



Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: <http://www.elsevier.com/locate/clnu>

Letter to the Editor

Yes, vitamin D can be a magic bullet

Dear Editor:

Reijnen and Soeters [1] recently reviewed evidence from observational studies and RCTs on vitamin D and various health outcomes and concluded: *“The high incidence of low vit D levels in disease related inflammatory states is predominantly based on reversed causality. Inflammation causes a decrease in total plasma Vit D due to a decrease of its binding protein, but active Vit D does not change. In practice the assessment of Vit D status is especially indicated in patients with symptoms of malabsorption, renal failure, hepatic failure, patients with low bone mineral density, patients prone to malnutrition and patients who lack sun exposure.”*

Evidently these authors are not considering mechanistic evidence. One review notes, *“The bone-centric guidelines recommend a target 25(OH)D concentration of 20 ng/mL (50 nmol/L), and age-dependent daily vitamin D doses of 400-800IU. The guidelines focused on pleiotropic effects of vitamin D recommend a target 25(OH)D concentration of 30 ng/mL (75 nmol/L), and age-, body weight-, disease-status, and ethnicity dependent vitamin D doses ranging between 400 and 2000IU/day.”* [2]

Regarding inflammatory disorders, meta-analysis of 28 studies showed that supplementation reduced serum hs-CRP by -0.20 ± 0.07 (95% CI -0.34 to -0.06; $p = 0.006$) ng/mL [3], and vitamin D suppresses pro-inflammatory and increases anti-inflammatory cytokine secretion [4].

RCT health outcomes depend on raising deficient circulating 25(OH)D concentrations to levels adequate to allow target tissue activation rather than on the dose given or on the tightly regulated circulating calcitriol levels which do not reflect deficiency. Vitamin D RCTs should be based on baseline and achieved circulating 25(OH)D concentrations since Western populations commonly include many non-deficient participants, reducing or abolishing the apparent benefits of supplementation. Significant benefits are commonly seen in deficient study subgroups as recently reported in two major recent RCTs, where cancer and type 2 diabetes mellitus development in pre-diabetes fell in subjects with deficiency or with low BMIs [5], as also reported in populations where deficiency is common.

Evidence for health benefits of better vitamin D status also comes from ecological studies where geographical variation of risk follows solar UVB doses, and health risks rise following low solar winter UVB and fall following high-summer sunshine; from Mendelian randomization demonstrations of health risk variation with gene variants relevant to vitamin-D₃ production and

activation, as supported by the many mechanistic benefits of activated hormonal vitamin D. Overall, the available evidence is compelling for increasing numbers of beneficial health outcomes with correction of deficiency [e.g. acute upper respiratory tract infections, cancer, insulin resistance, type 2 diabetes mellitus and many pregnancy and birth outcomes]. Furthermore, the authors would need a better hypothesis for the evolution of variations in human skin pigmentation than a balance between vitamin D production and protection against solar tissue damage if their contention were correct.

Conflict of Interest

WBG receives funding from Bio-Tech Phramacal, Inc. (Fayetteville, AR).

BJB has no conflicts of interest to disclose.

References

- [1] Reijnen PLM, Soeters PB. Vitamin D: a magic bullet or a myth? Clin Nutr 2020 Jan 10. <https://doi.org/10.1016/j.clnu.2019.12.028>. pii: S0261-5614(20)30004-2. [Epub ahead of print].
- [2] Pludowski P, Holick MF, Grant WB, Konstantynowicz J, Mascarenhas MR, Haq A, et al. Vitamin D supplementation guidelines. J Steroid Biochem Mol Biol 2018;175:125–35.
- [3] Mirhosseini N, Vatanparast H, Kimball SM. The association between serum 25(OH)D status and blood pressure in participants of a community-based program taking vitamin D supplements. Nutrients 2017;9:E1244.
- [4] Chun RF, Liu PT, Modlin RL, Adams JS, Hewison M. Impact of vitamin D on immune function: lessons learned from genome-wide analysis. Front Physiol 2014;5:151.
- [5] Grant WB, Boucher BJ. Why secondary analyses in vitamin D clinical trials are important and how to improve vitamin D clinical trial outcome analyses-A comment on “Extra-Skeletal effects of vitamin D. Nutrients 2019;11:E2182.

William B. Grant*

Sunlight, Nutrition, and Health Research Center, P.O. Box 641603, San Francisco, CA, 94164-1603, USA

Barbara J. Boucher

The Blizzard Institute Barts, The London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom

* Corresponding author.

E-mail addresses: wgrant@infionline.net (W.B. Grant).

2 February 2020

DOI of original article: <https://doi.org/10.1016/j.clnu.2020.03.023>.

<https://doi.org/10.1016/j.clnu.2020.03.021>

0261-5614/© 2020 Elsevier Ltd and European Society for Clinical Nutrition and Metabolism. All rights reserved.

Please cite this article as: Grant WB, Boucher BJ, Yes, vitamin D can be a magic bullet, Clinical Nutrition, <https://doi.org/10.1016/j.clnu.2020.03.021>