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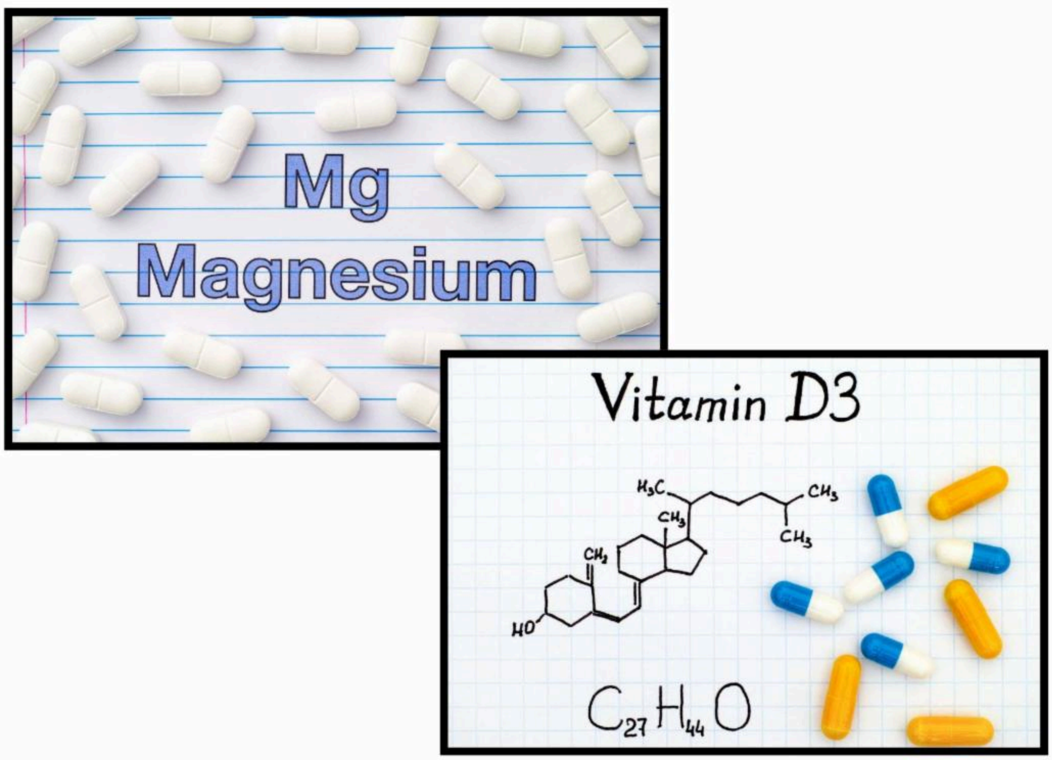

Researchers Finally Discover the Importance of Magnesium

by Wayne Persky

Anyone who has been following our magnesium and vitamin D recommendations will not be surprised by the results of a recently published research trial that should "open a few eyes" in the medical community by proving that magnesium is not just another electrolyte — it's essential for regulating vitamin D (Vanderbilt University Medical Center, 2025, December 30).[1]

For decades, vitamin D has been viewed as a paradox.

Observational studies consistently linked adequate vitamin D levels to lower risks of colorectal cancer, cardiovascular disease, fractures, and mortality. Yet large randomized trials have repeatedly failed to show clear benefits from vitamin D supplementation (alone).

Researchers at Vanderbilt University Medical Center finally did it right.

A new randomized clinical trial published in The American Journal of Clinical Nutrition, provides a compelling explanation for this disconnect (Sun et al., 2025).[2] The study showed that magnesium is not optional in vitamin D biology — it's an essential regulator. The studies redefine magnesium from a "supporting nutrient" into a master regulator of vitamin D metabolism, gut microbiome function, and colorectal cancer risk.

The Vanderbilt randomized trial demonstrated critical effects never previously shown in humans.

- Magnesium supplementation raised vitamin D levels in people who were deficient.
- Magnesium lowered vitamin D levels in people whose levels were already high.
- Rather than indiscriminately increasing vitamin D, magnesium normalized it, keeping levels within a physiologically optimal range.

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Magnesium is an essential regulator of Vitamin D.

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Magnesium also regulates the gut microbiome.

Note that the magnesium doses used in the trial were aligned with dietary intake, not simply megadoses.

This is vital insight.

Prior vitamin D trials assumed that “more is better.” The Vanderbilt data instead support a U-shaped risk curve, where both low and excessive vitamin D levels are associated with worse outcomes. The study shows that magnesium is the mechanism that keeps vitamin D in the protective middle zone. The trial helps explain a long-standing clinical mystery of why some patients take high doses of vitamin D, yet show little or no rise in blood levels

The lead investigator, Qi Dai, explained in the article that “Magnesium deficiency shuts down the vitamin D synthesis and metabolism pathway.”

That certainly wasn't news to most of us.

We've long been aware that magnesium is required for:

- Conversion of vitamin D to 25-hydroxyvitamin D (in the liver)
- Conversion to the active form, 1,25-dihydroxyvitamin D (in the kidneys)
- Vitamin D receptor signaling (VDR expression and function)
- Vitamin D transport and degradation (binding vitamin D to its transport protein in the blood)

Without adequate magnesium, vitamin D becomes biologically inert, regardless of the dose. This finding illustrates why “vitamin D resistance” is actually unrecognized magnesium deficiency.

Magnesium deficiency has long been a confounder in vitamin D research.

The implications are profound because magnesium deficiency is widespread. Up to 80% of U.S. adults fail to meet the RDA for magnesium. Deficiency is especially common in:

- Older adults
- Patients with chronic diarrhea
- Those using PPIs, diuretics, or certain antibiotics
- Individuals with metabolic or inflammatory diseases

Therefore, many vitamin D trials unknowingly tested vitamin D in a magnesium-deficient cohort, virtually guaranteeing inconsistent (unreliable) results.

The companion study from the Personalized Prevention of Colorectal Cancer Trial adds a second, equally important discovery.

Magnesium supplementation increased the abundance of two gut bacteria known to produce vitamin D locally in the gut, and suppress colorectal cancer. These organisms were:

- *Carnobacterium maltaromaticum*
- *Faecalibacterium prausnitzii*

Note that this effect occurred only in individuals with adequate Transient Receptor Potential Melastatin 7 (TRPM7) function.TRPM7 is a gene that codes for a unique protein also called TRPM7 central to magnesium transport and homeostasis. This confirms that genetics influence magnesium utilization, and introduces a critical dimension to vitamin D research.

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> **Genetics influence magnesium's roles.**

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> **Magnesium supplementation helps supress colorectal cancer.**

Vitamin D guidelines should be redone.

Current guidelines recommend testing for vitamin D level, and if the result is low, vitamin D intake should be increased. The correct approach should be to first verify that a patient's magnesium level is adequate (and corrected if necessary), before assessing vitamin D status.

The results of this study are especially important for IBD patients.

Patients with Crohn's, ulcerative colitis, and microscopic colitis (MC) find themselves victims of a perfect storm involving:

- Chronic intestinal inflammation
- Malabsorption
- Medication-induced mineral loss
- Heightened risk of osteoporosis

Magnesium deficiency is inherent in these diseases. Magnesium loss occurs via:

- Chronic diarrhea (osmotic + secretory)
- Reduced absorption in inflamed mucosa
- Increased renal wasting during inflammation
- PPI and diuretic use (very common in MC)
- Steroid exposure (even budesonide contributes indirectly)

This means that many IBD/MC patients are magnesium-deficient even when serum magnesium is "normal." The Vanderbilt trials explain why this matters. Clinicians commonly observe that:

- Patients take vitamin D
- Blood levels barely rise
- Bone density continues to decline

The Vanderbilt trial shows why.

Magnesium deficiency shuts down vitamin D synthesis, activation, transport, and receptor signaling. For IBD/MC patients (under medical care):

- Vitamin D is prescribed
- Magnesium deficiency is ignored
- Vitamin D becomes metabolically ineffective

This leads to the false conclusion that "Vitamin D doesn't work for IBD patients " The reality is: vitamin D cannot work without magnesium.

The real cause of bone loss in IBD/MC is:

- Chronic inflammation, which leads to osteoclast activation (bone resorption)
- Magnesium deficiency, which causes impaired bone mineralization
- Vitamin D resistance causes impaired calcium handling.

- Steroid exposure causes suppressed osteoblast activity (suppressed rebuilding of bone tissue).
- Hypogonadism or estrogen loss cause accelerated bone resorption.

Vitamin D alone addresses none of these issues adequately. Magnesium's role in bone health is independent and overriding.

Magnesium:

- Is required for hydroxyapatite formation. Hydroxyapatite (HA) is a naturally occurring mineral, a form of calcium phosphate, that makes up over 90% of tooth enamel and about 60-70% of bones.
- Determines whether calcium hardens bone or stays soluble
- Regulates parathyroid hormone (PTH)
- Controls vitamin D activation and degradation

Without magnesium:

- Calcium supplementation is inefficient.
- Vitamin D signaling is impaired.
- Bone becomes brittle, not dense.

This explains why many IBD/MC patients take calcium + vitamin D, yet still lose bone, and still experience fractures.

Serum tests provide misleading bone risk assessment.

Serum magnesium is a poor indicator because less than 1% of magnesium is in serum and serum magnesium levels are automatically tightly regulated by the body. Because of that, a deficiency is masked until it becomes truly severe. IBD/MC patients can be functionally magnesium-deficient for years, yet still show "normal" labs.

DEXA scans tend to underestimate fracture risk because bone quality (microarchitecture) deteriorates before density problems show up. Magnesium deficiency worsens bone fragility without large bone mass density (BMD) declines. This is why fractures often occur in IBD/MC patients with "osteopenia," not osteoporosis.

The take-home message from these trials:

The Vanderbilt trials show that vitamin D cannot be evaluated independently of magnesium level any more than calcium can be evaluated independently of vitamin D. These trial results suggest that:

- Vitamin D supplementation without magnesium is biologically incomplete.
- Magnesium status should be assessed before adjusting vitamin D doses.
- "Non-responders" to vitamin D may simply be magnesium-deficient.
- Any vitamin D trials that do not control for magnesium are flawed.
- Personalized supplementation (including genetics and microbiome effects) is necessary.

One can't help but wonder how the healthcare system will respond to this game changing data.

References

1. Vanderbilt University Medical Center. (2025, December 30). "Why your vitamin D supplements might not be working." ScienceDaily, Retrieved from https://www.sciencedaily.com/releases/2025/12/251228020010.htm
2. Sun, E., Zhu, X., Ness, R. M., Murff, H. J., Sun, S., Yu, C. . . . Dai, Q. (2025). Magnesium treatment increases gut microbiome synthesizing vitamin D and inhibiting colorectal cancer: results from a double-blind precision-based

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Contact Us:

Wayne Persky: wayne@perskyfarms.com
Rosalyn Upson (Newsletter Editor): rosalyn.upson@gmail.com