

Vitamin D may not provide protection from COVID-19 susceptibility or disease severity

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Observational studies have suggested that increased vitamin D levels may protect against COVID-19. However, these studies were inconclusive and possibly subject to confounding. A study published in *PLOS Medicine* by Guillaume Butler-Laporte and Tomoko Nakanishi at McGill University in Quebec, Canada, and colleagues suggests that



genetic evidence does not support vitamin D as a protective measure against COVID-19.

The ability of vitamin D to protect against severe COVID-19 illness is of great interest to public health experts, but has limited supporting evidence. To assess the relationship between vitamin D levels and COVID-19 susceptibility and severity, researchers conducted a Mendelian randomization study using genetic variants strongly associated with increased vitamin D levels. The authors analyzed genetic variants of 4,134 individuals with COVID-19, and 1,284,876 without COVID-19, from 11 countries to determine whether genetic predisposition for higher vitamin D levels were associated with less-severe disease outcomes in people with COVID-19.

The results showed no evidence for an association between genetically predicted vitamin D levels and COVID-19 susceptibility, hospitalization, or severe disease, suggesting that raising circulating vitamin D levels through supplementation may not improve COVID-19 outcomes in the general population. However, the study had several important limitations, including that the research did not include individuals with vitamin D deficiency, and it remains possible that truly deficient patients may benefit from supplementation for COVID-19 related protection and outcomes. Additionally, the genetic variants were obtained only from individuals of European ancestry, so future studies will be needed to determine the relationship with COVID-19 outcomes in other populations.

According to the authors, "Vitamin D supplementation as a public health measure to improve outcomes is not supported by this study. Most importantly, our results suggest that investment in other therapeutic or preventative avenues should be prioritized for COVID-19 randomized clinical trials".



Dr. Butler-Laporte notes, "Most vitamin D studies are very difficult to interpret since they cannot adjust for the known risk factors for severe COVID-19 (e.g. older age, institutionalization, having chronic diseases) which are also predictors of low vitamin D. Therefore, the best way to answer the question of the effect of vitamin D would be through randomized trials, but these are complex and resource intensive, and take a long time during a pandemic. Mendelian randomization can provide more clear insights into the role of risk factors like vitamin D because they can decrease potential bias from associated risk factors like institutionalization and chronic disease. In the past Mendelian randomization has consistently predicted results of large, expensive, and timely vitamin D trials. Here, this method does not show clear evidence that vitamin D supplementation would have a large effect on COVID-19 outcomes."

More information: Butler-Laporte G, Nakanishi T, Mooser V, Morrison DR, Abdullah T, Adeleye O, et al. (2021) Vitamin D and COVID-19 susceptibility and severity in the COVID-19 Host Genetics Initiative: A Mendelian randomization study. *PLoS Med* 18(6): e1003605. doi.org/10.1371/journal.pmed.1003605

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