

## **Incorrect and Misleading Claims Regarding Vitamin D**

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*In Response to Article Entitled:*

*'Optimisation of Vitamin D Status for Enhanced Immuno-Protection against Covid-19' by D.M McCartney et al –  
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McCartney and Byrne claim<sup>1</sup> we misrepresented the findings of Martineau<sup>2</sup> in our BMJ editorial.<sup>3</sup> They are wrong. The absolute risk reduction is the difference between the absolute risks in the control and intervention groups. In the meta-analysis by Martineau<sup>2</sup> this is 42%-40% = 2%. McCartney and Byrne divide this figure by the baseline absolute risk to get 4.8%, which is the relative risk reduction.

Unfortunately, they compound their error by equating an odds ratio of 0.88 with a 12% reduction in risk. The odds ratio only approximates the relative risk when the absolute risk is small. In the Martineau meta-analysis,<sup>2</sup> the absolute risk (42%) was not small, and thus the odds ratio substantially overestimates the relative risk.<sup>4</sup> The relative risk was actually about 0.93,<sup>4</sup> fairly close to the estimate of 4.8% by McCartney and Byrne.<sup>1</sup>

McCartney and Byrne then suggest that a 70% reduction in risk in those with baseline 25OHD <25 nmol/L from the Martineau meta-analysis could apply to Irish nursing home residents.<sup>1</sup> Notwithstanding the fact that they mean a 70% reduction in the odds (the relative risk reduction is about 48%), this finding is not generalizable. In the subgroup analysis McCartney and Byrne quote, there are 234 individuals with baseline 25OHD <25 nmol/L treated with daily or weekly vitamin D.<sup>2</sup> However, Table 1 shows that 225/243 individuals treated with daily/weekly vitamin D and 25OHD <25 nmol/L were infants or children (or all but 18).<sup>2</sup>

192/225 children were from a single study in school children in Mongolia which showed an extremely positive effect of 7 weeks of milk fortified with vitamin D compared to milk alone on parent-reported chest infections or colds occurring within the previous 3 months.<sup>5</sup> These results should be interpreted with extreme caution. The trial was cluster randomized by classroom with an undescribed (but small) number of clusters per treatment arm. In the Martineau meta-analysis, the study appears to have been analyzed as though children were individually randomized.<sup>2</sup> The data on colds or chest infections were not collected prospectively, instead gathered from parental recall for the preceding 3 months, of which the children were not taking vitamin D for 6 weeks.<sup>5</sup> The analysis was post-hoc and data for only 1 of the 5 different vitamin D arms have been reported.<sup>5</sup>

The claim that vitamin D supplementation prevents respiratory tract infections in the Martineau analysis, overall or in subgroups with 25OHD <25nmol/L, is largely or entirely dependent on this study. Applying fragile, post-hoc, selectively reported results from a cluster randomized trial of school children in Mongolia (or meta-analyses dependent on it) to Irish nursing home residents is both misleading and unwise.

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