



LINUS PAULING INSTITUTE

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VITAMIN D SUPPLEMENTS ON TRIAL: Are They “Useless”?

Earlier this summer, two studies on vitamin D caused a bit of a stir, inciting some media reports that proclaimed vitamin D supplements are “useless” for supporting bone and immune health. Here, we discuss the important findings from these vitamin D trials and provide some context and perspective.

In short, there is no reason to stop taking your vitamin D supplements.

Vitamin D is a fat-soluble, hormone-like molecule that plays an important role in health. Yet, many people in the world today are not getting enough vitamin D, especially in high northern or southern latitudes during the winter.

The primary source of vitamin D is sunlight exposure, as dietary sources are scarce. Because of the risk of skin damage and cancer from sunlight, many people turn to vitamin D supplements to meet their needs.

But questions have been raised about the need for vitamin D supplements and their role in maintaining health after the results of clinical trials reported no clear benefit in the people taking them.

Two recently published studies on vitamin D supplements – one on bone health and the other on immunity – have further fueled that argument. This has prompted recent editorials and media reports questioning the overall usefulness of vitamin D supplements.

As is often the case, this presents only one side of the story. At the Linus Pauling Institute, we believe that it is important to understand the designs of these clinical trials for a proper perspective on the conclusions. As we discuss below, neither study warrants a change to the Linus Pauling Institute’s recommendations on vitamin D supplements.

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Oregon State University
Linus Pauling Institute



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FROM THE DIRECTOR

Now more than ever before in our nation's history, health needs to be our highest priority.

It seems hard to imagine, but right now 60% of all adults in the United States have a chronic health problem – and this is only going to get worse. A wave of older adults is entering our healthcare system. In the next decade, one in five adults will be over the age of 65.

And while some will meet their later years with resilience, many will not. This is what we call an “aging tsunami” because its impact will overwhelm our healthcare system – that is, if we do nothing. The time to act is now.

Since the world is desperately in need of a paradigm shift, the Linus Pauling Institute will lead a new approach. Instead of us being reactive, let us start being *proactive* and change the face of health in this country – and the world.

On October 14, 2022, Oregon State University launched its second capital fundraising campaign. For this campaign, the Linus Pauling Institute will focus on moving the needle toward achieving optimal health. We know that this goal is within our reach – and you can help us achieve it.

In the upcoming months and years, you will be hearing more about our future plans to redefine healthcare. As we close in on our goals, you will also have new opportunities to engage with us and help shape the Institute's future.

My desire is to develop the tools you need to take charge of your health, so you can live better longer. At Oregon State University, we have the means to not only affect the nation but the entire world. I hope that you will join the Linus Pauling Institute in looking for innovative solutions to promote and optimize your health and vitality.

Please enjoy the first edition of our online-only newsletter. In this issue, we review the current state of nutrition research. The next issue will come in the late fall and provide more in-depth updates from our research programs.

Talk to you again in December,

A handwritten signature in black ink that reads "Emily".

INTRODUCING THE DRUG-NUTRIENT INTERACTIONS APP

Some dietary supplements can interfere with the action of drugs, and some drugs can influence how certain nutrients act in the body. It is incredibly important for physicians and consumers alike to be aware of potential interactions.

This is where the Institute's Drug-Nutrient Interactions (DNI) app plays an important role in healthcare. Developed from information in the Micronutrient Information Center and funded by a grant from Pfizer, Inc., this app is freely available for both Android and iOS devices.

The DNI app was developed to be a quick and easy reference for physicians, yet is simple enough for anyone to use. The app focuses on clinically relevant drug-nutrient interactions.



The VITAL Study: Vitamin D and Bone Fractures

In July 2022, the results of a randomized, placebo-controlled trial on vitamin D and bone fractures were published in *The New England Journal of Medicine*. These were new findings about the VITAL cohort – a group of approximately 26,000 older adults (50 years and older) from the Boston area.

In this recent paper, the authors looked at two groups: those that were given 2,000 IU of supplemental vitamin D to take daily and those that were given a placebo. Using surveys and medical records, the authors monitored the incidence of bone fracture in each participant. After five years, the data showed no difference in fracture risk between the two study groups – the placebo and vitamin D supplement groups had equal chances of breaking a bone.

Thus, the authors concluded that vitamin D supplements were ineffective in reducing fracture risk in this population.

Looking deeper into the data

The results of the VITAL trial were straightforward and logical: people taking vitamin D supplements did not see a reduction in bone fracture risk. Given what we know about vitamin D and bone health and the population studied, was this to be expected?

To explain further, let us describe the study in more detail.

The VITAL study recorded bone fractures, not bone mineral density. While fracture risk is related to bone mineral density, bone strength is influenced by physical activity and genetics.

Fracture risk is also influenced by how likely you are to sustain a potential bone-breaking injury, such as from a fall or motor vehicle accident.

Clearly, vitamin D cannot influence all of the factors that determine fracture risk. It is only one of the many components affecting bone mineral density. This makes bone fracture risk a limited parameter when evaluating the impact of vitamin D supplements.

And, participants in the VITAL cohort experienced below-average rates of bone fracture. The incidence of fracture in this group was about 1.1% per year, which is approximately four times lower than the average for similarly aged adults in the United States. A low rate of bone fracture makes it very difficult to detect the effect of any intervention, including vitamin D supplementation.

Why was the bone fracture risk so low? One reason might be that many participants in VITAL had higher than average levels of vitamin D before the study even started. In both the control and treatment groups, average baseline blood vitamin D concentrations were approximately 30 ng/mL. For context, the Linus Pauling Institute recommends achieving blood concentrations of 30 ng/mL or higher for optimal health.

Blood vitamin D levels were high in some of the study participants because they were allowed to take a daily supplement containing up to 800 IU of vitamin D if they desired. So while the placebo was given a supplement without vitamin D added, about 40% of the study participants continued to take vitamin D anyway.

Put plainly, VITAL was not designed to properly evaluate the effects of vitamin D on bone health or the effects of vitamin D supplements in those with low vitamin D status. Therefore, this report does not provide any evidence against the continued use of vitamin D supplements.

Vitamin D has a strong relationship to bone mineral density through its actions on calcium. Yet, bone mineral density can be influenced by 12 different vitamins and minerals.

See the Micronutrient Information Center on bone health for more: lpi.pub/BoneHealth

Previous studies on bone health have shown that bone mineral density appears to be negatively affected when blood vitamin D levels are below 20 ng/mL.

Another report on the VITAL cohort was published earlier in 2022. Interestingly, the use of vitamin D supplements was associated with a 22% lower risk of developing autoimmune diseases.

The CORONAVIT Study: Vitamin D and Immune Function

In September 2022, a clinical trial on COVID-19 and vitamin D was published in the research journal, *The BMJ*. This was a publication on the CORONAVIT cohort, a group of 6,200 participants ages 16 and older in the UK. This six-month trial examined whether vitamin D supplementation affected the risk of developing COVID-19 and other acute respiratory tract infections.

The CORONAVIT researchers randomly distributed the study participants into three groups. Two of the groups were designated as “vitamin D supplement groups.” Whether or not participants in these groups actually received these supplements depended on their initial vitamin D blood concentrations.

Only participants with blood vitamin D levels below 30 ng/mL (considered suboptimal vitamin D status) received either the 800 IU or 3,200 IU vitamin D supplement, depending on what group they were assigned. Those who had blood vitamin D concentrations above 30 ng/mL received no supplements, although they were still considered part of their assigned group.

The third group of participants was considered a control group. They were not given any supplements, nor was blood vitamin D measured at the start of the study.

At the end of the study, blood vitamin D concentrations were measured in randomly selected participants from all study groups. To determine if the use of vitamin D supplements had influenced the immune response, the authors periodically sent out questionnaires to all participants to see if they had gone to the doctor for a respiratory tract infection or had tested positive for COVID-19.

The final analysis showed equal numbers of respiratory tract infections in each group, whether the participants were assigned to a vitamin D supplement group or not. There was also no difference in the number of laboratory-confirmed COVID-19 cases among groups.

Looking deeper into the data

So, does the CORONAVIT trial suggest that vitamin D supplements are ineffective in the fight against respiratory tract infections? Not entirely. The unusual design of the CORONAVIT study makes it difficult to draw a solid connection between vitamin D status and infection risk.

The major concern was the treatment of the control group. This group was not provided any vitamin D supplements, but also not provided a placebo – so these participants were aware they were not getting vitamin D. As a consequence, about 50% of participants in the control group started taking vitamin D supplements despite being asked not to do so. Participants in the vitamin D supplementation groups, however, had little trouble following instructions.

Because blood vitamin D levels were not determined in the control group at the beginning of the study, we have no information on their initial vitamin D status. It is possible that these people had a lower risk of infection because they had sufficient vitamin D already.

At the end of the study, only 300 people in the control group (out of approximately 3,500) had their vitamin D blood concentrations measured. The likelihood that these participants were the ones who actually contracted a respiratory tract infection is pretty small.

And, in the groups provided with vitamin D supplements, supplementation was only partially effective. Approximately 40% of study participants in the 800 IU per day group and 15% in the 3,200 IU per day group did not reach the target of 30 ng/mL by the end of the study, potentially leaving these individuals vulnerable to infection.

Because of these design issues, the CORONAVIT trial revealed very little information of consequence about the use of vitamin D supplements in respiratory tract infections and COVID-19.

Bottom Line

Although the two studies discussed in this issue focus on vitamin D supplements, the response to their findings distract from the important messages about this vitamin. Establishing and maintaining adequate vitamin D status is vital to health, regardless if vitamin D comes from a supplement or some other source.

Many people can reach optimum vitamin D status easily with dietary supplements. But, this is not the only option available: diet and sunlight are alternatives. Regardless of the route you choose, it is important to get your blood vitamin D concentrations checked periodically.

While there are benefits associated with blood vitamin D levels at 30 ng/mL or above, vitamin D supplementation in individuals who already have vitamin D levels above 20 ng/mL may only result in subtle health benefits that require well-designed clinical trials to measure.

Ultimately, vitamin D is important for bone integrity and immune function, and vitamin D supplements continue to have their place for many people seeking to maintain good health. 🌞

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VITAMIN C AND SEPSIS: The End of the Story?

In June 2022, findings from the LOVIT study appear to show that intravenous vitamin C increases mortality in sepsis patients. Does this signal the end of IV vitamin C as a therapy for sepsis?

The LOVIT study is a randomized, placebo-controlled trial that investigated the impact of vitamin C in the treatment of sepsis. In this study, researchers enrolled participants with sepsis and provided standard sepsis treatments plus IV saline or IV vitamin C every six hours for four days. Response to the treatment was monitored, and treatments were evaluated over time.

At the end of the study, the authors found that IV vitamin C did not help sepsis patients. In fact, after 28 days, the group that received IV vitamin C had a 20% higher risk of death than the group that received the placebo.

Although there are many clinical trials that have tried IV vitamin C in the treatment of sepsis, few have suggested that vitamin C provides a benefit to sepsis patients. Combination therapy of IV vitamin C, thiamin, and hydrocortisone has not yielded any significant benefit to sepsis patients despite initial enthusiasm about this approach.

The LOVIT trial is the only trial to suggest that IV vitamin C harms sepsis patients. When we consider the mortality data from all of the trials on sepsis conducted to date, it does not appear that IV vitamin C causes harm.

Is there a path forward for IV vitamin C as a sepsis therapy? Earlier this year, a study from Korea suggested that IV vitamin C should be administered for at least five days to provide a significant benefit to sepsis patients. Since many randomized clinical trials only provided IV vitamin C for up to four days, extending the treatment period is one avenue to explore in future studies.

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