



# *Vitamin D and covid-19*

Article

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1 **Can current guidelines on vitamin D supplementation prevent or treat**  
2 **SARS-CoV-2 infection?**

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20 SARS-CoV-2 infection-related health crisis has led to unfounded or exaggerated claims  
21 on treatments. One area of controversy has been the role and dose of vitamin D supplementation  
22 in COVID-19<sup>1 2</sup>. Given the potential importance but prevailing uncertainty, the joint National  
23 Institute for Health and Care Excellence (NICE), Public Health England and Scientific  
24 Advisory Committee on Nutrition rapid guideline was recently published. It concluded that  
25 there was little evidence, highlighted the need for further research, and supported the existing  
26 government advice predicated on musculoskeletal health on vitamin D supplementation of  
27 400IU/day for adults and children between October and March, when people in the UK do not  
28 make sufficient vitamin D from sunlight. It also stressed that certain populations such as  
29 minority ethnic groups, should consider taking this dose throughout the year<sup>3</sup>. The guidance is  
30 timely, but questions remain.

### 31 **What is the evidence for a link between vitamin D and COVID-19?**

32 Vitamin D supplementation of 400-1000IU/day has a modest protective effect for acute  
33 respiratory infections<sup>4</sup>, providing indirect evidence for SARS-CoV-2 infection. There is,  
34 however, sparse research on a direct link.

35 The NICE review included one small randomised controlled trial (RCT) for COVID-  
36 19 treatment<sup>5</sup>, no RCTs for COVID-19 prevention, and 12 observational studies of associations  
37 between vitamin D status and COVID-19 incidence or treatment. Among 76 Spanish patients  
38 hospitalised with COVID-19, high-dose supplementation equivalent to 21,280IU  
39 cholecalciferol on admission day and 10,640IU on day 3 and 7, then weekly until discharge  
40 reduced disease severity<sup>5</sup>. We found two further RCTs with conflicting findings. Among 240  
41 Brazilian hospitalised patients with COVID-19, a single oral vitamin D<sub>3</sub> dose of 200,000IU  
42 versus placebo did not reduce the hospital length of stay<sup>6</sup>. In contrast, in 40 Indian SARS-CoV-  
43 2 positive Indians, infection vitamin D 60,000IU daily for 7 days, followed by the same dose  
44 either weekly or daily led to greater negative tests at 21 days<sup>7</sup>. These discrepancies highlight

45 the challenges of RCT design, with varying selection criteria, initial vitamin D status, the type,  
46 dose, and duration of supplementation, the endpoints studied, and risk of bias and study quality.

47 The observational evidence is inconsistent with some, but not all, studies reporting an  
48 association between vitamin D insufficiency and SARS-CoV-2 infection<sup>3 8</sup>. However, the  
49 observed link could be attributed to several confounding factors including age<sup>9</sup>, ethnicity<sup>10</sup>,  
50 genetic heterogeneity<sup>11</sup>, and obesity<sup>12 13</sup> which are incompletely or not accounted for in  
51 different studies.

52 High-quality evidence is currently lacking, but there is suggestive evidence for an  
53 immunomodulatory role of vitamin D for respiratory infections and contextual evidence of the  
54 shared risk factors between vitamin D deficiency and COVID-19 severity: older age, obesity,  
55 and minority ethnicity. There is also a correlation between seasonal decline of vitamin D and  
56 higher COVID-19 burden in high-latitude countries<sup>14</sup>. The available evidence cannot be  
57 ignored and makes a compelling case for further research.

### 58 **What next with the UK guidance on use of vitamin D supplementation?**

59 The recommendation of 400IU seems justifiable to maintain 25(OH)D levels >25nmol/l  
60 in 97.5% of the UK population, but it is unclear whether this level is appropriate for  
61 immunomodulatory actions for COVID-19. Guidance recommending 400IU/day vitamin D  
62 supplementation in the UK has been in existence for a while, but its implementation has not  
63 been ensured. Raising awareness of the relevance of vitamin D is therefore appropriate for  
64 musculoskeletal health, particularly during lockdowns. It may also be relevant for COVID-19,  
65 given the suggestive though not conclusive evidence of its potential role and the precautionary  
66 principle. We also need clear guidance on how to obtain vitamin D for vulnerable groups.  
67 Health care professionals can point people to the free NHS vitamin D supplement provisions  
68 for people at high risk<sup>15</sup> and for women and children who qualify for the Healthy Start scheme.

69 Clinicians also need to be aware that vegetarians or vegans would need guidance on appropriate  
70 sources of vitamin D supplements.

71 The public health emergency posed by COVID-19 demands the use of all promising  
72 solutions, therefore vitamin D remains a plausible candidate. However, policy  
73 recommendations need to ensure that the public are not falsely reassured regarding the role of  
74 vitamin D for COVID-19. These guidelines therefore must be accompanied with continued  
75 messaging on hand hygiene, face coverings, physical distancing, and the importance of vaccine  
76 uptake in culturally and linguistically adapted campaigns through local community groups.

77 The published guidelines have clearly articulated the currently unconvincing evidence  
78 of vitamin D for COVID-19; therefore, it is vital that ongoing and future trials evaluate the  
79 effect of vitamin D supplementation with improved design including attention to comparing  
80 different dosing regimens, initial vitamin D status, inclusion of different population subgroups,  
81 older participants and those with morbidities, and in settings including hospitalised patients  
82 and population-based samples. Ongoing trials such as COVIT-TRIAL<sup>16</sup> and CORONAVIT  
83 (NCT04579640), which is comparing the national recommendation with higher dosage  
84 (800IU/day and 3200IU/day), will be important to inform future guidance.

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90 Research Centre (BRC).

91

92 **Duality of Interest**

93 NGF is an honorary consultant public health physician with Public Health England. The views  
94 expressed are her own. KK is Director of the University of Leicester Centre for Black Minority  
95 Ethnic Health, Trustee of the South Asian Health Foundation, Chair of the Ethnicity Subgroup  
96 of SAGE and Member of Independent SAGE.

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