

Vitamin D status and ill health

Philippe Autier and colleagues¹ should be congratulated for providing a thorough overview and thoughtful discussion of the numerous studies showing associations between low serum concentrations of vitamin D and various causes of ill health in the context of the disappointing lack of response to oral vitamin D supplementation. The authors suggest that this finding might be attributable to reverse causation (ie, ill health lessens behaviour leading to exposure to the sun) or to systemic inflammation lowering vitamin D concentrations. We believe that they have overlooked another parsimonious and likely explanation: that circulating vitamin D is a biomarker for sunlight exposure, and that the sun is—for most people and when enjoyed in moderation—beneficial to health.

Exposure to ultraviolet light is carcinogenic to the skin, and extensive research has delineated the various mechanisms involved. Despite almost a century of work however, no reports suggest that exposure to sunlight shortens life. Conversely, two recent epidemiological studies show that although increased sun exposure was associated with increased incidence of melanoma, all-cause mortality was reduced;² and that the presence of non-melanoma skin cancer is associated with a 50% lower odds ratio for all-cause death.³ High blood pressure is the leading cause of disability-adjusted life-years, accounting for 18% of all deaths worldwide. Population blood pressure correlates directly with latitude and is lower in summer than winter. We have shown that human skin contains large stores of nitrogen oxides, which are mobilised to the systemic circulation by exposure of the body to ultraviolet A light, causing arterial vasodilatation and a decrease in blood pressure.⁴ This effect is independent of vitamin D. We also noted that the suppressive effects of ultraviolet radiation on immune-driven

diseases such as atopic dermatitis and asthma are independent of circulating vitamin D concentration, at least in animals.⁵ Vitamin D might also be involved in these processes, but the sun seems beneficial to health via a mechanism of action unrelated to vitamin D.

Public health advice on sun exposure, driven by dermatological concerns over skin cancer, has failed to take into account the possible benefits of sunlight. These benefits have become conflated with vitamin D, which we suggest only accounts for some of the positive aspects of sun exposure. Ultraviolet radiation has a wide range of biological effects other than carcinogenesis. In view of the epidemiological and mechanistic data showing improvements induced by sun in some of the major causes of disability-adjusted life-years, advice on healthy sun exposure needs to be reconsidered.

We declare that we have no competing interests.

**Martin Feelisch, Shelley Gorman,
*Richard B Weller**
r.weller@ed.ac.uk

Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton General Hospital, Southampton, UK (MF); Telethon Institute for Child Health Research, The University of Western Australia, Perth, WA, Australia (SG); and University of Edinburgh, MRC Centre for Inflammation Research, Edinburgh, UK (RBW)

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- 2 Yang L, Lof M, Veierod MB, Sandin S, Adami HO, Weiderpass E. Ultraviolet exposure and mortality among women in Sweden. *Cancer Epidemiol Biomarkers Prev* 2011; **20**: 683–90.
- 3 Brondum-Jacobsen P, Nordestgaard BG, Nielsen SF, Benn M. Skin cancer as a marker of sun exposure associates with myocardial infarction, hip fracture and death from any cause. *Int J Epidemiol* 2013; **42**: 1486–96.
- 4 Liu D, Fernandez BO, Hamilton A, et al. UVA irradiation of human skin vasodilates arterial vasculature and lowers blood pressure independently of nitric oxide synthase. *J Invest Dermatol* 2014; published online Feb 20. DOI:10.1038/jid.2014.27.
- 5 Gorman S, Scott NM, Tan DH et al. Acute erythral ultraviolet radiation causes systemic immunosuppression in the absence of increased 25-hydroxyvitamin D3 levels in male mice. *PLoS One* 2012; **7**: e46006.

In their Review,¹ Philippe Autier and colleagues reasoned that without evidence from randomised controlled trials, we cannot assume a causal association between vitamin D and prevention of chronic disease. We look forward to the results of large trials that are underway, but we hope that the results will not lead to years of debate, as happened with the Women's Health Initiative study.^{2–4} We should be mindful that individuals who are most deficient in vitamin D are the ones most likely to benefit from supplementation, and exercise caution when extrapolating to the general population (most of whom have adequate vitamin D status for their needs, at least in the summer and autumn at high latitudes). Despite concern about vitamin D deficiency in winter, no data exist to support the notion that the seasonal fall in circulating 25(OH)D to less than optimum concentrations in the winter months is directly associated with poor health outcomes. In this regard, small studies might provide a better controlled system for several analytical outcome measurements, with more frequent face-to-face contact with participants. Our randomised controlled trial⁵ of 300 older women tested two daily vitamin D doses (400 IU and 1000 IU) against placebo, with 87% completing the final visit, and was unique in that it was specifically designed to account for changes due to season, and participants attended follow-up twice a month for one year. The women, although outwardly healthy, started the trial with low vitamin D status (median 25[OH]D 34 nmol/L). Our study design uncovered a seasonal pattern of blood pressure that was independent of vitamin D treatment. As systolic blood pressure went down in the summer (by a mean of 6.6 mm Hg [SD 10.8]) and back up in the winter, the decrease was associated with increased vitamin D status in the placebo group. Thus, a causal association might have been assumed, but the same pattern was noted in both vitamin D treatment groups.