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Vitamin D and COVID-19: why the controversy?

“To help retain the peak of sunny summer health—to help maintain rugged resistance to winter colds and sickness—drink Schlitz [beer], with Sunshine Vitamin D”, reads an advertisement in the *American Magazine* from December, 1936.

The fascination with vitamin D supplementation began with the discovery in the early 1920s that vitamin D prevented rickets and was further driven by the recognition of other potential roles of vitamin D in non-skeletal outcomes, including immune function, cardiovascular health, and cancer. However, whereas data on the function of vitamin D in bone growth and maintenance is clear-cut and has informed practical clinical guidelines and public health policies over the years, evidence supporting the role of vitamin D in other health and disease processes, in particular in acute respiratory tract infection, remains patchy. Data from observational studies have suggested that vitamin D supplementation can lower the odds of developing respiratory infections, particularly in vitamin D-deficient groups, but randomised trials have yielded mixed results.

In *The Lancet Diabetes & Endocrinology*, the findings from a prespecified analysis from the D-Health randomised clinical trial in more than 20 000 Australian adults recruited from the general population suggest that monthly doses of vitamin D did not reduce the risk or severity of acute respiratory tract infections. Although the analysis showed a statistically significant effect on the overall duration of symptoms based on analysis of diary data, the reduction was small (0.5 days) and unlikely to be clinically meaningful. In a preprint deposited on medRxiv, the authors of a systematic review and meta-analysis based on aggregate data from trials, including data from the D-Health trial, concluded that vitamin D supplementation was safe and identified a small effect with respect to protection from acute respiratory tract infections associated with daily doses of 400–1000 IU vitamin D for up to 12 months, but acknowledged significant heterogeneity across trials.

The issue of vitamin D supplementation has been extensively debated, with strong arguments in favour and against. The COVID-19 pandemic has further escalated the discussion. It has long been clear that groups that traditionally exhibit vitamin D deficiency or insufficiency, such as older adults and nursing home residents, and

Black, Asian, and minority ethnic populations, are the same groups that have also been disproportionately impacted by COVID-19. Additionally, increased time spent indoors due to strict lockdowns and shielding triggered concerns that some people might not obtain the necessary physiological levels of vitamin D from sunlight.

On Dec 17, 2020, the National Institute for Health and Care Excellence (NICE), in collaboration with Public Health England and the Scientific Advisory Committee on Nutrition, published an updated rapid review of recent studies on vitamin D and COVID-19. Their recommendations support the current government advice, revised in April, 2020, during the first lockdown in the UK, for everyone to take vitamin D supplements to maintain bone and muscle health during the autumn and winter months. The recommendations are also in line with new guidance from the UK government, released on Dec 22, 2020, allowing extremely clinically vulnerable people to opt in to receive a free 4-month supply of daily vitamin D supplements—similar to an initiative launched earlier in Scotland. However, the rapid review concluded that sufficient evidence to support vitamin D supplementation with the aim of preventing or treating COVID-19 was still lacking and that the topic should be further investigated. Experts studying vitamin D welcomed the call for more research, but the lack of specific recommendations in the context of COVID-19 was also met with disappointment by many in the scientific community who have argued that vitamin D supplementation is generally safe and that any potential low toxicity would likely be strongly outweighed by any potential benefits in relation to protection from COVID-19.

NICE should continue to monitor new evidence as it is peer-reviewed and published, including results from several clinical trials on vitamin D and COVID-19 outcomes that are currently underway. However, particularly in countries where the pandemic situation continues to worsen (and will continue to do so during the winter months before the effects of vaccinations become perceptible), additional evidence could come in just too late. In an ideal world, all health decisions would be made based on overwhelming evidence, but a time of crisis may call for a slightly different set of rules.

■ *The Lancet Diabetes & Endocrinology*



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For the **D-Health analysis on vitamin D supplementation and respiratory infections** see **Articles** page 69

For the **systematic review and meta-analysis on vitamin D and prevention of acute respiratory infections** see *medRxiv* 2020; published online Nov 25, 2020. <https://www.medrxiv.org/content/10.1101/2020.07.14.20152728v3> (preprint)

For the **NICE guidelines on vitamin D use in the context of COVID-19** see <https://www.nice.org.uk/guidance/ng187>

For the **guidance on vitamin D supplementation for clinically extremely vulnerable groups** see <https://www.gov.uk/government/publications/vitamin-d-for-vulnerable-groups/vitamin-d-and-clinically-extremely-vulnerable-cev-guidance>