Published in final edited form as:

Am J Ophthalmol. 2014 November ; 158(5): 1079–1085. doi:10.1016/j.ajo.2014.07.033.

Myopia in Young Adults Is Inversely Related to an Objective Marker of Ocular Sun Exposure: The Western Australian Raine Cohort Study

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Abstract

PURPOSE—To determine the association between ocular sun exposure measured by conjunctival ultraviolet (UV) autofluorescence and myopic refractive error in young adults.

DESIGN—Cross-sectional study.

SETTING—Population-based cohort in Western Australia.

STUDY POPULATION—Total of 1344 mostly white subjects aged 19–22 years in the Western Australian Pregnancy Cohort (Raine) Eye Health Study.

OBSERVATION PROCEDURES—Cycloplegic autorefraction, conjunctival ultraviolet autofluorescence photography, participant questionnaire.

MAIN OUTCOME MEASURES—Prevalence of myopic refractive error (spherical equivalent less than -0.50 diopters) and area of conjunctival ultraviolet autofluorescence in mm^2 .

RESULTS—There was an inverse relationship between myopic refractive error and ocular sun exposure, with more than double the prevalence of myopia in the lowest quartile of conjunctival autofluorescence than the highest quartile (33.0% vs 15.6%). Median area of autofluorescence was

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ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported.

Contributions of authors: concept and design (C.M., J.S., S.Y., H.F., A.T., A.H., C.P., I.M., T.Y., M.C., D.M.), analysis and interpretation (C.M., J.S., S.Y.), writing the article (C.M.), critical revision of the article (C.M., J.S., S.Y., H.F., A.T., A.H., C.P., I.M., T.Y., M.C., D.M.), final approval of the article (C.M., J.S., S.Y., H.F., A.T., A.H., C.P., I.M., T.Y., M.C., D.M.), data collection (C.M., S.Y., H.F., A.T., D.M.), statistical expertise (J.S., S.Y.), obtaining funding (C.P., T.Y., M.C., D.M.).

significantly lower in myopic than in nonmyopic subjects (31.9 mm² vs 47.9 mm², $P < .001$). These differences remained significant after adjustment for age, sex, parental history of myopia, and subject level of education. The use of corrective lenses did not explain the lower conjunctival autofluorescence observed in myopic subjects.

CONCLUSIONS—In this young adult population, myopic refractive error was inversely associated with objectively measured ocular sun exposure, even after adjustment for potential confounders. This further supports the inverse association between outdoor activity and myopia.

Myopia is a major health issue worldwide.¹ It contributes to the burden of uncorrected refractive error, which is a leading cause of visual impairment² and a significant economic issue with billions of dollars of lost productivity globally.³ Low levels of myopia may be corrected with glasses, contact lenses, or refractive surgery; however, high myopia is associated with a substantial risk of potentially blinding ocular pathologies including myopic maculopathy,^{4,5} retinal detachment,⁶ glaucoma,⁷ and cataract.^{8,9}

Prevalence of myopia is increasing worldwide in many populations, with particularly steeper trajectories in east and southeast Asia.^{10,11} This rise in myopia, with corresponding rise in high myopia, is concurrent with myopigenic activities on a background of increasing urbanization of these populations.¹⁰ One activity underlying this association may be a reduction in time spent outdoors, with a recent meta-analysis revealing a reduction in odds of myopia of 2% for every additional hour spent outdoors per week.¹² The protective effect of outdoor activity has also been demonstrated in prospective studies^{13,14} and a randomized clinical trial.¹⁵

There are currently no widely used interventions to prevent development of myopia, and interventions proposed to reduce progression of myopia are limited by small effect sizes, rebound myopia, and side effects.^{16–18} If the protective association of increased outdoor time and reduced rates of myopia can be confirmed using objective measures of outdoor exposure, it will provide clear evidence of the need for further interventional trials in this area.

Conjunctival ultraviolet autofluorescence photography is an objective method of assessing ocular sun exposure and correlates strongly with outdoor time.¹⁹ This method avoids the inherent limitations, including subjectivity and recall bias, of measuring outdoor activity using participant recall via questionnaire. Preclinical sun damage on the conjunctiva is known to fluoresce under ultraviolet light,²⁰ a phenomenon that can be quantified with fixed focal-length photography and digital analysis (Figure 1). Using this technique, an inverse association between conjunctival ultraviolet autofluorescence and myopia was demonstrated in a population cohort from Norfolk Island, although findings were limited by a small sample size, wide age range of participants, and incomplete data on confounding variables.²¹ The current study was designed to further investigate the association between conjunctival ultraviolet autofluorescence and myopia in a larger population, and determine whether the association could be explained by confounding factors or the ultraviolet-blocking effect of corrective lenses.

METHODS

PARTICIPANTS

This was a population-based cross-sectional study of 1344 participants in the Western Australian Pregnancy Cohort (Raine) Study.^{22–24} Prospective ethical approval was obtained from the Human Research Ethics Committee at the University of Western Australia. The study was conducted in accordance with the tenets of the Declaration of Helsinki and informed consent was obtained from all participants.

The cohort was predominantly of white ethnicity: 90.3% of participants had a white mother, 90.0% had a white father, and for 85.5% of participants both parents were white. Chinese and Indian were the most common nonwhite ethnicities, with small numbers of participants having Indigenous Australian, Torres Strait Islander, Polynesian, or Vietnamese ethnicities. The recruitment and follow-up were performed in Perth, Western Australia, which has a subtropical climate with a latitude of 31°60s south.

Inclusion and exclusion criteria for the initial recruitment of the Raine cohort have been previously published.²⁴ There were no specific inclusion or exclusion criteria for the 21-year follow-up Raine Eye Health Study. All 2135 active members of the Raine cohort were invited to participate, and of these 1743 (81.6%) agreed to take part in the 21-year follow-up. During the 24-month period from March 2010 to February 2012, 1344 of those 1743 (77.1%) underwent the ophthalmic examination. There was no significant difference in age or sex between those who attended the eye examination and those who did not. Those who attended the eye examination were more likely to be of white ancestry (85.4% vs 80.1%, $P < .001$).

CONJUNCTIVAL ULTRAVIOLET AUTOFLUORESCENCE

High-resolution ultraviolet photographs of nasal and temporal conjunctiva were taken using a specially designed camera system.²⁵ A Nikon D100 (Nikon, Melville, New York, USA) digital camera with 105 mm 147 f/2.8 Micro Nikkor (Nikon, Melville, New York, USA) macro lens was used with an external electronic flash system including ultraviolet transmission filters (transmittance range 300–400 nm, peak 365 nm). The camera, lens, and flash system were mounted on a table with an adjustable subject headrest and joystick-controlled camera positioning assembly. Photographs were taken in a dark room so only ultraviolet fluorescence was recorded by the camera.

Analysis was performed using Adobe Photoshop CS4 Extend (Adobe Systems Inc, San Jose, California, USA). Four photographs were analyzed for each participant (left and right eyes, nasal and temporal conjunctiva). The area of fluorescence in mm² for each photograph was determined using Photoshop and added together to produce a total area of fluorescence in mm² for each participant.

MYOPIA AND HYPERMETROPIA

Cycloplegic autorefraction was performed using the Nidek ARK-510A (Nidek Co Ltd, Gamagori, Japan) autorefractor. Tropicamide 1% and phenylephrine 10% eye drops were

administered for mydriasis. Myopia was defined as spherical equivalent (sum of spherical error and half cylindrical error) less than -0.50 diopters. High myopia was defined as spherical equivalent less than -6.00 diopters. Hypermetropia was defined as spherical equivalent greater than $+0.50$ diopters. As the correlation between right and left eye spherical equivalent was high ($R = 0.955$), only right eye spherical equivalent was used in statistical analysis.

OTHER VARIABLES

Time spent outdoors, level of education (university studies started/completed), parental history of myopia, and use of glasses and contact lenses were determined by questionnaire. Body mass index (BMI) was calculated from height and weight measured at the time of the eye examination.

STATISTICAL ANALYSIS

Total conjunctival ultraviolet autofluorescence was analyzed in quartiles and in increments of 10 mm^2 . Continuous variables were assessed for normality and summarized using mean (standard deviation) or median (interquartile range [IQR]) as appropriate. Differences between categorical variables were assessed with the χ^2 test. Differences between continuous variables were assessed with the Mann-Whitney U test. Trends across categories were assessed using Cuzick's nonparametric test for trend.

Logistic regression was used to estimate the odds ratio (OR) and 95% confidence interval (95% CI) of myopia. Covariates that were statistically significant ($P < .05$) in univariable analyses were included in the multivariable models, in addition to age and sex. Separate multivariable models were constructed containing either total conjunctival ultraviolet autofluorescence or time spent outdoors, owing to the expected collinearity between the 2 covariates. Interaction was evaluated with the likelihood ratio test. All P values were 2-tailed. Statistical analyses were undertaken in Stata 10.1 for Macintosh (Stata-Corp, College Station, Texas, USA; 2009).

RESULTS

PREVALENCE OF MYOPIA

Of 1344 participants who attended the ophthalmic examination, 13 were excluded owing to absence of cycloplegic autorefraction (refused dilation) and 16 were excluded owing to inadequate or incomplete autofluorescence photographs. Thus, 1315 participants (97.8%) had complete autorefraction and conjunctival ultraviolet autofluorescence data.

Of 1328 participants with complete autorefraction data, mean age was 20.1 years (SD 0.46) and 684 (51.5%) were male. Three hundred eleven participants (23.7%) were myopic (95% CI 21.4–25.9). There was no significant difference between myopia prevalence in male subjects compared with female, 22.7% (95% CI 19.6–25.9) vs 24.6% (95% CI 21.3–28.0), $P = .410$.

Median conjunctival ultraviolet autofluorescence was lower in myopic subjects than in nonmyopic subjects, 31.9 mm^2 (IQR 10.6–55.9) vs 47.9 mm^2 (IQR 23.2–72.5), $P < .001$.

ASSOCIATIONS WITH MYOPIA

Variables associated with myopia are shown in Table 1. Increasing age, parental myopia, and tertiary education were associated with increased odds of myopia, although owing to the limited age range in the cohort (19–22 years) age only reached statistical significance in the adjusted model. Higher level of conjunctival ultraviolet autofluorescence was associated with decreased odds of myopia, as was participant recall of increased time outdoors during summer and winter. Sex, height, weight, and BMI were not associated with myopia.

As they were not significant in the univariable analysis, height, weight, and BMI were not included in the multivariable models (Table 2 and Table 3). Participant recall of time outdoors was not included in the multivariable analysis owing to its collinearity with conjunctival ultraviolet autofluorescence, but when it replaced conjunctival ultraviolet autofluorescence in the multivariable analysis it remained significantly inversely associated with myopia (data not shown). Conjunctival ultraviolet autofluorescence showed a stronger inverse association with myopia than participant recall of time outdoors. There was no interaction between education and conjunctival ultraviolet autofluorescence (p interaction = 0.482) or between parental myopia and conjunctival ultraviolet autofluorescence (p interaction = 0.141).

ANALYSIS BY INCREMENTS OF 10 MM²

Prevalence of myopia decreased with increasing conjunctival ultraviolet autofluorescence (Figure 2). For every 10 mm² reduction in total conjunctival ultraviolet autofluorescence, odds of myopia increased by 15% (OR 1.15, 95% CI 1.10–1.19, $P < .001$). This remained significant after adjustment for age, sex, educational level, and parental history of myopia (OR 1.12, 95% CI 1.08–1.19, $P < .001$).

ANALYSIS BY QUARTILES

Prevalence of myopia decreased with increasing quartiles of conjunctival ultraviolet autofluorescence. In the first quartile (least autofluorescence) prevalence of myopia was 33.0%. In the second quartile prevalence was 27.9%, in the third quartile prevalence was 18.0%, and in the fourth quartile (most autofluorescence) prevalence was 15.6%. This was statistically significant (trend across quartiles $P < .001$).

Participants in the first quartile had more than two and a half times the odds of myopia than participants in the fourth quartile (OR 2.67, 95% CI 1.83–3.89, $P < .001$). This remained significant after adjustment for age, sex, educational level, and parental history of myopia (OR 2.52, 95% CI 1.66–3.81, $P < .001$).

For every quartile increase in conjunctival ultraviolet autofluorescence, refraction increased by 0.24 diopters (95% CI 0.16–0.31, P trend $< .001$). After adjustment this remained significant, with refraction increasing by 0.21 diopters (95% CI 0.13–0.29, P trend $< .001$) for every quartile increase in conjunctival ultraviolet autofluorescence. When myopic subjects were considered alone, the effect of increasing quartiles was higher, with refraction increasing by 0.37 diopters (95% CI 0.17–0.56, $P < .001$) per quartile in the unadjusted analysis and 0.33 diopters (95% CI 0.14–0.53, P trend = .001) per quartile after adjustment.

USE OF GLASSES AND CONTACT LENSES

To determine whether the inverse relationship between conjunctival ultraviolet autofluorescence and myopia was attributable to a protective UV-blocking effect from corrective lenses (ie, whether the reduced autofluorescence in myopic subjects was attributable to lower amounts of UV light reaching the conjunctiva after being filtered by glasses or contact lenses), conjunctival ultraviolet autofluorescence was compared between myopic subjects who wore corrective lenses and hypermetropic subjects who wore corrective lenses. Conjunctival ultraviolet autofluorescence remained significantly lower in the myopic subjects compared to the hypermetropic subjects (median 31.9 mm² vs 43.8 mm², $P < .001$).

No difference in conjunctival ultraviolet autofluorescence was seen between myopic subjects who wore corrective lenses and those who did not (median 31.9 mm² vs 31.6 mm², $P = .821$). Similarly, no difference was seen between hypermetropic subjects who wore corrective lenses and those who did not (43.8 mm² vs 49.1 mm², $P = .144$). There remained no significant difference after adjustment for potential confounders.

HIGH MYOPIA AND OTHER REFRACTIVE ERROR

There were 17 participants with high myopia (spherical equivalent < -6.00 diopters). Median conjunctival ultraviolet autofluorescence in subjects with high myopia was 20.7 mm² (IQR 2.6–35.8). Eight participants were in the first quartile (least autofluorescence), 7 were in the second quartile, 2 were in the third quartile, and no participants were in the fourth quartile (P trend $< .001$). For every 10 mm² reduction in total conjunctival UV autofluorescence, odds of high myopia increased by 8% (OR 1.08, 95% CI 1.01–1.15, $P = .04$). Adjusted analyses were not performed owing to small numbers in the high myopic group.

There was no difference in median conjunctival ultraviolet autofluorescence between emmetropic and hypermetropic subjects, 47.4 mm² (IQR 22.6–72.2) vs 48.2 mm² (IQR 23.2–74.9), $P = .572$.

CONJUNCTIVAL ULTRAVIOLET AUTOFLUORESCENCE AND OUTDOOR EXPOSURE RECALL

Conjunctival ultraviolet autofluorescence showed a strong correlation with participant recall of time spent outdoors, even in winter when environmental UV radiation is relatively reduced (Table 4). Median conjunctival ultraviolet autofluorescence increased with longer duration of time outdoors in both summer and winter (P trend $< .001$). The season in which the eye examination was performed showed no association with measured conjunctival ultraviolet autofluorescence (data not shown).

DISCUSSION

The results of this study demonstrate a strong inverse relationship between myopia and conjunctival ultraviolet autofluorescence, an objective biomarker of ocular sun exposure and outdoor time.¹⁹ The relationship remained significant after adjustment for age, sex, educational level, and parental history of myopia. The difference in prevalence of myopia

between the groups appears to be clinically significant as well as statistically significant, with more than two and a half times the odds of myopia in the first quartile compared with the fourth.

The relationship between conjunctival ultraviolet autofluorescence and high myopia (spherical equivalent <-6.00 diopters) was also considered. Median conjunctival ultraviolet autofluorescence in the high myopic group was 20.7 mm^2 , significantly lower than in myopic subjects overall (31.9 mm^2) and nonmyopic subjects (47.9 mm^2). This demonstrates an interesting dose-response effect, with the lowest levels of autofluorescence seen in participants with the most severe myopia. Caution should be exercised in interpreting these results owing to small numbers of subjects with high myopia in the study population. Further studies looking specifically at conjunctival ultraviolet autofluorescence and high myopia are needed.

An inverse relationship between conjunctival ultraviolet autofluorescence and myopia has been previously reported in a population-based study of 636 Norfolk Island residents aged 15–89 years,²¹ although findings were limited by the population sample size and incomplete data on potential confounders. This study includes more than double the number of participants and reports the effect of parental myopia and level of education, important variables to consider when analyzing associations with myopia. The narrow age range of this study compared with the Norfolk Island population also reduces confounding by eliminating age cohort differences in outdoor activity patterns or myopia prevalence.

This study addresses the question of whether reduced conjunctival ultraviolet autofluorescence in myopic subjects might be attributable to a UV-protective effect from corrective lenses, rather than differences in outdoor time between the groups. The significantly lower autofluorescence in myopic subjects was still observed when only participants who wore corrective lenses were included in the analysis, indicating that a UV-protective effect was unlikely. Further evidence against a UV-protective effect was the observation that no differences in autofluorescence were observed between myopic subjects who wore corrective lenses and those who did not. This finding is interesting as most commercially available spectacle lenses have UV filters. It has been previously shown that light rays entering the eye obliquely are focused most intensely at the corneoscleral limbus²⁶ (the site of conjunctival ultraviolet autofluorescence), and it may be that these oblique rays are not blocked by conventional spectacle design. UV-filtering contact lenses, however, may provide some protection against oblique corneal rays. Further research into the protective effect of corrective lenses is needed.

Conjunctival ultraviolet autofluorescence was more strongly associated with myopia than was participant recall of time outdoors. This may indicate that autofluorescence photography is a more robust and reliable method of determining outdoor exposure than participant questionnaire. Certainly there is inherent imprecision in questionnaire categories (such as when estimating the proportion of the day spent outdoors), with potential for misclassification bias. Further, outdoor time may or may not directly represent sun exposure. It is also possible that ocular sun exposure, which conjunctival photography measures specifically, is more important in the process of emmetropization than systemic exposure.

The potential benefit of objective, rather than subjective, measurement of outdoor time is self-evident. One approach to objectively quantifying outdoor time and light exposure is the use of wearable light sensor devices, and these devices are currently being trialed in myopia research. They have the advantage of providing prospectively collected, detailed data on current light exposure, whereas conjunctival ultraviolet autofluorescence photography might better reflect cumulative lifetime light exposure. There may also be a consumer market for these devices, with growing interest generally in gadgets that provide quantified self-data (Tictrac dashboard, fitbit, Jawbone UP, Nike+FuelBand, and others).

Conjunctival ultraviolet autofluorescence photography has been shown to have high reliability, with intra-observer and inter-observer concordance correlation coefficients exceeding 0.900.¹⁹ The validity of the measurement as a biomarker of ocular sun exposure and outdoor time is supported by the strong correlation between total conjunctival ultraviolet autofluorescence and outdoor time measured by questionnaire (*P* trend across categories < .001).¹⁹ The reliability and validity of autofluorescence photography is a strength of this study. Other strengths include the large sample size and narrow age range of participants. The predominantly white ethnicity may reduce confounding by ethnic differences in patterns of conjunctival ultraviolet autofluorescence or myopia, but does limit application of the results to nonwhite populations.

It should be emphasized that the study has a cross-sectional design, and as such does not demonstrate a causal link between myopia and outdoor time, only an association. Any causality (if present) could be working in either direction, and it could be argued that different activity patterns between myopic and nonmyopic subjects might result in different levels of conjunctival ultraviolet autofluorescence. Clearly, prospective data on conjunctival ultraviolet autofluorescence and development or progression of myopia is needed. The longitudinal cohort design of the Raine Study does allow for further ophthalmic examinations to be performed at future follow-up assessments, and this has the potential to provide valuable prospective data.

Mechanisms underlying the association between outdoor time and myopia have been recently reviewed.¹² Although causality cannot be determined from this cross-sectional study, the study confirms a strong inverse relationship between ocular sun exposure and myopia. As increasing outdoor activity has potential as a low-risk intervention for preventing myopia, this study provides further evidence of the need for interventional trials, particularly given the rising burden of myopia worldwide.

Acknowledgments

Funding/support: Australian National Health and Medical Research Council, Canberra, Australia (App 102110), The University of Western Australia, Perth, West Australia, Raine Medical Research Foundation, Perth, West Australia, The University of Western Australia Faculty of Medicine, Dentistry and Health Sciences, Perth, West Australia, The Telethon Kids Institute, Perth, West Australia, The Women and Infants Research Foundation, Perth, West Australia, Curtin University, Perth, West Australia, The Alcon Research Institute, Fort Worth, Texas, USA, Telethon, Perth, West Australia, The Ophthalmic Research Institute of Australia, Sydney, West Australia, Australian Foundation for Prevention of Blindness Trust, Perth, West Australia, National Institutes of Health, National Eye Institute, Bethesda, Maryland, USA (R01 EY014685).

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FIGURE 1.

Conjunctival photographs of a young adult. (Left) Color photograph of the nasal conjunctiva. (Right) Conjunctival ultraviolet autofluorescence photograph of the same eye revealing fluorescence in area of sun damage.

FIGURE 2.

Myopia and conjunctival sun exposure in young adults. Myopia prevalence decreased with increasing area of conjunctival ultraviolet autofluorescence (participants with more sun exposure had less myopia).

TABLE 1

Univariable Associations With Myopia in a Population-Based Cohort of Young Adults

Variable	OR	95% CI	P
Age (per year)	1.20	0.91–1.60	.191
Sex (female)	1.11	0.86–1.44	.410
Parental myopia			
No parents	1 (ref)		
One parent	2.17	1.57–3.01	<.001
Both parents	3.37	2.01–5.31	<.001
Education level			
University started/completed	1.81	1.47–2.39	<.001
Height (per 10 cm)	0.94	0.82–1.07	.343
Weight (per 10 kg)	1.04	0.97–1.11	.296
Body mass index	1.02	0.99–1.04	.102
Time spent outdoors in summer			
Less than ½	2.00	1.18–3.42	.010
~ 1/2	1.37	0.79–2.37	.265
More than 3/4	1 (ref)		
Time outdoors in winter			
Mostly indoors	1.85	1.01–3.39	.046
50/50	1.18	0.63–2.21	.607
Mostly outdoors	1 (ref)		
Conjunctival ultraviolet autofluorescence (per 10 mm ² decrease)	1.15	1.10–1.19	<.001

TABLE 2

Multivariable Associations With Myopia in a Population-Based Cohort of Young Adults: Odds of Myopia Increased With Decreasing Conjunctival Ultraviolet Autofluorescence (Decreasing Ocular Sun Exposure)

Variable	OR	95% CI	P
Age (per year)	1.42	1.03–1.95	.03
Sex (female)	0.87	0.65–1.16	.34
Parental myopia			
No parents	1 (ref)		
One parent	1.98	1.41–2.78	<.001
Both parents	2.98	1.80–4.93	<.001
Education level			
University started/completed	1.66	1.24–2.22	.001
Conjunctival ultraviolet autofluorescence (per 10 mm ² decrease)	1.12	1.08–1.19	<.001

TABLE 3

Multivariable Associations With Myopia in a Population-Based Cohort of Young Adults: Conjunctival Ultraviolet Autofluorescence (Ocular Sun Exposure) Measured in Quartiles (First Quartile Had the Least Autofluorescence, Fourth Quartile Had the Most Autofluorescence)

Variable	OR	95% CI	P
Age (per year)	1.42	1.03–1.96	.03
Sex (female)	0.89	0.66–1.19	.43
Parental myopia			
No parents	1 (ref)		
One parent	2.01	1.44–2.83	<.001
Both parents	2.98	1.80–4.93	<.001
Education level			
University started/completed	1.67	1.25–2.23	.001
Conjunctival ultraviolet autofluorescence			
4th quartile (>69.8 mm ²)	1 (ref)		
3rd quartile (44.2–69.8 mm ²)	1.07	0.69–1.68	.760
2nd quartile (20.2–44.2 mm ²)	1.64	1.08–2.51	.021
1st quartile (>20.2 mm ²)	2.52	1.66–3.81	<.001

TABLE 4

Conjunctival Ultraviolet Autofluorescence (Ocular Sun Exposure) and Participant Recall of Outdoor Time Measured by Questionnaire

Questionnaire Response	Median Autofluorescence (mm ²)	Interquartile Range	P Trend
What part of the day do you spend outside in summer?			
None	24.8	11.0–55.8	<.001
Less than ¼ of the day	36.6	15.7–61.4	
½ of the day	48.4	27.7–73.7	
Greater than ¾ of the day	56.7	35.0–80.5	
Where has your recreation time usually been spent in winter?			
Mostly indoors	39.7	17.8–63.6	<.001
½ and ½	47.3	21.7–72.2	
Mostly outdoors	55.3	39.8–86.9	