



Vitamin D and covid-19

Benefits are possible but evidence is sparse, indirect, and inconclusive

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The covid-19 pandemic has led to many unfounded and exaggerated claims about possible treatments. One high profile controversy has been the role of vitamin D in the prevention and management of covid-19,^{1,2} so the National Institute for Health and Care Excellence (NICE), Public Health England, and the Scientific Advisory Committee on Nutrition rapid guideline is timely.³

The joint guidance concludes that there is little good evidence on vitamin D and covid-19, highlights the need for further research, and supports existing government advice that adults and children in the UK should take 10 µg (400 IU) a day between October and March, to optimise musculoskeletal health. It also recommends that certain populations such as minority ethnic groups, consider taking vitamin D throughout the year.

What's the evidence?

Vitamin D supplementation of 10-25 µg a day has a modest protective effect against acute respiratory infections,⁴ but research on a direct effect in covid-19 is sparse. The NICE review⁵ included one small randomised controlled trial of vitamin D as treatment,⁶ no trials of vitamin D as prevention, and 12 observational studies investigating associations between serum vitamin D concentrations and incidence or treatment of covid-19. The one small (n=76) low quality trial from Spain reported significantly reduced disease severity among patients given high dose vitamin D during their hospital admission.⁶

Two further trials not included in the NICE review reported conflicting findings. A single oral dose of 5000 µg of vitamin D₃ did not influence length of stay among Brazilian patients with severe covid-19 (n=240).⁷ In a smaller trial from India, however, (n=40) patients with mild or asymptomatic covid-19 were more likely to test negative at 21 days following daily vitamin D supplementation starting at 1500 µg.⁸ Differences in participants; type, dose, initial vitamin status, and duration of vitamin D supplementation; study endpoints; and risk of bias make interpretation of the trial evidence difficult.

Observational evidence is also inconsistent. Some, but not all, studies report an association between vitamin D deficiency and greater incidence or severity of SARS-CoV-2 infection.⁹ The extent of uncontrolled confounding by age,¹⁰ ethnicity,¹¹ genetic heterogeneity,¹² and obesity^{13,14} varies among studies, however, and probably accounts for at least some of the observed associations.

Though direct evidence of a link between vitamin D levels and covid-19 incidence or outcomes is lacking, indirect evidence of an immunomodulatory role of

vitamin D in respiratory infections exists. Other indirect evidence includes the similarity of the risk factors for both vitamin D deficiency and severe covid-19: older age, obesity, and minority ethnicity. Also, the correlation between seasonal decline of serum concentrations of vitamin D and higher burden of covid-19 in high latitude countries.¹⁵ Taken together, existing evidence supports a compelling case for further research.

Implications for guidance

Although the recommended 10 µg daily seems justifiable to maintain serum concentrations of 25-hydroxyvitamin D above 25 nmol/L, whether this is enough to gain any immunomodulatory benefits for patients with covid-19 remains unclear. UK guidance recommending 10 µg a day of vitamin D has been in existence for a while, but adherence is not guaranteed. Raising awareness of the relevance of vitamin D to musculoskeletal health is therefore appropriate, particularly during pandemic restrictions on movement. Evidence for a role in covid-19 remains suggestive only, but people may choose to take the recommended dose on the precautionary principle that it does no harm, may be beneficial, and improves bone health.

Vulnerable groups in particular need guidance on how to obtain vitamin D. Healthcare professionals can direct people at high risk to free NHS provision¹⁶ and eligible women and children to the Healthy Start scheme (<https://www.healthystart.nhs.uk/>). Vegetarians and vegans need more specific guidance on sources of vitamin D supplements that match their dietary choices.

It's important that people are not falsely reassured by vitamin D supplements, and guidance must stress the importance of hand hygiene, face coverings, physical distancing, and vaccination against covid-19 in culturally and linguistically appropriate campaigns through local community groups.

Further trials evaluating vitamin D supplements in the prevention and management of covid-19 are now justified, with particular attention to different doses, baseline vitamin D levels of participants, and effects on different population subgroups and in different settings, including hospitals. Ongoing trials such as Covit¹⁷ and Coronavit (NCT04579640), which compares three different doses, will help inform future guidance.

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