Sun exposure and intima-media thickness in the Mexican Teachers' Cohort

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Abstract

Background

Previous studies have evaluated how sun exposure affects cardiovascular health. In this sense, some evidence from ecological studies have found an inverse relationship between sun exposure and blood pressure or CVD. The aim of this study is to determine whether long-term sun exposure has a protective role in subclinical cardiovascular disease in adult Mexican women.

Methods

We conducted a cross-sectional analysis of a sample of women from the Mexican Teachers' Cohort (MTC) study. Sun exposure was assessed in the MTC 2008 baseline questionnaire, in which women were asked about their sun-related behavior. Vascular neurologists measured carotid intima-media thickness (IMT) using standard techniques. Multivariate linear regression models were used to estimate the percentage difference in mean IMT and 95% confidence intervals (95% CIs), according to categories of sun exposure and multivariate logistic regression models were used to estimate the odds ratio (OR) and 95% CIs for carotid atherosclerosis.

Results

The mean age of participants was 49.6 ± 5.5 years, the mean IMT was 0.678 ± 0.097 mm, and the mean accumulated hours of weekly sun exposure were 2.9 ± 1.9 . Prevalence of carotid atherosclerosis was 20.9%. Compared to women in the lowest category of sun exposure, the multivariate adjusted ORs of carotid atherosclerosis were 0.54 (95%CI: 0.24, 1.18) for women who were exposed 9 hours. For women who denied regular sun screen use, those in the higher exposure category (9 hours) had lower mean IMT compared to those in the lower category (multivariable-adjusted mean % difference = -2.67; 95%CI: -6.9, -1.5).

Conclusion

In general, we observed that cumulative sun exposure was inversely associated with IMT and subclinical carotid atherosclerosis. Our findings suggest that public health messages should also consider the sun's positive role for health, while still emphasizing the negative impacts of excessive exposure.

Introduction

According to the Global Burden of Disease (GBD) Study 2017, non-communicable diseases (NCDs) contribute to 73.4% of total deaths, globally (1). Within the NCDs, cardiovascular disease (CVD) is the

number one cause of death. In Mexico, NCDs represent 77% of total adult deaths, with CVD accounting for almost a quarter (24%) of these deaths (1).

Previous studies (2-4) have suggested that cardiovascular health differs according to weather, season and other environmental factors. Ultraviolet (UV) radiation from sun exposure has been widely established as a risk factor for skin cancer, especially melanoma. Consequently, public health recommendations focus on avoidance of excessive sun exposure (5). However, sun exposure is the main source of vitamin D (VD) in humans, since photons are required to convert 7-dehydrocholesterol in the epidermis into provitamin D₃ (6). Despite this fact, few studies have evaluated how sun exposure affects cardiovascular health. In this sense, some evidence from ecological studies have found an inverse relationship between sun exposure and blood pressure or CVD (7,8).

Different epidemiological studies have suggested that VD status has important implications on cardiovascular health. For example, low levels of VD have been associated with elevated blood pressure, coronary calcification, and CVD such as myocardial infarction and congestive heart failure (9,10). Moreover, a recent clinical trial conducted in Mexican adult women (11) has suggested that VD supplementation (4000 IU/d) may have a beneficial effect on some CVD risk factors.

Additionally, current investigations and recommendations on VD-related risk factors and outcomes have focused mainly on supplementation or dietary intake. However, since exposure to sun is the primary determinant of VD blood levels, exploring whether sun exposure is related to these outcomes is necessary. Also, more evidence to determine if this protective role exists and if it is short or long-term exposure that confers the protection is required, in addition to understanding this relationship in populations living in latitudes where there is more sunlight exposure (12-14). Adequate sun exposure could be an easy, affordable strategy to lower cardiovascular risk associated with VD deficiency. Thus, our main objective was to determine if long-term sun exposure has a protective role in subclinical cardiovascular disease in adult Mexican women. As an additional analysis, we also evaluated the short-term sun exposure and its association with subclinical cardiovascular disease.

Methods

Study population

We conducted a cross-sectional analysis of a sample of women from the Mexican Teachers' Cohort (MTC) study. The MTC is a prospective study with 115,314 female school teachers aged ≥ 25 years from 12 geographically and economically diverse states in Mexico. Details of the study design, methodology and participants' baseline characteristics have been published previously (15). In 2006 and 2008 we invited women to participate and respond a baseline questionnaire on demographic and reproductive characteristics, lifestyle, and medical conditions. Between September 2012 and June 2017, a random sample of 4,310 women were invited to participate in an ancillary study on subclinical cardiovascular disease (sCVD). There were seven sites where clinical evaluations took place. Women were eligible if they

lived in a 50 km radius from the clinical sites. For the central region of Mexico, clinical evaluations were conducted in Mexico City, while for the northern region evaluations were performed in Monterrey, Nuevo León. For the southeastern region of Mexico, we evaluated women in five clinical sites, four of them located in Chiapas (Tuxtla Gutiérrez, San Cristobal de las Casas, Comitán and Tapachula) and one in Yucatán (Mérida).

A total of 2,770 participants (64.2%) chose to participate in the study. Of these, we excluded women with missing data on sun exposure (n=223) or carotid intima-media thickness (IMT) measurement (n=282). Women who reported a previous diagnosis of stroke or myocardial infarction were also excluded (n=8). Finally, a total of 2,257 participants were included in our analysis.

Assessment of Sun Exposure and Sunscreen Use

In the MTC 2008 baseline questionnaire, women answered questions on their sun-related behavior by reporting their weekly average hours spent outdoors during the school year around midday (solar noon) at four different age periods: 12-18, 25-35, 36-59 and more than 60 years. Four multiple-choice answers were possible (all in hours): <1, 2-5, 6-8 and >8. Similar questions have been used in previous studies with validated questionnaires to assess sun exposure (16-18). Missing values of sun exposure were imputed. We used The R Package 'MICE' (July 27, 2018, Version 3.3.0). The package performs multiple imputations using Fully Conditional Specification (FCS). The variables we used to conduct the imputation were site, indigenous background, socioeconomic status, and smoking status.

Evaluation of Subclinical Carotid Atherosclerosis

Carotid intima media thickness (IMT) is a quantitative marker of vascular injury and increased carotid IMT is a measure of atherosclerotic burden and a predictor of subsequent cardiovascular events (19). Vascular neurologists measured IMT and detected carotid atherosclerotic plaques using a SonoSite™ MicroMaxx™ ultrasound and Asus™ laptop with M'AthStd Software™ (Intelligence in Medical Technologies, Paris, France). Researchers and a senior neurologist (C.C-B.) with extensive experience in carotid ultrasonography corroborated that study neurologists were appropriately trained and followed standardized procedures. Measurements of both carotid arteries were made according to international guidelines (20). Patients were positioned with their head rotated 0° to 30° and IMT was measured between the lumen-intima and media-adventitia interfaces on the far wall of the common carotid artery, at least 5 mm below its end where the carotid bifurcation was visible. Images of a 10-mm arterial segment were used to measure mean IMT for each common carotid artery from which overall mean was calculated. If neurologists could not obtain an adequate image they repeated this procedure on the near wall. Structures protruding into the arterial lumen by ≥ 0.5 mm or 50% of the surrounding IMT or IMT > 1.5 mm were considered an atherosclerotic plaque. Reproducibility was evaluated among 147 women from two different sites and showed high correlations: $r = 0.89$ (95%CI: 0.84, 0.93) for Chiapas and $r = 0.92$ (95%CI: 0.86, 0.96) for Yucatan.

Covariates

We obtained information on covariates based on self-reports from the 2008 baseline questionnaire. Covariates were updated based on information from clinical evaluations whenever possible. Baseline questionnaire included questions regarding indigenous background (defined as either the participant or her parents spoke an indigenous language), physical activity (METs/week) and regular sun screen use (yes or no). For physical activity, participants were asked how many hours per week they spent on moderate and vigorous recreational and non-recreational activities. Depending on the intensity of each activity, according to the U.S. Department of Health and Human Services Physical Activity Guidelines for Americans (21), a value of METs was assigned and then multiplied by the hours per week spent on each activity. The total METs were obtained by adding the METs per week per activity. Eight multiple-choice categories were possible ranging from none to >10 hours/week. The baseline questionnaire also included questions regarding the ownership of seven household assets: telephone, cell phone, internet access, microwave oven, car, computer and vacuum cleaner. We created a household asset score used as a proxy for socioeconomic status (SES). Then SES score was divided into tertiles in order to classify women as belonging to low, medium or high SES. Smoking status was updated with information from the clinical assessment in which women could choose from three categories: never, current, or past smoker. At the clinical sites, trained personnel who used standardized procedures performed anthropometric measurements. Body weight was assessed with an electronic digital scale (Tanita Corp; Arlington Heights, Illinois, USA) to the nearest 0.1 kg, with participants wearing minimum clothing and no shoes. Height was measured using an electronic digital scale (Seca Corp; Hamburg, Germany) to the nearest millimeter, with barefoot participants standing with their shoulders in a normal position. Body-mass index (BMI) was calculated as the weight in kilograms over height in meters squared (kg/m^2) and individuals were categorized as normal, overweight, and obese according to WHO criteria.

Statistical Analysis

Since the options for hours spent outdoors were asked in ranges, women were assigned to one of four categories of hours of sun exposure: 1, 3.5, 7 and 9. Our primary exposure was long-term sun exposure. We defined this exposure as the weekly hours spent outdoors at solar noon from age twelve to the clinical examination. Women were then categorized into quartiles of sun exposure according to this average. We also evaluated short-term and age period sun exposure. We defined short-term (recent) exposure as the hours spent outdoors at solar noon at the time when the IMT measurement was made. Women were assigned to one of four categories of sun exposure defined above. We also evaluated sun exposure for the four age periods: 12-18, 25-35, 36-59 and over 60 years. For this exposure women were classified into tertiles. We normalized the measurements of IMT by log-transformation. Carotid atherosclerosis was defined as mean left or right IMT of ≥ 0.8 mm or the presence of plaque. We used age-adjusted and multivariable-adjusted linear regression models to estimate the percentage difference in mean IMT and 95% confidence intervals (95% CIs) according to categories of sun exposure defined above and used the first category as reference. We used logistic regression models adjusted for age and multiple risk factors to estimate the odds ratio (OR) and 95% CIs for carotid atherosclerosis. Because evidence suggests that individuals from different ethnicities, as well as those who are obese, may have lower circulating levels of

vitamin D (22,23), we therefore explored effect measure modification by conducting stratified analyses by ethnicity (indigenous or not indigenous) and BMI (normal, overweight and obese). For the most recent sun exposure, we conducted sensitivity analyses excluding women without regular sunscreen use, as it modifies the absorption of UV radiation (23) and using a stricter definition for carotid atherosclerosis (mean left and right IMT ≥ 0.8 mm or the presence of plaque). All statistical tests were 2-sided, P -value < 0.05 was considered significant. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Table 1 presents general and sociodemographic characteristics of the 2,257 women included in the analysis. Of those invited, close to 70% chose to participate. Characteristics did not substantially vary between attendees and non-attendees. The mean age of participants was 49.6 ± 5.5 years, and the mean IMT was 0.678 ± 0.097 mm. The overall prevalence of carotid atherosclerosis was 20.9% ($n=471$). The mean accumulated hours of weekly sun exposure were 2.9 ± 1.9 for the whole study population.

Compared to women who spend less time under the sun, women with the highest sun exposure category (median 5.2 hours/week) were more likely to teach at rural areas and use sunscreen regularly. Women in the highest category of sun exposure reported higher levels of physical activity but were less likely to be in the highest tertile of the socioeconomic status score relative to women in the referent category. Also, a slightly higher prevalence of diabetes, hypertension, hypercholesterolemia was observed among women with the highest sun exposure. We observed a variation in sun exposure according to study site. The percentage of women from Chiapas and Monterrey decreased with increasing quartiles of sun exposure.

Compared to women in the lowest quartile of sun exposure, women in the highest quartile had lower mean IMT (age-adjusted mean % difference = -1.6; 95%CI: -3.0, -0.01). However, this association was no longer significant when additional confounders were included in the model (multivariable-adjusted mean % difference: -0.8; 95%CI: -2.3, 0.8). Compared to women in the lowest quartile of sun exposure, the multivariable adjusted ORs of carotid atherosclerosis were 0.89 (95%CI: 0.67, 1.21) for women in the second quartile, 0.93 (95%CI: 0.69, 1.24) for women in the third quartile and 0.88 (95%CI: 0.64, 1.16) for women in the fourth quartile. Compared to women with 1 hour of sun exposure, women with 9 hours of sun exposure had lower mean IMT (multivariable-adjusted mean % difference = -1.8; 95%CI: -4.8, -1.2). Compared to women in the lowest category of sun exposure, the multivariable adjusted ORs of carotid atherosclerosis were 1.04 (95%CI: 0.82, 1.32) for women exposed 3.5 hours, 0.82 (95%CI: 0.51, 1.33) for women exposed 7 hours and 0.54 (95%CI: 0.24, 1.18) for women who were exposed 9 hours (**Table 2**).

For exposure by age categories the magnitude of the effect for adjusted percentage difference seemed higher at increasing ages (-0.4 for 12-24, -0.6 for 25-35, -1.8 for 36-59). Likewise, the odds ratio for carotid atherosclerosis decreased with increasing ages (0.94 for 12-24, 0.92 for 25-35, 0.69 for 36-59). None of these analyses were statistically significant, but the p-trend for percentage difference for ages 36-59 was significant (P-trend 0.04) (**Table 3**).

For women who denied regular sun screen use, those in the higher exposure category (9 hours) had lower mean IMT compared to those in the lower category (multivariable-adjusted mean % difference = -2.67; 95%CI: -6.9, -1.5). The multivariable adjusted ORs for carotid atherosclerosis with women in the lowest category of exposure as reference were 0.97 (95%CI: 0.72, 1.30) for women exposed 3.5 hours, 0.72 (95%CI: 0.39, 1.35) for women exposed 7 hours and 0.45 (95%CI: 0.15, 1.35; *P*-trend = 0.13) for women who were exposed 9 hours **(Table 4)**.

In stratified analyses for BMI, we found that non-obese women in the highest quartile of sun exposure had a lower mean IMT compared to those in the lowest quartile (multivariable-adjusted mean % difference = -0.78; 95%CI 4.2, -2.8). For carotid atherosclerosis we did not find a significant association for non-obese women. Analyses for overweight participants did not show effect modification. In obese women the estimate was higher, but not significant. Nevertheless, the *p*-for interaction was not significant, suggesting statistical interaction (*P* for % difference = 0.52; *P* for OR = 0.12) **(Supplementary Table 1)**.

In sensitivity analyses using a stricter definition of carotid atherosclerosis (mean left and right IMT $\geq$ 0.8 mm or the presence of plaque) we did not find a statistically significant association between sun exposure and carotid atherosclerosis **(Supplementary Table 2)**.

Finally, in the multivariate adjusted percentage of differences of mean intima media thickness, for women with most recent exposure (no imputation), those in the higher exposure category (9 hours) had lower mean IMT compared to those in the lower category (multivariable-adjusted mean % difference = -2.8; 95%CI: -6.3, 0.8, *P*-trend = 0.04).

Discussion

To our knowledge this is the first study in Latin America that evaluates short- and long-term sun exposure and its association with subclinical cardiovascular disease. In general, we observed that cumulative sun exposure was inversely associated with IMT and subclinical carotid atherosclerosis; however, this relationship was not statistically significant. Furthermore, when we analyzed the association between sun exposure (hours/week) and [subclinical cardiovascular disease in](#) women without regular sun screen use, we found that women who were exposed to sun more than 9 hours a week had lower odds of carotid atherosclerosis.

The relation of sun exposure and cardiovascular disease has been analyzed in different countries around the world (16, 24-27). In the present study, sun exposure (more than 9 hours a week) was associated with lower odds of carotid atherosclerosis. This is consistent with previous results observed in the Swedish population; in which women with increased sun exposure habits had reduced CVD mortality, adjusted for socio-demographic variables, smoking and comorbidity (HR = 0.50; 95%CI: 0.40, 0.60).

There is rising evidence that sun exposure might play a protective role in mortality and cardiovascular outcomes (16,24,28). Historically, vitamin D synthesis has been the proposed mechanism for safe sun exposure, by modifying calcium influx into endothelial cells as well as effects on vascular tone (29). The

role of vitamin D as a negative regulator of the renin-angiotensin-aldosterone system has also been proposed (30). Since vitamin D deficiency has also been linked to adverse cardiovascular outcomes and cancer (14,31), several clinical trials with supplementation have been conducted to determine if improvement in cancer and cardiovascular outcomes occurred. Most trials have shown null results; one evaluated vitamin D supplementation and IMT (32) and a large randomized double-blind trial showed no improvement in cardiovascular outcomes or cancer after supplementation with high doses of vitamin D (2000 UI) (33). These results suggest that vitamin D might be related to cardiovascular health but not through a causal relationship. Vitamin D has been suggested as a marker of sun exposure (34).

Additionally, when we evaluated sun exposure according to age categories, we observed that in those women aged 36-59 years who had greater sun exposure, IMT was lower than in those of the lowest category of sun exposure (Difference = -1.8; 95%CI -3.7, 0.04; P-trend = 0.04). Moreover, when we analyzed the most recent exposure, we observed that the magnitude of the effect was stronger, but these results were not statistically significant probably due to small sample size. Recent evidence suggests sun exposure might have a protective role in cardiovascular disease explained by the mobilization of nitric oxide skin stores to systemic circulation, which reduces systolic blood pressure (35). In agreement with this, observational studies have shown a reduction in blood pressure in participants who were more sun-exposed, but these changes were not significant after adjusting for potential confounders (28). Since nitric oxide vasodilation is an immediate effect of sun exposure, cumulative exposure might not reflect the protective role. This is consistent with the higher effect observed in most recent exposure and with the p-trend on exposure from 36-59, which is the age category closest to the average age of participants at IMT measurement. Other studies have also shown a protective effect only from recent exposure (24).

Our analyses have several strengths, including a population-based design and the assessment of the exposure through an extensive questionnaire. There are few validated sun exposure questionnaires, and some studies have tried to assess sun exposure with estimations of UV radiation in geographical areas. However, questionnaires estimate sun exposure more effectively because they reflect actual behavior towards sun exposure. Ambient UV radiation and latitude provide rough estimates of UV exposure since individual behaviors regarding sun exposure vary widely within individuals and within life periods (36). Even if recall bias cannot be ruled out, asking for previous exposures allowed us to evaluate the differences between cumulative and most recent exposure and we did not assume that sun exposure habits do not change over time. Another strength is the high-quality assessment of IMT, which was conducted by standardized neurologists and with a high reproducibility technique. However, the possibility of random error cannot be ruled out. Evaluating short- and long-term sun exposure is also a strength, as well as assessing this exposure in sites with different latitudes and therefore different sun exposures.

It is important to mention some methodological limitations that might affect the interpretation of our results. First, since it is a cross-sectional study, causal inference is limited, but it is unlikely that carotid atherosclerosis of which the participants were not aware of could have changed sun exposure reports. Furthermore, although we adjusted for potential confounding factors, the presence of residual or

unmeasured confounding is possible. However, we were able to control confounding for common causes of sun exposure and atherosclerosis. A small number of participants and the limited variability of the exposure might limit the power of our study, but we believe this variability is representative of Mexican sun exposure habits.

Conclusions

Public health recommendations regarding sun exposure primarily focus on its avoidance and regular sunscreen use because of long-standing concerns regarding skin cancer. These recommendations tend to ignore that sun exposure is the main source of vitamin D and that oral supplements fail to substitute actual sun exposure (37). Rising evidence, including our study, suggest that historical recommendations of sun avoidance should be questioned and further investigated, in view of the potential health benefits of increasing sun exposure.

Our findings suggest that public health messages should consider a positive role for sun, while still emphasizing the negative impacts of excessive exposure. Future studies regarding the effects of differing long term and acute sun exposure on various risk factors conceptualized in terms of both disease and reactivity are needed to explore these relationships.

Declarations

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Ethics declarations

Ethics approval and consent to participate

The present study was developed and performed according to the Declaration of Helsinki guidelines. The Research, Ethics, and Biosecurity Committee at the National Institute of Public Health (INSP, by its Spanish acronym) evaluated and accepted the study protocol and informed consent forms. Written informed consent forms were obtained from each participant.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Abbreviations

GBD: Global Burden of Disease

NCDs: Non-communicable diseases

CVD: Cardiovascular disease

sCVD: Subclinical cardiovascular disease

UV: Ultraviolet

VD: Vitamin D

MTC: Mexican Teachers' Cohort

IMT: Intima-media thickness

INSP: National Institute of Public Health (Mexico)

METs: Metabolic equivalent of task

SES: Socio-economic status

BMI: Body mass index

WHO: World Health Organization

OR: Odds Ratio

CI: Confidence interval

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Tables

Table 1. Characteristics of 2,257 women from the Mexican Teachers' Cohort by weekly mean hours of sunlight exposure from age 12 to age of IMT measurement*				
Quartiles of sun exposure				
	Q1 <i>n=563</i>	Q2 <i>n=564</i>	Q3 <i>n=618</i>	Q4 <i>n=512</i>
Median (range) hours of weekly mean hours of sunlight exposure	1 (1-1.4)	1.8 (1.4-2.4)	3.5 (2.4-3.5)	5.2 (3.5-13.2)
Age, years [†]	50.8(6)	49.8(5)	49.1(5)	48.9 (6)
Speaks indigenous language ‡	10.3	14.4	15.1	14.9
Highest socioeconomic tertile	53.6	53.6	52.4	48.3
Teaches at rural site	11.6	13.4	13.2	17.0
Menopausal	61.4	59.7	53.8	56.5
Clinical site [†]				
Chiapas	31.6	29.9	25.1	25.9
Mexico City	11.0	12.9	15.9	20.0
Monterrey	35.9	30.5	29.1	26.9
Yucatán	21.9	26.6	29.9	27.1
Total intensity exercise, METS/week	27.1(28)	29.9(29)	33.8(29)	44.9(39)
Total alcohol servings per month	2.1(6)	2.1(3)	1.8(6)	2.1(6)
Smoking status				
Never	67.1	63.3	61.7	62
Past	23.9	26.7	27.1	27.8
Current	8.9	8.4	10.0	8.4
Diabetes	6.8	10.6	9.6	11.8
Hypertension	18.9	20.5	18.4	22.1
Hypercholesterolemia	23.9	26.2	25.7	26.8

Table 1. Characteristics of 2,257 women from the Mexican Teachers' Cohort by weekly mean hours of sunlight exposure from age 12 to age of IMT measurement*				
Quartiles of sun exposure				
	Q1 <i>n=563</i>	Q2 <i>n=564</i>	Q3 <i>n=618</i>	Q4 <i>n=512</i>
Body mass index, kg/m²				
Normal (< 25.0 kg/m ²), %	20.5	22.1	22.3	21.5
Overweight ([‡] 25.0-<30.0 kg/m ²), %	42.3	39.4	41.9	43.0
Obesity([‡] 30.0 kg/m ²), %	37.3	28.5	38.5	35.5
Vitamin D intake, UI/day	158.4(117)	161.7(125)	171.9(141)	175.5(117)
Vitamin D supplements, %	6.0	2.5	1.8	3.0
Regular sun screen use, %	37.5	41.0	36.7	44.3
* Values are percentages, mean ± SD and are adjusted to the age distribution of the study population				
† Values are not age-adjusted				
‡ Defined as either speaking an indigenous language or having a parent who did				

Table 2. Multivariate adjusted percentage of differences of mean intima media thickness and odds ratio for carotid atherosclerosis use in 2,257 women from the Mexican Teachers' Cohort* for cumulative sunlight exposure (quartiles) and most recent exposure.

Cumulative	Quartile 1 (n=563)	Quartile 2 (n=550)	Quartile 3 (n=633)	Quartile 4 (n=496)	P-trend
Difference, % (95% CI)					
Age-adjusted	Reference	0.5 (-1.0, 2.0)	1.0 (-2.0, 0.7)	-1.6 (-3.0, -0.01)	0.009
Age and site adjusted	Reference	0.3 (-1.1, 0.5)	-0.8(-2.3, 0.6)	-1.0 (-2.5, 1.8)	0.01
Multivariate [†]	Reference	0.4 (-1.0, 1.8)	-0.8 (-2.2, 0.7)	-0.8 (-2.3, 0.8)	0.11
Odds Ratio, % (95% CI)					
Age-adjusted	Reference	0.88 (0.66, 1.18)	0.88 (0.66, 1.17)	0.78(0.58, 1.07)	0.15
Age and site adjusted	Reference	0.89 (0.66, 1.19)	0.92 (0.68, 1.23)	0.85 (0.62, 1.16)	0.39
Multivariate [†]	Reference	0.89 (0.67, 1.21)	0.93 (0.69, 1.24)	0.88 (0.64, 1.16)	0.55
Most recent exposure	1 hour	3.5 hours	7 hours	9 hours	p-trend
Difference, % (95% CI)					
Age-adjusted	Reference	-0.8 (-6.2, 0.2)	-2.0 (-4.4, 0.3)	-2.9(-2.0, 0.4)	0.01
Age and site adjusted	Reference	-0.8 (-1.9, 0.4)	-1.6 (-3.7, 0.6)	-2.0 (-5.0, 0.3)	0.03
Multivariate [†]	Reference	-0.7 (-1.8, 0.04)	-1.3 (-3.4, 0.8)	-1.8 (-4.8, 1.2)	0.07
Odds Ratio, % (95% CI)					

Table 2. Multivariate adjusted percentage of differences of mean intima media thickness and odds ratio for carotid atherosclerosis use in 2,257 women from the Mexican Teachers' Cohort* for cumulative sunlight exposure (quartiles) and most recent exposure.

Cumulative	Quartile 1 (n=563)	Quartile 2 (n=550)	Quartile 3 (n=633)	Quartile 4 (n=496)	P-trend
Age-adjusted	Reference	0.7 (-1.8, 0.4)	-1.3 (-3.4, 0.8)	-1.8 (-4.8, 1.2)	0.05
Age and site adjusted	Reference	0.99 (0.79, 1.24)	0.72 (0.45, 1.17)	0.48 (0.22, 1.03)	0.14
Multivariate [†]	Reference	1.04 (0.83, 1.32)	0.82 (0.51, 1.33)	0.54 (0.25, 1.18)	0.23

*Values are percentage of differences (95% CI) and Odds Ratio (95% CI) unless otherwise specified.

[†] All models are multivariate analysis adjusted for age (continuous); indigenous (yes or no); site (Monterrey, Mexico City, Yucatan, Chiapas), smoking status (never, past, current), socioeconomic status (tertiles) and physical activity (continuous).

Table 3. Multivariate adjusted percentage differences of mean IMT and Odds Ratios (95% CI) by tertiles of sunlight exposure for age categories of exposure^{*, †}

	Tertile 1	Tertile 2	Tertile 3	p-trend
12-24	<i>n=697</i>	<i>n=1127</i>	<i>n=433</i>	
Difference, % (95% CI)	Reference	0.10(-1.1, 1.3)	-0.4(-1.9, 1.1)	0.62
Odds Ratio, (95% CI)	Reference	0.98 (0.77, 1.24)	0.94 (0.68, 1.29)	0.68
25-35	<i>n=881</i>	<i>n=1008</i>	<i>n=368</i>	
Difference, % (95% CI)	Reference	-0.40(-1.6, 0.7)	-0.60(-2.1, 1.0)	0.43
Odds Ratio, (95% CI)	Reference	0.99 (0.79, 1.26)	0.92 (0.66, 1.29)	0.66
36-59	<i>n=1259</i>	<i>n=773</i>	<i>n=211</i>	
Difference, % (95% CI)	Reference	-0.59(-1.7, 0.5)	-1.8(-3.7, 0.04)	0.04
Odds Ratio, (95% CI)	Reference	1.08 (0.86, 1.36)	0.69 (0.45, 1.08)	0.32

* Values are percentage of differences or odds ratio (95% CI) unless otherwise specified.

† Multivariate analysis were adjusted for age (continuous); indigenous (yes or no); site (Monterrey, Mexico City, Yucatan, Chiapas), smoking status (never, past or current), socioeconomic status (tertiles) and physical activity (continuous).

‡ Participants who were 60 or older were excluded since there were less than 90 women.

Table 4. Multivariable adjusted Percentage Differences of Mean IMT and Odds Ratios for Carotid Atherosclerosis (95% CI) by quartiles of sunlight exposure stratified by ethnicity and obesity*

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>P</i> -trend	<i>P</i> for interaction
Indigenoust	<i>n</i> =55	<i>n</i> =80	<i>n</i> =98	<i>n</i> =78		% Difference:
Difference, % (95% CI)	Reference	3.0 (-1.3, 7.4)	0.6 (-3.4, 4.6)	-0.7(-5.1, 3.6)	0.24	0.57
Odds Ratio, (95% CI)	Reference	1.97 (0.80, 4.88)	1.93 (0.79,4.69)	1.18 (0.44, 3.12)	0.88	OR: 0.17
Non indigenous	<i>n</i> =508	<i>n</i> =484	<i>n</i> =520	<i>n</i> =434		
Difference, % (95% CI)	Reference	0.08 (-1.5, 1.6)	-0.86 (-2.4, 0.7)	-0.73 (-2.4, 0.9)	0.22	
Odds Ratio, (95% CI)	Reference	0.81 (0.58, 1.10)	0.84 (0.61, 1.15)	0.86 (0.61, 1.21)	0.52	
Non-obese	<i>n</i> =111	<i>n</i> =125	<i>n</i> =136	<i>n</i> =114		% Difference:
Difference, % (95% CI)	Reference	0.26 (-3.0, 3.5)	-2.91 (-6.1, 0.3)	-0.79 (-4.2, -2.7)	0.27	0.51
Odds Ratio (95% CI)	Reference	0.59 (0.28, 1.25)	0.58 (0.27, 1.23)	1.15 (0.55, 2.39)	0.62	OR: 0.10
Overweight ‡	<i>n</i> =238	<i>n</i> =226	<i>n</i> =266	<i>n</i> =214		
Difference, % (95% CI)	Reference	-0.2(-1.9, 2.3)	-0.8(-2.2, 2.0)	-1.3(-3.5, 0.9)	0.19	
Odds Ratio (95% CI)	Reference	0.76(0.46, 1.24)	0.87 (0.54, 1.41)	0.62 (0.36, 1.05)	0.15	

Table 4. Multivariable adjusted Percentage Differences of Mean IMT and Odds Ratios for Carotid Atherosclerosis (95% CI) by quartiles of sunlight exposure stratified by ethnicity and obesity*

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>P</i> -trend	<i>P</i> for interaction
Obese §	<i>n</i> =214	<i>n</i> =213	<i>n</i> =216	<i>n</i> =184		
Difference, % (95% CI)	Reference	0.9 (-1.6, 3.4)	-0.10 (-2.6, 2.4)	-0.31 (-3.0, 2.4)	0.57	
Odds Ratio (95% CI)	Reference	1.23 (0.80, 1.90)	1.21 (0.78, 1.87)	1.0 (0.61, 1.62)	0.89	

* Multivariate analysis were adjusted for age (continuous); indigenous (yes or no, only in stratified for obesity); site (Monterrey, Mexico City, Yucatan, Chiapas), smoking status (never, past or current), socioeconomic status (tertiles) and physical activity (continuous).

† Defined as either speaking an indigenous language or having a parent who did

‡ Overweight; body mass index ≥ 25.0 – <30.0 kg/m²

§ Obesity; body mass index ≥ 30.0 kg/m²

Table 5. Multivariable adjusted Percentage Differences of Mean IMT and Odds Ratios for Carotid Atherosclerosis (95% CI) for current sunlight exposure by weekly hours of exposure for women without regular sun screen use (n=1338)					
	1 hr <i>n</i> =761	3.5 hr <i>n</i> =456	7 hr <i>n</i> =84	9 hr <i>n</i> =37	<i>P</i> trend
Percentage differences					
Age-adjusted	Reference	-1.13 (-2.7, 0.4)	-0.73(-3.8, 2.3)	-3.34 (-7.9, 1.1)	0.09
Multivariable ²	Reference	-1.29 (-2.8, 0.2)	-1.12 (-4.0, 1.8)	-2.67 (-6.9, 1.5)	0.07
Odds Ratio					
Age-adjusted	Reference	0.90 (0.68, 1.21)	0.69 (0.39, 1.28)	0.39 (0.14, 1.17)	0.05
Multivariable ³	Reference	0.97 (0.72, 1.30)	0.71 (0.38, 1.33)	0.45 (0.15, 1.35)	0.13

¹ Values are multivariable-adjusted odds ratio (95%) unless otherwise specified.

² Multivariate analysis were adjusted for age (continuous); indigenous (yes or no); site (Monterrey, Mexico City, Yucatan, Chiapas), smoking status (never, past or current), socioeconomic status (tertiles) and physical activity (continuous)

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