Endocrinology, Diabetes & Metabolism

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REVIEW ARTICLE OPEN ACCESS

Effects of Zinc Supplementation on Glycemic Control, Insulin Resistance, Inflammation and Oxidative Stress in Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Jessica Paola Loaiza-Giraldo[1] | Florencia Amigo-Fierro[2] | Camila Ignacia Cancino-Castro[2] | Matias Donoso-Emig[2] | Murtaja Satea[3] | Ignacia Farías-Quinteros[2] | Alejandro Bruna-Mejias[2] | Pablo Nova-Baeza[2] | Mathias Orellana-Donoso[4,5] | Héctor Gutiérrez-Espinoza[6,7] | Gloria Cifuentes-Suazo[8] | Juan Sanchis-Gimeno[9] | Maria Piagkou[10] | Vitor E. Valenti[11] | Jose E. Leon-Rojas[12,13] | Juan José Valenzuela-Fuenzalida[2,14]

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Zinc and Health Outcomes

- Zinc is an essential micronutrient that plays a crucial role in the metabolism of proteins, lipids, and nucleic acids, as well as in gene transcription. This micronutrient is critical for numerous physiological processes, including reproduction, immune function, and wound healing. At the cellular level, zinc is indispensable for the normal function of macrophages, neutrophils, natural killer cells, and the complement system.
- Despite being one of the most abundant trace elements in the human body, zinc cannot be stored in significant amounts and therefore requires regular dietary intake or supplementation to maintain adequate levels. Dietary sources include meat, fish, legumes, nuts, and other plant-based sources, although absorption efficiency varies depending on the food matrix.

McClung JP. Iron, Zinc, and Physical Performance. Biol Trace Elem Res. 2019 Mar;188(1):135-139.
Skalny AV, Aschner M, Tinkov AA. Zinc. Adv Food Nutr Res. 2021;96:251-310.

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2018 NHANES Data on Zinc Levels

- Approximately 3.8% of children (<10 y)
- 8.6% of males (≥10 y)
- 8.2% of females (≥10 y)
- Lower serum albumin and later day blood draw associated with lower levels

J Nutr 2018;148:1341–1351.

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RDI

Recommended daily elemental zinc intake for the prevention of zinc deficiency includes the following:

- 3 mg/d for children younger than 4
- 5 mg/d for children aged 4 to 8
- 8 mg/d for children aged 9 to 13
- 9 mg/d for nonpregnant, nonlactating women
- 11 mg/d for men
- 11 to 12 mg/d for pregnant and lactating women

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- 18 RCTs
- 1,023 participants with type 1, type 2, gestational and prediabetes
- Age average 44 years
- Interventions from 6 weeks to 1 year (average 19 weeks)
- Amount of Zn varied from 4 to 75 mg/day

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Results: Eighteen RCTs involving 1023 participants met the eligibility criteria. Zinc supplementation significantly increased plasma zinc concentrations (MD = 7.80; 95% CI 4.33 to 11.26) and improved insulin resistance, as reflected by reductions in serum insulin (MD = −2.50; 95% CI −4.69 to −0.31) and HOMA-IR (MD = −1.10; 95% CI −2.05 to −0.15). Total cholesterol decreased modestly but significantly (MD = −5.70; 95% CI −7.50 to −3.89), representing a relatively small absolute reduction, while LDL cholesterol showed a modest increase (MD = 3.46; 95% CI 1.48 to 5.43), although the clinical relevance of this finding remains uncertain. Inflammatory and oxidative stress markers improved, including reductions in C-reactive protein (SMD = −0.91; 95% CI −1.43 to −0.38) and malondialdehyde (SMD = −0.76; 95% CI −1.34 to −0.18), alongside an increase in total antioxidant capacity (SMD = 1.79; 95% CI 0.68 to 2.91).

Endocrinology, Diabetes & Metabolism, 2026; 9:e70264
https://doi.org/10.1002/edm2.70264

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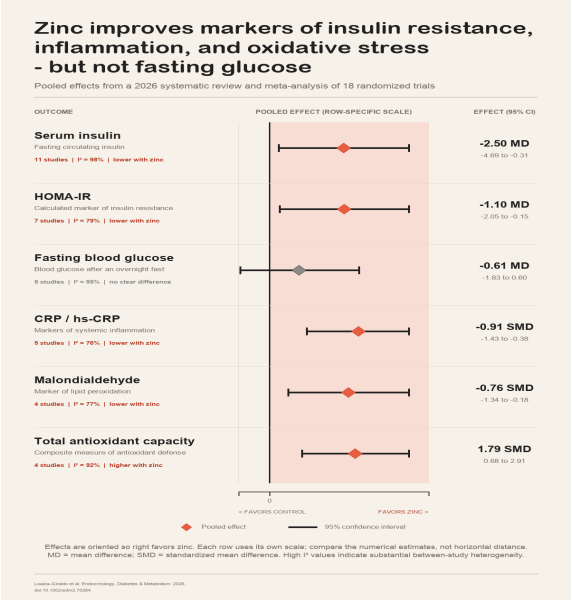

Endocrinology, Diabetes & Metabolism, 2026; 9:e70264

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Who is at higher risk for Zinc deficiency?

- Older adults due to lower food intake or reduced absorption
- Chronic acid suppression from proton pump inhibitors
- Individuals on a plant-based diet due to insufficient Zn content as well as phytates, which block absorption.
- Chronic GI issues e.g. celiac, Crohn's, post bariatric surgery
- Pregnant-nursing women

https://www.ncbi.nlm.nih.gov/books/NBK493231/

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Common Symptoms of Zinc Deficiency

- Loss of taste or smell
- Poor appetite
- Depressed Mood, ADHD, Anxiety
- Decreased Immunity
- Delayed/poor wound healing
- Diarrhea
- Hair Loss

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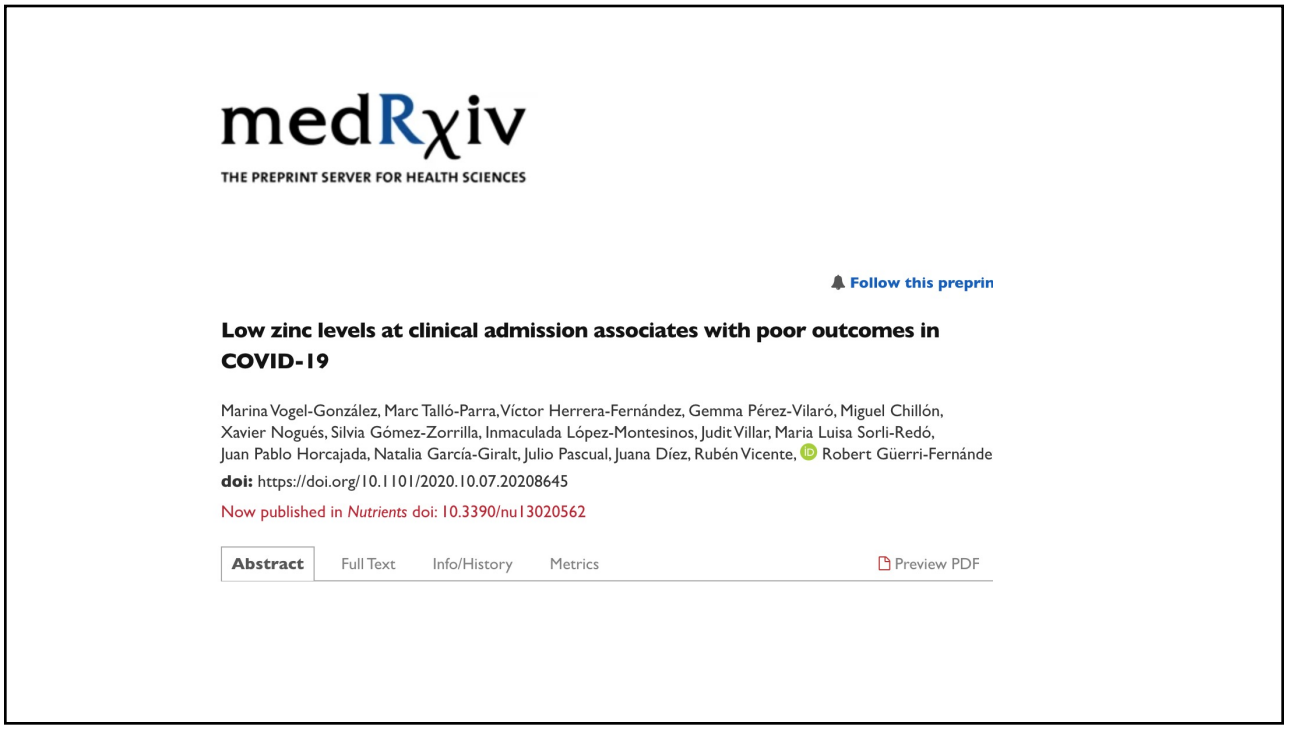

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European Journal of Epidemiology (2020) 35:1149–1156
https://doi.org/10.1007/s10654-020-00644-1

INFECTIOUS DISEASE EPIDEMIOLOGY

Check for updates

Serum copper-to-zinc-ratio and risk of incident infection in men: the Kuopio Ischaemic Heart Disease Risk Factor Study

In conclusion, our data suggest that an increased Cu/Zn-ratio and especially serum Cu concentration are associated with increased risk of incident infections in middle-aged and older men in Eastern Finland.

42–60 years and free of severe infectious disease at baseline in 1984–1989 from the prospective population-based Kuopio Ischaemic Heart Disease Risk Factor Study. The main outcome was an incident infection leading to hospitalization. Cox proportional hazards regression models were used for statistical analysis. During the average follow-up of 19.2 years, 636 incident first cases of infections were diagnosed. The hazard ratio (HR) of developing an incident infectious disease in the highest compared to the lowest Cu/Zn-ratio quartile after adjustment for age and baseline examination year was 1.35 [95% confidence interval (CI) = 1.07–1.69, *P*-trend across quartiles = 0.005]. The association was slightly attenuated after addi-

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Importance of Copper/Zinc Ratio

Why the Ratio Matters

- **Opposing Roles:** Copper and zinc are essential trace minerals that have a synergistic yet antagonistic relationship. They compete with each other for absorption in the gut and binding sites in cells.
- **Superior Indicator:** Evaluating the balance via a ratio is often more informative than looking at single nutrient levels alone. An abnormal balance can reveal hidden nutritional issues or chronic stress even if individual levels seem normal.
- **Ideal Proportion:** *A healthy ratio generally ranges from about 1 part copper to 8 to 10 parts zinc*.

Health Implications of Imbalances

- **High Ratio (Excess Copper or Low Zinc):** A high ratio is frequently linked to systemic inflammation, oxidative stress, infections, and chronic illnesses. It is also studied in relation to cardiovascular conditions, neurological issues, and certain cancers.

- **Low Ratio (Excess Zinc or Low Copper):** A low ratio can indicate a copper deficiency. This may impair red blood cell formation, iron metabolism, and nervous system function.

Nutrients 2021, 13, 946. https://doi.org/10.3390/nu13030946

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diseases

MDPI

Systematic Review

Zinc and Type 2 Diabetes: A Systematic Review with a Narrative

Zinc is mechanistically involved in insulin synthesis, antioxidant defense, and inflammation control, but current clinical evidence does not justify its use as a therapeutic agent in T2DM. Instead, assessment of zinc status and individualized correction of deficiency may represent a component of personalized nutritional support, particularly for patients with long disease duration, poordietary quality, or genetic predispositions affecting zinc metabolism.

Diseases 2025, 13, 396
https://doi.org/10.3390/diseases13120396

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BMC Cardiovascular Disorders https://doi.org/10.1186/s12872-026-06182-0

Article in Press

Zinc deficiency in patients with type 2 diabetes increases risk of cardiovascular diseases: Tehran

Zn deficiency is associated with a significantly increased risk of CVD events in patients with T2DM. Increased SZn concentration was associated with reduced risk of CVD events in patients with T2DM.

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Zahra Bahadoran, Fateme Ghafouri-Taleghani & Fereidoun Azizi

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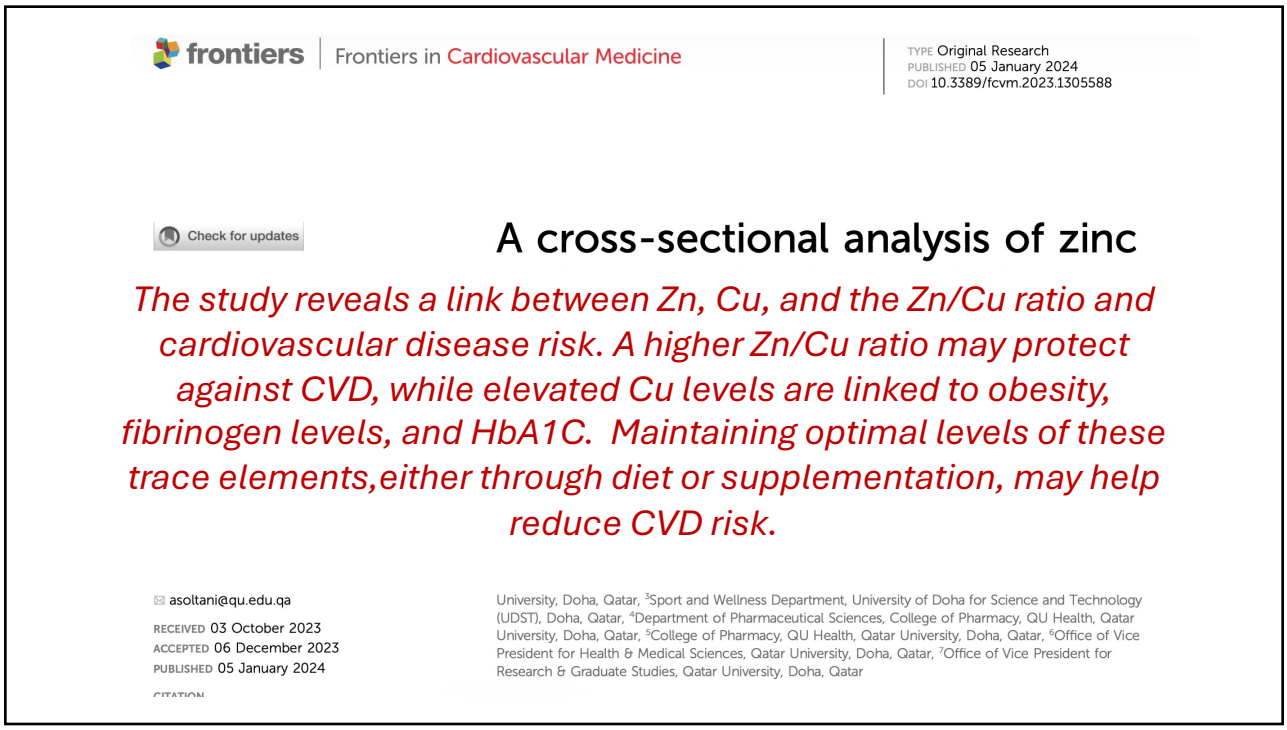

frontiers | Frontiers in Cardiovascular Medicine

TYPE Original Research
PUBLISHED 05 January 2024
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Check for updates

A cross-sectional analysis of zinc

The study reveals a link between Zn, Cu, and the Zn/Cu ratio and cardiovascular disease risk. A higher Zn/Cu ratio may protect against CVD, while elevated Cu levels are linked to obesity, fibrinogen levels, and HbA1C. Maintaining optimal levels of these trace elements,either through diet or supplementation, may help reduce CVD risk.

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