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Response

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We thank Dr Woodford for his interest in our article. In this we focus on the definition of vitamin D sufficiency as defined by serum 25(OH)D concentration and hence on the appropriate daily supplement to ensure this, particularly in countries such as the UK where the average serum 25(OH)D concentration falls by around 50% through winter.¹ He is sceptical about our support for 50 nmol/L as the appropriate target for sufficiency and cites as evidence for a much lower target level (10 nmol/L) a study that sought to define a 25(OH)D level below which the serum concentration of activated 1,25(OH)₂D can no longer be sustained.² Low levels of 1,25(OH)₂D are certainly a good predictor of mortality in patients with acute respiratory distress syndrome³ but, as we reported, less extreme degrees of vitamin D deficiency are commonly found in rickets. Moreover, serum concentrations of 1,25(OH)₂D may not be so relevant to immune function because immune cells and many epithelial cells are able to synthesise 1,25(OH)₂D from 25(OH)D locally.⁴ Unlike endocrine vitamin D metabolism by the kidneys, extra-renal production of 1,25(OH)₂D appears to be highly dependent on available 25(OH)D. The optimal level of 25(OH)D required for this process has yet to be determined but may be higher than the levels of 25(OH)D required to protect against rickets. In our article, we demonstrated the lack of evidence underlying the UK Scientific Advisory Committee on Nutrition (SACN) choice of 25 nmol/L as target for sufficiency and supported the 50 nmol/L target recommended by the European Food Safety Authority and the American Institute of Medicine (now National Academy of Medicine). Both these organisations have come to this conclusion by systematically reviewing a large body of evidence including musculoskeletal and adverse pregnancy-related health outcomes and they reference this extensively.^{5,6}

We have subsequently reviewed the substantial evidence linking vitamin D deficiency with severity of COVID-19.⁷ This includes seasonality-latitude-ultraviolet exposure; associations with obesity, ethnicity and living in institutions; and studies showing reduced severity with calcifediol (25(OH)D) treatment in hospital and vitamin D supplementation in the community. Previous studies with respiratory infections as the endpoint have also shown benefit from daily vitamin D supplementation.⁸ A single 1,000 IU / 25 µg capsule or tablet per day will usually cost less than 10p and there should be no significant risk of side-effects. In the Cochrane review cited by Woodford, significant hypercalcaemia was not reported (risk ratio (RR) 1.57; 95% confidence interval (CI) 0.8–3.05) for vitamin D given as D2, D3 or 25(OH)D without calcium nor were gastrointestinal symptoms increased (RR 0.95; 95% CI 0.79–1.14).⁹

Attention should urgently be paid to avoidance of vitamin D deficiency during this pandemic. ■

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Cardiac investigations after ischaemic stroke

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Editor – I read with great interest the paper by Helliwell *et al.*¹ The authors describe the case of a patient with stroke due to cardiac papillary fibroelastoma (CPF) successfully treated with systemic