Editorial Comment

Journal of INTERNAL MEDICINE

doi: 10.1111/joim.12248

Is there a golden mean for sun exposure?

Hardly a week goes by when the attention of the scientific press and the general public is not focused on a new report about the health effects of sunshine. Most studies of the effects of strong or prolonged ultraviolet radiation (UVR) exposure on the skin have emphasized the importance of sun avoidance and protection against sun exposure to reduce skin cancer risk. In recent years, though, these reports have competed for attention with studies about the health benefits and protective effects of vitamin D, and the potentially serious health risks caused by vitamin D insufficiency and deficiency. Because most vitamin D is produced in the skin by sun exposure, and specifically by DNA-damaging and carcinogenic UVB wavelengths, the development of tension within the medical community over the costs and benefits of sun exposure was inevitable.

Important data bearing on this dilemma come from the study of Lindqvist and colleagues in this issue. The authors report the results of a longitudinal cohort study designed to assess how all-cause mortality risk may be influenced by avoidance of active sun exposure. The population studied by Lindqvist *et al.* consisted of women had been recruited for a prospective 20-year follow-up of the Melanoma in Southern Sweden (MISS) cohort. Equal numbers of women aged 25–64 years with no history of cancer were invited into the study in 1990; 29,518 (74%) formally entered the study. The survey questions about sun exposure explored the frequency of activities that involved exposure of large surface areas of the body under strong sunlight or simulated sunlight; these activities included summertime sunbathing, vacation sunbathing and the use of tanning beds. Along with standard anthropometrics, hereditary disposition to malignant melanoma (MM) was assessed, smoking habits at the inception of the study were recorded, and level of exercise was categorized. Cases of MM and fatalities due to MM were dichotomized by Breslow thickness.

At the inception of the study in 1990, the investigators almost certainly did not anticipate that *avoidance* of sun exposure would be associated with an increase in all-cause mortality, but that is exactly what they discovered. Data available at that time indicated a strong causal relationship between sun exposure and MM, but no relationship between avoidance of sun exposure and increased mortality. In fact, in 1990, avoiding sun exposure was considered one of the healthiest things one could do because data on increased prevalence of skin cancers – especially amongst light-skinned people of European ancestry living in or even vacationing in sunny places – presented a dramatic picture of the risks of unprotected sun exposure. At that time, relatively few details were known about the relationship between sun exposure and the cutaneous production of vitamin D or other bioactive compounds, and there was no intimation that avoidance of sun exposure might pose a significant health risk.

The primary finding of Lindqvist *et al.* was that the mortality rate amongst sun avoiders in their cohort was approximately twice that of the most active sun exposers, yielding an excess mortality with a population attributable risk of 3%. This is a small effect, but very significant due to sample size and power. The authors are guarded in their discussion of the reasons why sun avoidance is associated with increased mortality. In previous studies, they speculated that this was due to insufficient vitamin D levels amongst sun avoiders, but cautioned that their results could not indicate a causal relationship. They are even more restrained here. They go to great lengths to point out that vitamin D is just one of several bioactive compounds produced by strong UVR solar ultraviolet exposure that may have an effect on morbidity and mortality. The 'dose-dependent' inverse relationship between sun exposure and all-cause mortality seen in their models is intriguing and supports the argument that some unidentified factor correlated with sun exposure is protective. Vitamin D is a strong candidate because of its myriad immune system boosting functions [1], but it probably cannot account entirely for the effects observed in the study. Cutaneous vitamin D production is strictly the product of UVB exposure, and southern Sweden boasts a highly seasonal UVB regime and a

long UVB-free winter. Studies show at the autumnal equinox (September 22), Boston, Massachusetts, at 42.5°N still receives ample UVB to catalyse vitamin D formation in the skin, but Malmö, Sweden, at 55.5°N does not (Fig. 1) [2]. One of the most interesting implications of the Lindqvist *et al.* data is that the most active sun exposers with the lowest mortality rates in the study were almost certainly experiencing high UVA loads because of their winter sun and tanning bed exposures. Thus, the mortality-reducing effects observed amongst the most active exposers probably were due to many factors including a suite of bioactive compounds produced by both UVB and UVA exposure: vitamin D and nitrous oxide, respectively. The skin is now recognized as harbouring a reservoir of nitric oxide (NO) metabolites, which are activated by UVA and which appear to exert a benign effect of cardiovascular homeostasis [3]. Sun avoiders thus lose out on both photosynthesized vitamin D and photoactivated NO.

Detailed data on the nature and duration of sun and tanning bed exposures of the MISS cohort would have helped significantly to illuminate the origin of the protective effects experienced by the active sun exposers in the Lindqvist *et al.* study. The ratio of UVB to UVA in sunlight varies according to latitude, season, time of day, levels of air pollution and other factors which were not possible to consider in the study [4]. Although UVA is present in sunlight throughout the year, UVB becomes more seasonal and attenuated with increasing latitude, resulting in significantly reduced potential for cutaneous biosynthesis of vitamin D [5]. Successful adaptations to high-latitude environments such as southern Sweden have been both biological and cultural, involving increasing amounts of vitamin D-rich foods in the diet to supplement seasonally photosynthesized vitamin D [6]. Throughout history and in most places, however, human vitamin D is derived primarily from sun exposure and not from food [7].

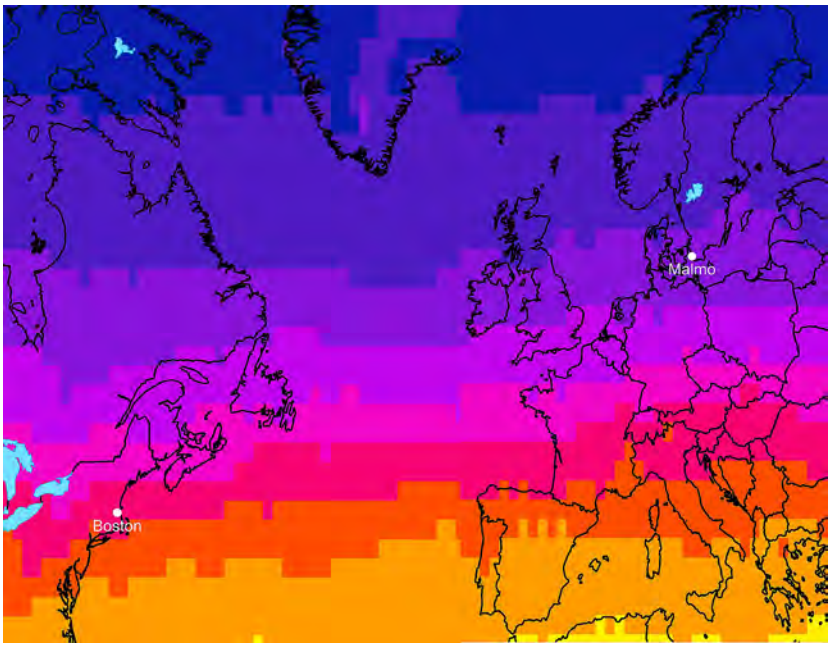

Fig. 1 *Visual comparison of 305 nm UVB levels for a portion of the Northern Hemisphere at the autumnal equinox (AE; 22 September), illustrating the difference in the potential for cutaneous vitamin D photosynthesis between Boston, Massachusetts, and Malmö, Sweden. At the AE, Boston receives 28 Jm^2; its annual mean is 23.9 Jm^2, and its annual maximum is 73 Jm^2. Malmö at the AE receives 12 Jm^2 with an annual mean of 11.6 Jm^2 and an annual maximum of 55 Jm^2. The breadth of the Atlantic Ocean has been reduced for purposes of display. Map based on remotely sensed data from the NASA Total Ozone Mapping Spectrometer flown aboard the Nimbus 7 satellite. Map and associated statistics created by George Chaplin and acknowledged with thanks.*

The biggest questions to emerge from the Lindqvist *et al.* study surround the nature and activity of the compounds produced by sun exposure and what happens in sun avoiders when these compounds are absent or present only at low levels. If this is primarily a vitamin D effect, then remedial measures such as additional food fortification or recommendations for vitamin supplementation can be implemented relatively easily, with no risk of additional skin cancers. Vitamin D deficiency is associated with increased susceptibility to infectious diseases such as tuberculosis and complex chronic diseases such as type 2 diabetes [8, 9], and it is widely accepted that that the high prevalence of vitamin D deficiency requires some kind of intervention.

What is a modern human supposed to do? If sun exposure is to be recommended, it should be of the wavelengths and energies to which a person's skin is adapted. Our ancestors spent most of their time outdoors, but did not sunbathe or subject themselves to intense prolonged solar irradiation on foreign holidays. With skin as the major interface with our physical environment, we faced changing solar conditions, outside, day by day. Only in the last few thousand years have large numbers of us spent significant amounts of time indoors, and only in the last century have large numbers of people engaged in the kinds of episodic sun exposure on weekends and foreign vacations – often leading to sunburns – that we consider normal today. In today's highly urbanized world, most people pursue indoor lifestyles whilst wearing concealing clothing. And, because of migration, many of us live under vastly different solar conditions than those of our ancestors. Understanding these changes will allow us to compensate for modernity through bespoke prescriptions for sun exposure and diet that are appropriate to our ancestry, location and lifestyle. The results of the Lindqvist *et al.* study indicate that we need to think about these things sooner rather than later.

Conflict of interest statement

The author is a member of the Scientific Advisory Board of L'Oréal.

N. G. Jablonski
From the Department of Anthropology, The Pennsylvania State University, University Park, PA, USA

References

1 Hewison M. Vitamin D and immune function: an overview. *Proc Nutr Soc* 2012; **71:** 50–61.
2 Webb AR, Kline L, Holick MF. Influence of season and latitude on the cutaneous synthesis of vitamin D_3: exposure to winter sunlight in Boston and Edmonton will not promote vitamin D_3 synthesis in human skin. *J Clin Endocrinol Metab* 1988; **67:** 373–8.
3 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; doi: 10.1038/jid.2014.27.
4 Jablonski NG, Chaplin G. Human skin pigmentation as an adaptation to UV radiation. *Proc Natl Acad Sci* 2010; **107:** 8962–8.
5 Jablonski NG, Chaplin G. The evolution of human skin coloration. *J Hum Evol* 2000; **39:** 57–106.
6 Chaplin G, Jablonski NG. The human environment and the vitamin D compromise: Scotland as a case study in human biocultural adaptation and disease susceptibility. *Hum Biol* 2013; **85:** 529–52.
7 Chen TC, Chimeh F, Lu Z *et al.* Factors that influence the cutaneous synthesis and dietary sources of vitamin D. *Arch Biochem Biophys* 2007; **460:** 213–7.
8 Gorham ED, Garland CF, Burgi AA *et al.* Lower prediagnostic serum 25-hydroxyvitamin D concentration is associated with higher risk of insulin-requiring diabetes: a nested case–control study. *Diabetologia* 2012; **55:** 3224–7.
9 Khoo AL, Chai L, Koenen H, Joosten I, Netea M, van der Ven A. Translating the role of vitamin D3 in infectious diseases. *Crit Rev Microbiol* 2012; **38:** 122–35.

Correspondence: Nina G. Jablonski, Evan Pugh Professor of Anthropology, The Pennsylvania State University, 409 Carpenter Building, University Park, PA, 16802, USA.
(fax: +1 814-863-1474; e-mail: ngj2@psu.edu).

