Hemilä’s response to professor Martineau

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Professor Martineau claims (27 Feb) that I was not correct when I stated (17 Feb) that they had interpreted the odds ratio (OR) as an approximation for the relative risk (RR). However, anyone can read from their abstract that “vitamin D supplementation reduced the risk of acute respiratory infection among all participants (adjusted odds ratio 0.88 ...” [1].

Given that in the medical literature OR is routinely used as an approximation of RR, their abstract states that vitamin D reduces the risk of respiratory infections by 12%. In my comment, I showed from the study-level data that the OR exaggerated the percentage effect of vitamin D more than two-fold. Thus, if we assume that the same ratio of two is also valid for the adjusted OR calculated by Martineau, then the correct estimate of the vitamin D effect would be a 6% reduction in the incidence of acute respiratory infections, which is substantially less than their abstract indicates. Martineau’s comments on the absolute effect size and NNT do not address my point.

I showed that the statistical significance of the pooled effect was not robust (17 Feb). The exclusion of two studies [2,3] led the pooled estimate to become nonsignificant. Martineau dismisses my sensitivity analysis on the basis that there are more than those two studies that have found a statistically significant benefit from vitamin D and he listed five [4-8]. However, four of those five trials he listed were conducted with quite special populations and therefore their findings cannot be directly extrapolated to the general population.

Majak (2011) restricted their trial to children with newly diagnosed asthma [4], Marchisio (2013) to children with a history of recurrent acute otitis media [5], Bergman (2012) to patients with antibody deficiency or increased susceptibility to respiratory tract infections [6], and Laaksi (2010) to young men undergoing military training [7]. Vitamin D may decrease the incidence of respiratory infections in children with asthma or in children with recurrent ear infections, etc. However, findings from those particular studies cannot be extrapolated to the population of ordinary children nor to the population of ordinary adults.

The only study in Martineau’s list [4-8] that appears potentially relevant for ordinary people is the Goodall (2014) trial which was carried out with university students in Canada [8]. However, the difference in clinical upper respiratory infections between the vitamin D and placebo groups in that study was not significant (P = 0.09, Table 2 in [8]). Thus, the 5th study in the list, that seems most relevant for ordinary people, was negative.
Martineau overlooks the ‘apples and oranges’ problem. When there is a highly significant heterogeneity among a set of trials, the existence of that heterogeneity indicates that no single estimate of effect, such as a 6% decrease in incidence, is applicable to all conditions of the included studies. Instead, different estimates should be examined for different conditions. Pooling heterogeneous studies to a single uniform estimate such as 6% does not guide further research, instead, considering the particular characteristics of the positive studies may suggest paths for future investigations.

Martineau investigated the potential role of certain variables such as vitamin D status. However, the selection of participants is also a highly relevant variable that may explain divergence between studies, but that source of variation was not considered [1]. Positive effects in certain special population groups indicates that the effects of vitamin D should be further studied in conditions close to those positive studies [2-7]. In any case, it does not seem appropriate to imply in the abstract that the benefits of vitamin D supplementation are universal and apply to all people [1].

References
[1] http://www.bmj.com/content/356/bmj.i6583