



# A systematic review and meta-analysis of the response of serum 25-hydroxyvitamin D concentration to vitamin D supplementation from RCTs from around the globe

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Received: 27 May 2020 / Revised: 21 June 2020 / Accepted: 14 July 2020  
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## To the Editor:

We have read with great interest the article entitled “A systematic review and meta-analysis of the response of serum 25-hydroxyvitamin D concentration to vitamin D supplementation from RCTs from around the globe” by Mo et al. [1]. The authors performed a meta-analysis on randomized controlled trials (RCTs) of vitamin D (VitD) supplementation to identify the association between VitD dose and serum 25(OH)D concentration, and to estimate optimal supplemental dose of vitamin D<sub>3</sub> for achieving circulating 25(OH)D concentrations greater than 75 nmol/L for different populations. A total of 136 articles were included with 19 studies in children (mean age 3–17 years) and found that there was a dose–response effect between dose and 25(OH)D concentration. The weighted mean (WM) increments in 25(OH)D concentration per 100 IU/day VitD were 1.6, 2.1, 1.4 nmol/L in the low, moderate, and high-dose groups, respectively. Baseline 25(OH)D concentration and age were significantly associated with achieved 25(OH)D concentration. For children, to reach sufficient 25(OH)D concentration, the recommended VitD intakes was 1340 IU/day. We would like to highlight some critical issues with the methodology of this report.

In the selection of studies for children, authors have omitted six studies, two from Middle East and North Africa region [2, 3], one from Finland [4], one from Australia [5], and two from the United States [6, 7], with over 800 participants, which examined the safety and efficacy of various

doses of VitD supplementation for improving the serum 25 (OH)D. The exclusion criteria did not justify excluding these studies. The exclusion of four large studies may skew the estimates and make them unreliable.

Furthermore, the authors declared that RCTs were included if the study participants were apparently healthy or patients with mild diseases with no known effects on VitD metabolism. The exact definition of being healthy or having only a mild illness is not clear. Authors had included study by Saad et al. [8], which was performed on children with autism spectrum disorder (ASD), a complex neurodevelopmental syndrome. The association between the risk of ASD and VitD insufficiency has been reported. On the other hand, some mild diseases with less effect on VitD metabolism such as obesity [9], atopic dermatitis [10], attention-deficit hyperactivity disorder [11], allergic rhinitis [12], asthma [13] may have been excluded.

In addition, study by Saad et al. [8] was retracted and this may cause flaw and bias other studies were included in the MENA region since only two.

Lastly, inception time of electronic literature searches has not been specified in this study. Considering that the inception date for various included databases i.e., MEDLINE/PubMed, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) is different, to homogenize the literature search of all online databases, it is better that a unique inception time be determined for the systematic review and applied for all databases.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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