# Vitamin-D and COVID-19: time for the profession to take a stand

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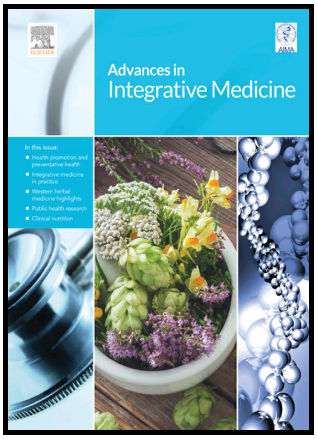


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**Vitamin-D and COVID-19: time for the profession to take a stand**

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The role of Vitamin-D in building immunity to viruses and respiratory illnesses is widely accepted. When the COVID-19 pandemic emerged earlier this year, it was too soon to show definitively that the vitamin would have a useful impact, although experts in nutritional medicine expected it would. Nearly a year into the pandemic, however, we have dozens of research papers from quality institutions around the world – including from the US, Spain, Israel and the UK. These demonstrate that optimal blood levels of 90-130nmol/L not only enhance immunity to COVID-19 but also reduce the severity of outcomes should infection occur. Some jurisdictions are already encouraging and supporting supplementation, with the UK the most recent to announce plans to supply Vitamin-D supplements to vulnerable residents to enhance COVID-19 defences. Australia should do the same – notwithstanding our current low case numbers, a resurgence of a virus can occur quickly, and we have a window of opportunity to prepare our population for that. Unfortunately, our Government is yet to act, citing the need for "more evidence". Such a conservative approach, when the risks associated with appropriate Vitamin-D supplementation are negligible, is foolish, dangerous and frustrating. However, as a profession, we are in a position to influence even without the backing of Government policy. We must advocate and inform not just at the political level, but importantly at the patient level. The elderly and those with darker skin are at

particular risk of Vitamin-D deficiency, while certain cohorts of our community, including those with comorbidities such as diabetes and obesity, are most vulnerable to the virus. We should be testing their Vitamin-D levels and ensuring they are at optimum levels to provide protection. Given an estimated 50% of Australians are deficient in Vitamin-D, most adults can benefit from a daily dose of 2,000-4,000 IU with no adverse risk, while some need substantially more. The medical professionals should do everything in their power to support the health of their patients.

Let's look at what we know about Vitamin-D and respiratory tract infections.

Acute respiratory tract infections are a major cause of global morbidity and mortality and are responsible for 10% of ambulatory and emergency department visits in the USA, and an estimated 2.65 million deaths worldwide in 2013.[1]

Observational studies have been reporting consistent independent associations between low serum/plasma concentrations of 25-hydroxy-Vitamin-D, the major circulating Vitamin-D metabolite, and susceptibility to acute respiratory tract infection.

A meta-analysis and systematic review of 25 randomised controlled trials involving 11,321 participants aged 0 to 95 concluded that Vitamin-D supplementation can indeed prevent acute respiratory tract infection with statistical significance (adjusted-odds-ratio 0.88, 95%CI 0.81-0.96, P<0.001). The effect was the greatest in those with deficient Vitamin-D levels.[1]

Prevalence of Vitamin-D deficiency is high, with one in four Australian adults (23%) being Vitamin-D deficiency, using standard reference ranges.[2]

However, standard reference ranges for biomarkers such as Vitamin-D are often below what is needed for optimal health. Many Vitamin-D experts advocate maintaining 25(OH)D levels at >75 nmol/L, whereas the standard upper reference is considered >50 nmol/L.[3] Optimal Vitamin-D levels have been associated with maximum mineral bone density, increased intestinal calcium absorption, decreased risk of osteoporosis and risk of fracture, higher serum phosphorus levels, increased performance speed, proximal muscle strength, and a significant decrease in the likelihood of chronic diseases such as cancers, auto-immune disease, osteoarthritis and diabetes.[3]

A study involving 139 healthy adults undergoing an integrative health check found that 80% of adults had sub-optimal Vitamin-D levels.[4]

In addition, several recent studies have linked Vitamin-D deficiency with risk and severity of COVID-19 infection and hospitalisation. For example, a study in Israel of more than 7800 individuals found that those with COVID-19 positive test results (n=782), had significantly lower Vitamin-D levels compared to those with negative COVID-19 tests. The study authors concluded that low plasma Vitamin- D levels are associated with increased risk and severity of COVID-19 infection and hospitalisation.[5] Also, a study conducted in Spain found that 80% of 216 COVID-19 hospital patients had Vitamin-D deficiency.[6] Indeed, many more authors have linked vitamin-D deficiency to severity of COVID-19.[7]

Vitamin-D protects against pathogens by exerting important regulatory functions on both the innate and adaptive immune system, including increased activity of white blood cells, improved T-cell defence, and reduction in inflammation through cytokine regulation.[8]

Some countries have now recognised the importance of Vitamin-D in the prevention of respiratory infections, including COVID-19, and have started to implement free Vitamin-D supplementation for the elderly and vulnerable, e.g. in the UK (Daily Mail, 8 Nov 2020: https://www.dailymail.co.uk/news/article-8925321/Millions-elderly-vulnerable-free-Vitamin-D-government.html).

Vitamin-D supplements, usually taken in doses of 1,000-5,000 IU per day and up to 10,000 IU/day for target groups, such as obese individuals, are regarded as safe.

The Benskin 2020 Review reported that 4,000-10,000 IU of Vitamin-D daily were safe and effective in preventing COVID-19 infection and disease severity.[9] The recommended oral Vitamin-D dose dependent on Vitamin-D serum levels are outlined in **Table 1**.[9,10]

In addition to Vitamin-D deficiency being linked to increased mortality, improvement of Vitamin-D status through supplementation also reduced progression of Parkinsons disease in the elderly.[11] Higher bolus doses of Vitamin-D, if required, have also proven safe and effective. For example, supplementation of 100,000-150,000 IU Vitamin-D daily for 2-3 months eradicated tuberculosis infection successfully in the 1940s.[12]

More recently, the Endocrine Society has recommended up to 10,000 IU/day, particularly for obese individuals.[10] In addition, recent studies reported on 15,000 to 40,000 IU of Vitamin-D taken daily for at least 6 months resulted in no apparent adverse effects.[9]

Closer to home, a New Zealand study in 2009 investigating the safety and efficacy of high dose Vitamin-D in the elderly, demonstrates that an IV-bolus of 50,000 IU/month for 3 months, or 500,000 IU once, were are safe and effective.[13]

In addition, an Australian study (2006) found that 100,000 IU of Vitamin-D3 given orally 3 monthly for 1-2 years is a practical, safe, effective and inexpensive way to meet the Vitamin-D3 requirement of aged care residents.[14]

In conclusion, adequate Vitamin-D levels are of great importance in the prevention and severity of acute respiratory infections. Vitamin-D protects against pathogens including viruses via the innate and adaptive immune system, involving white blood cells and T-cells. It is known, that a large proportion of Australians are Vitamin-D deficient, specifically older people. Research has proven Vitamin-D supplementation to be a key to alleviate Vitamin-D deficiency, and subsequently prevent the onset and severity of acute respiratory tract infections, and reduce morbidity and mortality. Supplementation of 4,000 IU Vitamin-D and up to 10,000 IU daily for several months are considered safe and effective in alleviating Vitamin-D deficiency and optimising plasma Vitamin-D levels.

Urgent action by the medical profession in Australia is needed to raise awareness about Vitamin-D and promote Vitamin-D supplementation.

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**Table 1: Classification of Vitamin-D levels (serum 25(OH)D levels) and recommended oral Vit-D dose[17]**

| **Classification** | **Nanograms (ng/ml)** | **Nanomoles (nmol/l)** | **Recommended oral VitD dose** |
|---|---|---|---|
| Normal or optimal | ≥30 | **≥75-120** | 400–4,000 IU/day |
| Insufficient | 21–29 | **51–74** | 4,000–6,000 IU/day |
| Deficient | 11–20 | **26–50** | 7,000 IU/day |
| Severely deficient (often not distinguished from deficient) | <10 | **25 or less** | 10,000 IU/day for 1 month |

Author statement:

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conflict of interest

The authors have no conflict of interest to declare.