


Comment

# Re: Scragg—Emerging Evidence of Thresholds for Beneficial Effects from Vitamin D Supplementation

Barbara J Boucher <sup>1,\*</sup> and William B. Grant <sup>2</sup> 

<sup>1</sup> The Blizard Institute, Barts & The London School of Medicine & Dentistry, Queen Mary University of London, London E1 2AT, UK

<sup>2</sup> Sunlight, Nutrition and Health Research Center, PO Box 641603, San Francisco, CA 94164-1603, USA; wgrant@infionline.net

\* Correspondence: bboucher@doctors.org.uk

Received: 4 March 2019; Accepted: 8 March 2019; Published: 13 June 2019



Scragg reports increasing evidence for differences in the thresholds for serum 25-hydroxyvitamin D [25(OH)D] concentration [vitamin D repletion] that need to be reached in populations observationally, or to be achieved by vitamin D supplementation in deficiency, before health benefits become apparent in different conditions [1]. Such variations are important as they add to the problems of developing adequate public health advice on desirable long-term vitamin D intakes and serum 25(OH)D concentrations at the population level. Additional evidence of such variations will assist in progressing the evolution of guidelines on optimal vitamin D intakes. Equally important will be the exclusion of confounding variations in threshold assessment due to differences in 25(OH)D assay methodology, since HMLC-TMS technology [2] normally gives higher results (often averaging about >5 nmol/L, but up to >33 nmol/L) than immunoassays [3]. Increasing compliance of laboratories providing 25(OH)D data with international quality control scheme requirements must be reducing assay unreliability. However, harmonization of older assay data with the newer “gold standard” methodology [4] will lead to the need to redefine the “cut-offs” classically used for defining deficiency and sufficiency. For example, standardised means of 49.7 nmol/L (48.2–51.3) and 49.3 nmol/L (47.4–51.2) by immunoassay were 62.0 nmol/L (58.9–65.1) and 60.9 nmol/L (57.1–64.7) in women and men respectively, after standardization to LC-MS/MS methodology [3]. However, such standardization will also increase the possibility of including older reports in further assessments of thresholds for various health benefits of increasing vitamin D status. It may be useful, therefore, to mention some additional reports of thresholds for health risk reduction from the existing literature that could prove useful in further analyses of data relevant to this important topic.

Reductions in abnormal insulin resistance have been reported after six months of supplementation with vitamin D at 4000 IU/day in deficient South-East Asian women living in New Zealand, but only in those women who achieved 25(OH)D values >80nmol/L [5], and, observationally, in obese black and white Americans at >65 nmol/L [6] and between 41.6 and 68.0 nmol/L in Hispanic black, Mexican American, and non-Hispanic white Americans [7]. Improved markers of bone health were found observationally with increasing serum 25(OH)D values >50 nmol/L in a study across 29 countries [8]. Literature review for features reducing fracture risks only found these at 25(OH)D values >50 nmol/L [9], while favourable responses to bisphosphonates in osteoporotic post-menopausal women required serum 25(OH)D concentrations >82 nmol/L [10]. Analyses of old and emerging data on thresholds for vitamin D efficacy using harmonized serum 25(OH)D concentrations, should, as Scragg points out, assist greatly in the development of optimal recommendations for long-term vitamin D<sub>3</sub> intakes and serum 25(OH)D concentrations, which would allow rationalisation of public health decisions on recommended daily intakes, according to demonstrable biological effects of different levels of vitamin D status in humans.

**Conflicts of Interest:** The authors have no conflicts of interest.

## References

1. Scragg, R. Emerging evidence of thresholds for beneficial effects from vitamin D supplementation. *Nutrients* **2018**, *10*, 561. [[CrossRef](#)] [[PubMed](#)]
2. Lensmeyer, G.L.; Wiebe, D.A.; Binkley, N.; Drezner, M.K. HPLC method for 25-hydroxyvitamin D measurement: comparison with contemporary assays. *Clin. Chem.* **2006**, *52*, 1120–1126. [[CrossRef](#)] [[PubMed](#)]
3. Rabenberg, M.; Scheidt-Nave, C.; Busch, M.A.; Thamm, M.; Rieckmann, N.; Durazo-Arvizu, R.; Dowling, K.G.; Skrabáková, Z.; Cashman, K.D.; Sempos, C.T.; et al. Implications of standardization of serum 25-hydroxyvitamin D data for the evaluation of vitamin D status in Germany, including a temporal analysis. *BMC Public Health*. **2018**, *18*, 845–858. [[CrossRef](#)] [[PubMed](#)]
4. Berry, D.J.; Dutton, J.; Fraser, W.D.; Jarvelin, M.R.; Hypponen, E. Harmonization study between LC-MS/MS and Diasporin RIA for measurement of 25-hydroxyvitamin D concentrations in a large population survey. *J. Clin. Lab. Anal.* **2017**, *31*. [[CrossRef](#)] [[PubMed](#)]
5. von Hurst, P.R.; Stonehouse, W.; Coad, J. Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitamin D deficient—A randomised placebo-controlled trial. *Br. J. Nutr.* **2010**, *103*, 549–556. [[CrossRef](#)] [[PubMed](#)]
6. Sorkin, J.D.; Vasalis, T.S.; Streeten, E.; Ryan, A.S.; Goldberg, A.P. Evidence for threshold effects of 25-hydroxyvitamin D on glucose tolerance and insulin resistance in black and white obese postmenopausal women. *J. Nutr.* **2014**, *144*, 734–742. [[CrossRef](#)] [[PubMed](#)]
7. Al-Khalidi, B.; Rotondi, M.A.; Kimball, S.M.; Ardern, C.I. Clinical utility of serum 25-hydroxyvitamin D in the diagnosis of insulin resistance and estimation of optimal 25-hydroxyvitamin D in U.S. adults. *Diabetes Res. Clin. Pract.* **2017**, *134*, 80–90. [[CrossRef](#)] [[PubMed](#)]
8. Kuchuk, N.P.; van Schoor, N.M.; Pluijm, S.M.; Chines, A.; Lips, P. Vitamin D status, parathyroid function, bone turnover, and BMD in postmenopausal women with osteoporosis: global perspective. *J. Bone. Min. Res.* **2009**, *24*, 693–701. [[CrossRef](#)] [[PubMed](#)]
9. Lips, P.; Bouillon, R.; van Schoor, N.M.; Vanderschueren, D.; Verschueren, S.; Kuckuk, N.; Milisen, K.; Boonen, S. Reducing fracture risk with calcium and vitamin D. *Clin. Endocrinol. (Oxf.)*. **2010**, *73*, 277–285. [[CrossRef](#)] [[PubMed](#)]
10. Carmel, A.S.; Shieh, A.; Bang, H.; Bockman, R.S. The 25(OH)D level needed to maintain a favourable biposphonate response is 33 ng/ml. *Osteoporos. Int.* **2012**, *23*, 2479–2487. [[CrossRef](#)] [[PubMed](#)]



© 2019 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).