

Vitamin D supplements may reduce risk of developing advanced cancer

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For many years, investigators have been trying to pin down the tantalizing connection between vitamin D and cancer. Epidemiological studies have found that people who live near the equator, where exposure to sunlight produces more vitamin D, have lower incidence and death rates from certain cancers. In cancer cells in the lab and in mouse models, vitamin D has also been found to slow cancer progression. But the results of randomized clinical trials in humans haven't yielded a clear answer. The Vitamin D and Omega-3 Trial (VITAL), which concluded in 2018, found that vitamin D did not reduce overall incidence of cancer, but hinted at a decreased risk of cancer deaths. Now, in a secondary analysis of VITAL, a team led by investigators at Brigham and Women's Hospital has narrowed in on the connection between taking vitamin D supplements and risk of metastatic or fatal cancer.

In a paper published in JAMA Network Open, the team reports that vitamin D was associated with an overall 17 percent risk reduction for [advanced cancer](#). When the team looked at only participants with a normal [body mass](#) index (BMI), they found a 38 percent risk reduction, suggesting that body

mass may influence the relationship between vitamin D and decreased risk of advanced [cancer](#).

"These findings suggest that vitamin D may reduce the risk of developing advanced cancers," said corresponding author Paulette Chandler, MD, MPH, a primary care physician and epidemiologist in the Brigham's Division of Preventive Medicine. "Vitamin D is a supplement that's readily available, cheap and has been used and studied for decades. Our findings, especially the strong risk reduction seen in individuals with [normal weight](#), provide new information about the relationship between vitamin D and advanced cancer."

The VITAL study was a rigorous, placebo-controlled study that took place over a span of more than five years. The VITAL study population included men who were 50 or older and women 55 or older who did not have cancer when the trial began. The study population was racially and ethnically diverse. VITAL was designed to test the independent effects of vitamin D and omega-3 supplements as well as to test for synergy between the two. Participants were divided into four groups: vitamin D (2000 IU/day) plus omega-3s; vitamin D plus placebo; omega-3s plus placebo; and placebos for both. Primary endpoints were major adverse cardiovascular events and incidence of cancer. VITAL did not find a statistical difference in overall cancer rates, but researchers did observe a reduction in cancer-related deaths.

In their secondary analysis, Chandler and colleagues followed up on the possible reduction in cancer deaths with an evaluation of advanced (metastatic or fatal) cancer among participants who did or did not take vitamin D supplements during the trial. They also examined the possible modifying effect of BMI.

Among the more than 25,000 participants in the VITAL study, 1,617 were diagnosed with invasive cancer over the next five years. This included a

broad mix of cancers (breast, prostate, colorectal, lung and more). Of the almost 13,000 participants who received vitamin D, 226 were diagnosed with advanced cancer compared to 274 who received the placebo. Of the 7,843 participants with a normal body mass index (BMI less than 25) taking vitamin D, only 58 were diagnosed with advanced cancer compared with 96 taking the placebo.

While the team's findings on BMI could be due to chance, there is previous evidence that body mass may affect vitamin D action. Obesity and associated inflammation may decrease the effectiveness of vitamin D, possibly by reducing vitamin D receptor sensitivity or altering vitamin D signaling. In addition, randomized trials of vitamin D and type 2 diabetes have found greater benefits of vitamin D in people with normal weights and no benefit among those with obesity.

Vitamin D deficiency is common among cancer patients, with one study reporting rates of vitamin D deficiency as high as 72 percent among cancer patients. There is also evidence that higher amounts of body fat are associated with increased risk for several cancers.

"Our findings, along with results from previous studies, support the ongoing evaluation of [vitamin D](#) supplementation for preventing metastatic cancer—a connection that is biologically plausible," said Chandler. "Additional studies focusing on cancer patients and investigating the role of BMI are warranted."

More information: Chandler PD et al. "Effect of Vitamin D3 Supplements on Development of Advanced Cancer" *JAMA Network Open* DOI: [10.1001/jamanetworkopen.2020.25850](https://doi.org/10.1001/jamanetworkopen.2020.25850)

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