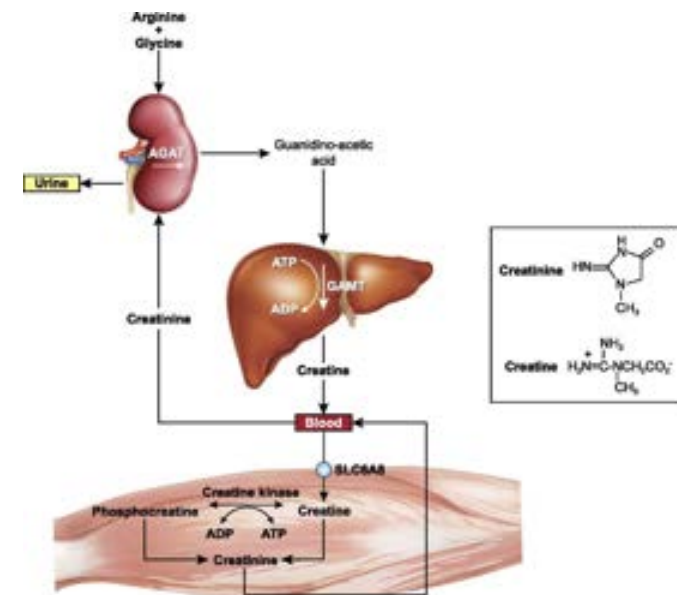


RB Kreider



JR Stout

- Some individuals are born with **rare deficiencies in creatine-related enzymes or transporters** (e.g., AGAT, GAMT, and CRTR) that reduce the ability to transport creatine into the cell or synthesize creatine.
- Individuals with creatine synthesis deficiencies and creatine transporter mutations typically present with **low brain Cr and PCr levels** that have been associated with **muscle myopathies (e.g., weakness), voluntary or involuntary movement disorders** that can affect **muscle function** and **coordination, speech development, epilepsy, cognitive and motor development delays, and/or autism**.
- High dose, long-term **CrM supplementation** (e.g., **0.3–0.8 g/kg/day**) has generally been found to **improve clinical outcomes**, particularly in patients with **AGAT and GAMT deficiencies**.



Chu et al. Drug Metabol Disposition, September 2016, 44 (9) 1498-1509



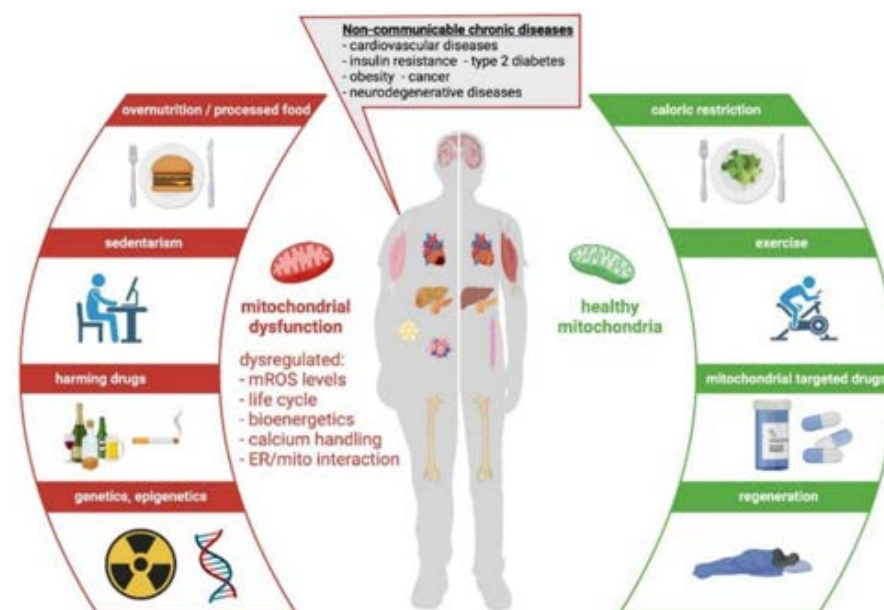
# Mitochondrial Dysfunction

Marshall et al., *Nutrients* 2022, 14(3), 529



Robert Percy Marshall, PhD

- CrM supplementation improves high-energy phosphate availability as well as has **antioxidative, neuroprotective, anti-lactatic, and calcium-homoeostatic effects**.
- These characteristics may have a **direct impact on mitochondria's survival** and health particularly during stressful conditions such as ischemia and injury.
- It appears that CrM supplementation may have a role in **improving cellular bioenergetics in several mitochondrial dysfunction-related diseases, ischemic conditions, and injury pathology** and thereby could provide therapeutic benefit in the management of these conditions.



# Medical Rehabilitation

Harmon et al. *Nutrients* 2021, 13(6), 1825



Kylie Harmon, cPhD

- Likely Effective:
  - Recovery from Exercise
  - Spinal Cord Injury
  - Arthritic Diseases
  - Muscular Dystrophy
- Possibly Effective
  - Acute Injury
  - Immobilization
  - COPD
  - Chronic Heart Failure
  - Mitochondrial Cytopathies
  - Charcot-Marie-Tooth Disease
- Not Likely Effective:
  - ALS
  - Multiple Sclerosis
  - Postoperative Orthopedic Recover
  - Parkinson's Disease



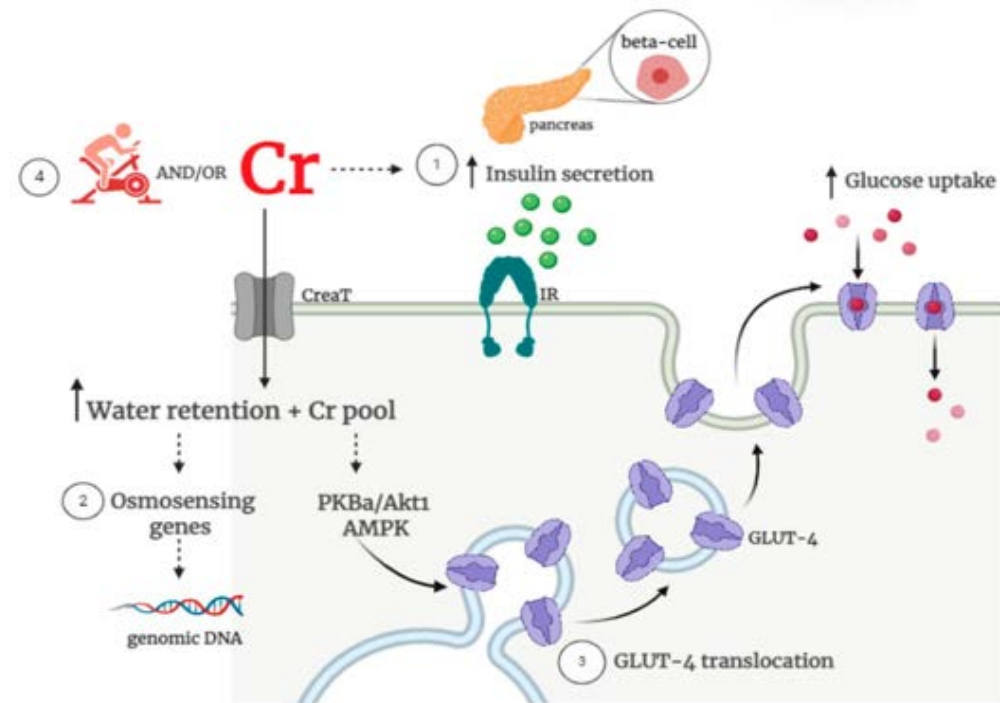
# Glucose Management and Diabetes

Solis et al. *Nutrients* 2021, 13(2), 570



Bruno Gualano, PhD

- CrM supplementation has the potential to promote changes in **glucose metabolism** that may favor a healthier metabolic profile, **particularly when combined with exercise training**.
- A few studies have **reported promising benefits of creatine on glucose control, especially with exercise**.
- **Additional large, longer-term, controlled trials involving T2DM** with variable disease severity and under different pharmacological treatments are necessary to draw firm conclusions on the efficacy and safety of creatine as an **anti-diabetic intervention**.



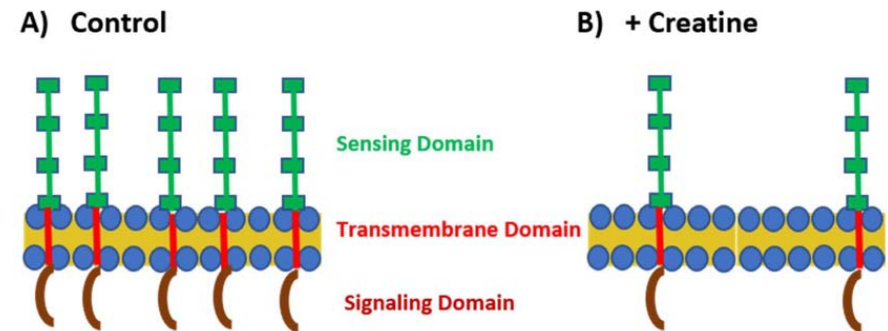
# Immune Response

*Bredahl et al. Nutrients 2021, 13(3), 751*

- Cr has diverse effects on components of the ***innate and adaptive immune response that are not trivial.***
- In conditions exacerbated by proinflammatory mediators, ***CR administration should be considered as an adjuvant therapy since it appears to ameliorate proinflammatory processes*** characteristic of an M1 phenotype, and all available data attest to its safety.
- Based on the current literature, there is clearly a path to justify the continued investigation of the ***potential influence that CR has upon the immune response,*** particularly in the realm of ***autoimmune and infectious diseases.***



Kristen Drescher, PhD



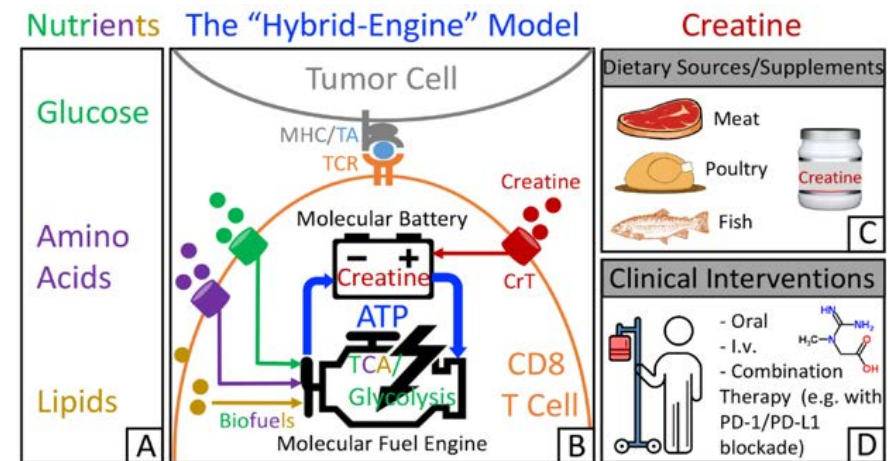
# T Cell Antitumor Immunity & Cancer Immunotherapy

Li and Yang. *Nutrients* 2021, 13(5), 1633



Lili Yang, PhD

- Creatine is an **important metabolic regulator conserving bioenergy to power CD8 T cell antitumor reactivity in a tumor microenvironment.**
- CrM supplementation has been shown **to enhance antitumor T cell immunity** in multiple preclinical mouse tumor models and, importantly, to synergize with other **cancer immunotherapy modalities**, such as the PD-1/PD-L1 blockade therapy, to improve antitumor efficacy.
- **New T cell immunotherapies, traditional chemotherapy, targeted therapy, and radiation therapy**, may also have improved therapeutic efficacy when combined with CrM supplementation.





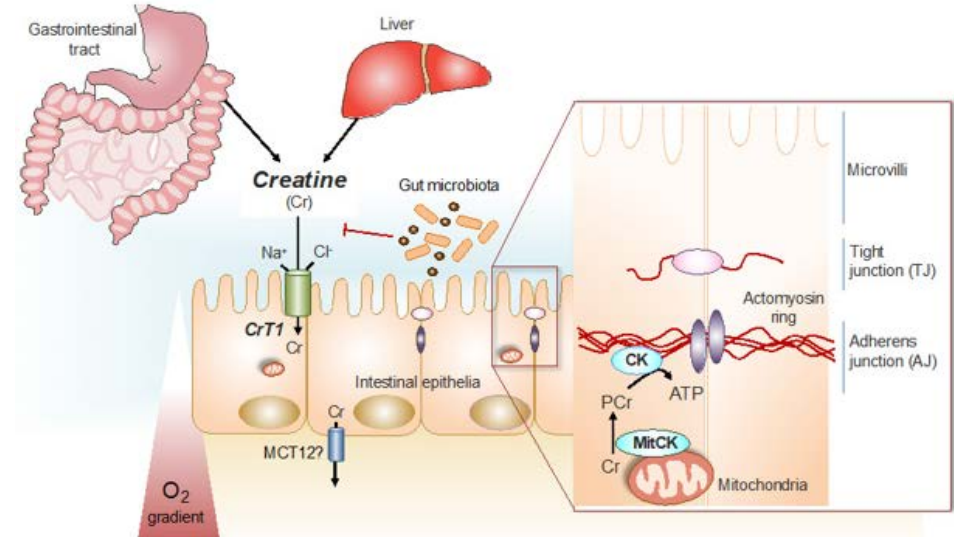
# Inflammatory Bowel Disease

Wallimann et al., *Nutrients* 2021, 13(5), 1429

- CrM supplementation, a pleiotropic cellular energy precursor, is likely to be effective in inducing a ***favorable response and/or remission in patients with inflammatory bowel diseases (IBD), like ulcerative colitis and/or Crohn's disease.***
- A current pilot clinical trial that incorporates the use of oral CrM at a dose of  $2 \times 7$  g per day, over an initial period of 2 months in conjunction with ongoing therapies (NCT02463305).
- Larger long-term CrM studies are warranted.
- ***CrM in reducing or alleviating the symptoms of IBD.***



Caroline H.T. Hall, MD, PhD



# Anti-Depressive Effects

Kreider & Stout, *Nutrients* 2021, 13(2), 447

- Reports since the **early 1980's** have suggested that creatine metabolism and/or availability may have **anti-depressive effects**.
- These studies and others have provided the basis for assessing the effects of **creatine** and/or creatine precursors like S-adenosyl-L-methionine (**SAMe**) and **GAA** affect brain phosphagen levels, markers of depression, and/or the therapeutic efficacy of anti-depressant medications.
- Although more research is needed, there is **some evidence suggesting that creatine may help individuals manage some types of depression and/or anxiety disorders, particularly when combined with choline**.
- Also evidence that depression risk is inversely related to dietary creatine intake.



Brent Kious, MD, PhD



Perry Renshaw, MD, PhD



# Creatine in COVID Recovery

*Kreider & Stout, Nutrients 2021, 13(2), 447*

*Creatine monohydrate  
supplementation may help people  
with chronic fatigue or long-COVID  
recover!*



# Post-Viral Chronic Fatigue

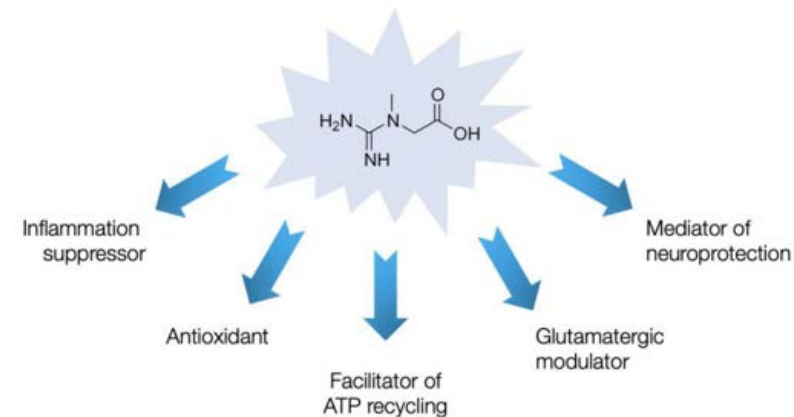
*Ostojic, Nutrients 2021, 13(2), 503*



Sergej Ostojic, MD, PhD

- **Chronic fatigue syndrome** (CFS), also known *as postviral fatigue syndrome* (PFS) or *myalgic encephalomyelitis* (ME), is characterized by fatigue and associated symptoms (e.g., muscle and joint pains, anxiety, cognitive and sleep disorders, intolerance to physical exertion) persisting more than six months in duration.
- Although the etiology is unknown, **CrM supplementation may improve functional capacity and help people with CFS conditions better manage this condition.**
- While more research is needed, there is some support that creatine and/or GAA may have some therapeutic benefit for patients with **CFS, PFS, EM, fibromyalgia, as well as patients with long-COVID.**

Possible mechanisms of creatine action in post-viral fatigue syndrome.



# Summary

- The **benefits of CrM supplementation go well beyond increasing muscle Cr and PCr levels** and thereby enhancing high-intensity exercise and training adaptations.
- Research has clearly shown **several health and/or potential therapeutic benefits** as we age and in clinical populations that may benefit by enhancing Cr and PCr levels.
- CrM may strengthen the immune system and help them manage chronic fatigue and/or recover from COVID.
- This provides a **great opportunity for additional research as well as to market creatine to the general population as a supplement to promote general health.**



[CreatineforHealth.com](http://CreatineforHealth.com)

# The Role of Creatine in Health and Disease



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*Disclosures:* Receive industry sponsored research grants and serve as a scientific and legal consultant.