



ORIGINAL ARTICLE

Sunlight Exposure and Breast Density: A Population-Based Study

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Purpose: This study aims to assess the association of sunlight exposure with breast cancer risk, measured by the breast density assessed from Tabár's mammographic pattern in Chinese women. Methods: A total of 676 premenopausal women were recruited to participate in this study, in which 650 completed a validated sunlight exposure questionnaire via telephone. The mammograms were classified according to Tabár's classification for parenchyma, and patterns IV & V and I, II & III indicated respectively high and low risk mammographic patterns for breast cancer. The odds ratios (OR) and 95% confidence intervals (Cls) for sun exposure-related variables were estimated using unconditional logistic regression with adjustment for potential confounders. Results: Among 646 participants, women with high breast cancer risk (Tabár's patterns IV &V) had less hours spent in the sun than those with low risk (I, II & III) at any age stage. A higher level of sunlight exposure was associated with a significantly lower risk having high risk Tabár's pattern. Women aged 40 to 44 years who were in the highest tertile of lifetime total hours spent in the sun had a multi-adjusted OR of 0.41 (95% CI, 0.18-0.92; *p* for trend = 0.03) compared with those in the lowest tertile (>2.19 hr/day vs. <1.32 hr/day). For hours spent in the sun across the ages of 6 to 12 years, the comparable OR was 0.37 (95% CI, 0.15-0.91; *p* for trend = 0.03). **Conclusion:** These findings suggest that higher sunlight exposure is related to a lower risk of having high risk breast density pattern in premenopausal women. Our results also suggest the most relevant period of exposure is during earlier life.

Key Words: Breast neoplasms, Mammographic density, Sunlight, Vitamin D

INTRODUCTION

There has been considerable interest in recent years as to whether vitamin D inhibits breast cancer development [1-3]. Vitamin D is produced when the skin to solar is exposed ultraviolet B (UVB) radiation, which is the primary source of vitamin D for most people [2,4]. Previtamin D from both diet and sunlight is hydroxylated in the liver into 25-hydroxyvitamin D (25(OH)D). 25(OH)D is then further hydroxylated into 1,25-dihydroxyvitamin D (1,25(OH)2D). 1,25(OH)2D is the biologically active metabolite that binds to nuclear vitamin D receptors in the intestine and bone, as well as breast tissues [5]. Experimental studies have shown the anticarcinogenic potential of vitamin D in different cell types, including normal and malignant breast cells, by affecting the induction of cell

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differentiation and apoptosis, as well as the inhibition of cell growth [1,3].

Epidemiological studies have conveyed the protective effect of sun exposure on breast cancer risk. Breast cancer mortality rates are higher in the north-eastern than in the southern United States [6], and are inversely correlated with solar radiation [6-8]. Studies have shown the association of reduced breast cancer risk with high early-life residential solar radiation or a usual residence in a region of high solar radiation and frequent adult recreational or occupational sun exposure [7,8]. In addition, high sun exposure was found to be associated with a reduced risk of advanced breast cancer [9].

A substantial body of evidence indicated that among the risk factors for breast cancer, mammographic parenchymal patterns have the strongest association with breast cancer risk [10,11]. Tabár's mammographic patterns IV and V have been shown to be associated with the known breast cancer risk factors, as well as with increased risk of disease [12,13]. It is reported that dense mammographic tissue is associated with breast epithelial hyperplasia and with stromal fibrosis, which may be in response to growth factors induced by circulating

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/ licenses/by-nc/3.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. levels of sex hormones (mitogenesis) [11,13].

Breast cancer is the most common cancer in Hong Kong women (approximately 2,100 new cases per year) and had the highest increase in incidence in 2007 among all cancers in Hong Kong [14]. There have no studies yet exploring whether sunlight exposure may reduce the risk of breast cancer in Asians. Recent evidence revealed that vitamin D deficiency (≤ 25 nmol/L) was indicated in 18% of Hong Kong women aged 18 to 40 years during the spring, and over 90% of women of reproductive age had insufficient levels of vitamin D (≤ 50 nmol/L) [15]. Therefore, this study aims to examine the relationship of sunlight exposure with breast cancer risk measured by breast density assessed from Tabár's mammographic pattern, in a population-based study of Hong Kong Chinese premenopausal women.

METHODS

Subjects and telephone survey

A total of 676 women from an ongoing population-based cohort study of breast density in premenopausal women were invited to participate in a questionnaire interview on sunlight exposure via telephone on a questionnaire interview on sunlight exposure. The participants had been recruited through stratified-cluster sampling from different housing types in Shatin, Hong Kong. A total of 3,250 households were selected from three housing types (public, private, and home ownership) according to the population ratio of 3:5:2. The housing estates and the housing blocks within the estates were randomly selected from these three housing strata. All households in the selected blocks were enumerated, and women between 35 and 45 years were interviewed by using a short questionnaire in order to determine their eligibility. Women who were eligible were invited to participate in the study. Two pretests (n=5)and n=22, respectively) conducted among women of similar age to the participants were first carried out from January to April 2010 before the study proper to start. A letter was first mailed to the potential subjects explaining the study, followed by a telephone call in order to arrange a time for a telephone interview. Among the 676 potential participants, 5 were excluded due to invalid telephone numbers (0.74%) (although they were valid at the baseline study). Of the remaining 671 women, 14 declined to participate, 3 answered parts of the questionnaire, 3 were too busy to complete the interview and 1 was only available beyond the study period. Thus, 650 completed the telephone questionnaire interview, providing a response rate of 96.9%. For quality control assessment, the sunlight exposure questionnaire was readministered after 2 weeks among a random sample (14.5%) of the study participants (n=94). All participants provided written, informed consent, and the reported study was approved by the Institutional Review Boards of the Chinese University of Hong Kong.

Questionnaires

The following information has been collected by assessors blinded to the mammographic results utilizing, standardized questionnaires/protocols that have been previously developed and successfully used: sociodemographic data (education, body measurements [weight, height, and calculated body mass index]), reproductive factors (age of menarche, breastfeeding and duration, times of pregnancies), hormonal use, physical activity (time spent in mild, moderate, and vigorous activities), and family history of breast cancer.

Sunlight exposure questionnaire

The sunlight exposure questionnaire was developed based on a literature review on sunlight exposure assessment [16-18], as well as on a sunlight exposure questionnaire that had previously been used in several epidemiological studies of cancer [19,20]. The questionnaire covers the skin reaction to sunlight exposure (always/easily burns; burns rarely/never; always/easily tans; tans rarely/never); time and frequency spent outdoors in the sun across different age groups (6-12, 13-19, and 20-34 years, and from 35 years to present); and personal protection. Questions relating to sunlight exposure in each age group included the following: residence (country, province, and city); outdoor activities in the sun and the average hours per day spent in the sun during the summer and the other 3 seasons, usual (usual was defined as >50% of the time) sun protection during the summer and the other 3 seasons, trips to summer climate locations during the winter and the frequency (none, once every 3-4 years, once every 2 years, every year); outdoor jobs in the sun and information on frequency (hours per day) and duration (number of weeks and months per season and total number of years); use of sunlamp or sunbed (with age when first used, age at last used, and total number of sessions over lifetime). The use of vitamin D supplements (cod liver oil, multivitamin, and other fish oil containing vitamin D) was also asked. The data in this study group indicated that the lifetime sunlight exposure questionnaire had sufficient content validity (98.4% of the questionnaire items with a valid content validity index [>0.84]), construct validity (two-factor construct was appropriate and no items [continuous variables] need to be excluded) and good reliability (intraclass correlation coefficient, 0.59-0.93) to measure the sun exposure of Hong Kong Chinese women [21].

Measurement of mammographic pattern

Mammograms of cranio-caudal (CC) and medio-lateraloblique (MLO) views were taken at the Department of Radiology and Organ Imaging, Prince of Wales Hospital in Hong Kong with dedicated mammographic equipment (Senographe DMR; General Electric Medical Systems, Milwaukee, USA) using computed radiography.

One trained research assistant was blinded to the identity of the subjects in order to classify the mammographic parenchymal patterns according to Tabár's classification system [13]. Both left and right CC and MLO views were used in the classification on the basis of extent and type of density: I, mammogram composed of scalloped contours with some lucent areas of fatty replacement, and 1 mm evenly distributed nodular densities; II, mammogram composed of almost entirely lucent areas of fatty replacement, and 1 mm evenly distributing nodular densities; III, prominent ducts in the retroareolar area; IV, extensive nodular and linear densities, with nodular size larger than normal lobules; V, homogenous, ground glasslike appearance with no perceptible features. Pattern I represented the classic appearance of the premenopausal breast. Pattern II represented the normal postmenopausal breast with glandular tissue replaced by fatty tissue. Pattern III indicated more periductal elastosis. Pattern IV perhaps represented proliferation. Pattern V represented extensive fibrosis, which might be, but was not necessarily, associated with any malignant or proliferative process. Gram et al. [13] presented a relationship of patterns IV and V with known breast cancer risk factors, and suggested that these patterns might be associated with increased risk of disease. The within-batch and betweenbatch agreement were 0.83 (n = 50) and 0.79 (n = 50) in the current study, respectively.

Statistical analysis

The final sample size for the statistical analysis was 646 after eliminating 4 subjects with missing mammographic films. Chi-square and Kolmogorov-Smirnov Z Test were used to examine the differences by high and low breast cancer risk (Tabár IV & V vs. I, II & III) in categorical and continuous variables, respectively. The association of breast cancer risk with sunlight exposure was evaluated using unconditional logistic regression, with high versus low risk (Tabár IV & V vs. I, II, & III), adjusting for age at the time of mammography measurement, height, weight, waist and hip circumferences, body mass index, age at menarche, ever pregnancy, ever breastfeeding, past use of contraceptives and hormonal replacement therapy, level of physical activity, family history of breast cancer in first-degree relatives (yes or no), education (highest completed degree: primary or less, secondary, some university or university graduate) and sun protection usage (yes or no). The covariates included in this study were factors related to breast cancer risk and sunlight exposure, as well as the data availability. The covariates in one model were not found to have high collinearity. As shown in a previous study [22], our data also portrayed that age was significantly associated with both sunlight exposure and mammographic density; thus, we stratified the analysis of the association of breast cancer risk with sunlight exposure among different age groups ($37 \le 40$, $40 \le 44$, and $45 \le 50$).

The analyses were conducted using the SPSS version 16.0 (SPSS Inc., Chicago, USA). All tests were two-sided with a significance level of p < 0.05.

RESULTS

The 277 and 369 low (Tabár's pattern I, II, & III) and high (IV & V) breast cancer risk subjects were included in the analysis (Table 1). The subjects with a low risk pattern were slightly older than those with high risk (43.99 years vs. 43.48 years). Statistically significant differences between low and high risk groups were observed with respect to waist-to-hip ratio, body mass index, height, physical activities index, education, and sun protection use from 35 years to present. There were no statistically significant differences between the low and high risk groups in terms of age at menarche, hormonal use, pregnancy, breastfeeding, number of live births, and family history of breast cancer. The subjects were more likely to spend more time in the sun during their younger ages. Figure 1 showed a declining trend of the total hours spent in the sun with increasing age stages, however, women with high risk breast pattern (Tabár pattern IV & V) had spent fewer hours in the sun than those with low risk (I, II, & III) at the various age stages. Sunlight exposure was only significantly associated with age and education, but not with other factors such as body mass index, physical activity, sun protection use and others (data not shown).

In the unconditional regression model, a statistically significant inverse association between time spent in the sun and breast cancer risk (Tabár IV & V vs. I, II, & III) was observed. Women aged 40 to 44 years who were in the highest tertile of lifetime total hours spent in the sun had an OR of 0.41 (95% CI, 0.18-0.92) of having high risk breast pattern compared with those in the lowest tertile (>2.19 hr/day vs. <1.32 hr/ day), with a significant linear trend across tertiles (*p* for trend = 0.03) after adjusting for other breast cancer risk factors, including age at mammography screening, age at menarche, ever pregnancy, ever breastfeeding, education, body mass index, waist-to-hip ratio, height, family history of breast

Voriable	Tabár's pattern (Iow vs. high breast cancer risk)						
Variable	Low (I, II, & III) (n=277)	High (IV & V) (n=369)	p-value*				
Age at time of screening mammography (yr)	43.99±2.79	43.48±3.11	0.03				
Age at menarche (yr)	12.85 ± 1.57	12.98±1.54	0.81				
Waist-to-hip ratio	0.84 ± 0.06	0.79 ± 0.05	0.00				
Body mass index (kg/m²)	25.05 ± 3.73	22.30 ± 2.52	0.00				
Height (cm)	155.96 ± 5.15	156.67 ± 5.04	0.08				
Physical activities index	24.01 ± 7.30	23.23 ± 6.58	0.01				
Total hours spent in the sun							
Lifetime (hr)	$28,970 \pm 16,572$	$27,618 \pm 14,804$	0.30				
6-12 yr	10,173±7,131	$9,300 \pm 6,659$	0.35				
13-19 yr	$9,750 \pm 6,689$	$9,299 \pm 6,766$	0.43				
20-34 yr	$7,997 \pm 6,103$	7,141±5,112	0.04				
≥35 yr	$7,596 \pm 6,229$	$7,094 \pm 5,547$	0.52				
Sun protection use							
6-12 yr							
Yes	53 (19)	56 (15)	0.18				
No	224 (81)	313 (85)					
13-19 yr							
Yes	81 (29)	99 (27)	0.50				
No	196 (71)	270 (73)					
20-34 yr							
Yes	175 (63)	240 (65)	0.63				
No	102 (37)	129 (35)					
≥35 yr							
Yes	232(84)	329 (89)	0.04				
No	45 (16)	40 (11)					
Education							
Primary school or less	43 (16)	35 (9)	0.04				
Secondary school	181 (65)	247 (67)					
Some university or university graduate	53 (19)	87 (24)					
Hormonal use							
Yes	211 (76)	295 (80)	0.22				
No	66 (24)	73 (20)					
Ever pregnant							
Yes	248 (90)	301 (82)	0.05				
No	28 (10)	66 (18)					
No. of live birth	1.88 ± 0.77	1.69 ± 0.81	0.06				
Ever breastfeeding							
Yes	123 (45)	146 (40)	0.24				
No	153 (55)	219 (60)					
Family history of breast cancer							
Yes	29 (10)	41 (11)	0.78				
No	247 (90)	325 (89)					

 Table 1. Sociodemographic characteristics and risk factors for breast cancer risk by Tabár's pattern in the 646 Hong Kong women

Values are presented as mean ± SD or number (%).

*Chi-square and Kolmogorov-Smirnov Z Test were used to examine the differences by high and low breast cancer risk (Tabár IV & V vs. I, II, & III) in categorical and continuous variables, respectively.

cancer, hormone replacement usage, physical activity and sun protection use (Table 2). Compared to those in the first tertile,

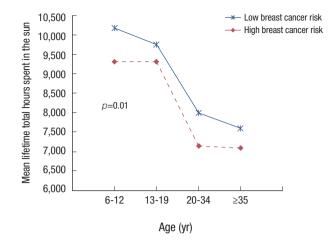


Figure 1. Tabár patterns (I, II, & III and IV & V indicates low and high breast cancer risk) vs. mean lifetime total hours spent in the sun.

subjects aged 40 to 44 years belonging to the highest tertile of hours spent in the sun during the ages of 6 to 12 years had a lower adjusted breast cancer risk (OR, 0.37; 95% CI, 0.15-0.91; *p* for trend = 0.03). The associations between sunlight exposure across age groups 13 to 19, 20 to 34, and over 35 years and breast cancer risk were not observed in women aged 40 to 44 years. There were no apparent differences in sunlight exposure duration between the high and low breast pattern risk groups for women aged 37 to 40 and 44 to 50 years.

No apparent differences were found between the two breast pattern risk groups for sunlight exposure during different seasons, the latitude where the subjects lived, vitamin D intake and skin reaction to sun (data not shown). Only 1 subject (0.15%) used the sunbed once and very few participants below the age of 35 years ever had trips to summer climate locations during winter seasons; hence, the risks of these factors could not be compared between the two comparison groups.

DISCUSSION

In this population-based cross-sectional study of premenopausal women, we observed an inverse association between lifetime sunlight exposure and breast cancer risk measured by breast density assessed from Tabár's mammographic parenchymal pattern. The reduced risk was particularly apparent for subjects aged 40 to 44 years with high sunlight exposure during the ages 6 to 12 years. Sun exposure is a major source of vitamin D. Evidence from both *in vitro* and *in vivo* studies revealed that high levels of vitamin D can be obtained from less than a minimal erythemal dose (slight reddening of the skin) of sunlight [23,24]. Previtamin D is hydroxylated in the liver into 25(OH)D. 25(OH)D is then further hydroxylated into 1,25(OH)2D. 1,25(OH)2D is the biologically active me-

		Age group											
Tertiles of total hours spent in the sun (average hours per day)		37-40 yr (n=73)				40-44 yr (n=207)			44-50 yr (n=366)				
	Unadjusted		A	Adjusted*		Unadjusted		Adjusted*		Unadjusted		Adjusted*	
	OR	95% Cl	OR	95% Cl	OR	95% Cl	OR	95% Cl	OR	95% Cl	OR	95% CI	
Lifetime (hr)													
< 19,618 (1.32)	1.00		1.00		1.00		1.00		1.00		1.00		
19,618-32,225 (1.32-2.19)	1.72	0.58-5.11	1.13	0.19-6.66	0.91	0.45-1.87	0.78	0.34-1.80	0.82	0.49-1.36	0.82	0.49-1.37	
32,225 (2.19)	2.89	0.68-12.35	4.94	0.72-34.02	0.48	0.24-0.94	0.41	0.18-0.92	0.83	0.50-1.38	0.85	0.51-1.41	
p for trend	0.13		0.11		0.03		0.03		0.29		0.92		
6-12 yr													
<5,384 (1.36)	1.00		1.00		1.00		1.00		1.00		1.00		
5,384-11,153 (1.36-2.50)	2.76	0.80-9.48	5.73	0.96-34.23	0.64	0.33-1.24	0.65	0.30-1.40	1.17	0.67-2.04	1.40	0.74-2.67	
>11,153 (2.50)	-		-		0.42	0.20-0.88	0.37	0.15-0.91	1.01	0.60-1.69	1.06	0.58-1.95	
p for trend	0.91		0.06		0.02		0.03		0.92		0.998		
13-19 yr													
<5,777 (1.50)	1.00		1.00		1.00		1.00		1.00		1.00		
5,777-10,446 (1.50-2.50)	3.04	0.97-9.58	4.91	0.97-24.89	0.98	0.51-1.89	0.77	0.35-1.70	0.88	0.51-1.52	0.74	0.39-1.39	
>10,446 (2.50)	-		-		0.63	0.31-1.30	0.62	0.26-1.46	0.95	0.57-1.57	0.97	0.54-1.74	
p for trend	0.06		0.06		0.24		0.27		0.98		0.995		
20-34 yr													
<4,308 (1.00)	1.00		1.00				1.00		1.00		1.00		
4,308-8,880 (1.00-2.00)	0.78	0.27-2.20	0.90	0.20-3.98	1.27	0.65-2.48	1.16	0.54-2.49	1.34	0.78-2.31	1.40	0.75-2.62	
>8,880 (2.00)	-		-		0.53	0.26-1.07	0.58	0.25-1.34	0.93	0.56-1.54	1.03	0.57-1.85	
p for trend	0.64		0.89		0.10		0.25		0.63		0.99		
≥35 yr													
< 3,930 (1.00)	1.00		1.00		1.00		1.00		1.00		1.00		
3,930-8,193 (1.00-2.00)	2.11	0.71-6.31	4.60	0.89-23.90	1.20	0.62-2.32	0.80	0.37-1.73	0.81	0.47-1.40	0.94	0.50-1.79	
>8,193 (2.00)	-		-		0.54	0.26-1.12	0.53	0.22-1.27	0.90	0.54-1.50	1.15	0.64-2.08	
p for trend	0.18		0.07		0.13		0.16		0.76		0.60		

OR = odds ratio; CI = confidence interval.

*All analyses were adjusted for age at the mammography screening, age at menarche, body mass index, waist-to-hip ratio, height, ever pregnancy, ever breastfeeding, education, family history of breast cancer, hormone replacement usage, physical activity and sun protection usage.

tabolite that binds to nuclear vitamin D receptors in the intestine and bone, as well as breast tissues [5]. Experimental studies have shown the anticarcinogenic potential of vitamin D in diverse kinds of cell types, including normal and malignant breast cells, by affecting the induction of cell differentiation and apoptosis as well as inhibition of cell growth [1,3].

Previous studies have suggested an inverse relationship between vitamin D and breast cancer [7,19]. In the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study, measures of sunlight exposure and dietary vitamin D intake were consistently associated with reduced risk of breast cancer, although the power was limited and many of the estimates did not reach statistical significance [7]. One large case-control study [19] reported an association between reduced breast cancer risks and increasing sun exposure from ages 10 to 19 (OR, 0.65; 95% CI, 0.58-0.85); yet, there was weaker evidence for the associations from ages 20 to 29 and no evidence for ages 45 to 54 years. The present study found that exposure during childhood, a critical period before breast development, was protective of breast cancer risk.

To our knowledge, this is the first study to examine the association between sun exposure and mammographic parenchymal patterns. To date, no studies had yet explored the mechanism as to why sun exposure has an effect on breast density. It is reported that extensive mammographic density and delayed breast involution are both associated with an increased risk of breast cancer and cumulative exposure of breast tissue to hormones and growth factors that stimulate cell division, as well as the accumulation of genetic damage in breast cells, are the major determinants of breast cancer incidence [22]. The protective influence of sun exposure on breast cancer risk measured by mammographic parenchymal patterns might be related to the anticarcinogenic potential of vitamin D on breast cells by affecting the induction of cell differentiation and apoptosis as well as the inhibition of cell growth [1,3].

This study used self-reports of personal sunlight exposure as a surrogate for vitamin D status. Although this study had no quantitative information on the intensity and duration of sunlight exposure or on other factors that influence vitamin D synthesis (e.g., skin pigmentation, medical conditions, and medications) [24], self-reported sunlight exposure has been reported in other studies to be a good surrogate for serum levels of 25(OH)D [25,26], which is the major circulating metabolite of vitamin D. The data in this study group has indicated that the lifetime sunlight exposure questionnaire had sufficient content validity to measure the sun exposure of Hong Kong Chinese women [21]. These data support the validity of our exposure measure in ranking the individuals according to sunlight exposure.

The accuracy of recall is a concern in this study. The reproducibility of sun exposure-related questions was examined in a number of studies over different time periods ranging from a few weeks to several years [27,28]. In general, these studies have found that sun exposure and outdoor activities, whether in childhood and adolescence or recent, could be reasonably and consistently recalled. Some questionnaires tended to focus on the total time in the sun and sun damage to the skin for studies of melanoma [28] or other outcomes [18,20]. In our study, the questionnaire was designed specifically to evaluate lifetime sun exposure-the major source of vitamin D; the validated results showed adequate content validity and reproducibility [21]. Although individuals are unlikely to be able to recall exactly how much time they spent outside, especially during childhood (6-12 years), the questionnaire is still able to roughly distinguish those who spent very little time versus those who spent considerable time outdoors. Due to the recall bias, our results on the protective effect of sun exposure on breast cancer risk might be biased toward either direction. Similarly, specific sun protection methods for those aged less than 35 years were also not collected due to the difficulty to recall except for the qualitative information, according to the results from the pretests.

Another concern for our study is the possible misclassification of mammographic patterns. However, almost all mammograms were taken using the same equipment (Senographe DMR). Furthermore, the assessment of mammographic patterns was performed by one trained reader using a computerassisted method. Thus, if present, the misclassification of mammographic patterns should be relatively small and most likely random. Another limitation of our study is that we did not obtain information of vitamin D supplementation alone other than multivitamins because most of the women did not take pure vitamin D supplements. Furthermore, our study used breast density measured by Tabár's mammographic pattern as a marker for breast cancer risk, which is not a direct association between sun exposure and the risk of breast cancer development. Nonetheless, our findings provide some insight into the potential for breast cancer prevention.

This study was cross-sectional in nature and did not allow us to determine the temporal associations. However, it is unlikely that mammographic patterns influence sunlight exposure in childhood, adolescent and young adulthood. The results might occur by chance because we have multiple comparisons; thus, the significance level of type I error would be smaller than 0.05 using Bonferroni correction. However, the correction will increase the probability of reducing "power" and result in the entire test to become irrelevant.

Other than influences on the vitamin D status, a number of other health benefits from sufficient levels of vitamin D have been identified. These include anticancer properties [8]; however, sun exposure has also been suspected of causing skin cancer [8].With respect to the risks and benefits of sun exposure, a balance is required between avoiding an increase in the risk of skin cancer by excessive sun exposure and achieving sufficient exposure in order to maintain adequate vitamin D levels [29]. Relatively short sun exposure time will maximize vitamin D generation, although the amount of vitamin D produced in a given time depends on the degree of skin coverage and skin color.

In conclusion, the present findings indicate that increased sunlight exposure throughout one's lifetime and across ages 6 to 12 years seem to be associated with a protective effect of breast cancer risk measured by breast density among Hong Kong premenopausal women. The research into the relationship between breast cancer and sunlight exposure create new opportunities in breast cancer prevention. Moreover, the timing of exposure seems to be crucial and additional work will be required in order to meet the challenge of assessing the prevention mechanism early in life. If confirmed, the results of this study would be particularly promising for the primary prevention of breast cancer due to the fact that sunlight exposure is a modifiable lifestyle factor.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

REFERENCES

- 1. Cui Y, Rohan TE. Vitamin D, calcium, and breast cancer risk: a review. Cancer Epidemiol Biomarkers Prev 2006;15:1427-37.
- Giovannucci E. The epidemiology of vitamin D and cancer incidence and mortality: a review (United States). Cancer Causes Control 2005;16:83-95.
- 3. Ingraham BA, Bragdon B, Nohe A. Molecular basis of the potential of vitamin D to prevent cancer. Curr Med Res Opin 2008;24:139-49.

- 4. Grant WB, Holick MF. Benefits and requirements of vitamin D for optimal health: a review. Altern Med Rev 2005;10:94-111.
- 5. Reichel H, Koeffler HP, Norman AW. The role of the vitamin D endocrine system in health and disease. N Engl J Med 1989;320:980-91.
- Garland FC, Garland CF, Gorham ED, Young JF. Geographic variation in breast cancer mortality in the United States: a hypothesis involving exposure to solar radiation. Prev Med 1990;19:614-22.
- John EM, Schwartz GG, Dreon DM, Koo J. Vitamin D and breast cancer risk: the NHANES I Epidemiologic follow-up study, 1971-1975 to 1992. National Health and Nutrition Examination Survey. Cancer Epidemiol Biomarkers Prev 1999;8:399-406.
- Freedman DM, Chang SC, Falk RT, Purdue MP, Huang WY, McCarty CA, et al. Serum levels of vitamin D metabolites and breast cancer risk in the prostate, lung, colorectal, and ovarian cancer screening trial. Cancer Epidemiol Biomarkers Prev 2008;17:889-94.
- John EM, Schwartz GG, Koo J, Wang W, Ingles SA. Sun exposure, vitamin D receptor gene polymorphisms, and breast cancer risk in a multiethnic population. Am J Epidemiol 2007;166:1409-19.
- Oza AM, Boyd NF. Mammographic parenchymal patterns: a marker of breast cancer risk. Epidemiol Rev 1993;15:196-208.
- Boyd NF, Lockwood GA, Byng JW, Tritchler DL, Yaffe MJ. Mammographic densities and breast cancer risk. Cancer Epidemiol Biomarkers Prev 1998;7:1133-44.
- Jakes RW, Duffy SW, Ng FC, Gao F, Ng EH. Mammographic parenchymal patterns and risk of breast cancer at and after a prevalence screen in Singaporean women. Int J Epidemiol 2000;29:11-9.
- 13. Gram IT, Funkhouser E, Tabár L. The Tabár classification of mammographic parenchymal patterns. Eur J Radiol 1997;24:131-6.
- Hong Kong Cancer Registry, Hospital Authority. 2012. http://www3. ha.org.hk/cancereg/. Accessed May 24th, 2013.
- 15. Woo J, Lam CW, Leung J, Lau WY, Lau E, Ling X, et al. Very high rates of vitamin D insufficiency in women of child-bearing age living in Beijing and Hong Kong. Br J Nutr 2008;99:1330-4.
- Godar DE. UV doses worldwide. Photochem Photobiol 2005;81:736-49.

- Webb AR. Who, what, where and when-influences on cutaneous vitamin D synthesis. Prog Biophys Mol Biol 2006;92:17-25.
- McCarty CA. Sunlight exposure assessment: can we accurately assess vitamin D exposure from sunlight questionnaires? Am J Clin Nutr 2008;87:1097S-101S.
- Knight JA, Lesosky M, Barnett H, Raboud JM, Vieth R. Vitamin D and reduced risk of breast cancer: a population-based case-control study. Cancer Epidemiol Biomarkers Prev 2007;16:422-9.
- Gilbert R, Metcalfe C, Oliver SE, Whiteman DC, Bain C, Ness A, et al. Life course sun exposure and risk of prostate cancer: population-based nested case-control study and meta-analysis. Int J Cancer 2009; 125:1414-23.
- Wu SH, Ho SC, Lam T. Validity and reproducibility of the Chinese lifetime sunlight exposure questionnaire. Scientific Report 2013. In press.
- Ginsburg OM, Martin LJ, Boyd NF. Mammographic density, lobular involution, and risk of breast cancer. Br J Cancer 2008;99:1369-74.
- Vieth R. The pharmacology of vitamin D, including fortification strategies. In: Feldman D, Pike JW, Glorieux FH, editors. Vitamin D. 2nd ed. Amsterdam: Elsevier Academic Press; 2005. p.995-1015.
- Holick MF. Environmental factors that influence the cutaneous production of vitamin D. Am J Clin Nutr 1995;61(3 Suppl): 638S-45S.
- 25. Webb AR, Pilbeam C, Hanafin N, Holick MF. An evaluation of the relative contributions of exposure to sunlight and of diet to the circulating concentrations of 25-hydroxyvitamin D in an elderly nursing home population in Boston. Am J Clin Nutr 1990;51:1075-81.
- Jacques PF, Felson DT, Tucker KL, Mahnken B, Wilson PW, Rosenberg IH, et al. Plasma 25-hydroxyvitamin D and its determinants in an elderly population sample. Am J Clin Nutr 1997;66:929-36.
- English DR, Armstrong BK, Kricker A, Fleming C. Sunlight and cancer. Cancer Causes Control 1997;8:271-83.
- van der Mei IA, Blizzard L, Ponsonby AL, Dwyer T. Validity and reliability of adult recall of past sun exposure in a case-control study of multiple sclerosis. Cancer Epidemiol Biomarkers Prev 2006;15:1538-44.
- 29. van der Rhee HJ, de Vries E, Coebergh JW. Does sunlight prevent cancer? A systematic review. Eur J Cancer 2006;42:2222-32.