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Research: Treatment

Vitamin supplementation and blood pressure in Type 2 diabetes

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Abstract

Aims Vitamin D levels are inversely related to blood pressure. Given that low sun exposure can create a greater reliance on dietary sources of vitamin D, we aimed to determine whether dietary vitamin D and blood pressure associations differ between periods of low and high sun exposure.

Methods Dietary intake, vitamin supplementation, blood pressure, and anthropometric parameters were assessed each season for 1 year (174 adults with Type 2 diabetes). Separate linear regression models were constructed for high and low sun exposure periods to examine associations of systolic blood pressure with dietary vitamin D intake and vitamin supplement use (adjusted for age, gender, BMI, ethnicity, smoking, alcohol, physical activity, antihypertensive medication and nutrient intake). Robustness of findings was confirmed with within-subject repeated measures analysis, including an interaction term for sun exposure period.

Results Vitamin D intake from food sources was low year-round and no conclusive association with blood pressure was identified during either period. Systolic blood pressure was 5.1 mmHg lower during the low sun exposure period (95% CI 0.5–9.7) in daily supplement users compared with non-users. The interaction term between supplement use and sun exposure period was significant (low sun exposure* no supplement, $P = 0.02$). Systolic blood pressure was relatively stable in users (low and high sun exposure periods, respectively, mean ± SE: 135.2 ± 2.6 mmHg and 134.2 ± 2.5 mmHg), but not in non-users (140.2 ± 2.7 mmHg and 130.5 ± 2.5 mmHg).

Conclusions Vitamin supplementation may stabilize systolic blood pressure in adults with Type 2 diabetes across seasons.

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Introduction

Careful attention to systolic blood pressure control in diabetes is critical to the prevention of cardiovascular disease complications [1]. Current diabetes care guidelines recommend that the average blood pressure should be maintained at less than 130/80 mmHg in diabetes [2–4]. However, it may be challenging to maintain stable, well-controlled blood pressure throughout the year. Several studies have detected higher blood pressure values during the autumn and winter months in a variety of populations. Specifically among adults with Type 2 diabetes, we recently determined systolic blood pressure values to be higher during the autumn and winter months compared with the spring and summer [5].

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Preventing such an increase is of potential clinical importance given that a recurrent annual increase in blood pressure could potentially result in vascular injury over time. The factors responsible for the autumn /winter blood pressure increase remain unclear. In our study, although there was a stepwise inverse relationship between blood pressure and pedometer-assessed daily steps in our cohort [6], seasonal differences in step counts did not explain seasonal differences in systolic blood pressure and there were no important seasonal differences in BMI [5].

We hypothesized that the rise in blood pressure could, in part, be the result of a lack of exposure to sunlight and changes in dietary habits during the autumn and winter months. Sunlight stimulates cutaneous production of vitamin D and is the primary source of this vitamin [7]. Some cross-sectional [8] and prospective studies [9,10] indicate that low serum vitamin D concentrations are associated with greater risk of hypertension. If the decline in sunlight-stimulated vitamin D production during the autumn and winter is not offset by increased intake through food sources or vitamin supplements, an increase in blood pressure could result. During the autumn and winter months, fruit and vegetables may be somewhat less available and this could also adversely impact blood pressure control given that the Dietary Approaches to Stop Hypertension (DASH) study has demonstrated that a low-fat diet that is rich in fruits, vegetables, and low-fat dairy products, can lower blood pressure [11,12].

Therefore, we used data from our observational cohort study to examine associations of systolic blood pressure with dietary vitamin D intake and vitamin supplement use, during periods of relatively high sun exposure (April–September) and low (October–March) sun exposure in adults with Type 2 diabetes.

Patients and methods

Study design and population

The analyses presented herein are based on data collected from 201 adults with Type 2 diabetes residing in Montreal, Canada. We specifically included the 174 subjects for whom data were available for both periods of high and low sun exposure, defined as April to September and October to March, respectively. Volunteer participants were recruited between June 2006 and June 2008 primarily through outpatient clinics affiliated with McGill University. All provided written informed consent. Study procedures were approved by the Institutional Review Board of McGill University and participating institutions. Procedures have been previously reported [13] but are summarized here.

Data collection

Assessments were conducted once per season over a 1-year follow-up period. These included blood pressure assessment (automated appropriate-sized cuff after 15 min seated period, left arm supported on the table; Omron HEM 747 IC; Omron Healthcare, Bannockburn, IL, USA), and direct assessment of anthropometric variables (weight, SECA 882 electronic scale, SECA Corporation, Hamburg, Germany; height, SECA 214 stadiometer, SECA Corporation). Dietary intake and vitamin supplement use were assessed through a bilingual (English and French), semiquantitative, self-administered Food Frequency Questionnaire (FFQ) that has previously been demonstrated to have good correlation with energy and nutrient intakes estimated from food records [14]. The Canadian Nutrient File is the standard reference food composition database that indicates the amount of nutrients in foods commonly consumed in Canada (Health Canada, Health Products and Food Branch). The Canadian Nutrient File 2007b, the eleventh version, was used to calculate the energy and nutrient composition of foods consumed; this is a computerized database that contains nutrient values of more than 5500 foods, including the most popular Canadian foods. The FFQ also queries use of vitamin supplement as daily, not daily or never. In terms of physical activity assessment, both direct measures and self-reported measures were employed in the present study. Step counts were assessed for 2 weeks each season using pedometers. The viewing window on which the step counts appeared was concealed with a cover and tamper-proof seal to reduce the likelihood that participants would alter activity in response to monitoring. Self-reported physical activity was measured with the International Physical Activity Questionnaire (short form, last 7 days). Mood was assessed by the score of Center for Epidemiologic Studies Depression scale (CES-D), with a score less than 16 considered indicative of depressed mood [15].

Statistical methods

Participant data were categorized into relatively high sun exposure (from April to September) and low (from October to March) sun exposure periods. For each subject, data were averaged over each period. Dietary intakes were compared with DASH diet recommendations [16]. Separate linear regression models were constructed for the periods with relatively high and low sun exposure to examine associations of systolic blood pressure with vitamin D intake (as a continuous variable) and with supplement use (divided into three classes: no; yes, daily; yes, not daily). The 95% confidence intervals were calculated for all regression coefficient estimates. The covariates included in the models were age, sex, BMI, physical activity (step counts and self-reported activity level), ethnicity (White/non-White), smoking, alcohol and number of antihypertensive medications. In addition, total energy and nutrients addressed in DASH diet recommendations (carbohydrate, protein, total fat, saturated fat, cholesterol, fibre, calcium, magnesium, sodium and potassium) were also considered as individual covariates. Because colinearity among the variables may affect the precision of the estimates, one variable from each pair of highly correlated variables (Spearman correlation coefficient ≥ 0.85), was removed. Given findings of these analyses, as a robustness check, within-subject repeated measures linear regression model was used, using an interaction term for the variable representing sun exposure period and supplement use. Statistical analyses were conducted using SAS (version 9.1, SAS Institute, Cary, NC, USA).

Results

Of the 201 participants enrolled in the original cohort, 174 had at least one visit during each of the high and low sun exposure periods and were included in our analyses. Over the 1-year follow-up period, there were a total of 651 study centre visits (average 3.7 visits per person), of which 342 (52.5%) were during the low sun exposure period and 309 (47.5%) during the high sun exposure period. The mean age of the subjects was 62.4 years (SD 10.6 years, range 27–85 years) and the median duration of diabetes was 8 years (inter-quartile range 3–13 years). Fifty two per cent were men; 69% were married, 10% were current smokers and 69% were Europid. Sixty two per cent had at least a college degree. The average alcohol consumption was 5.4 g/day (SD 10.0). Body-mass index ranged from 19.0 to 43.9 kg/m^2, with 46% being obese (BMI ≥ 30 kg/m^2). A higher proportion of men (30%) than women (7%) reported cardiovascular disease. Participants were, on average, at the stage 1 level of obesity and at the sedentary to low-active range of physical activity (Table 1), as per Tudor-Locke & Bassett's [17] step count classification scheme.

A mean systolic blood pressure greater than 130 mmHg was detected in 103 (59%) and 115 (66%) subjects during the high and low sun exposure periods, respectively. Systolic blood pressure was, on average, 3.0 mmHg higher (95% CI 1.2–4.8) and daily step count 507 lower (95% CI −773 to −241) during the low sun exposure period (Table 1). The number of antihypertensive medications and the proportion of subjects with depressed mood (36% in the high sun exposure and 33% in the low sun exposure months) did not differ between the two periods. Body-mass index tended to be stable across periods.

Vitamin D and supplements

Intakes of vitamin D from food sources and vitamin supplements did not differ by period. During both periods, about half of the subjects reported daily use of vitamin supplements (Table 2). While roughly half of the subjects aged 50 years and younger received vitamin D from food sources in the amount recommended as adequate intake (5 μg), in the age group over 70 years almost none met the adequate intake (15 μg) (Table 2).

Nutrients recommended in the DASH diet

Total energy intake did not differ between periods. Carbohydrate intake was higher during the low sun exposure period (Table 3). During both periods, levels of total fat and saturated fat intake were higher than the recommended levels of < 35% of energy [18,19] and < 7% of energy, respectively [20]. In addition, intake of micronutrients addressed in the DASH diet recommendations was similar across periods. Most subjects did not meet the recommended levels for potassium, calcium, magnesium and fibre, and consumed high amounts of cholesterol, saturated fat, fat and sodium (Fig. 1).

Associations between nutrients and blood pressure

There were no clinically important associations with systolic blood pressure of either vitamin D or any of the other micronutrients obtained from food sources. There were, however, important associations with use of vitamin supplements (Table 4). In a model including data only from the low sun exposure period, compared with regular supplement users, those who did not use vitamin supplementation had a higher systolic blood pressure (mean ± SE, non-users vs. users: 140.2 ± 2.7 mmHg vs. 135.2 ± 2.6 mmHg, 95% CI 0.5–9.7 mmHg). In contrast, in a model including only data from the high sun exposure period, systolic blood pressure in supplement non-users appeared lower, although an absence of difference or even slightly higher blood pressure could not be excluded (mean ± SE, non-users vs. users: 130.5 ± 2.5 vs. 134.2 ± 2.5 mmHg, 95% CI −8.3–1.0). In a within-subject repeated measures model that included an interaction term between period and use of vitamin supplements, a clinically important interaction effect between vitamin supplementation and sun exposure period was confirmed (β coefficient for the interaction term, low sun exposure period × no supplementation of 5.2; 95% CI 0.7–9.7, $P = 0.02$). As illustrated in Fig. 2, vitamin supplement users appeared to have stable systolic blood pressure levels across periods. In contrast, non-users, had lower blood pressure values during the higher sun exposure period and higher values during the lower sun exposure period.

Table 1 Blood pressure, physical activity and anthropometric variables during high and low sun exposure periods

	High sun exposure (April–September)	Low sun exposure (October–March)	Within-individual difference*	
			Estimate	95% CI
Blood pressure				
Systolic, mmHg	133.4 ± 1.1	136.4 ± 1.1	3.0	1.2–4.8
Diastolic, mmHg	78.8 ± 0.7	79.4 ± 0.7	0.6	−0.4 to 1.6
Physical activity				
Total physical activity, MET† min.wk^{-1}	2923.8 ± 198.8	2699.4 ± 198.1	−224.5	−574.9 to 125.9
Steps/day	5571.9 ± 194.1	5065.3 ± 192.5	−506.7	−772.5 to −240.9
Anthropometric measures				
BMI, kg/m^2	30.2 ± 0.4	30.2 ± 0.4	0.02	−0.1 to 0.1
Waist circumference, cm	102.0 ± 1.0	101.5 ± 1.0	−0.6	−1.1 to −0.05

Data are presented as mean ± SE, $n = 174$.
*The value for high sun exposure period subtracted from that of the low sun exposure period.
†MET, metabolic equivalent of task.

Table 2 Supplement use and dietary vitamin D intake during high and low sun exposure periods and distribution of dietary vitamin D intake by age group in each period

	High sun exposure (April–September)			Low sun exposure (October–March)		
Vitamin supplement use*						
No, *n* (%)	81 (47)			74 (43)		
Yes, not daily, *n* (%)	11 (6)			14 (8)		
Yes, daily, *n* (%)	80 (47)			86 (49)		
Vitamin D, μg/day, mean ± SD	5.2 ± 0.2			5.2 ± 0.2		
Distribution, μg/day, mean ± SD						
Age	≤ 50 years	51–70 years	> 70 years	≤ 50 years	51–70 years	> 70 years
5th	2.05	1.05	1.89	2.26	1.48	1.72
25th	3.64	2.80	2.97	3.91	2.91	3.29
50th	5.52	4.26	4.92	5.39	4.26	4.53
75th	7.70	6.52	7.00	9.22	6.76	6.29
95th	11.49	11.24	9.37	12.35	10.61	8.79
Vitamin D adequate intake, μg/day	5	10	15	5	10	15

Table 3 Dietary data for nutrients addressed in Dietary Approaches to Stop Hypertension (DASH) recommendations during high and low sun exposure periods

	High sun exposure (April–September)	Low sun exposure (October–March)	Within-individual difference*	
			Estimate	95% CI
Energy, kcal/day	1697.3 ± 51.7	1694.8 ± 50.8	−2.5	−81.3 to 76.2
Carbohydrates, % energy	43.2 ± 0.5	44.1 ± 0.5	0.9	0.1–1.7
Protein, % energy	19.4 ± 0.3	19.3 ± 0.3	−0.08	−0.5 to 0.4
Fat, % energy	36.8 ± 0.5	36.4 ± 0.5	−0.4	−1.2 to 0.3
Saturated fat, % energy	11.0 ± 0.2	10.8 ± 0.2	−0.2	−0.43 to 0.05
Cholesterol, mg/day	236.2 ± 8.8	233.3 ± 8.7	−2.9	−16.0 to 10.2
Fibre, g/day	17.4 ± 0.5	17.5 ± 0.5	0.1	−0.6 to 0.9
Calcium, mg/day	770.5 ± 28.3	785.4 ± 27.8	14.9	−31.2 to 61.0
Magnesium, mg/day	278.3 ± 8.8	282.7 ± 8.6	4.4	−10.7 to 19.5
Sodium, mg/day	2510.1 ± 95.2	2525.6 ± 93.6	15.5	−126.1 to 157.0
Potassium, mg/day	2736.3 ± 78.9	2756.7 ± 77.4	20.4	−106.8 to 147.5

Data are presented as mean ± SE or *n* (%), *n* = 174.
*The value for high sun exposure period subtracted from that for the low sun exposure period.

We repeated the analysis on a subsample of data, excluding the subjects with implausible energy intake ($n = 20$; i.e. outside the range of 500 to > 3500 kcal for women and 800–4000 for men) [21]. However, this exclusion did not change the associations reported.

Discussion

In our Type 2 diabetes cohort, nutritional factors in the control of blood pressure were clearly not optimal: there was a high prevalence of obesity and dietary intake conformed poorly to DASH recommendations. Intake of vitamins from food sources was low throughout the year (this included intake of vitamin D). Food-derived vitamin D did not demonstrate any conclusive association with blood pressure. However, compared with vitamin supplement users, participants who did not consume a daily vitamin supplement had a 5.1 mmHg higher systolic blood pressure during the low sun exposure months (October–March). Curiously, their systolic blood pressure values may have been somewhat lower during the high sun exposure months. On balance, however, their blood pressure levels were well-controlled and stable across periods.

The finding of a high prevalence of obesity (46%) among individuals with Type 2 diabetes was not unexpected and indicates that our participants would benefit from weight loss, an ongoing challenge in Type 2 diabetes. Body-mass index is known to be positively associated with blood pressure levels [22]. In addition, vitamin D intake was less than adequate for many individuals in our cohort. The partial sequestration of vitamin D in body fat may lead to a high level of vitamin D insufficiency in obese subjects [23].

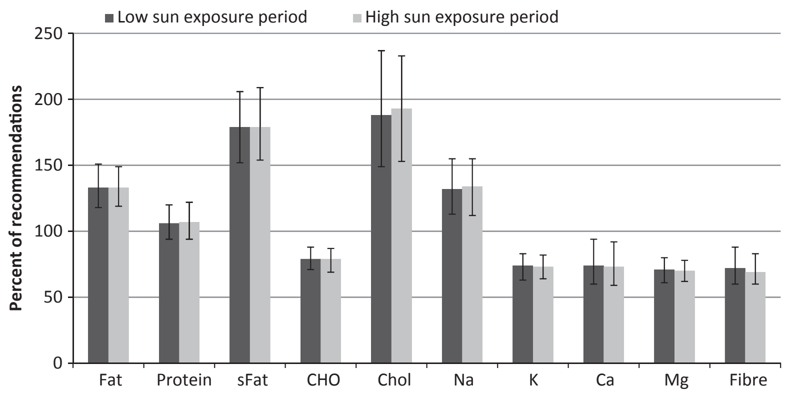

FIGURE 1 Median intakes of nutrients as per cent of Dietary Approaches to Stop Hypertension (DASH) recommendations. Error bars represent the 25 and75 percentiles. The DASH daily nutrient recommendations for 2100 calorie intake are: total fat, 27% of calories; saturated fat (sFat), 6% of calories; protein, 18% of calories; carbohydrate (CHO), 55% of calories; cholesterol (Chol), 150 mg; sodium (Na), 2300 mg; potassium (K), 4700 mg; calcium (Ca), 1250 mg; magnesium (Mg), 500 mg; fibre, 30 g.

Table 4 Estimated linear regression coefficients (β) and associated 95% confidence intervals for vitamin supplement use, with systolic blood pressure as outcome

Model	β	95% CI
Low sun exposure period		
Supplement		
Yes, daily	Reference	
Yes, not daily	4.5	−1.7 to 10.8
No	5.1	0.5–9.7
High sun exposure period		
Supplement		
Yes, daily	Reference	
Yes, not daily	−2.4	−9.9 to 5.0
No	−3.6	−8.3 to 1.0
Combined model, two periods		
Supplement		
Yes, daily	Reference	
Yes, not daily	−3.4	−10.1 to 3.2
No	−2.6	−7.0 to 1.6
Period		
High sun exposure	Reference	
Low sun exposure	−0.5	−3.8 to 2.9
Period by supplement interaction		
Low sun exposure period × not daily	6.2	−2.2 to 14.6
Low sun exposure period × no supplement	5.2	0.7–9.7

Adjusted for age, gender, BMI, ethnicity, smoking, alcohol, physical activity (total physical activity and steps/day), anti-hypertensive medication and intake of nutrients (glucose, total fibre, calcium, magnesium, sodium, cholesterol, saturated fat).

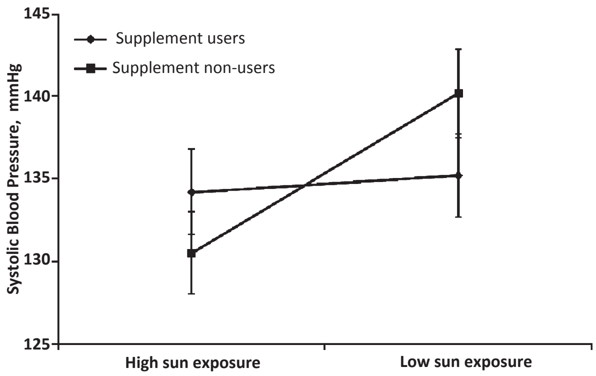

FIGURE 2 Least square mean systolic blood pressure ± SE during high and low sun exposure periods in separate regression models.

In our cohort, about half of the subjects reported the consumption of a vitamin supplement. This prevalence was similar to the prevalence reported in a population survey on 15 553 Canadian subjects aged 18–70 years, in which about 45% of subjects with chronic condition consumed a supplement in the previous month [24]. While routine vitamin supplementation is usually not recommended, the Canadian Diabetes Association recommends supplementation for vitamin D in individuals over 50 years old [19]. As we have reported, vitamin D intake from food sources was frequently inadequate. Although we did not have specific information concerning the vitamin content of the supplements used by our subjects, results of a survey on 26 735 multivitamin supplement users in the USA showed that among 123 different products, vitamin D content had a low variation, with many of the products containing 10 μg (400 IU) of vitamin D [13]. It should be noted that there is some evidence that very high vitamin D doses may increase fall risk, as in a trial [25] wherein older women were given an annual 500 000 IU dose; however, the vitamin D content of multivitamin supplements is well below this value. Supplementation is known to have a more important effect on vitamin D serum concentrations during low sun exposure months [26–28].

Given the stability of micronutrient intake and vitamin supplementation throughout the year, we believe that the association between vitamin supplementation and better blood pressure control during the low sun exposure months may be explained by the vitamin D content of the supplements. We cannot exclude the possibility that supplement use may be associated with better self-care behaviour: clearly, individuals who consume vitamin supplements have generally better socio-demographic factors associated with health [29], often make healthier food choices [30] and, in addition to supplements, consume more micronutrients, such as magnesium, from food sources [31,32]. However, in our analysis the positive effect of vitamin supplementation was observed after adjusting for the intakes of major food groups and specific micronutrients. We also adjusted for physical activity using objective (step counts) and self-report (questionnaire) measures.

In addition to vitamin D, combination of nutrients present in the supplements could be responsible for the observed lower blood pressure during the low sun exposure period. Particularly, the possibility of the role of the calcium–vitamin D combination cannot be excluded. Dietary vitamin D and calcium were inversely associated with the prevalence of metabolic syndrome in women over 45 years of age without diabetes [33]. However, in a large randomized placebo-controlled trial in postmenopausal women, vitamin D with calcium supplementation had no effect on incident hypertension during 7 years of follow-up [34]. There may thus be a need to better define the context in which vitamin D intake exerts a beneficial impact on blood pressure and cardiovascular disease (CVD) outcomes.

Currently, information on vitamin D status and risk of cardiovascular complications in diabetes is limited. Only one study tested the effect of vitamin D supplementation on 34 individuals with Type 2 diabetes (mean age 64 years) and hypovitaminosis D (vitamin D < 50 nmol/l). In this double-blind randomized clinical trial, a single high dose of vitamin D (100 000 IU) during winter caused a significant reduction in systolic blood pressure after 8 weeks follow-up. Beyond the fall in blood pressure, vitamin D supplementation improved endothelial function, possibly through anti-inflammatory actions [35]. In addition, evidence of an inverse association between vitamin D concentration and carotid artery intima media thickness, a marker of atherosclerosis [36], underlines the importance of adequacy of vitamin D in prevention of cardiovascular complications in diabetes. Our findings are consistent with these data and add to the growing body of evidence suggesting that vitamin D supplementation during periods of low sun exposure may improve blood pressure control in diabetes.

Nevertheless, our results raised the possibility that during high sun exposure months, supplement users may have a higher systolic blood pressure than non-users. This finding indicates that during the high sun exposure period, vitamin supplementation may have a neutral or even a potential harmful effect on blood pressure. We should note that there were no differences in the number of anti-hypertensive agents between periods of high and low sun exposure in either the supplement users or nonusers. However, we cannot rule out the possibility of dose adjustments: one possibility is that a higher blood pressure level during the low sun exposure period in non-users may have led to dose adjustments that contributed to a drop in blood pressure during the subsequent high sun exposure period. Further, although we accounted for dietary intake, as derived from food frequency questionnaire information, and for physical activity, through both objective measures (pedometer-assessed step counts) and self-report, given the challenges of accurately capturing dietary and physical activity information we cannot exclude the possibility of residual confounding.

There is no other obvious mechanism to explain a lower blood pressure level in supplement non-users during the high sun exposure period. However, this signal should not be ignored given that adverse effects of vitamin supplementations on cardiovascular outcomes have been recently reported in some studies. For example, folic acid supplementation was associated with an increase in heart events in the secondary prevention of cardiovascular disease (CVD), especially in individuals with diabetes [37]. In addition, in a randomized controlled trial on people with diabetes nephropathy, vitamin B supplementation compared with placebo was associated with an increase in vascular events [38]. In future clinical trials examining the impact of vitamin D on blood pressure and cardiovascular outcomes, it may be instructive to examine season-specific effects.

The strengths of our study include measurements of dietary intake, physical activity, vitamin supplementation, and blood pressure during both high and low sun exposure periods in the same cohort of participants. However, important limitations were absence of serum vitamin D concentrations and details concerning supplement use (type, content and duration of use).

In conclusion, our findings do demonstrate vitamin supplementation to be associated with a lower systolic blood pressure in adults with Type 2 diabetes during the months of the year characterized by low sun exposure. However, during periods of higher sun exposure, vitamin supplementation did not appear to confer benefit on systolic blood pressure control. Overall, systolic blood pressure was stable across high and low sun exposure periods in vitamin supplement users. We would re-emphasize, however, that while our findings suggested a blood pressure-lowering effect of vitamin supplementation during low sun exposure periods, we could not exclude the possibility of an adverse effect of vitamin supplementation on blood pressure during the high sun exposure period. Thus, before our findings can be translated into clinical practice, a clinical trial may be needed. Clearly, our findings provide justification for future studies to examine the impact of a dose response of vitamin D supplementation on blood pressure specifically during the months with low sun exposure.

Competing interests

Nothing to declare.

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